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The following report(s) provides findings from an FDA-initiated query using Sentinel. While Sentinel queries may be undertaken to assess potential medical product safety risks, they may also be initiated for various other reasons. Some examples include determining a rate or count of an identified health outcome of interest, examining medical product use, exploring the feasibility of future, more detailed analyses within Sentinel, and seeking to better understand Sentinel capabilities.

Data obtained through Sentinel are intended to complement other types of evidence such as preclinical studies, clinical trials, postmarket studies, and adverse event reports, all of which are used by FDA to inform regulatory decisions regarding medical product safety. The information contained in this report is provided as part of FDA's commitment to place knowledge acquired from Sentinel in the public domain as soon as possible. Any public health actions taken by FDA regarding products involved in Sentinel queries will continue to be communicated through existing channels.

FDA wants to emphasize that the fact that FDA has initiated a query involving a medical product and is reporting findings related to that query does not mean that FDA is suggesting health care practitioners should change their prescribing practices for the medical product or that patients taking the medical product should stop using it. Patients who have questions about the use of an identified medical product should contact their health care practitioners.

The following report contains a description of the request, request specifications, and results from the modular program run(s).

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## Overview for Request cder\_mpl1r\_wp014\_nsdp\_v01, Report 1 of 8

**Request ID:** cder\_mpl1r\_wp014\_nsdp\_v01. This is report 1 of 8.

**Request Description:** FDA has requested execution of the Cohort Identification and Descriptive Analysis (CIDA) tool, version 2.1.1, to investigate heart failure diagnoses following new use of attention deficit hyperactivity disorder (ADHD) medications. This report presents results for all amphetamines. Results for all methylphenidates, strattera, and all stimulants are presented in separate reports.

**Data Source:** Data from January 1, 2000 to March 3, 2016 from 15 health plans contributing to the Sentinel Distributed Database (SDD) are included in this report.

**Study Design:** This request was designed to identify exposures and follow-up time. The exposure of interest and the occurrence of the health outcome of interest during exposed time were identified. The number of exposure episodes, number of individuals, number of events, and days at-risk in the SDD were calculated overall and were stratified by age group, sex, and year.

**Exposure of Interest:** The exposures of interest were amphetamines, which were defined using National Drug Codes (NDCs). Please refer to Appendix A for a list of generic and brand names of amphetamines included in this request.

**Cohort Eligibility Criteria:** Patients were required to be continuously enrolled in plans with both medical and drug coverage for at least 6 months (183 days) before their dispensing date, during which gaps in coverage of up to 45 days were allowed. Members were excluded if they had any ADHD medication or the outcome of interest in the 6 months (183 days) prior to exposure initiation. The following age groups were included in the cohort: 0-21, 22-44, 45-64, 65+ years.

**Follow-Up Time:** Follow-up time for the outcome was determined by the length of the exposure episodes. Exposure episode lengths were defined using outpatient pharmacy dispensing days supplied to create a sequence of continuous exposure. Exposure episodes were considered continuous if gaps in days supply were less than 90 days. The end date of each exposure episode was extended by 90 additional days. Sensitivity analyses were performed using a 30-day episode gap and 30-day exposure extension period. Follow-up began on the day on which the first exposure of interest was dispensed and continued until the first occurrence of any of the following: 1) the outcome of interest; 2) any codes defining incidence criteria; 3) disenrollment; 4) the study end date (March, 2016); 5) the end date of the data provided by each Data Partner; or 6) the end of the exposure episode. Only the first valid incident exposure episode that occurred during the study period was included per patient.

This report examines different blackout periods which are numbers of days at the beginning of the ADHD medication episode where if an outcome occurs, it is not attributed to the exposure and the person is omitted from the analysis. The blackout periods examined are 90 days, 180 days, 270 days, 365 days, 730 days, and 1,095 days. Episodes that were at least as long as the blackout period were required.

**Outcome of Interest:** Heart failure was defined using any of the ICD-9-CM diagnosis codes listed in Appendix B. This event had to be incident (no heart failure events in the 183 days prior to exposure initiation). The event could happen in any care setting. However, if the event happened in the inpatient or institutionalized care setting, the event had to be flagged as a principal diagnosis.

**Please refer to Appendix C for detailed specifications.**

**Limitations:** Algorithms to define exposures and outcomes are imperfect and, therefore, may be misclassified.

**Notes:** Please contact the Sentinel Operations Center Query Fulfillment Team (production@mini-sentinel.org) for questions and to provide comments/suggestions for future enhancements to this document.

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**Glossary of Terms for Analyses Using  
Cohort Identification and Descriptive Analysis (CIDA) Tool\***

**Amount Supplied** - number of units (pills, tablets, vials) dispensed. Net amount per NDC per dispensing. This is equivalent to the "RxAmt" value in the MSCDM.

**Blackout Period** - number of days at the beginning of a treatment episode that events are to be ignored. If an event occurs during the blackout period, the episode is excluded.

**Care Setting** - type of medical encounter or facility where the exposure, event, or condition code was recorded. Possible care settings include: Inpatient Hospital Stay (IP), Non-Acute Institutional Stay (IS), Emergency Department (ED), Ambulatory Visit (AV), and Other Ambulatory Visit (OA). For laboratory results, possible care settings include: Emergency department (E), Home (H), Inpatient (I), Outpatient (O), or Unknown or Missing (U). Along with the Principal Diagnosis Indicator, forms the Care Setting/PDX parameter.

**Cohort Definition (drug/exposure)** - indicates how the cohort will be defined: (1) 01: Cohort includes only the first valid incident treatment episode during the query period; (2) 02: Cohort includes all valid incident treatment episodes during the query period; (3) 03: Cohort includes all valid incident treatment episodes during the query period until an event

**Days Supplied** - number of days supplied for all dispensings in qualifying treatment episodes.

**Eligible Members** - number of members eligible for an incident treatment episode (defined by the drug/exposure and event washout periods) with drug and medical coverage during the query period.

**Enrollment Gap** - number of days allowed between two consecutive enrollment periods without breaking a "continuously enrolled" sequence.

**Episodes** - treatment episodes; length of episode is determined by days supplied in one dispensing or consecutive dispensings bridged by the episode gap.

**Episode Gap** - number of days allowed between two (or more) consecutive exposures (dispensings/procedures) to be considered the same treatment episode.

**Event Deduplication** - specifies how events are counted by the MP algorithm: (0) 0: Counts all occurrences of an HOI during an exposure episode; (1) 1: de-duplicates occurrences of the same HOI code and code type on the same day; (2) 2: de-duplicates occurrences of the same HOI group on the same day (e.g., de-duplicates at the group level).

**Exposure Episode Length** - number of days after exposure initiation that is considered "exposed time."

**Exposure Extension Period** - number of days post treatment period in which the outcomes/events are counted for a treatment episode.

**Lookback Period (pre-existing condition)** - number of days wherein a member is required to have evidence of pre-existing condition (diagnosis/procedure/drug dispensing).

**Member-Years** - sum of all days of enrollment with medical and drug coverage\*\* in the query period preceded by an exposure washout period all divided by **365.25**.

**Minimum Days Supplied** - specifies a minimum number of days in length of the days supplied for the episode to be considered.

**Minimum Episode Duration** - specifies a minimum number of days in length of the episode for it to be considered.

**Principal Diagnosis (PDX)** - diagnosis or condition established to be chiefly responsible for admission of the patient to the hospital. 'P' = principal diagnosis, 'S' = secondary diagnosis, 'X' = unspecified diagnosis, '.' = blank. Along with the Care Setting values, forms the Caresetting/PDX parameter.

**Query Period** - period in which the modular program looks for exposures and outcomes of interest.

**Treatment Episode Truncation Indicator** - indicates whether observation of the incident query code during follow-up requires truncation of valid treatment episodes. A value of Y indicates that the treatment episodes should be truncated at the first occurrence of an incident query code. A value of N indicates that the treatment episodes should not be truncated at the occurrence of the incident query code.

**Users** - number of members with exposure during the query period. Member must have no evidence of exposure(s) of interest (defined by incidence criteria) in the prior washout period. A user may only be counted once in a query period.

**Washout Period (drug/exposure)\*\*** - number of days a user is required to have no evidence of prior exposure (drug dispensing/procedure) and continuous drug and medical coverage prior to an incident treatment episode.

**Washout Period (event/outcome)\*\*** - number of days a user is required to have no evidence of a prior event (procedure/diagnosis) and continuous drug and medical coverage prior to an incident treatment episode.

**Years at Risk** - number of days supplied plus any episode gaps and exposure extension periods all divided by 365.25.

\*all terms may not be used in this report

\*\*incident treatment episodes must be incident to both the exposure and the event

**Table 1a: Summary of Incident Amphetamine Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, and Blackout Period**

New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>30-Day Episode Gap/Extension Period</b>													
<b>0-Day Blackout Period</b>													
1,169,730	1,169,730	6,156,359	198,288,883	297,573,899	644,216.0	1,874	110,278,913	305,292,626.1	10.61	169.52	5.26	32.21	29.09
<b>90-Day Blackout Period</b>													
650,173	650,173	5,649,361	185,776,441	272,439,231	420,332.7	1,107	100,795,198	276,395,375.1	6.45	285.73	8.69	32.88	26.34
<b>180-Day Blackout Period</b>													
362,718	362,718	4,846,316	161,200,407	238,863,174	307,348.5	780	93,629,250	250,244,733.8	3.87	444.42	13.36	33.26	25.38
<b>270-Day Blackout Period</b>													
241,712	241,712	4,181,457	140,317,564	209,934,118	236,184.5	586	80,082,581	228,167,810.7	3.02	580.52	17.30	33.56	24.81
<b>365-Day Blackout Period</b>													
170,083	170,083	3,591,292	121,550,849	183,364,258	184,330.3	446	72,081,132	207,160,668.0	2.36	714.66	21.11	33.85	24.20
<b>730-Day Blackout Period</b>													
62,981	62,981	2,085,250	72,565,609	111,722,383	79,912.1	224	48,757,177	144,830,482.3	1.29	1152.18	33.11	34.80	28.03
<b>1,095-Day Blackout Period</b>													
27,766	27,766	1,208,454	43,169,074	67,584,643	37,387.4	99	34,276,055	102,931,993.9	0.81	1554.75	43.52	35.72	26.48
<b>90-Day Episode Gap/Extension Period</b>													
<b>0-Day Blackout Period</b>													
1,169,730	1,169,730	8,198,613	265,362,592	398,873,235	1,021,878.5	2,727	110,278,913	305,292,626.1	10.61	226.86	7.01	32.37	26.69
<b>90-Day Blackout Period</b>													
988,312	988,312	7,946,263	259,776,403	391,275,492	760,723.0	1,854	100,795,198	276,008,719.2	9.81	262.85	8.04	32.69	24.37
<b>180-Day Blackout Period</b>													
616,660	616,660	7,436,264	245,648,004	364,599,077	591,289.6	1,362	93,629,249	250,068,895.3	6.59	398.35	12.06	33.03	23.03
<b>270-Day Blackout Period</b>													
442,941	442,941	6,786,616	225,849,895	337,472,905	470,504.7	1,057	80,082,580	228,069,035.9	5.53	509.89	15.32	33.28	22.47
<b>365-Day Blackout Period</b>													
325,952	325,952	6,076,412	203,576,663	306,111,952	375,512.7	841	72,081,131	207,104,557.6	4.52	624.56	18.64	33.50	22.40
<b>730-Day Blackout Period</b>													
130,088	130,088	3,847,927	131,756,551	201,917,885	169,678.2	406	48,757,177	144,821,017.5	2.67	1012.83	29.58	34.24	23.93
<b>1,095-Day Blackout Period</b>													
59,194	59,194	2,337,116	81,792,111	127,656,888	80,636.3	196	34,276,055	102,929,943.2	1.73	1381.76	39.48	35.00	24.31

**Table 1b: Rate of Heart Failure Outcomes at Different Stages of Amphetamine Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, and Blackout Period**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>30-Day Episode Gap/Extension Period</b>			
Days 0-90	767	223,883	34.3
Days 91-180	327	112,984	28.9
Days 181-270	194	71,164	27.3
Days 271-365	140	51,854	27.0
Days 366-730	222	104,418	21.3
Days 731-1,095	125	42,525	29.4
<b>90-Day Episode Gap/Extension Period</b>			
Days 0-90	873	261,156	33.4
Days 91-180	492	169,433	29.0
Days 181-270	305	120,785	25.3
Days 271-365	216	94,992	22.7
Days 366-730	435	205,835	21.1
Days 731-1,095	210	89,042	23.6

**Table 2a: Summary of Incident Amphetamine Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>30-Day Episode Gap/Extension Period</b>														
<b>0 Day Blackout Period</b>														
00-21 Years	558,702	558,702	2,590,925	84,126,050	107,052,925	280,200.2	479	33,425,289	84,072,316.3	16.71	150.57	4.64	32.47	17.09
22-44 Years	444,252	444,252	2,592,947	82,116,417	130,269,587	261,873.1	531	45,747,439	95,902,747.4	9.71	184.84	5.84	31.67	20.28
45-64 Years	157,031	157,031	933,285	30,672,849	57,827,883	97,578.4	698	32,647,050	90,461,977.4	4.81	195.33	5.94	32.87	71.53
65+ Years	9,745	9,745	39,202	1,373,567	2,423,504	4,564.3	166	10,950,623	34,855,585.0	0.89	140.95	4.02	35.04	363.70
<b>90-Day Blackout Period</b>														
00-21 Years	305,512	305,512	2,341,432	77,946,049	99,190,877	173,662.9	295	30,664,758	76,531,927.8	9.96	255.13	7.66	33.29	16.99
22-44 Years	254,381	254,381	2,406,744	77,544,766	123,048,377	176,139.3	308	41,121,997	85,421,048.7	6.19	304.84	9.46	32.22	17.49
45-64 Years	85,808	85,808	866,875	29,041,260	47,973,564	67,742.2	431	30,234,919	82,556,324.9	2.84	338.44	10.10	33.50	63.62
65+ Years	4,472	4,472	34,310	1,244,366	2,226,413	2,788.2	73	9,846,439	31,886,073.8	0.45	278.26	7.67	36.27	261.81
<b>180-Day Blackout Period</b>														
00-21 Years	155,474	155,474	1,930,157	65,196,857	83,526,410	122,462.6	203	28,477,129	69,578,636.2	5.46	419.34	12.41	33.78	16.58
22-44 Years	152,228	152,228	2,111,680	68,703,442	109,936,917	130,547.0	221	37,550,116	76,110,165.3	4.05	451.32	13.87	32.53	16.93
45-64 Years	52,595	52,595	775,277	26,221,956	43,456,239	52,281.4	307	28,250,994	75,302,353.9	1.86	498.56	14.74	33.82	58.72
65+ Years	2,421	2,421	29,202	1,078,152	1,943,609	2,057.5	49	9,283,150	29,253,578.4	0.26	445.33	12.06	36.92	238.15
<b>270-Day Blackout Period</b>														
00-21 Years	97,522	97,522	1,623,219	55,396,292	71,509,160	92,742.3	164	24,382,852	63,666,711.9	4.00	568.04	16.64	34.13	17.68
22-44 Years	105,179	105,179	1,841,965	60,421,285	97,408,820	100,201.0	156	31,629,281	68,431,478.4	3.33	574.46	17.51	32.80	15.57
45-64 Years	37,381	37,381	691,066	23,558,206	39,305,071	41,647.0	228	24,593,145	69,091,555.5	1.52	630.22	18.49	34.09	54.75
65+ Years	1,630	1,630	25,207	941,781	1,711,067	1,594.2	38	8,263,236	26,978,064.9	0.20	577.78	15.46	37.36	238.36
<b>365-Day Blackout Period</b>														
00-21 Years	65,919	65,919	1,372,029	47,276,684	61,391,717	72,232.7	126	21,971,316	58,013,539.7	3.00	717.19	20.81	34.46	17.44
22-44 Years	75,171	75,171	1,585,544	52,418,423	85,163,024	77,423.8	118	27,913,055	61,257,811.1	2.69	697.32	21.09	33.06	15.24
45-64 Years	27,817	27,817	611,779	21,030,656	35,288,504	33,424.1	175	22,307,462	63,127,724.2	1.25	756.04	21.99	34.38	52.36
65+ Years	1,176	1,176	21,940	825,086	1,521,013	1,249.8	27	7,724,030	24,761,592.9	0.15	701.60	18.66	37.61	216.04
<b>730-Day Blackout Period</b>														
00-21 Years	24,216	24,216	800,767	28,412,455	37,203,597	31,981.7	59	14,939,259	40,913,457.4	1.62	1173.29	33.07	35.48	18.45
22-44 Years	27,009	27,009	893,213	30,240,961	50,495,827	31,874.3	56	17,763,710	40,908,458.3	1.52	1119.66	33.07	33.86	17.57
45-64 Years	11,316	11,316	378,782	13,421,242	23,078,683	15,529.8	98	15,594,476	44,997,975.3	0.73	1186.04	33.47	35.43	63.10
65+ Years	440	440	12,488	490,951	944,276	526.4	11	5,590,290	18,010,591.4	0.08	1115.80	28.38	39.31	208.98
<b>1,095-Day Blackout Period</b>														
00-21 Years	11,000	11,000	476,777	17,386,393	23,097,918	15,398.7	27	10,527,068	29,229,558.3	1.04	1580.58	43.34	36.47	17.53
22-44 Years	11,337	11,337	496,072	17,138,478	29,075,028	14,008.1	24	11,867,570	28,139,999.6	0.96	1511.73	43.76	34.55	17.13
45-64 Years	5,265	5,265	229,467	8,379,201	14,881,081	7,724.6	44	11,226,165	32,398,416.5	0.47	1591.49	43.58	36.52	56.96
65+ Years	164	164	6,138	265,002	530,616	256.0	4	4,147,057	13,164,019.5	0.04	1615.87	37.43	43.17	156.27
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														

**Table 2a: Summary of Incident Amphetamine Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
00-21 Years	558,702	558,702	3,639,976	118,751,819	152,149,437	476,293.6	669	33,425,289	84,072,316.3	16.71	212.55	6.52	32.62	14.05
22-44 Years	444,252	444,252	3,284,927	104,354,501	168,006,141	387,691.5	741	45,747,439	95,902,747.4	9.71	234.90	7.39	31.77	19.11
45-64 Years	157,031	157,031	1,221,756	40,417,224	75,400,210	150,410.2	1,061	32,647,050	90,461,977.4	4.81	257.38	7.78	33.08	70.54
65+ Years	9,745	9,745	51,954	1,839,048	3,317,447	7,483.3	256	10,950,623	34,855,585.0	0.89	188.72	5.33	35.40	342.10
<b>90-Day Blackout Period</b>														
00-21 Years	470,380	470,380	3,522,669	116,200,344	148,957,199	352,385.3	470	30,664,758	76,353,655.5	15.34	247.04	7.49	32.99	13.34
22-44 Years	373,639	373,639	3,182,472	102,062,901	164,709,289	288,252.2	500	41,095,222	85,294,135.7	9.09	273.16	8.52	32.07	17.35
45-64 Years	135,736	135,736	1,190,905	39,721,832	74,371,842	114,831.0	733	30,227,882	82,484,617.5	4.49	292.64	8.77	33.35	63.83
65+ Years	8,557	8,557	50,217	1,791,326	3,237,163	5,254.5	151	9,844,664	31,876,310.5	0.87	209.34	5.87	35.67	287.37
<b>180-Day Blackout Period</b>														
00-21 Years	293,912	293,912	3,288,918	109,694,134	141,103,420	271,518.5	350	28,477,128	69,485,817.9	10.32	373.22	11.19	33.35	12.89
22-44 Years	235,707	235,707	2,974,916	96,308,461	156,081,069	223,291.2	377	37,532,478	76,054,943.9	6.28	408.59	12.62	32.37	16.88
45-64 Years	82,743	82,743	1,126,707	37,972,332	64,347,243	92,464.4	546	28,247,708	75,277,855.8	2.93	458.92	13.62	33.70	59.05
65+ Years	4,298	4,298	45,723	1,673,077	3,067,345	4,015.5	89	9,282,353	29,250,277.8	0.46	389.27	10.64	36.59	221.64
<b>270-Day Blackout Period</b>														
00-21 Years	207,583	207,583	2,987,136	100,355,466	129,633,748	214,438.7	287	24,382,852	63,613,594.5	8.51	483.45	14.39	33.60	13.38
22-44 Years	170,732	170,732	2,711,102	88,399,685	144,355,065	176,784.2	280	31,618,330	68,401,869.6	5.40	517.77	15.88	32.61	15.84
45-64 Years	61,618	61,618	1,046,947	35,558,670	60,637,489	76,065.2	423	24,591,061	69,077,335.9	2.51	577.08	16.99	33.96	55.61
65+ Years	3,008	3,008	41,431	1,536,074	2,846,602	3,216.7	67	8,262,734	26,976,236.0	0.36	510.66	13.77	37.08	208.29
<b>365-Day Blackout Period</b>														
00-21 Years	149,137	149,137	2,656,428	89,825,795	116,418,989	170,330.7	224	21,971,315	57,983,110.0	6.79	602.30	17.81	33.81	13.15
22-44 Years	126,995	126,995	2,422,514	79,518,440	130,700,610	139,918.6	223	27,906,607	61,241,349.5	4.55	626.15	19.08	32.82	15.94
45-64 Years	47,587	47,587	960,055	32,830,572	56,359,905	62,650.7	342	22,306,056	63,119,566.6	2.13	689.91	20.17	34.20	54.59
65+ Years	2,233	2,233	37,415	1,401,856	2,632,449	2,612.9	52	7,723,717	24,760,531.5	0.29	627.79	16.76	37.47	199.02
<b>730-Day Blackout Period</b>														
00-21 Years	58,315	58,315	1,682,830	58,082,228	75,864,314	76,797.6	95	14,939,259	40,908,227.1	3.90	996.01	28.86	34.51	12.37
22-44 Years	49,365	49,365	1,487,349	49,810,073	83,991,848	60,693.1	109	17,762,637	40,906,122.0	2.78	1009.02	30.13	33.49	17.96
45-64 Years	21,453	21,453	653,611	22,925,229	40,245,042	30,998.6	183	15,594,153	44,996,364.1	1.38	1068.63	30.47	35.07	59.03
65+ Years	955	955	24,137	939,021	1,816,682	1,188.8	19	5,590,198	18,010,304.3	0.17	983.27	25.27	38.90	159.82
<b>1,095-Day Blackout Period</b>														
00-21 Years	26,714	26,714	1,037,688	36,578,109	48,317,008	36,756.0	52	10,527,068	29,228,331.4	2.54	1369.25	38.84	35.25	14.15
22-44 Years	21,537	21,537	868,142	29,585,477	50,939,100	27,496.3	47	11,867,389	28,139,630.9	1.81	1373.70	40.31	34.08	17.09
45-64 Years	10,573	10,573	418,547	15,087,376	27,303,678	15,766.5	87	11,226,098	32,398,020.4	0.94	1426.97	39.59	36.05	55.18
65+ Years	370	370	12,739	541,149	1,097,102	617.6	10	4,147,029	13,163,960.6	0.09	1462.56	34.43	42.48	161.92



**Table 2b: Rate of Heart Failure Outcomes at Different Stages of Amphetamine Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>30-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
00-21 Years	184	106,537	17.3
22-44 Years	223	85,734	26.0
45-64 Years	267	29,836	89.5
65+ Years	93	1,776	523.6
<b>Days 91-180</b>			
00-21 Years	92	51,200	18.0
22-44 Years	87	45,592	19.1
45-64 Years	124	15,461	80.2
65+ Years	24	731	328.4
<b>Days 181-270</b>			
00-21 Years	39	29,720	13.1
22-44 Years	65	30,346	21.4
45-64 Years	79	10,634	74.3
65+ Years	11	463	237.4
<b>Days 271-365</b>			
00-21 Years	38	20,510	18.5
22-44 Years	38	22,777	16.7
45-64 Years	53	8,223	64.5
65+ Years	11	344	319.3
<b>Days 366-730</b>			
00-21 Years	67	40,251	16.6
22-44 Years	62	45,549	13.6
45-64 Years	77	17,894	43.0
65+ Years	16	723	221.2
<b>Days 731-1,095</b>			
00-21 Years	32	16,583	19.3
22-44 Years	32	17,866	17.9
45-64 Years	54	7,805	69.2
65+ Years	7	270	258.9
<b>90-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			

**Table 2b: Rate of Heart Failure Outcomes at Different Stages of Amphetamine Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
00-21 Years	199	123,908	16.1
22-44 Years	241	99,439	24.2
45-64 Years	328	35,579	92.2
65+ Years	105	2,229	471.1
<b>Days 91-180</b>			
00-21 Years	120	80,867	14.8
22-44 Years	123	64,961	18.9
45-64 Years	187	22,367	83.6
65+ Years	62	1,239	500.4
<b>Days 181-270</b>			
00-21 Years	63	57,080	11.0
22-44 Years	97	46,507	20.9
45-64 Years	123	16,399	75.0
65+ Years	22	799	275.4
<b>Days 271-365</b>			
00-21 Years	63	44,108	14.3
22-44 Years	57	36,866	15.5
45-64 Years	81	13,415	60.4
65+ Years	15	604	248.4
<b>Days 366-730</b>			
00-21 Years	129	93,533	13.8
22-44 Years	114	79,225	14.4
45-64 Years	159	31,652	50.2
65+ Years	33	1,424	231.7
<b>Days 731-1,095</b>			
00-21 Years	43	40,042	10.7
22-44 Years	62	33,197	18.7
45-64 Years	96	15,232	63.0
65+ Years	9	571	157.6

**Table 3a: Summary of Incident Amphetamine Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>30-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
Female	548,464	548,464	3,037,413	97,698,609	146,358,801	315,651.4	913	56,071,657	158,263,520.2	9.78	178.13	5.54	32.17	28.92
Male	621,218	621,218	3,118,738	100,583,602	151,205,194	328,542.1	961	54,201,546	147,016,390.6	11.46	161.91	5.02	32.25	29.25
Unknown	48	48	208	6,672	9,904	22.5	0	5,710	12,715.4	8.41	139.00	4.33	32.08	0.00
<b>90-Day Blackout Period</b>														
Female	309,232	309,232	2,805,906	91,998,866	137,876,579	210,265.1	546	51,322,049	143,483,942.2	6.03	297.51	9.07	32.79	25.97
Male	340,920	340,920	2,843,282	93,771,844	134,553,545	210,054.4	561	49,468,322	132,900,119.2	6.89	275.06	8.34	32.98	26.71
Unknown	21	21	173	5,731	9,107	13.2	0	4,827	11,313.7	4.35	272.90	8.24	33.13	0.00
<b>180-Day Blackout Period</b>														
Female	178,074	178,074	2,439,832	80,870,951	122,242,230	155,977.7	382	47,747,103	130,099,110.8	3.73	454.14	13.70	33.15	24.49
Male	184,634	184,634	2,406,354	80,324,993	116,613,522	151,361.5	398	45,877,987	120,135,483.9	4.02	435.05	13.03	33.38	26.29
Unknown	10	10	130	4,463	7,422	9.3	0	4,160	10,139.2	2.40	446.30	13.00	34.33	0.00
<b>270-Day Blackout Period</b>														
Female	121,342	121,342	2,127,404	71,120,440	108,312,183	120,834.9	283	40,899,023	118,792,959.5	2.97	586.12	17.53	33.43	23.42
Male	120,365	120,365	2,053,945	69,193,464	101,615,551	115,342.0	303	39,180,257	109,365,638.4	3.07	574.86	17.06	33.69	26.27
Unknown	5	5	108	3,660	6,384	7.7	0	3,301	9,212.8	1.51	732.00	21.60	33.89	0.00
<b>365-Day Blackout Period</b>														
Female	86,639	86,639	1,840,511	62,053,028	95,178,713	94,680.2	208	36,882,927	108,016,096.5	2.35	716.23	21.24	33.72	21.97
Male	83,441	83,441	1,750,687	59,494,814	88,179,994	89,643.7	238	35,195,289	99,136,218.3	2.37	713.02	20.98	33.98	26.55
Unknown	3	3	94	3,007	5,551	6.5	0	2,916	8,353.3	1.03	1002.33	31.33	31.99	0.00
<b>730-Day Blackout Period</b>														
Female	32,547	32,547	1,077,779	37,332,444	58,587,909	41,145.2	100	25,089,970	75,941,546.2	1.30	1147.03	33.11	34.64	24.30
Male	30,433	30,433	1,007,404	35,231,181	53,130,506	38,761.9	124	23,665,314	68,883,059.8	1.29	1157.66	33.10	34.97	31.99
Unknown	1	1	67	1,984	3,968	5.0	0	1,893	5,876.3	0.53	1984.00	67.00	29.61	0.00
<b>1,095-Day Blackout Period</b>														
Female	14,397	14,397	626,323	22,217,516	35,377,936	19,134.2	39	17,741,982	54,257,818.5	0.81	1543.20	43.50	35.47	20.38
Male	13,368	13,368	582,064	20,949,574	32,202,739	18,249.2	60	16,532,754	48,669,941.6	0.81	1567.14	43.54	35.99	32.88
Unknown	1	1	67	1,984	3,968	4.0	0	1,319	4,233.8	0.76	1984.00	67.00	29.61	0.00
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
Female	548,464	548,464	4,037,721	130,468,224	197,435,288	496,225.8	1,353	56,071,657	158,263,520.2	9.78	237.88	7.36	32.31	27.27

**Table 3a: Summary of Incident Amphetamine Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
Male	621,218	621,218	4,160,594	134,884,600	201,424,480	525,615.4	1,374	54,201,546	147,016,390.6	11.46	217.13	6.70	32.42	26.14
Unknown	48	48	298	9,768	13,467	37.4	0	5,710	12,715.4	8.41	203.50	6.21	32.78	0.00
<b>90-Day Blackout Period</b>														
Female	465,578	465,578	3,922,119	127,915,570	193,924,137	373,421.4	929	51,322,049	143,312,314.7	9.07	274.75	8.42	32.61	24.88
Male	522,695	522,695	4,023,864	131,851,501	197,338,324	387,275.1	925	49,468,322	132,685,099.6	10.57	252.25	7.70	32.77	23.88
Unknown	39	39	280	9,332	13,031	26.5	0	4,827	11,304.8	8.08	239.28	7.18	33.33	0.00
<b>180-Day Blackout Period</b>														
Female	294,371	294,371	3,687,256	121,423,831	184,481,129	293,131.6	692	47,747,102	130,026,823.5	6.17	412.49	12.53	32.93	23.61
Male	322,270	322,270	3,748,772	124,216,099	180,106,213	298,138.4	670	45,877,987	120,031,942.3	7.02	385.44	11.63	33.14	22.47
Unknown	19	19	236	8,074	11,735	19.6	0	4,160	10,129.5	4.57	424.95	12.42	34.21	0.00
<b>270-Day Blackout Period</b>														
Female	214,821	214,821	3,386,810	112,335,359	171,793,496	235,139.8	538	40,899,023	118,752,275.8	5.25	522.93	15.77	33.17	22.88
Male	228,109	228,109	3,399,605	113,507,567	165,669,279	235,349.0	519	39,180,256	109,307,556.3	5.82	497.60	14.90	33.39	22.05
Unknown	11	11	201	6,969	10,130	16.0	0	3,301	9,203.8	3.33	633.55	18.27	34.67	0.00
<b>365-Day Blackout Period</b>														
Female	160,468	160,468	3,052,304	101,917,502	156,620,708	188,836.3	423	36,882,927	107,993,269.0	4.35	635.13	19.02	33.39	22.40
Male	165,478	165,478	3,023,940	101,653,297	149,482,401	186,662.8	418	35,195,288	99,102,942.2	4.70	614.30	18.27	33.62	22.39
Unknown	6	6	168	5,864	8,843	13.6	0	2,916	8,346.4	2.06	977.33	28.00	34.90	0.00
<b>730-Day Blackout Period</b>														
Female	65,773	65,773	1,962,425	66,964,992	104,937,306	86,395.4	201	25,089,970	75,937,591.8	2.62	1018.12	29.84	34.12	23.27
Male	64,311	64,311	1,885,361	64,786,718	96,973,319	83,273.7	205	23,665,314	68,877,555.2	2.72	1007.40	29.32	34.36	24.62
Unknown	4	4	141	4,841	7,260	9.1	0	1,893	5,870.5	2.11	1210.25	35.25	34.33	0.00
<b>1,095-Day Blackout Period</b>														
Female	30,315	30,315	1,200,370	41,848,950	66,699,352	41,124.1	92	17,741,982	54,257,036.9	1.71	1380.47	39.60	34.86	22.37
Male	28,877	28,877	1,136,623	39,939,505	60,951,867	39,506.3	104	16,532,754	48,668,672.5	1.75	1383.09	39.36	35.14	26.32
Unknown	2	2	123	3,656	5,670	5.9	0	1,319	4,233.8	1.52	1828.00	61.50	29.72	0.00

**Table 3b: Rate of Heart Failure Outcomes at Different Stages of Amphetamine Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>30-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
Female	367	105,386	34.8
Male	400	118,488	33.8
Unknown	0	9	0.0
<b>Days 91-180</b>			
Female	164	54,287	30.2
Male	163	58,693	27.8
Unknown	0	4	0.0
<b>Days 181-270</b>			
Female	99	35,143	28.2
Male	95	36,020	26.4
Unknown	0	2	0.0
<b>Days 271-365</b>			
Female	75	26,155	28.7
Male	65	25,698	25.3
Unknown	0	1	0.0
<b>Days 366-730</b>			
Female	108	53,535	20.2
Male	114	50,882	22.4
Unknown	0	1	0.0
<b>Days 731-1,095</b>			
Female	61	22,011	27.7
Male	64	20,513	31.2
Unknown	0	1	0.0
<b>90-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
Female	424	122,804	34.5
Male	449	138,340	32.5

**Table 3b: Rate of Heart Failure Outcomes at Different Stages of Amphetamine Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
Unknown	0	11	0.0
<b>Days 91-180</b>			
Female	237	80,290	29.5
Male	255	89,137	28.6
Unknown	0	7	0.0
<b>Days 181-270</b>			
Female	154	57,992	26.6
Male	151	62,789	24.0
Unknown	0	4	0.0
<b>Days 271-365</b>			
Female	115	46,303	24.8
Male	101	48,686	20.7
Unknown	0	2	0.0
<b>Days 366-730</b>			
Female	222	102,441	21.7
Male	213	103,389	20.6
Unknown	0	4	0.0
<b>Days 731-1,095</b>			
Female	109	45,271	24.1
Male	101	43,767	23.1
Unknown	0	3	0.0

**Table 4a: Summary of Incident Amphetamine Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member - Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>30-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
200	4,445	4,445	16,868	769,345	1,687,901	2,478.3	16	6,528,534	2,996,066.8	0.68	173.08	3.79	45.61	64.56
200	10,026	10,026	35,423	1,490,644	3,002,630	4,997.1	39	7,127,377	5,952,300.9	1.41	148.68	3.53	42.08	78.05
200	9,488	9,488	38,426	1,599,921	2,944,078	5,204.7	37	7,278,258	6,050,303.3	1.30	168.63	4.05	41.64	71.09
200	14,597	14,597	87,118	3,225,555	8,054,261	10,084.0	67	7,271,066	6,022,844.4	2.01	220.97	5.97	37.03	66.44
200	12,006	12,006	67,706	2,550,712	6,668,842	7,977.4	79	7,706,827	6,267,195.9	1.56	212.45	5.64	37.67	99.03
200	11,527	11,527	63,770	2,379,863	3,901,306	7,431.4	83	7,950,033	6,557,957.1	1.45	206.46	5.53	37.32	111.69
200	27,030	27,030	157,820	5,508,445	8,611,497	17,575.3	107	19,421,917	11,592,037.9	1.39	203.79	5.84	34.90	60.88
200	44,869	44,869	271,286	9,127,529	14,147,717	29,175.8	168	23,618,253	17,146,278.6	1.90	203.43	6.05	33.65	57.58
200	97,121	97,121	569,870	18,574,497	34,141,073	59,714.8	191	44,315,751	27,985,579.6	2.19	191.25	5.87	32.59	31.99
200	143,528	143,528	855,047	27,513,867	39,571,569	88,557.9	208	45,694,875	35,453,462.7	3.14	191.70	5.96	32.18	23.49
201	149,830	149,830	897,177	28,634,201	40,492,691	92,327.6	210	43,543,185	33,937,855.2	3.44	191.11	5.99	31.92	22.75
201	150,803	150,803	878,291	27,872,033	38,867,947	90,383.0	185	42,124,991	33,129,469.7	3.58	184.82	5.82	31.73	20.47
201	148,452	148,452	834,164	26,497,572	36,777,919	86,343.4	143	41,090,454	32,445,579.6	3.61	178.49	5.62	31.77	16.56
201	143,836	143,836	715,229	22,523,846	31,368,832	74,350.0	177	40,939,000	32,116,700.6	3.51	156.59	4.97	31.49	23.81
201	139,259	139,259	533,308	16,264,982	22,191,662	54,893.2	137	41,865,439	31,987,415.3	3.33	116.80	3.83	30.50	24.96
201	62,913	62,913	134,856	3,755,871	5,143,974	12,722.0	27	34,431,982	15,651,578.6	1.83	59.70	2.14	27.85	21.22
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>90-Day Blackout Period</b>														
200	2,324	2,324	14,416	695,522	1,542,732	1,559.2	9	6,271,153	2,822,041.0	0.37	299.28	6.20	48.25	57.72
200	4,944	4,944	29,946	1,327,852	2,689,901	2,972.2	27	6,793,824	5,669,267.6	0.73	268.58	6.06	44.34	90.84
200	4,987	4,987	34,266	1,486,152	2,848,562	3,370.9	22	6,958,530	5,742,173.2	0.72	298.01	6.87	43.37	65.26
200	8,423	8,423	86,517	3,265,522	8,653,904	7,750.4	44	6,908,604	5,723,800.0	1.22	387.69	10.27	37.74	56.77
200	6,836	6,836	63,284	2,448,859	5,445,985	5,727.6	50	7,430,434	5,972,756.7	0.92	358.23	9.26	38.70	87.30
200	6,329	6,329	58,966	2,261,319	3,700,914	5,248.9	65	7,585,997	6,192,543.0	0.83	357.29	9.32	38.35	123.83
200	14,573	14,573	145,519	5,194,487	8,123,403	12,331.4	68	18,302,765	10,875,594.6	0.80	356.45	9.99	35.70	55.14
200	24,188	24,188	250,078	8,578,067	13,293,579	20,438.2	92	22,143,045	16,087,169.9	1.09	354.64	10.34	34.30	45.01
200	52,105	52,105	522,103	17,345,579	25,325,381	40,768.5	117	41,872,078	25,735,715.4	1.24	332.90	10.02	33.22	28.70
200	79,774	79,774	788,622	25,802,902	37,154,350	60,336.6	134	42,518,050	32,619,147.7	1.88	323.45	9.89	32.72	22.21
201	86,178	86,178	837,054	27,140,687	38,461,748	63,245.1	110	40,747,336	31,352,254.8	2.11	314.94	9.71	32.42	17.39
201	87,312	87,312	821,712	26,507,563	36,956,128	61,431.0	108	39,638,828	30,721,455.0	2.20	303.60	9.41	32.26	17.58
201	88,069	88,069	784,868	25,322,378	35,180,505	57,934.8	85	39,225,141	30,217,850.5	2.25	287.53	8.91	32.26	14.67
201	84,943	84,943	663,897	21,274,579	29,644,922	46,595.5	106	38,516,700	29,756,177.6	2.21	250.46	7.82	32.04	22.75
201	81,601	81,601	477,261	14,863,042	20,284,348	27,670.4	64	39,116,110	29,216,724.7	2.09	182.14	5.85	31.14	23.13
201	17,587	17,587	70,852	2,261,931	3,132,870	2,952.2	6	22,986,350	7,690,703.3	0.77	128.61	4.03	31.92	20.32
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>180-Day Blackout Period</b>														
200	1,151	1,151	11,881	583,839	1,339,362	1,148.5	9	6,000,891	2,668,690.0	0.19	507.25	10.32	49.14	78.36
200	2,377	2,377	24,101	1,091,858	2,256,644	2,117.4	18	6,564,580	5,409,238.5	0.36	459.34	10.14	45.30	85.01
200	2,520	2,520	28,621	1,272,855	2,507,885	2,544.4	15	6,682,703	5,451,652.9	0.38	505.10	11.36	44.47	58.95
200	4,793	4,793	78,299	2,980,664	8,379,420	6,326.3	41	6,656,319	5,455,605.7	0.72	621.88	16.34	38.07	64.81
200	3,946	3,946	56,410	2,208,827	4,561,370	4,558.1	35	7,094,001	5,703,535.4	0.56	559.76	14.30	39.16	76.79
200	3,583	3,583	52,094	2,026,160	3,357,947	4,163.6	48	7,316,229	5,856,393.8	0.49	565.49	14.54	38.89	115.28
200	8,398	8,398	129,333	4,673,768	7,360,667	9,760.3	55	17,580,806	10,225,742.4	0.48	556.53	15.40	36.14	56.35
200	14,031	14,031	222,421	7,709,753	12,052,818	16,123.8	58	21,032,171	15,128,114.1	0.67	549.48	15.85	34.66	35.97
200	29,861	29,861	459,677	15,426,113	22,717,790	31,450.5	79	39,175,224	23,704,111.6	0.76	516.60	15.39	33.56	25.12
200	45,661	45,661	692,316	22,874,156	33,228,644	46,112.9	106	40,462,722	30,039,482.2	1.13	500.96	15.16	33.04	22.99
200	50,112	50,112	736,434	24,094,581	34,413,367	47,917.5	82	38,827,367	29,006,004.2	1.29	480.81	14.70	32.72	17.11
201	50,362	50,362	721,275	23,481,320	32,956,881	46,222.9	70	37,854,554	28,493,060.2	1.33	466.25	14.32	32.56	15.14
201	51,745	51,745	687,836	22,382,969	31,320,799	42,516.5	60	36,994,842	28,143,157.8	1.40	432.56	13.29	32.54	14.11
201	49,022	49,022	567,495	18,349,077	25,747,763	31,838.1	71	36,850,226	27,545,062.6	1.33	374.30	11.58	32.33	22.30

**Table 4a: Summary of Incident Amphetamine Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member - Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
200	40,459	40,459	349,982	11,073,933	15,289,547	13,908.4	33	36,397,236	23,813,298.8	1.11	273.71	8.65	31.64	23.73
201	4,697	4,697	28,141	970,534	1,372,270	639.4	0	13,594,744	3,601,583.5	0.35	206.63	5.99	34.49	0.00
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>270-Day Blackout Period</b>														
200	716	716	10,119	506,196	1,198,313	919.4	8	5,556,728	2,575,586.1	0.13	706.98	14.13	50.02	87.01
200	1,471	1,471	20,458	933,716	1,975,912	1,656.5	13	6,239,349	5,172,510.0	0.24	634.75	13.91	45.64	78.48
200	1,570	1,570	24,584	1,105,901	2,229,627	2,060.4	13	6,328,271	5,194,966.1	0.25	704.40	15.66	44.98	63.09
200	3,403	3,403	71,693	2,743,484	7,933,418	5,363.9	35	6,272,918	5,219,168.3	0.54	806.20	21.07	38.27	65.25
200	2,766	2,766	50,831	2,006,439	4,054,429	3,774.3	29	6,684,275	5,464,609.6	0.41	725.39	18.38	39.47	76.84
200	2,386	2,386	46,475	1,829,078	3,051,826	3,484.5	44	6,845,038	5,563,516.6	0.35	766.59	19.48	39.36	126.27
200	5,797	5,797	116,173	4,231,948	6,721,591	8,068.4	50	16,123,676	9,730,777.8	0.36	730.02	20.04	36.43	61.97
200	9,666	9,666	199,175	6,963,680	10,990,807	13,308.2	42	19,515,997	14,308,561.3	0.50	720.43	20.61	34.96	31.56
200	20,526	20,526	408,942	13,831,798	20,536,483	25,451.5	59	34,992,008	22,233,188.9	0.59	673.87	19.92	33.82	23.18
200	31,546	31,546	614,743	20,446,284	29,898,302	36,944.2	76	36,930,872	27,866,190.1	0.85	648.14	19.49	33.26	20.57
201	34,556	34,556	651,151	21,449,416	30,870,421	37,919.4	60	35,510,617	27,028,635.7	0.97	620.71	18.84	32.94	15.82
201	34,720	34,720	636,634	20,858,987	29,405,216	36,248.8	53	34,706,199	26,589,200.8	1.00	600.78	18.34	32.76	14.62
201	36,302	36,302	604,976	19,812,098	27,880,105	32,211.9	43	33,869,422	26,423,096.5	1.07	545.76	16.67	32.75	13.35
201	33,776	33,776	484,488	15,772,953	22,290,409	22,140.9	46	33,842,511	25,608,869.9	1.00	466.99	14.34	32.56	20.78
201	21,941	21,941	237,559	7,663,050	10,640,237	6,573.1	15	31,997,240	18,155,638.1	0.69	349.26	10.83	32.26	22.82
201	570	570	3,456	162,536	257,023	59.0	0	9,128,292	1,033,294.9	0.06	285.15	6.06	47.03	0.00
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>365-Day Blackout Period</b>														
200	472	472	8,722	441,672	1,076,035	765.8	8	5,308,581	2,486,855.0	0.09	935.75	18.48	50.64	104.47
200	1,027	1,027	17,662	815,592	1,742,063	1,337.2	10	5,774,614	4,927,922.5	0.18	794.15	17.20	46.18	74.78
200	1,089	1,089	21,671	981,793	2,027,318	1,738.0	11	5,831,116	4,955,041.8	0.19	901.55	19.90	45.30	63.29
200	2,543	2,543	65,415	2,522,651	7,300,858	4,614.3	32	5,852,891	4,990,202.0	0.43	992.00	25.72	38.56	69.35
200	1,982	1,982	45,023	1,805,225	3,602,622	3,185.1	25	6,394,907	5,222,423.6	0.31	910.81	22.72	40.10	78.49
200	1,745	1,745	41,903	1,660,668	2,795,418	2,970.3	36	6,234,521	5,289,580.4	0.28	951.67	24.01	39.63	121.20
200	4,223	4,223	104,287	3,830,323	6,134,715	6,800.9	40	14,954,009	9,251,910.9	0.28	907.01	24.70	36.73	58.82
200	7,223	7,223	179,697	6,337,176	10,102,473	11,176.6	29	17,881,956	13,524,180.4	0.40	877.36	24.88	35.27	25.95
200	14,960	14,960	364,075	12,396,141	18,547,640	20,962.8	47	32,595,353	20,830,088.9	0.46	828.62	24.34	34.05	22.42
200	22,883	22,883	543,789	18,202,825	26,785,562	30,055.4	60	32,136,251	25,757,516.5	0.71	795.47	23.76	33.47	19.96
201	25,098	25,098	573,266	19,004,358	27,472,348	30,393.2	50	31,160,199	25,150,968.2	0.81	757.21	22.84	33.15	16.45
201	25,305	25,305	559,930	18,459,372	26,129,488	28,762.7	37	30,529,927	24,734,824.1	0.83	729.48	22.13	32.97	12.86
201	26,673	26,673	526,501	17,345,259	24,504,543	24,300.1	32	32,126,387	24,743,679.3	0.83	650.29	19.74	32.94	13.17
201	24,455	24,455	407,043	13,338,310	18,935,329	14,787.1	26	29,561,474	23,711,875.2	0.83	545.42	16.64	32.77	17.58
201	10,405	10,405	132,308	4,409,484	6,207,847	2,480.9	3	24,793,139	11,583,599.1	0.42	423.79	12.72	33.33	12.09
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>730-Day Blackout Period</b>														
200	219	219	6,238	324,889	833,332	452.3	6	4,472,279	2,102,708.9	0.05	1483.51	28.48	52.08	132.64
200	375	375	10,449	511,615	1,138,432	691.2	5	4,798,149	4,155,900.9	0.08	1364.31	27.86	48.96	72.34
200	448	448	14,891	691,498	1,508,705	1,053.8	8	4,865,986	4,226,375.8	0.09	1543.52	33.24	46.44	75.91
200	1,294	1,294	49,554	1,948,970	5,361,962	2,834.0	26	5,026,238	4,274,351.5	0.26	1506.16	38.30	39.33	91.74
200	804	804	30,310	1,264,905	2,352,311	1,935.5	12	5,309,626	4,319,477.1	0.15	1573.26	37.70	41.73	62.00
200	801	801	29,847	1,220,168	2,089,564	1,790.9	20	5,224,881	4,518,675.0	0.15	1523.31	37.26	40.88	111.68
200	1,920	1,920	74,346	2,786,296	4,519,160	4,006.2	10	12,089,133	7,673,184.6	0.16	1451.20	38.72	37.48	24.96
200	3,301	3,301	126,883	4,563,231	7,411,321	6,347.1	14	14,483,359	10,818,869.6	0.23	1382.38	38.44	35.96	22.06
200	6,662	6,662	248,055	8,617,375	13,100,052	11,047.1	27	24,136,632	16,019,341.0	0.28	1293.51	37.23	34.74	24.44
200	9,852	9,852	359,657	12,253,226	18,134,407	15,023.2	32	23,895,008	19,743,604.9	0.41	1243.73	36.51	34.07	21.30
201	10,420	10,420	365,158	12,331,541	17,910,349	14,213.1	29	23,494,226	19,387,442.4	0.44	1183.45	35.04	33.77	20.40
201	11,350	11,350	362,575	12,175,670	17,426,659	12,005.5	21	24,770,418	19,571,224.9	0.46	1072.75	31.94	33.58	17.49



**Table 4a: Summary of Incident Amphetamine Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member - Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
200	10,795	10,795	300,477	10,109,031	14,380,091	7,245.3	9	24,553,358	18,843,977.4	0.44	936.45	27.83	33.64	12.42
201	4,740	4,740	106,810	3,767,194	5,556,039	1,267.0	5	18,916,120	9,175,348.4	0.25	794.77	22.53	35.27	39.46
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>1,095-Day Blackout Period</b>														
200	104	104	4,040	222,906	589,833	295.6	3	3,815,327	1,806,473.6	0.03	2143.33	38.85	55.17	101.49
200	178	178	7,035	346,725	815,592	434.1	3	4,106,403	3,609,935.8	0.04	1947.89	39.52	49.29	69.10
200	256	256	11,175	532,693	1,234,639	715.7	4	4,274,307	3,683,678.5	0.06	2080.83	43.65	47.67	55.89
200	702	702	35,901	1,456,073	3,647,431	1,893.3	17	4,276,082	3,584,244.3	0.16	2074.18	51.14	40.56	89.79
200	481	481	23,151	988,151	1,737,107	1,303.4	6	4,485,160	3,756,838.2	0.11	2054.37	48.13	42.68	46.03
200	446	446	21,808	914,909	1,581,628	1,186.9	5	4,515,056	3,941,062.1	0.10	2051.37	48.90	41.95	42.13
200	1,130	1,130	56,078	2,130,174	3,499,613	2,544.1	5	9,875,015	6,410,390.6	0.11	1885.11	49.63	37.99	19.65
200	1,881	1,881	92,942	3,395,068	5,592,236	3,862.8	8	11,686,175	8,935,346.8	0.16	1804.93	49.41	36.53	20.71
200	3,633	3,633	172,693	6,101,588	9,349,115	6,149.3	12	18,692,512	12,887,402.7	0.19	1679.49	47.53	35.33	19.51
200	5,136	5,136	240,735	8,324,469	12,276,130	7,879.0	18	18,567,989	15,598,977.0	0.28	1620.81	46.87	34.58	22.85
201	5,656	5,656	244,612	8,383,157	12,255,468	6,531.8	14	19,671,829	15,782,068.5	0.29	1482.17	43.25	34.27	21.43
201	5,634	5,634	216,865	7,428,470	10,707,227	3,931.4	4	19,626,102	15,303,570.9	0.29	1318.51	38.49	34.25	10.17
201	2,529	2,529	81,419	2,944,691	4,298,625	659.9	0	17,017,025	7,632,004.9	0.15	1164.37	32.19	36.17	0.00
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
200	4,445	4,445	25,026	1,152,988	2,509,250	4,450.6	22	6,528,534	2,996,066.8	0.68	259.39	5.63	46.07	49.43
200	10,026	10,026	55,273	2,335,761	4,642,788	9,463.1	49	7,127,377	5,952,300.9	1.41	232.97	5.51	42.26	51.78
200	9,488	9,488	57,881	2,400,319	4,752,964	9,334.3	49	7,278,258	6,050,303.3	1.30	252.98	6.10	41.47	52.49
200	14,597	14,597	131,712	4,858,234	12,183,767	17,423.3	102	7,271,066	6,022,844.4	2.01	332.82	9.02	36.89	58.54
200	12,006	12,006	93,950	3,580,368	8,651,923	13,082.7	101	7,706,827	6,267,195.9	1.56	298.21	7.83	38.11	77.20
200	11,527	11,527	92,006	3,457,178	5,670,766	12,603.8	104	7,950,033	6,557,957.1	1.45	299.92	7.98	37.58	82.51
200	27,030	27,030	222,568	7,785,096	12,261,470	29,294.6	152	19,421,917	11,592,037.9	1.39	288.02	8.23	34.98	51.89
200	44,869	44,869	380,047	12,800,702	20,084,552	48,263.7	227	23,618,253	17,146,278.6	1.90	285.29	8.47	33.68	47.03
200	97,121	97,121	782,053	25,589,134	44,602,989	97,461.5	276	44,315,751	27,985,579.6	2.19	263.48	8.05	32.72	28.32
200	143,528	143,528	1,173,443	37,858,922	54,697,738	144,032.3	322	45,694,875	35,453,462.7	3.14	263.77	8.18	32.26	22.36
201	149,830	149,830	1,222,408	39,117,740	55,594,124	149,336.6	331	43,543,185	33,937,855.2	3.44	261.08	8.16	32.00	22.16
201	150,803	150,803	1,182,114	37,617,061	52,718,993	144,836.1	277	42,124,991	33,129,469.7	3.58	249.45	7.84	31.82	19.13
201	148,452	148,452	1,101,311	35,070,215	48,863,264	136,385.9	226	41,090,454	32,445,579.6	3.61	236.24	7.42	31.84	16.57
201	143,836	143,836	907,868	28,606,930	39,931,017	113,223.7	275	40,939,000	32,116,700.6	3.51	198.89	6.31	31.51	24.29
201	139,259	139,259	627,705	19,137,430	26,217,407	77,219.4	183	41,865,439	31,987,415.3	3.33	137.42	4.51	30.49	23.70
201	62,913	62,913	143,248	3,994,514	5,490,223	15,466.8	31	34,431,982	15,651,578.6	1.83	63.49	2.28	27.89	20.04
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>90-Day Blackout Period</b>														
200	3,975	3,975	24,356	1,136,162	2,477,776	3,414.3	15	6,271,153	2,822,041.0	0.63	285.83	6.13	46.65	43.93
200	9,179	9,179	54,102	2,304,301	4,584,050	7,097.4	37	6,792,762	5,668,612.1	1.35	251.04	5.89	42.59	52.13
200	8,587	8,587	56,546	2,364,600	4,696,006	7,121.3	33	6,954,580	5,739,507.7	1.23	275.37	6.59	41.82	46.34
200	12,931	12,931	129,413	4,803,261	12,114,070	14,082.0	77	6,902,748	5,719,981.0	1.87	371.45	10.01	37.12	54.68
200	10,396	10,396	91,586	3,524,894	8,443,971	10,363.8	70	7,423,310	5,967,879.4	1.40	339.06	8.81	38.49	67.54
200	10,074	10,074	89,954	3,409,713	5,601,321	10,011.2	85	7,576,763	6,185,903.1	1.33	338.47	8.93	37.91	84.90
200	23,727	23,727	218,437	7,695,940	12,128,173	23,164.3	109	18,291,640	10,867,225.1	1.30	324.35	9.21	35.23	47.06
200	39,398	39,398	372,072	12,615,561	19,812,371	38,013.8	144	22,126,822	16,075,259.4	1.78	320.21	9.44	33.91	37.88
200	83,413	83,413	762,508	25,152,712	44,008,481	75,496.2	191	41,847,719	25,718,249.5	1.99	301.54	9.14	32.99	25.30

**Table 4a: Summary of Incident Amphetamine Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member - Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
200	124,026	124,026	1,146,506	37,260,423	53,913,207	111,515.3	235	42,479,226	32,592,536.4	2.92	300.42	9.24	32.50	21.07
201	130,101	130,101	1,195,496	38,523,950	54,791,376	115,399.0	215	40,690,560	31,313,081.0	3.20	296.11	9.19	32.22	18.63
201	130,986	130,986	1,156,473	37,070,467	52,016,509	110,860.6	185	39,565,848	30,670,537.1	3.31	283.01	8.83	32.05	16.69
201	130,389	130,389	1,078,392	34,588,861	48,242,388	102,828.8	160	39,139,329	30,157,134.1	3.33	265.27	8.27	32.07	15.56
201	125,655	125,655	883,989	28,091,803	39,256,741	80,725.9	188	38,420,497	29,687,571.1	3.27	223.56	7.04	31.78	23.29
201	119,531	119,531	600,047	18,526,870	25,411,038	45,862.0	102	39,016,072	29,146,971.5	3.06	155.00	5.02	30.88	22.24
201	25,944	25,944	86,386	2,706,885	3,778,014	4,767.2	8	22,933,913	7,676,229.7	1.13	104.34	3.33	31.33	16.78
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>180-Day Blackout Period</b>														
200	2,370	2,370	21,934	1,056,048	2,317,980	2,650.3	15	6,000,891	2,668,690.0	0.39	445.59	9.25	48.15	56.60
200	5,299	5,299	49,085	2,144,829	4,276,410	5,433.3	26	6,564,090	5,409,082.4	0.81	404.76	9.26	43.70	47.85
200	5,154	5,154	53,455	2,288,559	4,657,059	5,773.1	28	6,680,764	5,450,644.5	0.77	444.04	10.37	42.81	48.50
200	8,544	8,544	131,558	4,912,150	12,864,946	12,546.6	70	6,653,206	5,453,879.5	1.28	574.92	15.40	37.34	55.79
200	6,671	6,671	88,307	3,445,247	7,143,998	8,716.3	50	7,089,937	5,701,152.4	0.94	516.45	13.24	39.01	57.36
200	6,235	6,235	86,023	3,304,427	5,437,401	8,393.7	65	7,310,691	5,852,977.9	0.85	529.98	13.80	38.41	77.44
200	14,485	14,485	206,894	7,376,782	11,674,957	19,054.7	92	17,573,949	10,221,217.3	0.82	509.27	14.28	35.65	48.28
200	24,136	24,136	352,631	12,079,326	19,001,861	31,226.5	92	21,023,286	15,122,349.6	1.15	500.47	14.61	34.25	29.46
200	51,151	51,151	717,641	23,886,620	35,220,911	60,848.1	128	39,162,626	23,696,227.7	1.31	466.98	14.03	33.28	21.04
200	77,966	77,966	1,083,386	35,485,713	51,504,109	89,614.6	187	40,444,186	30,028,740.7	1.93	455.14	13.90	32.75	20.87
201	84,225	84,225	1,140,231	37,016,461	52,855,928	93,001.5	166	38,799,075	28,989,770.3	2.17	439.49	13.54	32.46	17.85
201	85,072	85,072	1,103,474	35,650,186	50,124,490	88,594.6	135	37,815,970	28,470,444.2	2.25	419.06	12.97	32.31	15.24
201	86,911	86,911	1,032,846	33,365,103	46,679,594	80,600.0	117	36,947,098	28,114,032.9	2.35	383.90	11.88	32.30	14.52
201	82,477	82,477	831,563	26,650,655	37,317,300	58,803.6	137	36,793,927	27,510,707.2	2.24	323.13	10.08	32.05	23.30
201	67,870	67,870	496,741	15,611,381	21,577,025	24,909.6	54	36,339,426	23,781,809.4	1.87	230.02	7.32	31.43	21.68
201	8,094	8,094	40,495	1,374,517	1,945,109	1,123.1	0	13,578,385	3,597,169.3	0.60	169.82	5.00	33.94	0.00
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>270-Day Blackout Period</b>														
200	1,602	1,602	20,006	968,549	2,159,048	2,178.6	14	5,556,728	2,575,586.1	0.29	604.59	12.49	48.41	64.26
200	3,506	3,506	44,326	1,952,755	3,926,826	4,412.3	22	6,239,186	5,172,485.1	0.56	556.98	12.64	44.05	49.86
200	3,476	3,476	49,113	2,118,017	4,566,200	4,823.2	25	6,327,413	5,194,617.7	0.55	609.33	14.13	43.13	51.83
200	6,455	6,455	126,110	4,725,762	12,740,320	10,987.4	63	6,271,413	5,218,443.0	1.03	732.11	19.54	37.47	57.34
200	4,931	4,931	83,737	3,287,703	6,570,582	7,500.4	42	6,682,098	5,463,488.9	0.74	666.74	16.98	39.26	56.00
200	4,537	4,537	80,990	3,128,431	5,169,616	7,205.2	58	6,841,809	5,561,670.2	0.66	689.54	17.85	38.63	80.50
200	10,790	10,790	195,115	6,997,590	11,116,678	16,173.6	81	16,119,491	9,728,200.1	0.67	648.53	18.08	35.86	50.08
200	17,836	17,836	330,881	11,396,878	18,015,907	26,383.2	67	19,510,661	14,305,279.3	0.91	638.98	18.55	34.44	25.39
200	38,061	38,061	670,201	22,444,007	33,245,388	50,444.3	98	34,984,497	22,228,715.3	1.09	589.69	17.61	33.49	19.43
200	57,591	57,591	1,007,812	33,193,630	48,361,941	73,873.3	149	36,920,083	27,860,143.7	1.56	576.37	17.50	32.94	20.17
201	62,889	62,889	1,063,521	34,716,526	49,773,583	76,242.3	126	35,493,829	27,019,417.7	1.77	552.03	16.91	32.64	16.53
201	63,249	63,249	1,026,905	33,355,508	47,058,099	71,850.6	103	34,682,396	26,575,912.7	1.82	527.37	16.24	32.48	14.34
201	65,618	65,618	960,506	31,201,064	43,799,001	63,471.3	85	33,838,924	26,405,303.8	1.94	475.50	14.64	32.48	13.39
201	61,514	61,514	757,624	24,422,192	34,324,442	42,472.6	98	33,805,893	25,587,460.0	1.82	397.02	12.32	32.24	23.07
201	39,823	39,823	364,214	11,682,836	16,235,129	12,373.9	26	31,962,362	18,139,955.5	1.25	293.37	9.15	32.08	21.01
201	1,063	1,063	5,555	258,447	410,147	112.6	0	9,120,268	1,032,356.9	0.12	243.13	5.23	46.53	0.00
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>365-Day Blackout Period</b>														
200	1,097	1,097	17,901	878,387	2,001,149	1,833.2	14	5,308,581	2,486,855.0	0.21	800.72	16.32	49.07	76.37
200	2,513	2,513	39,919	1,771,923	3,596,530	3,644.5	18	5,774,592	4,927,921.4	0.44	705.10	15.88	44.39	49.39
200	2,491	2,491	44,773	1,940,567	4,279,767	4,104.9	23	5,830,777	4,954,926.0	0.43	779.03	17.97	43.34	56.03
200	5,076	5,076	119,433	4,493,712	12,161,232	9,608.3	57	5,852,169	4,989,874.3	0.87	885.29	23.53	37.63	59.32
200	3,729	3,729	77,470	3,071,706	5,929,941	6,457.6	36	6,393,675	5,221,827.6	0.58	823.73	20.78	39.65	55.75
200	3,488	3,488	75,875	2,952,825	4,902,691	6,275.2	49	6,232,682	5,288,534.8	0.56	846.57	21.75	38.92	78.08
200	8,102	8,102	180,902	6,529,029	10,428,892	13,848.3	69	14,951,423	9,250,351.0	0.54	805.85	22.33	36.09	49.83

**Table 4a: Summary of Incident Amphetamine Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member - Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
200	13,699	13,699	307,742	10,666,580	16,995,060	22,507.0	51	17,878,780	13,522,158.5	0.77	778.64	22.46	34.66	22.66
200	28,821	28,821	617,462	20,781,571	30,964,535	42,133.1	81	32,590,874	20,827,407.9	0.88	721.06	21.42	33.66	19.22
200	43,621	43,621	923,813	30,569,353	44,728,349	61,176.7	117	32,130,177	25,753,910.9	1.36	700.79	21.18	33.09	19.12
200	47,891	47,891	974,790	31,962,860	46,009,245	62,569.1	113	31,150,587	25,145,581.1	1.54	667.41	20.35	32.79	18.06
201	48,244	48,244	939,222	30,657,444	43,371,995	58,254.0	78	30,516,009	24,726,915.6	1.58	635.47	19.47	32.64	13.39
201	50,822	50,822	875,645	28,578,702	40,242,974	49,186.1	66	32,107,108	24,732,662.1	1.58	562.33	17.23	32.64	13.42
201	46,585	46,585	667,568	21,630,455	30,519,221	29,050.7	63	29,539,192	23,698,358.2	1.58	464.32	14.33	32.40	21.69
201	19,773	19,773	213,897	7,091,549	9,980,372	4,864.0	6	24,776,986	11,577,273.2	0.80	358.65	10.82	33.15	12.34
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>730-Day Blackout Period</b>														
200	499	499	13,242	668,320	1,593,675	1,106.5	10	4,472,279	2,102,708.9	0.11	1339.32	26.54	50.47	90.37
200	1,038	1,038	27,200	1,246,742	2,603,266	1,998.6	9	4,798,149	4,155,900.9	0.22	1201.10	26.20	45.84	45.03
200	1,093	1,093	32,902	1,453,230	3,435,073	2,520.2	14	4,865,979	4,226,375.2	0.22	1329.58	30.10	44.17	55.55
200	2,600	2,600	94,604	3,605,005	9,061,683	6,074.3	43	5,026,163	4,274,326.4	0.52	1386.54	36.39	38.11	70.79
200	1,704	1,704	57,731	2,346,561	4,228,353	4,029.5	17	5,309,447	4,319,395.2	0.32	1377.09	33.88	40.65	42.19
200	1,719	1,719	58,453	2,327,989	3,933,816	3,927.8	27	5,224,549	4,518,508.6	0.33	1354.27	34.00	39.83	68.74
200	3,920	3,920	137,329	5,026,318	8,165,645	8,303.6	19	12,088,547	7,672,859.3	0.32	1282.22	35.03	36.60	22.88
200	6,601	6,601	230,717	8,120,068	13,167,354	13,119.7	22	14,482,512	10,818,358.1	0.46	1230.13	34.95	35.19	16.77
200	13,419	13,419	448,067	15,309,959	23,146,823	22,861.6	50	24,135,565	16,018,697.4	0.56	1140.92	33.39	34.17	21.87
200	20,157	20,157	659,070	22,092,088	32,573,624	31,732.7	60	23,893,587	19,742,724.3	0.84	1096.00	32.70	33.52	18.91
201	21,654	21,654	677,290	22,523,170	32,721,880	30,653.0	57	23,492,209	19,386,235.3	0.92	1040.14	31.28	33.25	18.60
201	23,291	23,291	661,347	21,860,454	31,236,045	25,369.0	43	24,767,320	19,569,444.4	0.94	938.58	28.39	33.05	16.95
201	22,796	22,796	558,434	18,513,633	26,269,766	15,431.3	24	24,548,922	18,841,420.7	0.93	812.14	24.50	33.15	15.55
201	9,597	9,597	191,541	6,663,014	9,780,881	2,550.4	11	18,912,990	9,174,062.8	0.51	694.28	19.96	34.79	43.13
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>1,095-Day Blackout Period</b>														
200	261	261	9,393	492,219	1,236,561	735.8	7	3,815,327	1,806,473.6	0.07	1885.90	35.99	52.40	95.13
200	510	510	19,116	889,630	1,917,116	1,286.2	5	4,106,403	3,609,935.8	0.12	1744.37	37.48	46.54	38.87
200	648	648	25,341	1,141,949	2,613,274	1,663.5	8	4,274,307	3,683,678.5	0.15	1762.27	39.11	45.06	48.09
200	1,511	1,511	72,465	2,824,289	6,655,143	4,083.4	28	4,276,081	3,584,244.3	0.35	1869.15	47.96	38.97	68.57
200	1,023	1,023	45,110	1,867,837	3,240,782	2,711.1	11	4,485,139	3,756,832.2	0.23	1825.84	44.10	41.41	40.57
200	999	999	44,542	1,818,314	3,107,043	2,644.9	7	4,514,996	3,941,035.4	0.22	1820.13	44.59	40.82	26.47
200	2,286	2,286	105,152	3,895,868	6,419,988	5,325.4	11	9,874,868	6,410,320.3	0.23	1704.23	46.00	37.05	20.66
200	3,897	3,897	176,166	6,267,661	10,319,402	8,074.4	15	11,685,923	8,935,216.7	0.33	1608.33	45.21	35.58	18.58
200	7,456	7,456	323,523	11,193,874	17,088,466	12,926.9	25	18,692,146	12,887,185.4	0.40	1501.32	43.39	34.60	19.34
200	10,842	10,842	461,240	15,635,341	23,107,461	16,905.8	35	18,567,525	15,598,682.0	0.58	1442.11	42.54	33.90	20.70
201	12,256	12,256	478,128	16,076,307	23,536,119	14,382.9	31	19,671,174	15,781,668.8	0.62	1311.71	39.01	33.62	21.55
201	12,094	12,094	420,393	14,097,138	20,305,889	8,441.9	12	19,625,187	15,302,993.4	0.62	1165.63	34.76	33.53	14.21
201	5,411	5,411	156,547	5,591,684	8,109,645	1,454.0	1	17,016,100	7,631,676.8	0.32	1033.39	28.93	35.72	6.88
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
201	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Amphetamine Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>30-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
2000	7	919	76.2
2001	12	2,025	59.3
2002	15	1,834	81.8
2003	23	2,334	98.6
2004	29	2,250	128.9
2005	18	2,182	82.5
2006	39	5,244	74.4
2007	76	8,738	87.0
2008	74	18,946	39.1
2009	74	28,221	26.2
2010	100	29,083	34.4
2011	77	28,952	26.6
2012	58	28,409	20.4
2013	71	27,754	25.6
2014	73	27,223	26.8
2015	21	9,770	21.5
2016	0	0	---
<b>Days 91-180</b>			
2000	0	411	0.0
2001	9	855	105.3
2002	7	827	84.7
2003	3	1,424	21.1
2004	15	1,170	128.3
2005	17	1,085	156.6
2006	13	2,571	50.6
2007	34	4,314	78.8
2008	38	9,318	40.8
2009	28	14,224	19.7
2010	28	15,328	18.3
2011	38	15,208	25.0
2012	25	15,418	16.2
2013	35	14,757	23.7
2014	31	13,762	22.5
2015	6	2,313	25.9
2016	0	0	---



**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Amphetamine Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>Days 181-270</b>			
2000	1	229	43.6
2001	5	461	108.5
2002	2	484	41.3
2003	6	962	62.3
2004	6	784	76.5
2005	4	679	58.9
2006	5	1,692	29.6
2007	16	2,816	56.8
2008	20	5,999	33.3
2009	30	9,169	32.7
2010	22	9,998	22.0
2011	17	9,974	17.0
2012	17	10,305	16.5
2013	25	9,697	25.8
2014	18	7,335	24.5
2015	0	580	0.0
2016	0	0	---
<b>Days 271-365</b>			
2000	0	154	0.0
2001	3	319	94.0
2002	2	322	62.0
2003	3	750	40.0
2004	4	589	67.9
2005	8	514	155.6
2006	10	1,268	78.9
2007	13	2,132	61.0
2008	12	4,489	26.7
2009	16	6,889	23.2
2010	10	7,526	13.3
2011	16	7,486	21.4
2012	11	7,912	13.9
2013	20	7,354	27.2
2014	12	4,092	29.3
2015	0	59	0.0
2016	0	0	---
<b>Days 366-730</b>			

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Amphetamine Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	<b>New Episodes with Events</b>	<b>Years at Risk</b>	<b>New Episodes with Events per 10,000 Years at Risk</b>
2000	2	313	63.8
2001	5	646	77.4
2002	3	684	43.8
2003	6	1,780	33.7
2004	13	1,250	104.0
2005	16	1,179	135.7
2006	30	2,795	107.3
2007	15	4,829	31.1
2008	20	9,916	20.2
2009	28	15,032	18.6
2010	21	16,180	13.0
2011	16	16,757	9.5
2012	23	17,055	13.5
2013	21	13,520	15.5
2014	3	2,481	12.1
2015	0	0	---
2016	0	0	---
<b>Days 731-1,095</b>			
2000	3	157	191.4
2001	2	257	77.8
2002	4	338	118.3
2003	9	941	95.7
2004	6	632	94.9
2005	15	604	248.4
2006	5	1,462	34.2
2007	6	2,484	24.2
2008	15	4,898	30.6
2009	14	7,144	19.6
2010	15	7,681	19.5
2011	17	8,074	21.1
2012	9	6,585	13.7
2013	5	1,267	39.5
2014	0	0	---
2015	0	0	---
2016	0	0	---
<b>90-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Amphetamine Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
2000	7	1,036	67.5
2001	12	2,366	50.7
2002	16	2,213	72.3
2003	25	3,341	74.8
2004	31	2,719	114.0
2005	19	2,593	73.3
2006	43	6,130	70.1
2007	83	10,250	81.0
2008	85	21,965	38.7
2009	87	32,517	26.8
2010	116	33,938	34.2
2011	92	33,976	27.1
2012	66	33,557	19.7
2013	87	32,498	26.8
2014	81	31,357	25.8
2015	23	10,700	21.5
2016	0	0	---
<b>Days 91-180</b>			
2000	0	764	0.0
2001	11	1,664	66.1
2002	5	1,348	37.1
2003	7	1,535	45.6
2004	20	1,647	121.4
2005	20	1,618	123.6
2006	17	4,110	41.4
2007	52	6,787	76.6
2008	63	14,648	43.0
2009	48	21,901	21.9
2010	49	22,397	21.9
2011	50	22,266	22.5
2012	43	22,229	19.3
2013	51	21,922	23.3
2014	48	20,952	22.9
2015	8	3,644	22.0
2016	0	0	---
<b>Days 181-270</b>			
2000	1	472	21.2

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Amphetamine Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
2001	4	1,021	39.2
2002	3	950	31.6
2003	7	1,559	44.9
2004	8	1,216	65.8
2005	7	1,189	58.9
2006	11	2,881	38.2
2007	25	4,843	51.6
2008	30	10,404	28.8
2009	38	15,741	24.1
2010	40	16,759	23.9
2011	32	16,744	19.1
2012	32	17,129	18.7
2013	39	16,331	23.9
2014	28	12,536	22.3
2015	0	1,011	0.0
2016	0	0	---
<b>Days 271-365</b>			
2000	0	345	0.0
2001	4	768	52.1
2002	2	718	27.8
2003	6	1,379	43.5
2004	6	1,043	57.5
2005	9	930	96.8
2006	12	2,325	51.6
2007	16	3,876	41.3
2008	17	8,311	20.5
2009	32	12,697	25.2
2010	13	13,673	9.5
2011	25	13,597	18.4
2012	19	14,285	13.3
2013	35	13,422	26.1
2014	20	7,510	26.6
2015	0	113	0.0
2016	0	0	---
<b>Days 366-730</b>			
2000	4	727	55.0
2001	9	1,646	54.7



**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Amphetamine Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	<b>New Episodes with Events</b>	<b>Years at Risk</b>	<b>New Episodes with Events per 10,000 Years at Risk</b>
2002	9	1,585	56.8
2003	14	3,534	39.6
2004	19	2,428	78.3
2005	22	2,347	93.7
2006	50	5,545	90.2
2007	29	9,387	30.9
2008	31	19,272	16.1
2009	57	29,444	19.4
2010	56	31,916	17.5
2011	35	32,885	10.6
2012	42	33,755	12.4
2013	52	26,500	19.6
2014	6	4,864	12.3
2015	0	0	---
2016	0	0	---
<b>Days 731-1,095</b>			
2000	3	371	80.9
2001	4	712	56.1
2002	6	857	70.0
2003	15	1,991	75.3
2004	6	1,318	45.5
2005	20	1,283	155.9
2006	8	2,978	26.9
2007	7	5,045	13.9
2008	25	9,935	25.2
2009	25	14,827	16.9
2010	26	16,270	16.0
2011	31	16,927	18.3
2012	23	13,977	16.5
2013	11	2,550	43.1
2014	0	0	---
2015	0	0	---
2016	0	0	---

**Appendix A: List of Generic and Brand Names Used to Define the Exposures and Exposure Incidence in this Request**

Generic Name	Brand Name
<b>Amphetamines</b>	
DEXTROAMPHETAMINE SULFATE	Dexedrine Spansule
DEXTROAMPHETAMINE SULFATE	dextroamphetamine
DEXTROAMPHETAMINE SULFATE	Dexedrine
DEXTROAMPHETAMINE SULFATE	DextroStat
DEXTROAMPHETAMINE SULFATE	Zenzedi
DEXTROAMPHETAMINE SULFATE	ProCentra
DEXTROAMPHETAMINE SULFATE	Liquadd
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	Amphetamine Salt Combo
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	Adderall XR
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	Adderall
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	dextroamphetamine-amphetamine
LISDEXAMFETAMINE DIMESYLATE	Vyvanse
METHAMPHETAMINE HCL	Desoxyn
AMPHETAMINE SULFATE	Evekeo
METHAMPHETAMINE HCL	methamphetamine
<b>Methylphenidates</b>	
DEXMETHYLPHENIDATE HCL	dexmethylphenidate
DEXMETHYLPHENIDATE HCL	Focalin XR
DEXMETHYLPHENIDATE HCL	Focalin
METHYLPHENIDATE HCL	Methylin
METHYLPHENIDATE HCL	Ritalin LA
METHYLPHENIDATE HCL	methylphenidate
METHYLPHENIDATE HCL	Concerta
METHYLPHENIDATE HCL	Metadate CD
METHYLPHENIDATE HCL	Aptensio XR
METHYLPHENIDATE HCL	Ritalin
METHYLPHENIDATE HCL	Ritalin SR
METHYLPHENIDATE HCL	Metadate ER
METHYLPHENIDATE HCL	Quillivant XR
METHYLPHENIDATE HCL	Methylin ER
<b>Strattera</b>	
ATOMOXETINE HCL	Strattera

**Appendix B: Codes used to define Heart Failure in this Request**

<b>Code</b>	<b>Code Type</b>	<b>Description</b>
398.91	ICD-9-CM Diagnosis	Rheumatic heart failure (congestive)
402.01	ICD-9-CM Diagnosis	Malignant hypertensive heart disease with heart failure
402.11	ICD-9-CM Diagnosis	Benign hypertensive heart disease with heart failure
402.91	ICD-9-CM Diagnosis	Unspecified hypertensive heart disease with heart failure
404.01	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.03	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic kidney disease stage V or end stage renal disease
404.11	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, benign, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.13	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, benign, with heart failure and chronic kidney disease stage V or end stage renal disease
404.91	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, unspecified, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.93	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, unspecified, with heart failure and chronic kidney disease stage V or end stage renal disease
422.90	ICD-9-CM Diagnosis	Acute myocarditis, unspecified
425.4	ICD-9-CM Diagnosis	Other primary cardiomyopathies
425.9	ICD-9-CM Diagnosis	Secondary cardiomyopathy, unspecified
428	ICD-9-CM Diagnosis	Heart Failure
428.0	ICD-9-CM Diagnosis	Congestive heart failure, unspecified
428.1	ICD-9-CM Diagnosis	Left heart failure
428.2	ICD-9-CM Diagnosis	Systolic heart failure
428.20	ICD-9-CM Diagnosis	Systolic heart failure, unspecified
428.21	ICD-9-CM Diagnosis	Acute systolic heart failure
428.22	ICD-9-CM Diagnosis	Chronic systolic heart failure
428.23	ICD-9-CM Diagnosis	Acute on chronic systolic heart failure
428.3	ICD-9-CM Diagnosis	Diastolic heart failure
428.30	ICD-9-CM Diagnosis	Diastolic heart failure, unspecified
428.31	ICD-9-CM Diagnosis	Acute diastolic heart failure
428.32	ICD-9-CM Diagnosis	Chronic diastolic heart failure
428.33	ICD-9-CM Diagnosis	Acute on chronic diastolic heart failure
428.4	ICD-9-CM Diagnosis	Combined systolic and diastolic heart failure
428.40	ICD-9-CM Diagnosis	Combined systolic and diastolic heart failure, unspecified
428.41	ICD-9-CM Diagnosis	Acute combined systolic and diastolic heart failure
428.42	ICD-9-CM Diagnosis	Chronic combined systolic and diastolic heart failure
428.43	ICD-9-CM Diagnosis	Acute on chronic combined systolic and diastolic heart failure
428.9	ICD-9-CM Diagnosis	Heart failure, unspecified

**Modular Program Specifications for cder\_mpl1r\_wp014\_nsdp\_v01 Report 1 of 8**

Sentinel's Cohort Identification and Descriptive Analysis (CIDA) tool was used to investigate heart failure following treatment with select attention deficit and hyperactivity disorder (ADHD) medications. In total, 49 scenarios were examined with four different exposures, seven different blackout periods, and two different episode gaps/exposure extension periods. The four exposures are all amphetamines, all methylphenidates, strattera, and all stimulants (which include all amphetamines, all methylphenidates, and strattera). **The outcome is heart failure, defined as any heart failure ICD-9-CM diagnosis code (398.91, 402.x1, 402.x3, 404.x1, 404.x3, 422.90, 425.4, 425.9, 428.xx) in any care setting with a primary discharge diagnosis (PDX) value of P (principal) for those diagnoses in the inpatient care setting.** See below for a description of each of these scenarios. The query period was from January 1, 2000 to March 3, 2016 and the enrollment gap was set at 45 days. Age groups were split as follows: 0-21, 22-44, 45-64, 65+.

Enrollment Gap	45 Days
Age Groups	0-21, 22-44, 45-64, 65+
Query Period	January 1, 2000 - Current
Coverage Requirement	Medical and Drug
Enrollment Requirement	183 Days

Drug/Exposure											Event/Outcome					
Scenario	Incident exposure	Incident w/ respect to:	Episode Truncation at Incident Exposure	Episode Truncation at Death	Washout (days)	Cohort Definition	Episode Gap	Exposure Extension Period	Min Episode Duration	Min Days Supplied	Event/ Outcome	Care Setting/PDX	Incident with Respect to Setting/PDX	Incident w/ respect to Care Setting/PDX	Washout (days)	Blackout Period
1	All Amphetamines	All Stimulants	Yes	No	183	01	90	90	0	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	0
2	All Amphetamines	All Stimulants	Yes	No	183	01	90	90	90	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	90
3	All Amphetamines	All Stimulants	Yes	No	183	01	90	90	180	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	180
4	All Amphetamines	All Stimulants	Yes	No	183	01	90	90	270	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	270
5	All Amphetamines	All Stimulants	Yes	No	183	01	90	90	365	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	365
6	All Amphetamines	All Stimulants	Yes	No	183	01	90	90	730	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	730
7	All Amphetamines	All Stimulants	Yes	No	183	01	90	90	1095	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	1095
8	All Amphetamines	All Stimulants	Yes	No	183	01	30	30	0	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	0
9	All Amphetamines	All Stimulants	Yes	No	183	01	30	30	90	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	90
10	All Amphetamines	All Stimulants	Yes	No	183	01	30	30	180	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	180
11	All Amphetamines	All Stimulants	Yes	No	183	01	30	30	270	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	270
12	All Amphetamines	All Stimulants	Yes	No	183	01	30	30	365	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	365
13	All Amphetamines	All Stimulants	Yes	No	183	01	30	30	730	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	730
14	All Amphetamines	All Stimulants	Yes	No	183	01	30	30	1095	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	1095

ICD-9, ICD-10, HCPDS, and CPT codes are provided by Optum360. NDC codes are checked against First Data Bank's "National Drug Data File (NDDF\*) Plus."

Cohort Definition of 01 will only consider the first incident episode for each user during the query period that satisfies the washout period.

Note: Episodes are automatically truncated at outcome.

### Disclaimer

The following report(s) provides findings from an FDA-initiated query using Sentinel. While Sentinel queries may be undertaken to assess potential medical product safety risks, they may also be initiated for various other reasons. Some examples include determining a rate or count of an identified health outcome of interest, examining medical product use, exploring the feasibility of future, more detailed analyses within Sentinel, and seeking to better understand Sentinel capabilities.

Data obtained through Sentinel are intended to complement other types of evidence such as preclinical studies, clinical trials, postmarket studies, and adverse event reports, all of which are used by FDA to inform regulatory decisions regarding medical product safety. The information contained in this report is provided as part of FDA's commitment to place knowledge acquired from Sentinel in the public domain as soon as possible. Any public health actions taken by FDA regarding products involved in Sentinel queries will continue to be communicated through existing channels.

FDA wants to emphasize that the fact that FDA has initiated a query involving a medical product and is reporting findings related to that query does not mean that FDA is suggesting health care practitioners should change their prescribing practices for the medical product or that patients taking the medical product should stop using it. Patients who have questions about the use of an identified medical product should contact their health care practitioners.

The following report contains a description of the request, request specifications, and results from the modular program run(s).

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## Overview for Request cder\_mpl1r\_wp014\_nsdp\_v01, Report 2 of 8

**Request ID:** cder\_mpl1r\_wp014\_nsdp\_v01. This is report 2 of 8.

**Request Description:** FDA has requested execution of the Cohort Identification and Descriptive Analysis (CIDA) tool, version 2.1.1, to investigate heart failure diagnoses following new use of attention deficit hyperactivity disorder (ADHD) medications. This report presents results for all methylphenidates. Results for all amphetamines, strattera, and all stimulants are presented in separate reports.

**Data Source:** Data from January 1, 2000 to March 3, 2016 from 15 health plans contributing to the Sentinel Distributed Database (SDD) are included in this report.

**Study Design:** This request was designed to identify exposures and follow-up time. The exposure of interest and the occurrence of the health outcome of interest during exposed time were identified. The number of exposure episodes, number of individuals, number of events, and days at-risk in the SDD were calculated overall and were stratified by age group, sex, and year.

**Exposure of Interest:** The exposures of interest were methylphenidates, which were defined using National Drug Codes (NDCs). Please refer to Appendix A for a list of generic and brand names of methylphenidates included in this request.

**Cohort Eligibility Criteria:** Patients were required to be continuously enrolled in plans with both medical and drug coverage for at least 6 months (183 days) before their dispensing date, during which gaps in coverage of up to 45 days were allowed. Members were excluded if they had any ADHD medication or the outcome of interest in the 6 months (183 days) prior to exposure initiation. The following age groups were included in the cohort: 0-21, 22-44, 45-64, 65+ years.

**Follow-Up Time:** Follow-up time for the outcome was determined by the length of the exposure episodes. Exposure episode lengths were defined using outpatient pharmacy dispensing days supplied to create a sequence of continuous exposure. Exposure episodes were considered continuous if gaps in days supply were less than 90 days. The end date of each exposure episode was extended by 90 additional days. Sensitivity analyses were performed using a 30-day episode gap and 30-day exposure extension period. Follow-up began on the day on which the first exposure of interest was dispensed and continued until the first occurrence of any of the following: 1) the outcome of interest; 2) any codes defining incidence criteria; 3) disenrollment; 4) the study end date (March, 2016); 5) the end date of the data provided by each Data Partner; or 6) the end of the exposure episode. Only the first valid incident exposure episode that occurred during the study period was included per patient.

This report examines different blackout periods which is a number of days at the beginning of the ADHD medication episode where if an outcome occurs, it is not attributed to the exposure and the person is omitted from the analysis. The blackout periods examined were 90 days, 180 days, 270 days, 365 days, 730 days, and 1,095 days. Episodes that were at least as long as the blackout period were required.

**Outcome of Interest:** Heart failure was defined using any of the ICD-9-CM diagnosis codes listed in Appendix B. This event had to be incident (no heart failure events in the 183 days prior to exposure initiation). The event could happen in any care setting. However, if the event happened in the inpatient or institutionalized care setting, the event had to be flagged as a principal diagnosis.

**Please refer to Appendix C for detailed specifications.**

**Limitations:** Algorithms to define exposures and outcomes are imperfect and, therefore, may be misclassified.

**Notes:** Please contact the Sentinel Operations Center Query Fulfillment Team ([production@mini-sentinel.org](mailto:production@mini-sentinel.org)) for questions and to provide comments/suggestions for future enhancements to this document.

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**Glossary of Terms for Analyses Using  
Cohort Identification and Descriptive Analysis (CIDA) Tool\***

**Amount Supplied** - number of units (pills, tablets, vials) dispensed. Net amount per NDC per dispensing. This is equivalent to the "RxAmt" value in the MSCDM.

**Blackout Period** - number of days at the beginning of a treatment episode that events are to be ignored. If an event occurs during the blackout period, the episode is excluded.

**Care Setting** - type of medical encounter or facility where the exposure, event, or condition code was recorded. Possible care settings include: Inpatient Hospital Stay (IP), Non-Acute Institutional Stay (IS), Emergency Department (ED), Ambulatory Visit (AV), and Other Ambulatory Visit (OA). For laboratory results, possible care settings include: Emergency department (E), Home (H), Inpatient (I), Outpatient (O), or Unknown or Missing (U). Along with the Principal Diagnosis Indicator, forms the Care Setting/PDX parameter.

**Cohort Definition (drug/exposure)** - indicates how the cohort will be defined: (1) 01: Cohort includes only the first valid incident treatment episode during the query period; (2) 02: Cohort includes all valid incident treatment episodes during the query period; (3) 03: Cohort includes all valid incident treatment episodes during the query period until an event

**Days Supplied** - number of days supplied for all dispensings in qualifying treatment episodes.

**Eligible Members** - number of members eligible for an incident treatment episode (defined by the drug/exposure and event washout periods) with drug and medical coverage during the query period.

**Enrollment Gap** - number of days allowed between two consecutive enrollment periods without breaking a "continuously enrolled" sequence.

**Episodes** - treatment episodes; length of episode is determined by days supplied in one dispensing or consecutive dispensings bridged by the episode gap.

**Episode Gap** - number of days allowed between two (or more) consecutive exposures (dispensings/procedures) to be considered the same treatment episode.

**Event Deduplication** - specifies how events are counted by the MP algorithm: (0) 0: Counts all occurrences of an HOI during an exposure episode; (1) 1: de-duplicates occurrences of the same HOI code and code type on the same day; (2) 2: de-duplicates occurrences of the same HOI group on the same day (e.g., de-duplicates at the group level).

**Exposure Episode Length** - number of days after exposure initiation that is considered "exposed time."

**Exposure Extension Period** - number of days post treatment period in which the outcomes/events are counted for a treatment episode.

**Lookback Period (pre-existing condition)** - number of days wherein a member is required to have evidence of pre-existing condition (diagnosis/procedure/drug dispensing).

**Member-Years** - sum of all days of enrollment with medical and drug coverage\*\* in the query period preceded by an exposure washout period all divided by 365.25.

**Minimum Days Supplied** - specifies a minimum number of days in length of the days supplied for the episode to be considered.

**Minimum Episode Duration** - specifies a minimum number of days in length of the episode for it to be considered.

**Principal Diagnosis (PDX)** - diagnosis or condition established to be chiefly responsible for admission of the patient to the hospital. 'P' = principal diagnosis, 'S' = secondary diagnosis, 'X' = unspecified diagnosis, '.' = blank. Along with the Care Setting values, forms the Caresetting/PDX parameter.

**Query Period** - period in which the modular program looks for exposures and outcomes of interest.

**Treatment Episode Truncation Indicator** - indicates whether observation of the incident query code during follow-up requires truncation of valid treatment episodes. A value of Y indicates that the treatment episodes should be truncated at the first occurrence of an incident query code. A value of N indicates that the treatment episodes should not be truncated at the occurrence of the incident query code.

**Users** - number of members with exposure during the query period. Member must have no evidence of exposure(s) of interest (defined by incidence criteria) in the prior washout period. A user may only be counted once in a query period.

**Washout Period (drug/exposure)\*\*** - number of days a user is required to have no evidence of prior exposure (drug dispensing/procedure) and continuous drug and medical coverage prior to an incident treatment episode.

**Washout Period (event/outcome)\*\*** - number of days a user is required to have no evidence of a prior event (procedure/diagnosis) and continuous drug and medical coverage prior to an incident treatment episode.

**Years at Risk** - number of days supplied plus any episode gaps and exposure extension periods all divided by 365.25.

\*all terms may not be used in this report

\*\*incident treatment episodes must be incident to both the exposure and the event



**Table 1a: Summary of Incident Methylphenidate Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, and Blackout Period**

New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>30-Day Episode Gap/Extension Period</b>													
<b>0-Day Blackout Period</b>													
788,617	788,617	3,405,316	117,642,651	178,675,704	390,002.4	1,904	110,278,917	305,293,872.1	7.15	149.18	4.32	34.55	48.82
<b>90-Day Blackout Period</b>													
394,021	394,021	2,998,408	107,506,390	161,243,842	242,780.3	893	100,795,204	276,386,648.9	3.91	272.84	7.61	35.85	36.78
<b>180-Day Blackout Period</b>													
203,408	203,408	2,484,867	91,114,723	136,901,394	176,207.7	599	93,629,252	250,239,168.0	2.17	447.94	12.22	36.67	33.99
<b>270-Day Blackout Period</b>													
130,217	130,217	2,108,562	78,562,958	118,535,082	136,854.4	431	80,082,582	228,163,500.2	1.63	603.32	16.19	37.26	31.49
<b>365-Day Blackout Period</b>													
90,472	90,472	1,804,318	68,263,413	103,461,195	109,074.3	346	72,081,132	207,156,631.6	1.26	754.53	19.94	37.83	31.72
<b>730-Day Blackout Period</b>													
34,932	34,932	1,083,933	43,052,989	65,734,436	52,781.8	144	48,757,177	144,828,333.7	0.72	1232.48	31.03	39.72	27.28
<b>1,095-Day Blackout Period</b>													
16,924	16,924	672,818	28,098,181	43,265,966	28,280.8	72	34,276,055	102,931,045.7	0.49	1660.26	39.76	41.76	25.46
<b>90-Day Episode Gap/Extension Period</b>													
<b>0-Day Blackout Period</b>													
788,617	788,617	4,560,999	159,196,790	242,071,428	633,986.8	2,776	110,278,917	305,293,872.1	7.15	201.87	5.78	34.90	43.79
<b>90-Day Blackout Period</b>													
645,686	645,686	4,371,726	154,983,858	235,502,067	461,343.7	1,579	100,795,204	276,005,493.3	6.41	240.03	6.77	35.45	34.23
<b>180-Day Blackout Period</b>													
371,111	371,111	4,000,042	144,540,261	218,356,725	353,604.0	1,060	93,629,250	250,056,153.2	3.96	389.48	10.78	36.13	29.98
<b>270-Day Blackout Period</b>													
257,949	257,949	3,603,394	131,909,774	199,464,954	281,844.4	779	80,082,580	228,058,323.4	3.22	511.38	13.97	36.61	27.64
<b>365-Day Blackout Period</b>													
185,908	185,908	3,198,050	118,511,647	179,769,865	226,709.1	631	72,081,131	207,094,074.1	2.58	637.47	17.20	37.06	27.83
<b>730-Day Blackout Period</b>													
74,129	74,129	2,038,486	78,677,134	120,463,201	109,633.0	278	48,757,177	144,815,465.6	1.52	1061.35	27.50	38.60	25.36
<b>1,095-Day Blackout Period</b>													
35,624	35,624	1,291,926	52,093,395	80,984,678	57,845.0	139	34,276,055	102,927,638.0	1.04	1462.31	36.27	40.32	24.03

**Table 1b: Rate of Heart Failure Outcomes at Different Stages of Methylphenidate Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, and Blackout Period**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>30-Day Episode Gap/Extension Period</b>			
Days 0-90	1,011	147,222	68.7
Days 91-180	294	66,573	44.2
Days 181-270	168	39,353	42.7
Days 271-365	85	27,780	30.6
Days 366-730	202	56,293	35.9
Days 731-1,095	72	24,501	29.4
<b>90-Day Episode Gap/Extension Period</b>			
Days 0-90	1,197	172,643	69.3
Days 91-180	519	107,740	48.2
Days 181-270	281	71,760	39.2
Days 271-365	148	55,135	26.8
Days 366-730	353	117,076	30.2
Days 731-1,095	139	51,788	26.8

**Table 2a: Summary of Incident Methylphenidate Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>30-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
00-21 Years	516,115	516,115	2,338,448	81,357,091	107,508,153	268,128.5	389	33,425,291	83,982,133.7	15.44	157.63	4.53	34.79	14.51
22-44 Years	155,267	155,267	575,421	19,123,754	36,360,185	65,089.6	214	45,769,117	96,000,653.3	3.39	123.17	3.71	33.23	32.88
45-64 Years	95,859	95,859	413,484	14,548,563	29,805,882	48,097.4	587	32,651,934	90,474,224.7	2.94	151.77	4.31	35.19	122.04
65+ Years	21,376	21,376	77,963	2,613,243	5,001,484	8,686.9	714	10,949,553	34,836,860.4	1.95	122.25	3.65	33.52	821.92
<b>90-Day Blackout Period</b>														
00-21 Years	275,910	275,910	2,095,353	75,364,070	98,569,530	170,205.7	251	30,664,761	76,480,712.9	9.00	273.15	7.59	35.97	14.75
22-44 Years	66,439	66,439	479,546	16,686,539	31,424,160	37,103.5	115	41,133,833	85,464,614.6	1.62	251.16	7.22	34.80	30.99
45-64 Years	43,249	43,249	360,180	13,214,294	26,887,187	30,628.4	253	30,237,658	82,561,797.6	1.43	305.54	8.33	36.69	82.60
65+ Years	8,423	8,423	63,329	2,241,487	4,362,964	4,842.7	274	9,846,046	31,879,523.8	0.86	266.12	7.52	35.39	565.80
<b>180-Day Blackout Period</b>														
00-21 Years	142,353	142,353	1,736,527	63,851,041	83,092,039	123,243.3	181	28,477,130	69,553,837.5	5.00	448.54	12.20	36.77	14.69
22-44 Years	33,284	33,284	387,889	13,825,217	26,356,125	26,146.7	70	37,555,453	76,128,704.0	0.89	415.37	11.65	35.64	26.77
45-64 Years	23,436	23,436	308,670	11,565,426	23,753,671	23,368.6	184	28,252,413	75,305,693.1	0.83	493.49	13.17	37.47	78.74
65+ Years	4,335	4,335	51,781	1,873,039	3,699,558	3,449.2	164	9,283,001	29,250,933.3	0.47	432.07	11.94	36.17	475.48
<b>270-Day Blackout Period</b>														
00-21 Years	90,505	90,505	1,472,522	54,987,028	71,446,732	95,708.0	129	24,382,853	63,653,142.6	3.71	607.56	16.27	37.34	13.48
22-44 Years	21,032	21,032	322,878	11,708,234	22,622,562	19,759.0	50	31,631,977	68,440,681.3	0.66	556.69	15.35	36.26	25.30
45-64 Years	15,882	15,882	269,533	10,266,211	21,259,609	18,763.9	132	24,593,957	69,092,919.6	0.65	646.41	16.97	38.09	70.35
65+ Years	2,798	2,798	43,629	1,601,485	3,206,180	2,623.5	120	8,263,132	26,976,756.7	0.34	572.37	15.59	36.71	457.40
<b>365-Day Blackout Period</b>														
00-21 Years	62,548	62,548	1,260,249	47,748,650	61,954,700	76,396.9	106	21,971,316	58,005,046.5	2.85	763.39	20.15	37.89	13.87
22-44 Years	14,427	14,427	271,368	10,003,187	19,569,491	15,348.6	40	27,914,408	61,262,457.0	0.52	693.37	18.81	36.86	26.06
45-64 Years	11,541	11,541	236,051	9,138,959	19,153,068	15,308.0	107	22,307,895	63,128,162.8	0.52	791.87	20.45	38.72	69.90
65+ Years	1,956	1,956	36,650	1,372,617	2,783,936	2,020.8	93	7,723,962	24,760,965.2	0.25	701.75	18.74	37.45	460.20
<b>730-Day Blackout Period</b>														
00-21 Years	24,575	24,575	766,317	30,382,779	39,179,985	36,979.2	43	14,939,259	40,911,337.4	1.64	1236.33	31.18	39.65	11.63
22-44 Years	4,931	4,931	148,749	5,789,687	11,779,147	6,918.3	19	17,763,776	40,908,733.1	0.28	1174.14	30.17	38.92	27.46
45-64 Years	4,744	4,744	149,432	6,093,407	13,154,245	8,013.3	50	15,594,505	44,997,792.2	0.30	1284.44	31.50	40.78	62.40
65+ Years	682	682	19,435	787,116	1,621,060	871.0	32	5,590,262	18,010,470.9	0.12	1154.13	28.50	40.50	367.39
<b>1,095-Day Blackout Period</b>														
00-21 Years	12,040	12,040	477,655	19,905,606	25,767,473	19,609.2	19	10,527,068	29,228,781.6	1.14	1653.29	39.67	41.67	9.69
22-44 Years	2,203	2,203	87,251	3,573,977	7,336,663	3,608.8	10	11,867,524	28,139,960.6	0.19	1622.32	39.61	40.96	27.71

**Table 2a: Summary of Incident Methylphenidate Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
45-64 Years	2,419	2,419	97,924	4,179,730	9,242,189	4,619.1	27	11,226,155	32,398,309.9	0.22	1727.88	40.48	42.68	58.45
65+ Years	262	262	9,988	438,868	919,641	443.6	16	4,147,049	13,163,993.7	0.06	1675.07	38.12	43.94	360.65
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
00-21 Years	516,115	516,115	3,187,314	111,853,314	147,991,589	441,305.9	545	33,425,291	83,982,133.7	15.44	216.72	6.18	35.09	12.35
22-44 Years	155,267	155,267	728,975	24,571,510	47,164,397	101,879.9	294	45,769,117	96,000,653.3	3.39	158.25	4.69	33.71	28.86
45-64 Years	95,859	95,859	545,312	19,375,884	40,227,395	76,929.4	855	32,651,934	90,474,224.7	2.94	202.13	5.69	35.53	111.14
65+ Years	21,376	21,376	99,398	3,396,082	6,688,046	13,871.6	1,082	10,949,553	34,836,860.4	1.95	158.87	4.65	34.17	780.01
<b>90-Day Blackout Period</b>														
00-21 Years	428,657	428,657	3,074,331	109,410,389	144,611,456	327,904.0	381	30,664,761	76,274,018.6	13.98	255.24	7.17	35.59	11.62
22-44 Years	120,035	120,035	681,790	23,490,460	45,279,176	68,653.2	179	41,114,495	85,376,627.9	2.92	195.70	5.68	34.45	26.07
45-64 Years	79,623	79,623	522,777	18,852,573	39,227,910	55,659.0	473	30,231,980	82,494,636.5	2.63	236.77	6.57	36.06	84.98
65+ Years	17,371	17,371	92,828	3,230,436	6,383,526	9,127.5	546	9,843,731	31,860,210.3	1.76	185.97	5.34	34.80	598.19
<b>180-Day Blackout Period</b>														
00-21 Years	263,110	263,110	2,848,916	103,087,140	135,602,394	253,744.8	296	28,477,128	69,435,562.4	9.24	391.80	10.83	36.18	11.67
22-44 Years	59,550	59,550	595,161	21,014,639	40,399,600	49,726.5	109	37,544,114	76,092,722.6	1.59	352.89	9.99	35.31	21.92
45-64 Years	40,924	40,924	476,459	17,572,749	36,576,868	43,523.4	337	28,250,085	75,282,961.1	1.45	429.40	11.64	36.88	77.43
65+ Years	7,527	7,527	79,506	2,865,733	5,777,863	6,609.4	318	9,281,982	29,244,907.0	0.81	380.73	10.56	36.04	481.13
<b>270-Day Blackout Period</b>														
00-21 Years	185,301	185,301	2,577,058	94,361,424	123,760,117	202,229.8	226	24,382,851	63,581,322.6	7.60	509.23	13.91	36.62	11.18
22-44 Years	39,150	39,150	522,295	18,736,375	36,372,202	38,607.3	81	31,625,419	68,422,408.0	1.24	478.58	13.34	35.87	20.98
45-64 Years	28,535	28,535	433,769	16,237,786	34,069,412	35,770.1	246	24,592,594	69,080,995.5	1.16	569.05	15.20	37.43	68.77
65+ Years	4,963	4,963	70,272	2,574,189	5,263,224	5,237.2	226	8,262,513	26,973,597.3	0.60	518.68	14.16	36.63	431.53
<b>365-Day Blackout Period</b>														
00-21 Years	133,676	133,676	2,289,810	84,799,660	111,188,048	162,414.8	192	21,971,315	57,961,663.9	6.08	634.37	17.13	37.03	11.82
22-44 Years	27,368	27,368	453,364	16,502,113	32,346,942	30,394.3	66	27,910,569	61,252,351.7	0.98	602.97	16.57	36.40	21.71
45-64 Years	21,231	21,231	392,531	14,890,709	31,446,842	29,697.9	203	22,307,021	63,121,056.5	0.95	701.37	18.49	37.94	68.35
65+ Years	3,633	3,633	62,345	2,319,165	4,788,032	4,202.1	170	7,723,569	24,759,002.0	0.47	638.36	17.16	37.20	404.55
<b>730-Day Blackout Period</b>														
00-21 Years	53,465	53,465	1,462,455	56,241,238	73,331,052	77,498.2	82	14,939,259	40,902,163.2	3.58	1051.93	27.35	38.46	10.58
22-44 Years	9,861	9,861	268,789	10,281,052	20,821,159	14,152.6	33	17,763,044	40,907,141.3	0.56	1042.60	27.26	38.25	23.32
45-64 Years	9,358	9,358	269,329	10,653,922	23,139,375	16,006.3	94	15,594,281	44,996,182.4	0.60	1138.48	28.78	39.56	58.73
65+ Years	1,445	1,445	37,913	1,500,922	3,171,616	1,975.9	69	5,590,126	18,009,978.7	0.26	1038.70	26.24	39.59	349.21

**Table 2a: Summary of Incident Methylphenidate Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>1,095-Day Blackout Period</b>														
00-21 Years	25,584	25,584	921,793	37,011,516	48,634,798	40,035.4	38	10,527,068	29,226,394.7	2.43	1446.67	36.03	40.15	9.49
22-44 Years	4,515	4,515	164,458	6,598,961	13,631,339	7,497.1	20	11,867,350	28,139,567.7	0.38	1461.56	36.42	40.13	26.68
45-64 Years	4,919	4,919	184,114	7,575,958	16,775,442	9,270.6	48	11,226,081	32,397,829.5	0.44	1540.14	37.43	41.15	51.78
65+ Years	606	606	21,561	906,960	1,943,100	1,041.8	33	4,146,995	13,163,846.1	0.15	1496.63	35.58	42.06	316.75

**Table 2b: Rate of Heart Failure Outcomes at Different Stages of Methylphenidate Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>30-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
00-21 Years	138	97,923	14.1
22-44 Years	99	27,986	35.4
45-64 Years	334	17,469	191.2
65+ Years	440	3,844	1,144.6
<b>Days 91-180</b>			
00-21 Years	70	46,962	14.9
22-44 Years	45	10,957	41.1
45-64 Years	69	7,260	95.0
65+ Years	110	1,394	789.3
<b>Days 181-270</b>			
00-21 Years	52	27,535	18.9
22-44 Years	20	6,388	31.3
45-64 Years	52	4,605	112.9
65+ Years	44	826	532.9
<b>Days 271-365</b>			
00-21 Years	23	19,311	11.9
22-44 Years	10	4,410	22.7
45-64 Years	25	3,456	72.3
65+ Years	27	603	448.0
<b>Days 366-730</b>			
00-21 Years	63	39,418	16.0
22-44 Years	21	8,430	24.9
45-64 Years	57	7,295	78.1
65+ Years	61	1,150	530.5
<b>Days 731-1,095</b>			
00-21 Years	24	17,370	13.8
22-44 Years	9	3,309	27.2
45-64 Years	23	3,394	67.8
65+ Years	16	427	374.4
<b>90-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
00-21 Years	164	113,402	14.5

**Table 2b: Rate of Heart Failure Outcomes at Different Stages of Methylphenidate Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
22-44 Years	115	33,227	34.6
45-64 Years	382	21,270	179.6
65+ Years	536	4,744	1,129.8
<b>Days 91-180</b>			
00-21 Years	85	74,159	11.5
22-44 Years	70	18,927	37.0
45-64 Years	136	12,136	112.1
65+ Years	228	2,518	905.4
<b>Days 181-270</b>			
00-21 Years	70	51,515	13.6
22-44 Years	28	11,119	25.2
45-64 Years	91	7,753	117.4
65+ Years	92	1,372	670.5
<b>Days 271-365</b>			
00-21 Years	34	39,815	8.5
22-44 Years	15	8,213	18.3
45-64 Years	43	6,072	70.8
65+ Years	56	1,035	541.0
<b>Days 366-730</b>			
00-21 Years	110	84,917	13.0
22-44 Years	33	16,242	20.3
45-64 Years	109	13,692	79.6
65+ Years	101	2,226	453.7
<b>Days 731-1,095</b>			
00-21 Years	44	37,463	11.7
22-44 Years	13	6,656	19.5
45-64 Years	46	6,736	68.3
65+ Years	36	934	385.4

**Table 3a: Summary of Incident Methylphenidate Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>30-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
Female	322,076	322,076	1,328,680	45,431,582	72,894,885	151,970.8	953	56,071,657	158,291,175.6	5.74	141.06	4.13	34.19	62.71
Male	466,517	466,517	2,076,575	72,209,100	105,778,300	238,024.0	951	54,201,550	146,989,993.4	8.61	154.78	4.45	34.77	39.95
Unknown	24	24	61	1,969	2,519	7.5	0	5,710	12,703.1	4.20	82.04	2.54	32.28	0.00
<b>90-Day Blackout Period</b>														
Female	154,116	154,116	1,151,565	40,987,306	64,671,514	92,294.0	439	51,322,051	143,495,405.1	3.00	265.95	7.47	35.59	47.57
Male	239,895	239,895	1,846,798	66,517,547	96,570,373	150,483.2	454	49,468,326	132,879,945.0	4.85	277.28	7.70	36.02	30.17
Unknown	10	10	45	1,537	1,955	3.1	0	4,827	11,298.8	2.07	153.70	4.50	34.16	0.00
<b>180-Day Blackout Period</b>														
Female	78,704	78,704	947,194	34,530,594	54,793,888	66,524.7	282	47,747,103	130,104,661.7	1.65	438.74	12.03	36.46	42.39
Male	124,699	124,699	1,537,642	56,583,007	82,106,116	109,681.5	317	45,877,989	120,124,383.2	2.72	453.76	12.33	36.80	28.90
Unknown	5	5	31	1,122	1,390	1.5	0	4,160	10,123.1	1.20	224.40	6.20	36.19	0.00
<b>270-Day Blackout Period</b>														
Female	50,229	50,229	800,393	29,669,887	47,425,912	51,392.4	204	40,899,023	118,795,695.5	1.23	590.69	15.93	37.07	39.69
Male	79,986	79,986	1,308,148	48,892,306	71,108,405	85,461.1	227	39,180,258	109,358,597.8	2.04	611.26	16.35	37.38	26.56
Unknown	2	2	21	765	765	0.9	0	3,301	9,206.9	0.61	382.50	10.50	36.43	0.00
<b>365-Day Blackout Period</b>														
Female	34,739	34,739	681,529	25,676,862	41,328,939	40,721.3	167	36,882,927	108,017,255.8	0.94	739.14	19.62	37.68	41.01
Male	55,732	55,732	1,122,772	42,586,046	62,131,751	68,352.4	179	35,195,289	99,131,022.6	1.58	764.12	20.15	37.93	26.19
Unknown	1	1	17	505	505	0.6	0	2,916	8,353.3	0.34	505.00	17.00	29.71	0.00
<b>730-Day Blackout Period</b>														
Female	13,039	13,039	400,703	15,917,241	26,107,181	19,472.6	63	25,089,970	75,941,310.4	0.52	1220.74	30.73	39.72	32.35
Male	21,893	21,893	683,230	27,135,748	39,627,255	33,309.2	81	23,665,314	68,881,147.0	0.93	1239.47	31.21	39.72	24.32
Unknown	0	0	0	0	0	0.0	0	1,893	5,876.3	0.00	---	---	---	---
<b>1,095-Day Blackout Period</b>														
Female	6,192	6,192	245,469	10,271,103	17,021,136	10,420.1	31	17,741,982	54,257,626.7	0.35	1658.77	39.64	41.84	29.75
Male	10,732	10,732	427,349	17,827,078	26,244,830	17,860.6	41	16,532,754	48,669,185.2	0.65	1661.11	39.82	41.72	22.96
Unknown	0	0	0	0	0	0.0	0	1,319	4,233.8	0.00	---	---	---	---
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
Female	322,076	322,076	1,773,644	61,392,229	98,620,099	247,985.4	1,352	56,071,657	158,291,175.6	5.74	190.61	5.51	34.61	54.52
Male	466,517	466,517	2,787,288	97,802,182	143,448,400	385,990.2	1,424	54,201,550	146,989,993.4	8.61	209.64	5.97	35.09	36.89
Unknown	24	24	67	2,379	2,929	11.2	0	5,710	12,703.1	4.20	99.13	2.79	35.51	0.00
<b>90-Day Blackout Period</b>														
Female	261,007	261,007	1,692,082	59,560,844	95,676,265	177,756.8	757	51,322,051	143,335,036.4	5.09	228.20	6.48	35.20	42.59



**Table 3a: Summary of Incident Methylphenidate Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
Male	384,662	384,662	2,679,586	95,420,863	139,823,185	283,580.7	822	49,468,326	132,659,165.3	7.78	248.06	6.97	35.61	28.99
Unknown	17	17	58	2,151	2,617	6.1	0	4,827	11,291.6	3.52	126.53	3.41	37.09	0.00
<b>180-Day Blackout Period</b>														
Female	144,427	144,427	1,532,028	55,049,893	87,726,641	134,794.6	491	47,747,103	130,035,530.3	3.02	381.16	10.61	35.93	36.43
Male	226,677	226,677	2,467,971	89,488,656	130,627,954	218,806.0	569	45,877,987	120,010,499.8	4.94	394.78	10.89	36.26	26.00
Unknown	7	7	43	1,712	2,130	3.4	0	4,160	10,123.1	1.68	244.57	6.14	39.81	0.00
<b>270-Day Blackout Period</b>														
Female	99,258	99,258	1,374,102	50,079,118	80,068,187	107,132.5	367	40,899,023	118,757,086.3	2.43	504.53	13.84	36.44	34.26
Male	158,689	158,689	2,229,265	81,829,481	119,395,592	174,709.5	412	39,180,256	109,292,030.2	4.05	515.66	14.05	36.71	23.58
Unknown	2	2	27	1,175	1,175	2.3	0	3,301	9,206.9	0.61	587.50	13.50	43.52	0.00
<b>365-Day Blackout Period</b>														
Female	71,344	71,344	1,216,524	44,907,282	72,201,675	85,989.2	299	36,882,927	107,994,457.9	1.93	629.45	17.05	36.91	34.77
Male	114,562	114,562	1,981,499	73,603,190	107,567,016	140,718.1	332	35,195,288	99,091,268.5	3.26	642.47	17.30	37.15	23.59
Unknown	2	2	27	1,175	1,175	1.8	0	2,916	8,347.6	0.69	587.50	13.50	43.52	0.00
<b>730-Day Blackout Period</b>														
Female	28,059	28,059	768,119	29,656,987	48,593,537	41,615.7	129	25,089,970	75,936,798.6	1.12	1056.95	27.38	38.61	31.00
Male	46,069	46,069	1,270,357	49,019,477	71,868,995	68,017.1	149	23,665,314	68,872,795.3	1.95	1064.04	27.58	38.59	21.91
Unknown	1	1	10	670	670	0.2	0	1,893	5,871.7	0.53	670.00	10.00	67.00	0.00
<b>1,095-Day Blackout Period</b>														
Female	13,385	13,385	484,964	19,580,302	32,635,467	22,094.8	64	17,741,982	54,256,451.9	0.75	1462.85	36.23	40.37	28.97
Male	22,239	22,239	806,962	32,513,093	48,349,212	35,750.2	75	16,532,754	48,666,952.3	1.35	1461.99	36.29	40.29	20.98
Unknown	0	0	0	0	0	0.0	0	1,319	4,233.8	0.00	---	---	---	---

**Table 3b: Rate of Heart Failure Outcomes at Different Stages of Methylphenidate Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Episodes with Events	Years at Risk	New Episodes with Events per 01,000 Years at Risk
<b>30-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
Female	514	59,677	86.1
Male	497	87,541	56.8
Unknown	0	4	0.0
<b>Days 91-180</b>			
Female	157	25,769	60.9
Male	137	40,802	33.6
Unknown	0	2	0.0
<b>Days 181-270</b>			
Female	78	15,132	51.5
Male	90	24,220	37.2
Unknown	0	1	0.0
<b>Days 271-365</b>			
Female	37	10,671	34.7
Male	48	17,109	28.1
Unknown	0	0	0.0
<b>Days 366-730</b>			
Female	104	21,249	48.9
Male	98	35,043	28.0
Unknown	0	1	0.0
<b>Days 731-1,095</b>			
Female	32	9,052	35.3
Male	40	15,449	25.9
Unknown	0	0	---
<b>90-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
Female	595	70,229	84.7
Male	602	102,409	58.8
Unknown	0	5	0.0
<b>Days 91-180</b>			
Female	266	42,962	61.9

**Table 3b: Rate of Heart Failure Outcomes at Different Stages of Methylphenidate Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Episodes with Events	Years at Risk	New Episodes with Events per 01,000 Years at Risk
Male	253	64,775	39.1
Unknown	0	3	0.0
<b>Days 181-270</b>			
Female	124	27,662	44.8
Male	157	44,096	35.6
Unknown	0	1	0.0
<b>Days 271-365</b>			
Female	68	21,143	32.2
Male	80	33,991	23.5
Unknown	0	1	0.0
<b>Days 366-730</b>			
Female	170	44,374	38.3
Male	183	72,701	25.2
Unknown	0	2	0.0
<b>Days 731-1,095</b>			
Female	65	19,521	33.3
Male	74	32,267	22.9
Unknown	0	0	0.0

**Table 4a: Summary of Incident Methylphenidate Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>30-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
2000	5,613	5,613	20,176	964,508	2,113,161	3,121.7	33	6,528,534	2,996,066.8	0.86	171.83	3.59	47.80	105.71
2001	13,930	13,930	55,664	2,413,257	4,709,608	7,843.9	67	7,126,797	5,951,991.0	1.95	173.24	4.00	43.35	85.42
2002	13,306	13,306	56,271	2,635,297	4,754,478	8,311.8	70	7,275,947	6,048,905.9	1.83	198.05	4.23	46.83	84.22
2003	18,679	18,679	105,098	4,303,498	8,488,198	13,303.7	94	7,267,208	6,020,250.4	2.57	230.39	5.63	40.95	70.66
2004	16,943	16,943	85,871	3,621,450	8,342,632	11,349.6	101	7,701,178	6,263,171.3	2.20	213.74	5.07	42.17	88.99
2005	17,084	17,084	81,922	3,501,707	5,989,955	11,058.0	103	7,941,951	6,552,168.0	2.15	204.97	4.80	42.74	93.14
2006	31,749	31,749	152,486	5,780,810	8,825,247	18,694.1	113	19,411,790	11,584,595.3	1.64	182.08	4.80	37.91	60.45
2007	48,513	48,513	235,652	8,447,379	12,386,693	27,497.2	189	23,605,215	17,136,640.4	2.06	174.13	4.86	35.85	68.73
2008	76,380	76,380	351,295	12,039,576	17,401,363	39,796.6	187	44,299,773	27,972,989.8	1.72	157.63	4.60	34.27	46.99
2009	96,854	96,854	436,366	14,701,857	21,009,882	48,975.4	215	45,682,539	35,441,580.4	2.12	151.79	4.51	33.69	43.90
2010	93,246	93,246	427,495	14,292,256	20,271,392	47,535.2	170	43,541,802	33,931,638.3	2.14	153.27	4.58	33.43	35.76
2011	91,172	91,172	418,142	13,788,770	19,306,874	45,980.5	152	42,137,841	33,131,645.4	2.16	151.24	4.59	32.98	33.06
2012	84,284	84,284	374,521	12,236,368	17,118,255	41,150.7	129	41,117,768	32,456,965.9	2.05	145.18	4.44	32.67	31.35
2013	78,699	78,699	317,572	10,167,165	14,899,239	34,695.6	151	40,980,381	32,137,167.9	1.92	129.19	4.04	32.02	43.52
2014	71,549	71,549	226,581	7,044,952	10,501,915	24,718.1	103	41,914,661	32,013,481.9	1.71	98.46	3.17	31.09	41.67
2015	30,616	30,616	60,204	1,703,801	2,556,811	5,970.4	27	34,463,590	15,654,613.3	0.89	55.65	1.97	28.30	45.22
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>90-Day Blackout Period</b>														
2000	2,912	2,912	17,050	866,985	1,888,243	1,955.2	18	6,271,153	2,822,041.0	0.46	297.73	5.86	50.85	92.06
2001	6,915	6,915	47,991	2,189,720	4,230,460	5,049.1	36	6,793,584	5,669,191.0	1.02	316.66	6.94	45.63	71.30
2002	7,051	7,051	49,888	2,467,190	4,408,471	5,711.0	46	6,957,777	5,741,791.5	1.01	349.91	7.08	49.45	80.55
2003	10,762	10,762	102,629	4,284,100	8,745,645	10,115.1	61	6,907,143	5,722,963.8	1.56	398.08	9.54	41.74	60.31
2004	9,511	9,511	78,709	3,444,066	6,444,476	8,085.8	56	7,428,017	5,971,223.7	1.28	362.11	8.28	43.76	69.26
2005	9,277	9,277	74,297	3,318,713	5,640,160	7,809.6	62	7,582,379	6,190,218.3	1.22	357.74	8.01	44.67	79.39
2006	16,410	16,410	136,621	5,378,078	8,142,535	12,596.0	66	18,297,942	10,872,270.8	0.90	327.73	8.33	39.36	52.40
2007	24,586	24,586	210,835	7,811,396	11,377,699	18,248.2	89	22,136,595	16,082,602.4	1.11	317.72	8.58	37.05	48.77
2008	37,340	37,340	310,036	10,976,058	15,800,228	25,360.6	74	41,864,142	25,729,668.2	0.89	293.95	8.30	35.40	29.18
2009	47,244	47,244	383,200	13,341,225	18,903,880	30,654.4	94	42,511,105	32,612,795.0	1.11	282.39	8.11	34.82	30.66
2010	46,742	46,742	380,007	13,118,774	18,424,870	30,124.6	71	40,745,669	31,348,092.6	1.15	280.66	8.13	34.52	23.57
2011	46,404	46,404	373,085	12,679,842	17,571,519	28,985.9	52	39,644,257	30,721,004.3	1.17	273.25	8.04	33.99	17.94
2012	44,004	44,004	335,749	11,302,909	15,681,109	25,504.8	57	39,238,881	30,222,006.2	1.12	256.86	7.63	33.66	22.35
2013	40,888	40,888	280,138	9,249,817	13,509,373	20,002.7	66	38,537,989	29,764,761.4	1.06	226.22	6.85	33.02	33.00
2014	36,156	36,156	188,691	6,094,391	9,019,721	11,248.5	42	39,141,526	29,228,044.3	0.92	168.56	5.22	32.30	37.34
2015	7,819	7,819	29,482	983,126	1,455,454	1,328.8	3	22,991,526	7,687,974.4	0.34	125.74	3.77	33.35	22.58
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>180-Day Blackout Period</b>														
2000	1,389	1,389	13,935	719,514	1,569,897	1,447.4	14	6,000,891	2,668,690.0	0.23	518.01	10.03	51.63	96.73
2001	3,423	3,423	39,964	1,859,199	3,570,355	3,838.5	24	6,564,510	5,409,226.2	0.52	543.15	11.68	46.52	62.52
2002	3,781	3,781	42,651	2,184,229	3,895,780	4,500.8	38	6,682,521	5,451,561.1	0.57	577.69	11.28	51.21	84.43
2003	6,118	6,118	92,260	3,905,991	8,188,054	8,298.9	43	6,655,830	5,455,338.8	0.92	638.44	15.08	42.34	51.81
2004	5,425	5,425	68,746	3,068,295	5,552,461	6,362.2	42	7,093,083	5,702,982.0	0.76	565.58	12.67	44.63	66.02
2005	5,131	5,131	64,463	2,964,872	5,050,544	6,208.9	45	7,314,826	5,855,599.5	0.70	577.84	12.56	45.99	72.48
2006	9,161	9,161	118,033	4,749,335	7,188,426	9,698.7	44	17,578,850	10,224,461.6	0.52	518.43	12.88	40.24	45.37
2007	13,277	13,277	180,727	6,827,741	9,938,441	13,946.5	69	21,029,491	15,126,291.7	0.63	514.25	13.61	37.78	49.47
2008	19,786	19,786	262,551	9,469,758	13,662,473	18,945.8	47	39,171,896	23,701,625.0	0.51	478.61	13.27	36.07	24.81
2009	24,213	24,213	320,708	11,384,143	16,116,205	22,673.3	65	40,459,409	30,036,640.2	0.60	470.17	13.25	35.50	28.67
2010	24,375	24,375	319,342	11,220,122	15,741,060	22,190.1	44	38,826,091	29,003,826.1	0.63	460.31	13.10	35.14	19.83
2011	24,531	24,531	313,903	10,858,731	15,006,165	21,170.6	30	37,856,685	28,492,493.7	0.65	442.65	12.80	34.59	14.17
2012	23,455	23,455	280,310	9,596,979	13,300,756	18,065.2	38	37,001,167	28,144,783.8	0.63	409.17	11.95	34.24	21.03
2013	21,491	21,491	227,730	7,635,816	11,228,033	13,123.4	37	36,860,350	27,548,817.5	0.58	355.30	10.60	33.53	28.19
2014	15,850	15,850	128,093	4,253,028	6,277,911	5,436.2	19	36,408,467	23,816,720.7	0.44	268.33	8.08	33.20	34.95

**Table 4a: Summary of Incident Methylphenidate Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2015	2,002	2,002	11,451	416,970	614,832	301.2	0	13,592,915	3,600,110.2	0.15	208.28	5.72	36.41	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>270-Day Blackout Period</b>														
2000	838	838	11,869	619,866	1,357,539	1,173.3	12	5,556,728	2,575,586.1	0.15	739.70	14.16	52.23	102.27
2001	2,193	2,193	34,916	1,639,354	3,149,689	3,156.7	18	6,239,344	5,172,509.4	0.35	747.54	15.92	46.95	57.02
2002	2,475	2,475	37,166	1,949,806	3,494,600	3,746.6	29	6,328,222	5,194,941.6	0.39	787.80	15.02	52.46	77.40
2003	4,319	4,319	84,390	3,595,833	7,674,345	7,078.1	37	6,272,716	5,219,079.8	0.69	832.56	19.54	42.61	52.27
2004	3,669	3,669	61,033	2,765,283	4,873,017	5,298.0	36	6,683,871	5,464,402.3	0.55	753.69	16.63	45.31	67.95
2005	3,409	3,409	56,819	2,669,708	4,576,475	5,216.5	33	6,844,370	5,563,161.4	0.50	783.14	16.67	46.99	63.26
2006	5,973	5,973	102,839	4,207,648	6,391,720	7,911.5	35	16,122,677	9,730,155.1	0.37	704.44	17.22	40.91	44.24
2007	8,694	8,694	157,198	6,031,242	8,831,812	11,331.5	41	19,514,670	14,307,637.8	0.45	693.72	18.08	38.37	36.18
2008	12,786	12,786	226,211	8,279,756	12,014,574	15,080.2	34	34,990,210	22,231,893.5	0.37	647.56	17.69	36.60	22.55
2009	15,655	15,655	275,925	9,915,982	14,069,518	17,925.3	49	36,928,902	27,864,615.5	0.42	633.41	17.63	35.94	27.34
2010	15,938	15,938	276,196	9,813,398	13,777,131	17,494.7	28	35,509,599	27,027,255.2	0.45	615.72	17.33	35.53	16.00
2011	15,978	15,978	269,043	9,413,330	13,000,785	16,373.9	20	34,707,016	26,588,672.3	0.46	589.14	16.84	34.99	12.21
2012	15,541	15,541	239,093	8,271,733	11,465,747	13,472.2	22	33,872,841	26,423,846.2	0.46	532.25	15.38	34.60	16.33
2013	14,130	14,130	189,110	6,398,624	9,433,279	8,936.1	27	33,847,980	25,610,769.6	0.42	452.84	13.38	33.84	30.21
2014	8,266	8,266	84,593	2,890,097	4,285,292	2,620.4	10	32,002,272	18,156,272.3	0.26	349.64	10.23	34.16	38.16
2015	353	353	2,161	101,298	139,558	39.2	0	9,126,865	1,032,702.0	0.04	286.96	6.12	46.88	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>365-Day Blackout Period</b>														
2000	582	582	10,406	550,989	1,209,407	989.2	11	5,308,581	2,486,855.0	0.11	946.72	17.88	52.95	111.20
2001	1,543	1,543	30,773	1,463,843	2,815,397	2,675.6	13	5,774,614	4,927,922.5	0.27	948.70	19.94	47.57	48.59
2002	1,771	1,771	33,067	1,765,384	3,174,333	3,215.7	25	5,831,095	4,955,029.5	0.30	996.83	18.67	53.39	77.74
2003	3,207	3,207	76,820	3,304,947	7,155,348	6,129.1	29	5,852,796	4,990,165.7	0.55	1030.54	23.95	43.02	47.31
2004	2,682	2,682	54,711	2,503,837	4,361,730	4,487.0	30	6,394,702	5,222,330.4	0.42	933.57	20.40	45.76	66.86
2005	2,511	2,511	51,174	2,441,100	4,239,179	4,487.5	28	6,234,197	5,289,419.1	0.40	972.16	20.38	47.70	62.39
2006	4,269	4,269	90,834	3,769,563	5,753,517	6,620.6	32	14,953,445	9,251,568.1	0.29	883.01	21.28	41.50	48.33
2007	6,288	6,288	139,564	5,419,603	7,979,807	9,467.7	36	17,881,201	13,523,642.6	0.35	861.90	22.20	38.83	38.02
2008	8,960	8,960	196,865	7,298,476	10,635,675	12,339.5	26	32,594,226	20,829,297.4	0.27	814.56	21.97	37.07	21.07
2009	11,023	11,023	240,023	8,733,162	12,393,732	14,580.0	41	32,134,970	25,756,528.5	0.34	792.27	21.77	36.38	28.12
2010	11,295	11,295	239,963	8,620,559	12,147,880	14,060.2	20	31,159,274	25,149,997.6	0.36	763.22	21.25	35.92	14.22
2011	11,307	11,307	232,250	8,214,190	11,326,635	12,929.3	14	30,530,008	24,734,275.6	0.37	726.47	20.54	35.37	10.83
2012	11,051	11,051	204,077	7,132,274	9,860,361	10,133.6	16	32,128,068	24,743,886.3	0.34	645.40	18.47	34.95	15.79
2013	9,895	9,895	155,422	5,312,656	7,834,983	5,909.7	21	29,564,154	23,712,744.5	0.33	536.90	15.71	34.18	35.53
2014	4,088	4,088	48,369	1,732,830	2,573,211	1,049.5	4	24,794,126	11,582,968.7	0.16	423.88	11.83	35.83	38.11
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>730-Day Blackout Period</b>														
2000	267	267	7,314	404,603	873,340	602.7	5	4,472,279	2,102,708.9	0.06	1515.37	27.39	55.32	82.95
2001	673	673	21,318	1,056,170	2,064,614	1,645.7	8	4,798,149	4,155,900.9	0.14	1569.35	31.68	49.54	48.61
2002	802	802	22,771	1,299,014	2,363,620	2,026.8	12	4,865,986	4,226,375.8	0.16	1619.72	28.39	57.05	59.21
2003	1,662	1,662	58,747	2,589,724	5,432,658	3,863.0	13	5,026,237	4,274,348.9	0.33	1558.20	35.35	44.08	33.65
2004	1,149	1,149	37,097	1,798,742	3,049,674	2,749.8	18	5,309,605	4,319,468.4	0.22	1565.48	32.29	48.49	65.46
2005	1,156	1,156	36,118	1,806,022	3,185,799	2,784.7	10	5,224,829	4,518,657.1	0.22	1562.30	31.24	50.00	35.91
2006	1,872	1,872	61,380	2,670,685	4,106,768	3,824.9	13	12,089,022	7,673,124.2	0.15	1426.65	32.79	43.51	33.99
2007	2,720	2,720	93,974	3,792,626	5,627,498	5,344.9	17	14,483,174	10,818,764.4	0.19	1394.35	34.55	40.36	31.81
2008	3,829	3,829	130,740	5,008,151	7,354,522	6,600.9	14	24,136,324	16,019,132.5	0.16	1307.95	34.14	38.31	21.21
2009	4,641	4,641	155,913	5,853,766	8,300,918	7,462.6	18	23,894,572	19,743,300.9	0.19	1261.32	33.59	37.55	24.12
2010	4,774	4,774	153,052	5,677,364	7,961,895	6,750.0	3	23,493,792	19,387,106.5	0.20	1189.23	32.06	37.09	4.44
2011	4,963	4,963	148,084	5,379,493	7,393,684	5,519.4	7	24,770,016	19,570,868.5	0.20	1083.92	29.84	36.33	12.68
2012	4,510	4,510	116,922	4,193,250	5,777,235	3,063.2	6	24,553,189	18,843,670.9	0.18	929.77	25.93	35.86	19.59

**Table 4a: Summary of Incident Methylphenidate Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure**

Extension Period, Blackout Period, and Year	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2013	1,914	1,914	40,503	1,523,379	2,242,212	543.2	0	18,915,723	9,174,905.8	0.10	795.91	21.16	37.61	0.00
2014	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>1,095-Day Blackout Period</b>														
2000	154	154	5,479	310,119	681,631	403.0	4	3,815,327	1,806,473.6	0.04	2013.76	35.58	56.60	99.26
2001	400	400	16,142	825,428	1,600,954	1,123.9	2	4,106,403	3,609,935.8	0.10	2063.57	40.36	51.14	17.79
2002	476	476	17,189	1,019,802	1,887,778	1,412.5	5	4,274,307	3,683,678.5	0.11	2142.44	36.11	59.33	35.40
2003	927	927	42,414	1,969,297	3,773,390	2,640.1	7	4,276,082	3,584,244.3	0.22	2124.38	45.75	46.43	26.51
2004	713	713	28,705	1,424,070	2,406,683	1,838.9	5	4,485,159	3,756,838.2	0.16	1997.29	40.26	49.61	27.19
2005	717	717	28,001	1,436,611	2,584,015	1,877.0	4	4,515,037	3,941,060.2	0.16	2003.64	39.05	51.31	21.31
2006	1,052	1,052	43,971	1,983,994	3,085,561	2,414.7	9	9,874,979	6,410,374.7	0.11	1885.93	41.80	45.12	37.27
2007	1,571	1,571	67,986	2,846,315	4,235,236	3,292.1	13	11,686,099	8,935,307.6	0.13	1811.79	43.28	41.87	39.49
2008	2,085	2,085	90,980	3,582,269	5,298,148	3,813.4	10	18,692,366	12,887,317.5	0.11	1718.11	43.64	39.37	26.22
2009	2,509	2,509	106,138	4,097,819	5,775,166	4,046.2	11	18,567,791	15,598,836.8	0.14	1633.25	42.30	38.61	27.19
2010	2,626	2,626	102,451	3,898,908	5,425,650	3,179.9	0	19,671,563	15,781,878.6	0.13	1484.73	39.01	38.06	0.00
2011	2,600	2,600	91,863	3,429,957	4,711,557	1,920.2	2	19,625,773	15,303,338.1	0.13	1319.21	35.33	37.34	10.42
2012	1,094	1,094	31,499	1,273,592	1,800,197	318.9	0	17,016,652	7,631,761.7	0.06	1164.16	28.79	40.43	0.00
2013	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2014	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
2000	5,613	5,613	29,646	1,430,593	3,067,463	5,513.6	47	6,528,534	2,996,066.8	0.86	254.87	5.28	48.26	85.24
2001	13,930	13,930	80,498	3,522,217	6,892,595	13,701.2	108	7,126,797	5,951,991.0	1.95	252.85	5.78	43.76	78.83
2002	13,306	13,306	80,756	3,768,044	6,785,468	14,018.1	106	7,275,947	6,048,905.9	1.83	283.18	6.07	46.66	75.62
2003	18,679	18,679	153,114	6,236,961	12,180,360	22,132.3	132	7,267,208	6,020,250.4	2.57	333.90	8.20	40.73	59.64
2004	16,943	16,943	118,284	5,067,573	10,870,661	18,474.6	146	7,701,178	6,263,171.3	2.20	299.10	6.98	42.84	79.03
2005	17,084	17,084	115,509	4,984,021	8,389,120	18,425.3	145	7,941,951	6,552,168.0	2.15	291.74	6.76	43.15	78.70
2006	31,749	31,749	210,814	8,033,524	12,212,788	31,087.3	155	19,411,790	11,584,595.3	1.64	253.03	6.64	38.11	49.86
2007	48,513	48,513	323,815	11,666,856	17,233,431	45,575.2	259	23,605,215	17,136,640.4	2.06	240.49	6.67	36.03	56.83
2008	76,380	76,380	479,567	16,583,288	24,072,172	66,008.9	261	44,299,773	27,972,989.8	1.72	217.12	6.28	34.58	39.54
2009	96,854	96,854	595,810	20,235,096	29,025,512	81,453.9	314	45,682,539	35,441,580.4	2.12	208.92	6.15	33.96	38.55
2010	93,246	93,246	580,266	19,562,089	27,796,279	78,336.9	271	43,541,802	33,931,638.3	2.14	209.79	6.22	33.71	34.59
2011	91,172	91,172	558,410	18,558,868	26,132,463	74,790.0	241	42,137,841	33,131,645.4	2.16	203.56	6.12	33.24	32.22
2012	84,284	84,284	493,520	16,226,197	22,832,361	66,273.0	195	41,117,768	32,456,965.9	2.05	192.52	5.86	32.88	29.42
2013	78,699	78,699	407,477	13,115,232	19,304,830	54,751.9	221	40,980,381	32,137,167.9	1.92	166.65	5.18	32.19	40.36
2014	71,549	71,549	269,304	8,385,352	12,539,418	35,995.1	143	41,914,661	32,013,481.9	1.71	117.20	3.76	31.14	39.73
2015	30,616	30,616	64,209	1,820,879	2,736,508	7,449.5	32	34,463,590	15,654,613.3	0.89	59.47	2.10	28.36	42.96
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>90-Day Blackout Period</b>														
2000	5,000	5,000	28,745	1,407,002	3,015,881	4,206.6	32	6,271,153	2,822,041.0	0.80	281.40	5.75	48.95	76.07
2001	12,627	12,627	78,520	3,470,829	6,789,507	10,441.5	71	6,792,255	5,668,342.4	1.86	274.87	6.22	44.20	68.00
2002	11,893	11,893	78,794	3,720,176	6,673,415	10,947.5	77	6,952,509	5,738,247.2	1.71	312.80	6.63	47.21	70.34
2003	16,441	16,441	150,265	6,171,780	12,067,706	17,873.5	91	6,899,304	5,717,648.6	2.38	375.39	9.14	41.07	50.91
2004	14,695	14,695	115,259	4,994,759	10,683,044	14,638.9	91	7,418,196	5,964,230.5	1.98	339.90	7.84	43.34	62.16
2005	14,823	14,823	112,765	4,930,499	8,283,961	14,629.1	93	7,569,502	6,180,776.2	1.96	332.62	7.61	43.72	63.57
2006	27,384	27,384	205,239	7,914,966	12,013,898	23,965.8	101	18,282,521	10,860,580.6	1.50	289.04	7.49	38.56	42.14
2007	41,596	41,596	314,642	11,458,274	16,899,831	34,697.4	141	22,115,193	16,066,672.6	1.88	275.47	7.56	36.42	40.64
2008	63,385	63,385	461,761	16,173,424	23,462,751	49,034.3	131	41,833,390	25,706,994.6	1.52	255.16	7.29	35.03	26.72
2009	80,538	80,538	573,845	19,736,570	28,274,340	59,971.8	174	42,468,379	32,581,875.3	1.90	245.06	7.13	34.39	29.01

**Table 4a: Summary of Incident Methylphenidate Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2010	76,814	76,814	559,209	19,102,789	27,082,150	57,904.1	144	40,689,574	31,307,542.7	1.89	248.69	7.28	34.16	24.87
2011	75,145	75,145	538,081	18,126,247	25,487,883	54,892.3	131	39,578,145	30,672,694.7	1.90	241.22	7.16	33.69	23.86
2012	69,932	69,932	475,669	15,843,074	22,274,302	47,846.6	112	39,165,519	30,167,940.1	1.79	226.55	6.80	33.31	23.41
2013	65,258	65,258	390,387	12,743,359	18,755,060	37,543.9	121	38,459,674	29,706,153.2	1.70	195.28	5.98	32.64	32.23
2014	57,693	57,693	250,691	7,969,285	11,902,661	20,432.7	64	39,061,473	29,169,845.5	1.48	138.13	4.35	31.79	31.32
2015	12,462	12,462	37,854	1,220,825	1,835,677	2,317.7	5	22,946,618	7,673,908.3	0.54	97.96	3.04	32.25	21.57
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>180-Day Blackout Period</b>														
2000	2,971	2,971	25,810	1,303,809	2,783,521	3,244.6	23	6,000,891	2,668,690.0	0.50	438.85	8.69	50.52	70.89
2001	7,128	7,128	71,199	3,241,156	6,299,926	8,189.9	50	6,563,875	5,409,019.1	1.09	454.71	9.99	45.52	61.05
2002	7,245	7,245	73,828	3,583,441	6,400,635	8,948.2	62	6,680,089	5,450,335.8	1.08	494.61	10.19	48.54	69.29
2003	10,782	10,782	151,957	6,260,544	12,683,334	15,787.0	74	6,651,899	5,453,120.6	1.62	580.65	14.09	41.20	46.87
2004	9,321	9,321	109,019	4,823,084	8,751,054	12,133.6	65	7,087,654	5,699,731.5	1.32	517.44	11.70	44.24	53.57
2005	9,121	9,121	105,855	4,738,097	7,932,595	12,079.8	69	7,307,226	5,850,827.4	1.25	519.47	11.61	44.76	57.12
2006	16,259	16,259	191,153	7,528,298	11,377,229	19,284.4	75	17,569,167	10,218,028.8	0.93	463.02	11.76	39.38	38.89
2007	24,103	24,103	291,769	10,818,030	15,935,736	27,607.3	103	21,016,974	15,118,013.1	1.15	448.83	12.11	37.08	37.31
2008	35,931	35,931	423,955	15,092,109	21,887,019	38,281.2	78	39,154,962	23,690,499.3	0.92	420.03	11.80	35.60	20.38
2009	45,245	45,245	525,196	18,357,087	26,213,228	46,359.1	119	40,437,243	30,022,481.9	1.12	405.73	11.61	34.95	25.67
2010	44,519	44,519	517,190	17,940,327	25,336,034	45,178.9	91	38,797,115	28,985,314.6	1.15	402.98	11.62	34.69	20.14
2011	44,216	44,216	498,302	17,023,757	23,841,346	42,418.3	77	37,821,282	28,469,639.7	1.17	385.01	11.27	34.16	18.15
2012	41,872	41,872	441,473	14,908,749	20,910,474	36,275.6	76	36,960,879	28,117,974.0	1.13	356.06	10.54	33.77	20.95
2013	39,026	39,026	356,426	11,795,484	17,390,924	26,497.2	69	36,815,476	27,518,676.8	1.06	302.25	9.13	33.09	26.04
2014	29,513	29,513	198,626	6,481,777	9,658,959	10,736.3	29	36,362,740	23,789,126.4	0.81	219.62	6.73	32.63	27.01
2015	3,859	3,859	18,284	644,512	954,713	582.6	0	13,575,849	3,594,674.2	0.28	167.02	4.74	35.25	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>270-Day Blackout Period</b>														
2000	1,975	1,975	23,448	1,189,217	2,534,236	2,659.6	19	5,556,728	2,575,586.1	0.36	602.14	11.87	50.72	71.44
2001	4,774	4,774	64,931	2,975,931	5,775,462	6,803.8	37	6,239,134	5,172,478.2	0.77	623.36	13.60	45.83	54.38
2002	5,032	5,032	67,948	3,365,200	6,011,036	7,616.3	52	6,327,152	5,194,516.6	0.80	668.76	13.50	49.53	68.27
2003	8,094	8,094	145,007	6,000,186	12,346,370	13,755.1	62	6,270,756	5,218,106.9	1.29	741.31	17.92	41.38	45.07
2004	6,726	6,726	101,792	4,552,088	8,045,574	10,380.7	53	6,680,865	5,462,785.4	1.01	676.79	15.13	44.72	51.06
2005	6,499	6,499	98,589	4,480,860	7,506,794	10,403.0	50	6,839,991	5,560,624.8	0.95	689.47	15.17	45.45	48.06
2006	11,737	11,737	177,108	7,048,230	10,654,421	16,071.1	62	16,116,779	9,726,480.5	0.73	600.51	15.09	39.80	38.58
2007	17,086	17,086	267,719	10,035,019	14,791,627	22,851.3	66	19,507,053	14,302,805.7	0.88	587.32	15.67	37.48	28.88
2008	25,433	25,433	387,097	13,932,035	20,232,921	31,126.8	60	34,979,879	22,225,410.9	0.73	547.79	15.22	35.99	19.28
2009	31,675	31,675	477,028	16,850,229	24,053,053	37,435.8	93	36,915,582	27,856,331.2	0.86	531.97	15.06	35.32	24.84
2010	31,483	31,483	471,927	16,532,037	23,344,665	36,553.0	60	35,491,945	27,016,403.5	0.89	525.11	14.99	35.03	16.41
2011	31,598	31,598	454,279	15,676,399	21,930,979	33,802.5	51	34,684,951	26,574,909.0	0.91	496.12	14.38	34.51	15.09
2012	30,307	30,307	401,936	13,696,643	19,197,452	28,103.2	52	33,847,164	26,407,227.6	0.90	451.93	13.26	34.08	18.50
2013	28,129	28,129	318,210	10,622,971	15,683,738	18,807.9	47	33,818,805	25,591,829.7	0.83	377.65	11.31	33.38	24.99
2014	16,701	16,701	142,622	4,783,891	7,120,340	5,399.4	15	31,974,052	18,141,691.8	0.52	286.44	8.54	33.54	27.78
2015	700	700	3,753	168,838	236,286	74.8	0	9,117,591	1,031,135.3	0.08	241.20	5.36	44.99	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>365-Day Blackout Period</b>														
2000	1,340	1,340	20,931	1,072,039	2,283,820	2,238.1	17	5,308,581	2,486,855.0	0.25	800.03	15.62	51.22	75.96
2001	3,458	3,458	58,865	2,727,825	5,292,523	5,749.6	29	5,774,593	4,927,921.3	0.60	788.84	17.02	46.34	50.44
2002	3,672	3,672	62,094	3,117,794	5,585,828	6,552.6	46	5,830,685	4,954,892.5	0.63	849.07	16.91	50.21	70.20
2003	6,302	6,302	136,229	5,669,186	11,843,040	11,983.0	54	5,851,850	4,989,731.6	1.08	899.59	21.62	41.62	45.06
2004	5,149	5,149	94,426	4,265,959	7,461,784	8,938.8	44	6,393,117	5,221,514.5	0.81	828.50	18.34	45.18	49.22
2005	4,950	4,950	91,427	4,208,140	7,061,832	9,024.4	44	6,231,626	5,287,992.2	0.79	850.13	18.47	46.03	48.76
2006	8,625	8,625	161,598	6,504,723	9,865,418	13,556.4	57	14,949,756	9,249,327.9	0.58	754.17	18.74	40.25	42.05
2007	12,709	12,709	243,933	9,237,595	13,670,251	19,140.2	55	17,876,518	13,520,609.4	0.71	726.85	19.19	37.87	28.74

**Table 4a: Summary of Incident Methylphenidate Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2008	18,463	18,463	348,339	12,661,087	18,456,906	25,635.3	45	32,587,883	20,825,314.2	0.57	685.75	18.87	36.35	17.55
2009	22,949	22,949	427,914	15,260,345	21,790,012	30,598.5	79	32,127,013	25,751,404.4	0.71	664.97	18.65	35.66	25.82
2010	23,231	23,231	425,652	15,047,308	21,281,116	29,783.4	46	31,148,589	25,143,266.7	0.75	647.73	18.32	35.35	15.44
2011	23,213	23,213	406,866	14,153,199	19,763,872	27,018.1	37	30,516,503	24,725,648.8	0.76	609.71	17.53	34.79	13.69
2012	22,680	22,680	358,934	12,322,077	17,238,723	21,529.9	37	32,111,521	24,733,253.5	0.71	543.30	15.83	34.33	17.19
2013	20,664	20,664	275,456	9,266,920	13,709,472	12,742.9	36	29,545,798	23,700,402.4	0.70	448.46	13.33	33.64	28.25
2014	8,503	8,503	85,386	2,997,450	4,465,266	2,217.8	5	24,779,756	11,575,939.7	0.34	352.52	10.04	35.10	22.55
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>730-Day Blackout Period</b>														
2000	597	597	15,274	812,094	1,724,317	1,366.9	8	4,472,279	2,102,708.9	0.13	1360.29	25.58	53.17	58.53
2001	1,492	1,492	42,309	2,016,599	3,949,106	3,447.6	17	4,798,149	4,155,900.9	0.31	1351.61	28.36	47.66	49.31
2002	1,700	1,700	45,369	2,379,584	4,316,605	4,064.8	23	4,865,982	4,226,375.3	0.35	1399.76	26.69	52.45	56.58
2003	3,273	3,273	107,695	4,566,121	9,181,083	7,538.6	35	5,026,150	4,274,322.0	0.65	1395.09	32.90	42.40	46.43
2004	2,331	2,331	68,318	3,229,781	5,632,212	5,504.7	27	5,309,381	4,319,377.3	0.44	1385.58	29.31	47.28	49.05
2005	2,400	2,400	69,533	3,303,851	5,676,405	5,689.9	20	5,224,358	4,518,432.5	0.46	1376.60	28.97	47.51	35.15
2006	4,004	4,004	117,107	4,876,249	7,408,022	7,833.5	23	12,088,174	7,672,640.1	0.33	1217.84	29.25	41.64	29.36
2007	5,653	5,653	172,841	6,752,652	10,089,303	10,765.8	28	14,481,972	10,818,011.5	0.39	1194.53	30.58	39.07	26.01
2008	7,953	7,953	241,157	9,021,753	13,276,354	13,721.2	21	24,134,707	16,018,115.3	0.33	1134.38	30.32	37.41	15.30
2009	9,836	9,836	291,641	10,676,218	15,357,773	15,641.1	34	23,892,462	19,741,949.8	0.41	1085.42	29.65	36.61	21.74
2010	10,220	10,220	289,270	10,502,990	14,883,100	14,508.9	14	23,491,045	19,385,316.3	0.44	1027.69	28.30	36.31	9.65
2011	10,545	10,545	274,995	9,792,178	13,677,634	11,658.6	17	24,766,390	19,568,557.0	0.43	928.61	26.08	35.61	14.58
2012	9,824	9,824	223,255	7,826,465	10,933,082	6,685.9	11	24,548,667	18,840,727.0	0.40	796.67	22.73	35.06	16.45
2013	4,301	4,301	79,722	2,920,599	4,358,206	1,205.6	0	18,912,128	9,173,031.8	0.23	679.05	18.54	36.63	0.00
2014	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>1,095-Day Blackout Period</b>														
2000	324	324	11,147	615,556	1,302,959	921.3	6	3,815,327	1,806,473.6	0.08	1899.86	34.40	55.22	65.12
2001	847	847	31,940	1,568,138	3,088,628	2,314.6	9	4,106,403	3,609,935.8	0.21	1851.40	37.71	49.10	38.88
2002	1,003	1,003	34,768	1,877,824	3,464,056	2,752.4	12	4,274,307	3,683,678.5	0.23	1872.21	34.66	54.01	43.60
2003	1,870	1,870	80,867	3,549,089	6,938,555	5,053.7	20	4,276,081	3,584,244.2	0.44	1897.91	43.24	43.89	39.58
2004	1,423	1,423	53,775	2,594,364	4,579,242	3,707.1	11	4,485,130	3,756,827.5	0.32	1823.17	37.79	48.24	29.67
2005	1,451	1,451	54,222	2,641,274	4,645,659	3,832.3	9	4,514,934	3,941,011.8	0.32	1820.31	37.37	48.71	23.48
2006	2,213	2,213	84,768	3,648,962	5,629,398	4,873.6	14	9,874,745	6,410,256.7	0.22	1648.88	38.30	43.05	28.73
2007	3,196	3,196	126,449	5,094,352	7,687,100	6,540.0	21	11,685,702	8,935,087.4	0.27	1593.98	39.56	40.29	32.11
2008	4,305	4,305	170,836	6,555,998	9,673,078	7,880.1	12	18,691,777	12,886,952.3	0.23	1522.88	39.68	38.38	15.23
2009	5,378	5,378	204,087	7,668,488	11,009,368	8,387.9	18	18,567,039	15,598,345.3	0.29	1425.90	37.95	37.57	21.46
2010	5,686	5,686	200,593	7,427,612	10,512,084	6,885.0	3	19,670,525	15,781,220.7	0.29	1306.30	35.28	37.03	4.36
2011	5,524	5,524	175,331	6,389,898	8,957,743	3,992.7	4	19,624,451	15,302,467.0	0.28	1156.75	31.74	36.44	10.02
2012	2,404	2,404	63,143	2,461,840	3,496,809	704.2	0	17,015,298	7,631,137.2	0.14	1024.06	26.27	38.99	0.00
2013	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2014	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---



**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Methylphenidate Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>30-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
2000	15	1,167	128.6
2001	31	2,795	110.9
2002	24	2,601	92.3
2003	33	3,189	103.5
2004	45	3,264	137.9
2005	41	3,248	126.2
2006	47	6,098	77.1
2007	100	9,249	108.1
2008	113	14,436	78.3
2009	121	18,321	66.0
2010	99	17,411	56.9
2011	100	16,995	58.8
2012	72	15,646	46.0
2013	85	14,693	57.9
2014	61	13,470	45.3
2015	24	4,642	51.7
2016	0	0	---
<b>Days 91-180</b>			
2000	4	508	78.8
2001	12	1,211	99.1
2002	8	1,210	66.1
2003	18	1,816	99.1
2004	14	1,724	81.2
2005	17	1,601	106.2
2006	22	2,897	75.9
2007	20	4,302	46.5
2008	27	6,415	42.1
2009	29	7,981	36.3
2010	27	7,934	34.0
2011	22	7,815	28.2
2012	19	7,440	25.5
2013	29	6,879	42.2
2014	23	5,812	39.6
2015	3	1,028	29.2
2016	0	0	---
<b>Days 181-270</b>			
2000	2	274	73.0
2001	6	682	88.0
2002	9	754	119.3
2003	6	1,221	49.1
2004	6	1,064	56.4
2005	12	992	120.9
2006	9	1,787	50.4
2007	28	2,615	107.1

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Methylphenidate Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	<b>New Episodes with Events</b>	<b>Years at Risk</b>	<b>New Episodes with Events per 10,000 Years at Risk</b>
2008	13	3,866	33.6
2009	16	4,748	33.7
2010	16	4,695	34.1
2011	10	4,797	20.8
2012	16	4,593	34.8
2013	10	4,187	23.9
2014	9	2,816	32.0
2015	0	262	0.0
2016	0	0	---
<b>Days 271-365</b>			
2000	1	184	54.3
2001	5	481	103.9
2002	4	531	75.3
2003	8	949	84.3
2004	6	811	74.0
2005	5	729	68.6
2006	3	1,291	23.2
2007	5	1,864	26.8
2008	8	2,741	29.2
2009	8	3,345	23.9
2010	8	3,435	23.3
2011	6	3,445	17.4
2012	6	3,339	18.0
2013	6	3,026	19.8
2014	6	1,571	38.2
2015	0	39	0.0
2016	0	0	---
<b>Days 366-730</b>			
2000	6	386	155.3
2001	5	1,030	48.5
2002	13	1,189	109.3
2003	16	2,266	70.6
2004	12	1,737	69.1
2005	18	1,703	105.7
2006	19	2,796	68.0
2007	19	4,123	46.1
2008	12	5,739	20.9
2009	23	7,117	32.3
2010	17	7,310	23.3
2011	7	7,410	9.4
2012	10	7,070	14.1
2013	21	5,367	39.1
2014	4	1,050	38.1
2015	0	0	---
2016	0	0	---

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Methylphenidate Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>Days 731-1,095</b>			
2000	1	200	50.1
2001	6	522	115.0
2002	7	614	114.0
2003	6	1,223	49.1
2004	13	911	142.7
2005	6	908	66.1
2006	4	1,410	28.4
2007	4	2,053	19.5
2008	4	2,787	14.3
2009	7	3,416	20.5
2010	3	3,570	8.4
2011	5	3,599	13.9
2012	6	2,744	21.9
2013	0	543	0.0
2014	0	0	---
2015	0	0	---
2016	0	0	---
<b>90-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
2000	15	1,307	114.8
2001	37	3,260	113.5
2002	29	3,071	94.4
2003	41	4,259	96.3
2004	55	3,836	143.4
2005	52	3,796	137.0
2006	54	7,122	75.8
2007	118	10,878	108.5
2008	130	16,975	76.6
2009	140	21,482	65.2
2010	127	20,433	62.2
2011	110	19,898	55.3
2012	83	18,426	45.0
2013	100	17,208	58.1
2014	79	15,562	50.8
2015	27	5,132	52.6
2016	0	0	---
<b>Days 91-180</b>			
2000	9	962	93.6
2001	21	2,252	93.3
2002	15	1,999	75.0
2003	17	2,087	81.5
2004	26	2,505	103.8
2005	24	2,549	94.1
2006	26	4,681	55.5

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Methylphenidate Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	<b>New Episodes with Events</b>	<b>Years at Risk</b>	<b>New Episodes with Events per 10,000 Years at Risk</b>
2007	38	7,090	53.6
2008	53	10,753	49.3
2009	55	13,613	40.4
2010	53	12,725	41.6
2011	54	12,474	43.3
2012	36	11,571	31.1
2013	52	11,047	47.1
2014	35	9,696	36.1
2015	5	1,735	28.8
2016	0	0	---
<b>Days 181-270</b>			
2000	4	585	68.4
2001	13	1,386	93.8
2002	10	1,332	75.1
2003	12	2,032	59.1
2004	12	1,753	68.5
2005	19	1,677	113.3
2006	13	3,213	40.5
2007	37	4,756	77.8
2008	18	7,154	25.2
2009	26	8,923	29.1
2010	31	8,626	35.9
2011	26	8,616	30.2
2012	24	8,172	29.4
2013	22	7,689	28.6
2014	14	5,337	26.2
2015	0	508	0.0
2016	0	0	---
<b>Days 271-365</b>			
2000	2	421	47.5
2001	8	1,054	75.9
2002	6	1,064	56.4
2003	8	1,772	45.1
2004	9	1,442	62.4
2005	6	1,379	43.5
2006	5	2,515	19.9
2007	11	3,711	29.6
2008	15	5,491	27.3
2009	14	6,837	20.5
2010	14	6,770	20.7
2011	14	6,784	20.6
2012	15	6,573	22.8
2013	11	6,065	18.1
2014	10	3,182	31.4
2015	0	75	0.0

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Methylphenidate Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
2016	0	0	---
<b>Days 366-730</b>			
2000	9	871	103.3
2001	12	2,302	52.1
2002	23	2,488	92.5
2003	19	4,444	42.7
2004	17	3,434	49.5
2005	24	3,334	72.0
2006	34	5,723	59.4
2007	27	8,374	32.2
2008	24	11,914	20.1
2009	45	14,957	30.1
2010	32	15,275	20.9
2011	20	15,359	13.0
2012	26	14,844	17.5
2013	36	11,537	31.2
2014	5	2,218	22.5
2015	0	0	---
2016	0	0	---
<b>Days 731-1,095</b>			
2000	2	446	44.9
2001	8	1,133	70.6
2002	11	1,312	83.8
2003	15	2,485	60.4
2004	16	1,798	89.0
2005	11	1,858	59.2
2006	9	2,960	30.4
2007	7	4,226	16.6
2008	9	5,841	15.4
2009	16	7,253	22.1
2010	11	7,624	14.4
2011	13	7,666	17.0
2012	11	5,982	18.4
2013	0	1,206	0.0
2014	0	0	---
2015	0	0	---
2016	0	0	---

**Appendix A: List of Generic and Brand Names Used To Define the Exposures and Exposure Incidence in this Request**

Generic Name	Brand Name
<b>Amphetamines</b>	
DEXTROAMPHETAMINE SULFATE	Dexedrine Spansule
DEXTROAMPHETAMINE SULFATE	dextroamphetamine
DEXTROAMPHETAMINE SULFATE	Dexedrine
DEXTROAMPHETAMINE SULFATE	DextroStat
DEXTROAMPHETAMINE SULFATE	Zenzedi
DEXTROAMPHETAMINE SULFATE	ProCentra
DEXTROAMPHETAMINE SULFATE	Liquadd
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	Amphetamine Salt Combo
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	Adderall XR
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	Adderall
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	dextroamphetamine-amphetamine
LISDEXAMFETAMINE DIMESYLATE	Vyvanse
METHAMPHETAMINE HCL	Desoxyn
AMPHETAMINE SULFATE	Evekeo
METHAMPHETAMINE HCL	methamphetamine
<b>Methylphenidates</b>	
DEXMETHYLPHENIDATE HCL	dexmethylphenidate
DEXMETHYLPHENIDATE HCL	Focalin XR
DEXMETHYLPHENIDATE HCL	Focalin
METHYLPHENIDATE HCL	Methylin
METHYLPHENIDATE HCL	Ritalin LA
METHYLPHENIDATE HCL	methylphenidate
METHYLPHENIDATE HCL	Concerta
METHYLPHENIDATE HCL	Metadate CD
METHYLPHENIDATE HCL	Aptensio XR
METHYLPHENIDATE HCL	Ritalin
METHYLPHENIDATE HCL	Ritalin SR
METHYLPHENIDATE HCL	Metadate ER
METHYLPHENIDATE HCL	Quillivant XR
METHYLPHENIDATE HCL	Methylin ER
<b>Strattera</b>	
ATOMOXETINE HCL	Strattera

**Appendix B: Codes Used To Define Heart Failure in this Request**


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<b>Code</b>	<b>Code Type</b>	<b>Description</b>
398.91	ICD-9-CM Diagnosis	Rheumatic heart failure (congestive)
402.01	ICD-9-CM Diagnosis	Malignant hypertensive heart disease with heart failure
402.11	ICD-9-CM Diagnosis	Benign hypertensive heart disease with heart failure
402.91	ICD-9-CM Diagnosis	Unspecified hypertensive heart disease with heart failure
404.01	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.03	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic kidney disease stage V or end stage renal disease
404.11	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, benign, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.13	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, benign, with heart failure and chronic kidney disease stage V or end stage renal disease
404.91	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, unspecified, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.93	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, unspecified, with heart failure and chronic kidney disease stage V or end stage renal disease
422.90	ICD-9-CM Diagnosis	Acute myocarditis, unspecified
425.4	ICD-9-CM Diagnosis	Other primary cardiomyopathies
425.9	ICD-9-CM Diagnosis	Secondary cardiomyopathy, unspecified
428	ICD-9-CM Diagnosis	Heart Failure
428.0	ICD-9-CM Diagnosis	Congestive heart failure, unspecified
428.1	ICD-9-CM Diagnosis	Left heart failure
428.2	ICD-9-CM Diagnosis	Systolic heart failure
428.20	ICD-9-CM Diagnosis	Systolic heart failure, unspecified
428.21	ICD-9-CM Diagnosis	Acute systolic heart failure
428.22	ICD-9-CM Diagnosis	Chronic systolic heart failure
428.23	ICD-9-CM Diagnosis	Acute on chronic systolic heart failure
428.3	ICD-9-CM Diagnosis	Diastolic heart failure
428.30	ICD-9-CM Diagnosis	Diastolic heart failure, unspecified
428.31	ICD-9-CM Diagnosis	Acute diastolic heart failure
428.32	ICD-9-CM Diagnosis	Chronic diastolic heart failure
428.33	ICD-9-CM Diagnosis	Acute on chronic diastolic heart failure
428.4	ICD-9-CM Diagnosis	Combined systolic and diastolic heart failure
428.40	ICD-9-CM Diagnosis	Combined systolic and diastolic heart failure, unspecified
428.41	ICD-9-CM Diagnosis	Acute combined systolic and diastolic heart failure
428.42	ICD-9-CM Diagnosis	Chronic combined systolic and diastolic heart failure
428.43	ICD-9-CM Diagnosis	Acute on chronic combined systolic and diastolic heart failure
428.9	ICD-9-CM Diagnosis	Heart failure, unspecified

**Modular Program Specifications for cder\_mpl1r\_wp014\_nsdp\_v01 Report 2 of 8**

Sentinel's Cohort Identification and Descriptive Analysis (CIDA) tool was used to investigate heart failure following treatment with select attention deficit and hyperactivity disorder (ADHD) medications. In total, 49 scenarios were examined with four different exposures, seven different blackout periods, and two different episode gaps/exposure extension periods. The four exposures are all amphetamines, all methylphenidates, strattera, and all stimulants (which include all amphetamines, all methylphenidates, and strattera). **The outcome is heart failure, defined as any heart failure ICD-9-CM diagnosis code (398.91, 402.x1, 402.x3, 404.x1, 404.x3, 422.90, 425.4, 425.9, 428.xx) in any care setting with a primary discharge diagnosis (PDX) value of P (principal) for those diagnoses in the inpatient care setting.** See below for a description of each of these scenarios. The query period was from January 1, 2000 to March 3, 2016 and the enrollment gap was set at 45 days. Age groups were split as follows: 0-21, 22-44, 45-64, 65+.

Enrollment Gap	45 Days
Age Groups	0-21, 22-44, 45-64, 65+
Query Period	January 1, 2000 - Current
Coverage Requirement	Medical and Drug
Enrollment Requirement	183 Days

Scenario	Drug/Exposure										Event/Outcome					
	Incident exposure	Incident w/ respect to:	Episode Truncation at Incident Exposure	Episode Truncation at Death	Washout (days)	Cohort Definition	Episode Gap	Exposure Extension Period	Min Episode Duration	Min Days Supplied	Event/ Outcome	Care Setting/PDX	Incident with Respect to Setting/PDX	Incident w/ respect to Care Setting/PDX	Washout (days)	Blackout Period
1	All Methylphenidates	All Stimulants	Yes	No	183	01	90	90	0	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	0
2	All Methylphenidates	All Stimulants	Yes	No	183	01	90	90	90	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	90
3	All Methylphenidates	All Stimulants	Yes	No	183	01	90	90	180	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	180
4	All Methylphenidates	All Stimulants	Yes	No	183	01	90	90	270	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	270
5	All Methylphenidates	All Stimulants	Yes	No	183	01	90	90	365	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	365
6	All Methylphenidates	All Stimulants	Yes	No	183	01	90	90	730	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	730
7	All Methylphenidates	All Stimulants	Yes	No	183	01	90	90	1095	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	1095
8	All Methylphenidates	All Stimulants	Yes	No	183	01	30	30	0	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	0
9	All Methylphenidates	All Stimulants	Yes	No	183	01	30	30	90	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	90
10	All Methylphenidates	All Stimulants	Yes	No	183	01	30	30	180	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	180
11	All Methylphenidates	All Stimulants	Yes	No	183	01	30	30	270	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	270
12	All Methylphenidates	All Stimulants	Yes	No	183	01	30	30	365	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	365
13	All Methylphenidates	All Stimulants	Yes	No	183	01	30	30	730	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	730
14	All Methylphenidates	All Stimulants	Yes	No	183	01	30	30	1095	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	1095

ICD-9, ICD-10, HCPCS, and CPT codes are provided by Optum360. NDC codes are checked against First Data Bank's "National Drug Data File (NDDF®) Plus."

Cohort Definition of 01 will only consider the first incident episode for each user during the query period that satisfies the washout period.

Note: Episodes are automatically truncated at outcome.



### Disclaimer

The following report(s) provides findings from an FDA-initiated query using Sentinel. While Sentinel queries may be undertaken to assess potential medical product safety risks, they may also be initiated for various other reasons. Some examples include determining a rate or count of an identified health outcome of interest, examining medical product use, exploring the feasibility of future, more detailed analyses within Sentinel, and seeking to better understand Sentinel capabilities.

Data obtained through Sentinel are intended to complement other types of evidence such as preclinical studies, clinical trials, postmarket studies, and adverse event reports, all of which are used by FDA to inform regulatory decisions regarding medical product safety. The information contained in this report is provided as part of FDA's commitment to place knowledge acquired from Sentinel in the public domain as soon as possible. Any public health actions taken by FDA regarding products involved in Sentinel queries will continue to be communicated through existing channels.

FDA wants to emphasize that the fact that FDA has initiated a query involving a medical product and is reporting findings related to that query does not mean that FDA is suggesting health care practitioners should change their prescribing practices for the medical product or that patients taking the medical product should stop using it. Patients who have questions about the use of an identified medical product should contact their health care practitioners.

The following report contains a description of the request, request specifications, and results from the modular program run(s).

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### Overview for Request cder\_mpl1r\_wp014\_nsdp\_v01, Report 3 of 8

**Request ID:** cder\_mpl1r\_wp014\_nsdp\_v01. This is report 3 of 8.

**Request Description:** FDA has requested execution of the Cohort Identification and Descriptive Analysis (CIDA) tool, version 2.1.1, to investigate heart failure diagnoses following new use of attention deficit hyperactivity disorder (ADHD) medications. This report presents results for all ADHD medications. Results for all methylphenidates, strattera, and all amphetamines are presented in separate reports.

**Data Source:** Data from January 1, 2000 to March 3, 2016 from 15 health plans contributing to the Sentinel Distributed Database (SDD) are included in this report.

**Study Design:** This request was designed to identify exposures and follow-up time. The exposure of interest and the occurrence of the health outcome of interest during exposed time were identified. The number of exposure episodes, number of individuals, number of events, and days at-risk in the SDD were calculated overall and were stratified by age group, sex, and year.

**Exposure of Interest:** The exposures of interest were ADHD medications, which were defined using National Drug Codes (NDCs). Please refer to Appendix A for a list of generic and brand names of ADHD medications included in this request.

**Cohort Eligibility Criteria:** Patients were required to be continuously enrolled in plans with both medical and drug coverage for at least 6 months (183 days) before their dispensing date, during which gaps in coverage of up to 45 days were allowed. Members were excluded if they had any ADHD medication or the outcome of interest in the 6 months (183 days) prior to exposure initiation. The following age groups were included in the cohort: 0-21, 22-44, 45-64, 65+ years.

**Follow-Up Time:** Follow-up time for the outcome was determined by the length of the exposure episodes. Exposure episode lengths were defined using outpatient pharmacy dispensing days supplied to create a sequence of continuous exposure. Exposure episodes were considered continuous if gaps in days supply were less than 90 days. The end date of each exposure episode was extended by 90 additional days. Sensitivity analyses were performed using a 30-day episode gap and 30-day exposure extension period. Follow-up began on the day on which the first exposure of interest was dispensed and continued until the first occurrence of any of the following: 1) the outcome of interest; 2) any codes defining incidence criteria; 3) disenrollment; 4) the study end date (March, 2016); 5) the end date of the data provided by each Data Partner; or 6) the end of the exposure episode. Only the first valid incident exposure episode that occurred during the study period was included per patient.

This report examines different blackout periods which is a number of days at the beginning of the ADHD medication episode where if an outcome occurs, it is not attributed to the exposure and the person is omitted from the analysis. The blackout periods examined were 90 days, 180 days, 270 days, 365 days, 730 days, and 1,095 days. Episodes that were at least as long as the blackout period were required.

**Outcome of Interest:** Heart failure was defined using any of the ICD-9-CM diagnosis codes listed in Appendix B. This event had to be incident (no heart failure events in the 183 days prior to exposure initiation). The event could happen in any care setting. However, if the event happened in the inpatient or institutionalized care setting, the event had to be flagged as a principal diagnosis.

**Please refer to Appendix C for detailed specifications.**

**Limitations:** Algorithms to define exposures and outcomes are imperfect and, therefore, may be misclassified.

**Notes:** Please contact the Sentinel Operations Center Query Fulfillment Team ([production@mini-sentinel.org](mailto:production@mini-sentinel.org)) for questions and to provide comments/suggestions for future enhancements to this document.

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**Glossary of Terms for Analyses Using  
Cohort Identification and Descriptive Analysis (CIDA) Tool\***

**Amount Supplied** - number of units (pills, tablets, vials) dispensed. Net amount per NDC per dispensing. This is equivalent to the "RxAmt" value in the MSCDM.

**Blackout Period** - number of days at the beginning of a treatment episode that events are to be ignored. If an event occurs during the blackout period, the episode is excluded.

**Care Setting** - type of medical encounter or facility where the exposure, event, or condition code was recorded. Possible care settings include: Inpatient Hospital Stay (IP), Non-Acute Institutional Stay (IS), Emergency Department (ED), Ambulatory Visit (AV), and Other Ambulatory Visit (OA). For laboratory results, possible care settings include: Emergency department (E), Home (H), Inpatient (I), Outpatient (O), or Unknown or Missing (U). Along with the Principal Diagnosis Indicator, forms the Care Setting/PDX parameter.

**Cohort Definition (drug/exposure)** - indicates how the cohort will be defined: (1) 01: Cohort includes only the first valid incident treatment episode during the query period; (2) 02: Cohort includes all valid incident treatment episodes during the query period; (3) 03: Cohort includes all valid incident treatment episodes during the query period until an event

**Days Supplied** - number of days supplied for all dispensings in qualifying treatment episodes.

**Eligible Members** - number of members eligible for an incident treatment episode (defined by the drug/exposure and event washout periods) with drug and medical coverage during the query period.

**Enrollment Gap** - number of days allowed between two consecutive enrollment periods without breaking a "continuously enrolled" sequence.

**Episodes** - treatment episodes; length of episode is determined by days supplied in one dispensing or consecutive dispensings bridged by the episode gap.

**Episode Gap** - number of days allowed between two (or more) consecutive exposures (dispensings/procedures) to be considered the same treatment episode.

**Event Deduplication** - specifies how events are counted by the MP algorithm: (0) 0: Counts all occurrences of an HOI during an exposure episode; (1) 1: de-duplicates occurrences of the same HOI code and code type on the same day; (2) 2: de-duplicates occurrences of the same HOI group on the same day (e.g., de-duplicates at the group level).

**Exposure Episode Length** - number of days after exposure initiation that is considered "exposed time."

**Exposure Extension Period** - number of days post treatment period in which the outcomes/events are counted for a treatment episode.

**Lookback Period (pre-existing condition)** - number of days wherein a member is required to have evidence of pre-existing condition (diagnosis/procedure/drug dispensing).

**Member-Years** - sum of all days of enrollment with medical and drug coverage\*\* in the query period preceded by an exposure washout period all divided by 365.25.

**Minimum Days Supplied** - specifies a minimum number of days in length of the days supplied for the episode to be considered.

**Minimum Episode Duration** - specifies a minimum number of days in length of the episode for it to be considered.

**Principal Diagnosis (PDX)** - diagnosis or condition established to be chiefly responsible for admission of the patient to the hospital. 'P' = principal diagnosis, 'S' = secondary diagnosis, 'X' = unspecified diagnosis, '.' = blank. Along with the Care Setting values, forms the Caresetting/PDX parameter.

**Query Period** - period in which the modular program looks for exposures and outcomes of interest.

**Treatment Episode Truncation Indicator** - indicates whether observation of the incident query code during follow-up requires truncation of valid treatment episodes. A value of Y indicates that the treatment episodes should be truncated at the first occurrence of an incident query code. A value of N indicates that the treatment episodes should not be truncated at the occurrence of the incident query code.

**Users** - number of members with exposure during the query period. Member must have no evidence of exposure(s) of interest (defined by incidence criteria) in the prior washout period. A user may only be counted once in a query period.

**Washout Period (drug/exposure)\*\*** - number of days a user is required to have no evidence of prior exposure (drug dispensing/procedure) and continuous drug and medical coverage prior to an incident treatment episode.

**Washout Period (event/outcome)\*\*** - number of days a user is required to have no evidence of a prior event (procedure/diagnosis) and continuous drug and medical coverage prior to an incident treatment episode.

**Years at Risk** - number of days supplied plus any episode gaps and exposure extension periods all divided by 365.25.

\*all terms may not be used in this report

\*\*incident treatment episodes must be incident to both the exposure and the event

**Table 1a: Summary of Attention Deficit and Hyperactivity Disorder (ADHD) Medications and Subsequent Heart Failures in the Sentinel Distributed Database (SDD) between January 1, 2000 and March 3, 2016 by Episode Gap/Exposure Extension Period, and Blackout Period**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>30-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
	2,012,948	2,012,948	11,936,403	399,949,179	601,749,024	1,260,550.9	4,419	110,278,682	304,304,394.9	18.25	198.69	5.93	33.51	35.06
<b>90-Day Blackout Period</b>														
	1,200,184	1,200,184	11,328,166	386,443,542	572,198,938	877,520.2	2,610	100,795,003	275,892,445.4	11.91	321.99	9.44	34.11	29.74
<b>180-Day Blackout Period</b>														
	688,592	688,592	9,996,909	345,758,118	513,929,271	673,565.5	1,909	93,629,082	250,025,376.7	7.35	502.12	14.52	34.59	28.34
<b>270-Day Blackout Period</b>														
	469,209	469,209	8,836,951	308,837,338	461,420,642	539,333.3	1,480	80,082,426	228,048,606.8	5.86	658.21	18.83	34.95	27.44
<b>365-Day Blackout Period</b>														
	339,341	339,341	7,795,629	275,206,086	413,295,402	438,507.1	1,219	72,081,003	207,089,837.5	4.71	811.00	22.97	35.30	27.80
<b>730-Day Blackout Period</b>														
	141,681	141,681	5,044,258	184,019,643	279,362,639	220,597.6	626	48,757,079	144,813,994.6	2.91	1298.83	35.60	36.48	28.38
<b>1,095-Day Blackout Period</b>														
	71,035	71,035	3,285,583	123,815,611	189,604,379	119,657.2	318	34,275,987	102,927,190.1	2.07	1743.02	46.25	37.68	26.58
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
	2,012,948	2,012,948	16,515,427	556,240,445	836,290,269	2,069,820.7	6,617	110,278,682	304,304,395.3	18.25	276.33	8.20	33.68	31.97
<b>90-Day Blackout Period</b>														
	1,801,284	1,801,284	16,186,890	548,682,833	825,480,891	1,602,003.3	4,434	100,794,994	275,083,403.6	17.87	304.61	8.99	33.90	27.68
<b>180-Day Blackout Period</b>														
	1,173,718	1,173,718	15,656,992	536,082,502	798,806,288	1,311,554.6	3,380	93,629,069	249,592,471.2	12.54	456.74	13.34	34.24	25.77
<b>270-Day Blackout Period</b>														
	869,111	869,111	14,656,513	505,948,245	755,612,447	1,087,698.7	2,726	80,082,419	227,783,729.5	10.85	582.14	16.86	34.52	25.06
<b>365-Day Blackout Period</b>														
	659,282	659,282	13,464,695	468,409,213	701,440,765	902,824.3	2,292	72,080,997	206,925,967.7	9.15	710.48	20.42	34.79	25.39
<b>730-Day Blackout Period</b>														
	295,753	295,753	9,442,432	337,097,621	509,990,074	469,843.4	1,201	48,757,078	144,776,386.3	6.07	1139.79	31.93	35.70	25.56
<b>1,095-Day Blackout Period</b>														
	152,025	152,025	6,413,717	235,083,828	358,973,699	257,216.9	641	34,275,987	102,916,687.7	4.44	1546.35	42.19	36.65	24.92

**Table 1b: Rate of Heart Failure Outcomes at Different Stages of Attention Deficit and Hyperactivity Disorder (ADHD) Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, and Blackout Period**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>30-Day Episode Gap/Extension Period</b>			
Days 0-90	1,809	383,031	47.2
Days 91-180	701	203,955	34.4
Days 181-270	429	134,232	32.0
Days 271-365	261	100,826	25.9
Days 366-730	593	217,909	27.2
Days 731-1,095	308	100,940	30.5
<b>90-Day Episode Gap/Extension Period</b>			
Days 0-90	2,183	467,817	46.7
Days 91-180	1,054	290,449	36.3
Days 181-270	654	223,856	29.2
Days 271-365	434	184,874	23.5
Days 366-730	1,091	432,981	25.2
Days 731-1,095	560	212,627	26.3

**Table 2a: Summary of Attention Deficit and Hyperactivity Disorder (ADHD) Medications and Subsequent Heart Failures in the Sentinel Distributed Database (SDD) between January 1, 2000 and March 3, 2016 by Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>30-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
00-21 Years	1,088,618	1,088,618	6,530,449	222,592,085	291,654,296	698,204.8	1,115	33,425,181	83,528,803.1	32.57	204.47	6.00	34.09	15.97
22-44 Years	628,325	628,325	3,694,758	119,096,205	198,333,810	377,937.0	896	45,694,947	95,661,496.4	13.75	189.55	5.88	32.23	23.71
45-64 Years	264,657	264,657	1,586,243	53,972,523	103,754,070	170,308.3	1,500	32,630,564	90,298,927.4	8.11	203.93	5.99	34.03	88.08
65+ Years	31,348	31,348	124,953	4,288,366	8,006,848	14,100.8	908	10,944,649	34,815,168.0	2.86	136.80	3.99	34.32	643.94
<b>90-Day Blackout Period</b>														
00-21 Years	675,308	675,308	6,259,299	217,006,783	283,826,637	490,262.3	826	30,664,666	76,225,253.1	22.02	321.34	9.27	34.67	16.85
22-44 Years	363,623	363,623	3,467,410	113,696,537	188,684,605	257,848.6	543	41,094,326	85,313,243.6	8.85	312.68	9.54	32.79	21.06
45-64 Years	147,526	147,526	1,494,118	51,889,935	92,432,789	120,937.9	868	30,226,740	82,484,102.6	4.88	351.73	10.13	34.73	71.77
65+ Years	13,727	13,727	107,339	3,850,287	7,254,907	8,471.4	373	9,843,548	31,869,846.2	1.39	280.49	7.82	35.87	440.30
<b>180-Day Blackout Period</b>														
00-21 Years	374,946	374,946	5,498,006	193,524,427	252,932,694	377,629.0	650	28,477,056	69,441,100.7	13.17	516.14	14.66	35.20	17.21
22-44 Years	216,469	216,469	3,062,353	101,574,859	169,923,158	194,365.7	386	37,538,049	76,067,200.2	5.77	469.24	14.15	33.17	19.86
45-64 Years	89,810	89,810	1,346,137	47,344,011	84,756,862	95,339.0	643	28,246,940	75,270,666.9	3.18	527.16	14.99	35.17	67.44
65+ Years	7,367	7,367	90,413	3,314,821	6,316,556	6,231.6	230	9,281,699	29,246,408.9	0.79	449.96	12.27	36.66	369.08
<b>270-Day Blackout Period</b>														
00-21 Years	249,979	249,979	4,857,210	172,829,800	226,358,021	305,382.9	522	24,382,789	63,591,561.6	10.25	691.38	19.43	35.58	17.09
22-44 Years	150,079	150,079	2,691,766	90,110,291	151,943,867	151,650.6	290	31,622,764	68,409,135.4	4.75	600.42	17.94	33.48	19.12
45-64 Years	64,271	64,271	1,210,495	43,012,890	77,561,383	77,458.8	496	24,590,683	69,073,787.1	2.61	669.24	18.83	35.53	64.03
65+ Years	4,880	4,880	77,480	2,884,357	5,557,371	4,841.0	172	8,262,338	26,974,122.7	0.59	591.06	15.88	37.23	355.30
<b>365-Day Blackout Period</b>														
00-21 Years	179,271	179,271	4,307,063	154,806,205	203,067,077	252,059.1	452	21,971,260	57,968,414.7	8.16	863.53	24.03	35.94	17.93
22-44 Years	108,372	108,372	2,340,848	79,073,790	134,649,434	119,283.6	233	27,909,271	61,245,335.8	3.88	729.65	21.60	33.78	19.53
45-64 Years	48,219	48,219	1,081,064	38,809,885	70,661,539	63,354.8	404	22,305,870	63,116,744.6	2.16	804.87	22.42	35.90	63.77
65+ Years	3,479	3,479	66,654	2,516,206	4,917,351	3,809.6	130	7,723,430	24,759,342.5	0.45	723.26	19.16	37.75	341.25
<b>730-Day Blackout Period</b>														
00-21 Years	78,979	78,979	2,928,682	108,506,211	142,973,625	134,210.5	248	14,939,215	40,902,097.3	5.29	1373.86	37.08	37.05	18.48
22-44 Years	40,803	40,803	1,376,828	47,868,311	84,402,618	52,619.0	119	17,762,787	40,906,106.1	2.30	1173.16	33.74	34.77	22.62
45-64 Years	20,601	20,601	700,838	26,119,791	48,902,987	32,054.8	207	15,594,066	44,995,680.4	1.32	1267.89	34.02	37.27	64.58
65+ Years	1,298	1,298	37,910	1,525,330	3,083,408	1,713.3	52	5,590,114	18,010,110.9	0.23	1175.14	29.21	40.24	303.50
<b>1,095-Day Blackout Period</b>														
00-21 Years	42,120	42,120	2,010,266	76,765,481	102,129,900	76,249.9	133	10,527,029	29,226,038.3	4.00	1822.54	47.73	38.19	17.44
22-44 Years	18,092	18,092	803,747	28,723,140	51,731,020	25,101.9	56	11,867,299	28,139,462.8	1.52	1587.62	44.43	35.74	22.31
45-64 Years	10,306	10,306	451,443	17,450,168	33,902,451	17,413.1	104	11,226,036	32,397,781.2	0.92	1693.20	43.80	38.65	59.73
65+ Years	517	517	20,127	876,822	1,841,009	892.4	25	4,147,006	13,163,907.8	0.12	1695.98	38.93	43.56	280.15
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
00-21 Years	1,088,618	1,088,618	9,468,010	323,572,706	425,635,364	1,203,101.8	1,694	33,425,181	83,528,803.1	32.57	297.23	8.70	34.18	14.08

**Table 2a: Summary of Attention Deficit and Hyperactivity Disorder (ADHD) Medications and Subsequent Heart Failures in the Sentinel Distributed Database (SDD) between January 1, 2000 and March 3, 2016 by Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
22-44 Years	628,325	628,325	4,763,056	154,260,340	260,068,475	574,495.3	1,259	45,694,947	95,661,496.8	13.75	245.51	7.58	32.39	21.91
45-64 Years	264,657	264,657	2,120,489	72,694,243	139,641,629	269,308.1	2,262	32,630,564	90,298,927.4	8.11	274.67	8.01	34.28	83.99
65+ Years	31,348	31,348	163,872	5,713,156	10,944,801	22,915.6	1,402	10,944,649	34,815,168.0	2.86	182.25	5.23	34.86	611.81
<b>90-Day Blackout Period</b>														
00-21 Years	990,732	990,732	9,315,522	320,087,375	421,143,890	947,944.2	1,325	30,664,659	75,834,144.6	32.31	323.08	9.40	34.36	13.98
22-44 Years	547,108	547,108	4,638,899	151,431,437	255,796,846	430,440.5	864	41,047,135	85,076,030.2	13.33	276.79	8.48	32.64	20.07
45-64 Years	236,729	236,729	2,076,469	71,656,476	137,956,863	207,837.8	1,496	30,212,611	82,333,179.9	7.84	302.69	8.77	34.51	71.98
65+ Years	26,715	26,715	156,000	5,507,545	10,583,292	15,780.7	749	9,839,361	31,840,048.9	2.72	206.16	5.84	35.30	474.63
<b>180-Day Blackout Period</b>														
00-21 Years	674,357	674,357	9,125,549	316,320,257	416,384,347	788,111.3	1,142	28,477,046	69,186,962.2	23.68	469.07	13.53	34.66	14.49
22-44 Years	342,434	342,434	4,395,175	144,949,529	245,293,989	340,048.8	645	37,505,445	75,957,391.4	9.13	423.29	12.84	32.98	18.97
45-64 Years	144,171	144,171	1,995,988	69,710,592	127,205,493	171,373.8	1,136	28,239,933	75,212,142.9	5.11	483.53	13.84	34.93	66.29
65+ Years	12,756	12,756	140,280	5,102,124	9,922,460	12,020.6	457	9,279,629	29,235,974.7	1.37	399.98	11.00	36.37	380.18
<b>270-Day Blackout Period</b>														
00-21 Years	503,580	503,580	8,608,746	300,613,057	395,813,896	659,910.3	977	24,382,782	63,427,130.0	20.65	596.95	17.10	34.92	14.81
22-44 Years	249,117	249,117	4,047,934	134,602,645	229,368,367	274,223.6	509	31,601,893	68,348,390.1	7.88	540.32	16.25	33.25	18.56
45-64 Years	107,689	107,689	1,873,266	66,054,481	121,217,116	143,833.2	909	24,586,163	69,039,863.3	4.38	613.38	17.40	35.26	63.20
65+ Years	8,725	8,725	126,567	4,678,062	9,213,068	9,731.6	331	8,260,993	26,968,346.1	1.06	536.17	14.51	36.96	340.13
<b>365-Day Blackout Period</b>														
00-21 Years	382,289	382,289	7,962,189	280,001,182	368,769,092	553,087.1	860	21,971,254	57,863,549.3	17.40	732.43	20.83	35.17	15.55
22-44 Years	186,720	186,720	3,654,348	122,453,189	210,173,276	220,999.7	416	27,896,347	61,210,351.1	6.69	655.81	19.57	33.51	18.82
45-64 Years	83,782	83,782	1,733,995	61,679,411	113,985,033	120,784.6	763	22,302,813	63,096,320.0	3.76	736.19	20.70	35.57	63.17
65+ Years	6,491	6,491	114,163	4,275,431	8,513,363	7,952.9	253	7,722,544	24,755,747.3	0.84	658.67	17.59	37.45	318.12
<b>730-Day Blackout Period</b>														
00-21 Years	177,128	177,128	5,783,837	208,102,358	275,308,263	297,941.8	485	14,939,214	40,876,103.3	11.86	1174.87	32.65	35.98	16.28
22-44 Years	76,271	76,271	2,348,994	80,724,129	142,702,935	103,108.1	213	17,760,204	40,900,307.7	4.29	1058.39	30.80	34.37	20.66
45-64 Years	39,577	39,577	1,235,496	45,349,002	85,996,554	64,904.4	393	15,593,257	44,990,882.4	2.54	1145.84	31.22	36.71	60.55
65+ Years	2,777	2,777	74,105	2,922,132	5,982,322	3,889.1	110	5,589,793	18,009,092.8	0.50	1052.26	26.69	39.43	282.84
<b>1,095-Day Blackout Period</b>														
00-21 Years	94,626	94,626	4,082,535	150,453,098	200,658,827	168,194.7	282	10,527,029	29,218,306.8	8.99	1589.98	43.14	36.85	16.77
22-44 Years	35,328	35,328	1,446,663	50,922,012	92,091,828	50,740.1	102	11,866,724	28,138,306.8	2.98	1441.41	40.95	35.20	20.10
45-64 Years	20,873	20,873	841,191	31,888,911	62,381,515	36,173.1	201	11,225,788	32,396,435.0	1.86	1527.76	40.30	37.91	55.57
65+ Years	1,198	1,198	43,328	1,819,807	3,841,529	2,109.1	56	4,146,889	13,163,639.1	0.29	1519.04	36.17	42.00	265.52



**Table 2b: Rate of Heart Failure Outcomes at Different Stages of Attention Deficit and Hyperactivity Disorder (ADHD) Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>30-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
00-21 Years	289	207,943	13.9
22-44 Years	353	120,088	29.4
45-64 Years	632	49,370	128.0
65+ Years	535	5,629	950.4
<b>Days 91-180</b>			
00-21 Years	176	112,633	15.6
22-44 Years	157	63,483	24.7
45-64 Years	225	25,599	87.9
65+ Years	143	2,240	638.5
<b>Days 181-270</b>			
00-21 Years	128	72,246	17.7
22-44 Years	96	42,715	22.5
45-64 Years	147	17,880	82.2
65+ Years	58	1,391	417.1
<b>Days 271-365</b>			
00-21 Years	70	53,324	13.1
22-44 Years	57	32,367	17.6
45-64 Years	92	14,104	65.2
65+ Years	42	1,031	407.2
<b>Days 366-730</b>			
00-21 Years	204	117,849	17.3
22-44 Years	114	66,665	17.1
45-64 Years	197	31,300	62.9
65+ Years	78	2,096	372.1
<b>Days 731-1,095</b>			
00-21 Years	115	57,961	19.8
22-44 Years	63	27,517	22.9
45-64 Years	103	14,642	70.3
65+ Years	27	821	328.9
<b>90-Day Episode Gap/Extension Period</b>			

**Table 2b: Rate of Heart Failure Outcomes at Different Stages of Attention Deficit and Hyperactivity Disorder (ADHD) Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>Days 0-90</b>			
00-21 Years	369	255,158	14.5
22-44 Years	395	144,055	27.4
45-64 Years	766	61,470	124.6
65+ Years	653	7,135	915.2
<b>Days 91-180</b>			
00-21 Years	183	159,833	11.4
22-44 Years	219	90,392	24.2
45-64 Years	360	36,464	98.7
65+ Years	292	3,760	776.6
<b>Days 181-270</b>			
00-21 Years	165	128,201	12.9
22-44 Years	136	65,825	20.7
45-64 Years	227	27,541	82.4
65+ Years	126	2,289	550.4
<b>Days 271-365</b>			
00-21 Years	117	106,823	11.0
22-44 Years	93	53,224	17.5
45-64 Years	146	23,049	63.3
65+ Years	78	1,779	438.5
<b>Days 366-730</b>			
00-21 Years	375	255,145	14.7
22-44 Years	203	117,892	17.2
45-64 Years	370	55,880	66.2
65+ Years	143	4,064	351.9
<b>Days 731-1,095</b>			
00-21 Years	203	129,747	15.6
22-44 Years	111	52,368	21.2
45-64 Years	192	28,731	66.8
65+ Years	54	1,780	303.4

**Table 3a: Summary of Attention Deficit and Hyperactivity Disorder (ADHD) Medications and Subsequent Heart Failures in the Sentinel Distributed Database (SDD) between January 1, 2000 and March 3, 2016 by Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>30-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
Female	897,388	897,388	5,309,261	176,261,944	271,247,645	558,644.4	2,144	56,071,570	157,855,915.2	16.00	196.42	5.92	33.20	38.38
Male	1,115,480	1,115,480	6,626,744	223,674,717	330,484,423	701,866.1	2,275	54,201,402	146,435,798.3	20.58	200.52	5.94	33.75	32.41
Unknown	80	80	398	12,518	16,957	40.4	0	5,710	12,681.4	14.01	156.48	4.98	31.45	0.00
<b>90-Day Blackout Period</b>														
Female	530,465	530,465	5,018,075	169,595,832	259,248,930	387,194.0	1,240	51,321,978	143,287,832.7	10.34	319.71	9.46	33.80	32.03
Male	669,676	669,676	6,309,737	216,836,291	312,934,185	490,301.6	1,370	49,468,198	132,593,323.3	13.54	323.79	9.42	34.37	27.94
Unknown	43	43	354	11,419	15,823	24.7	0	4,827	11,289.4	8.91	265.56	8.23	32.26	0.00
<b>180-Day Blackout Period</b>														
Female	308,098	308,098	4,431,849	151,803,670	233,226,512	296,358.8	868	47,747,039	130,015,568.6	6.45	492.71	14.38	34.25	29.29
Male	380,474	380,474	5,564,796	193,945,521	280,690,145	377,189.2	1,041	45,877,883	119,999,690.3	8.29	509.75	14.63	34.85	27.60
Unknown	20	20	264	8,927	12,614	17.4	0	4,160	10,117.8	4.81	446.35	13.20	33.81	0.00
<b>270-Day Blackout Period</b>														
Female	211,872	211,872	3,920,394	135,656,689	209,470,119	236,225.3	669	40,898,957	118,748,126.1	5.18	640.28	18.50	34.60	28.32
Male	257,326	257,326	4,916,331	173,173,062	251,939,752	303,093.8	811	39,180,168	109,291,274.3	6.57	672.97	19.11	35.22	26.76
Unknown	11	11	226	7,587	10,771	14.2	0	3,301	9,206.5	3.33	689.73	20.55	33.57	0.00
<b>365-Day Blackout Period</b>														
Female	153,646	153,646	3,450,221	120,574,761	187,307,055	190,617.8	536	36,882,874	107,989,676.2	4.17	784.76	22.46	34.95	28.12
Male	185,688	185,688	4,345,206	154,624,831	225,978,969	247,877.4	683	35,195,213	99,091,808.1	5.28	832.71	23.40	35.59	27.55
Unknown	7	7	202	6,494	9,378	11.9	0	2,916	8,353.3	2.40	927.71	28.86	32.15	0.00
<b>730-Day Blackout Period</b>														
Female	62,728	62,728	2,182,088	78,797,240	124,754,266	92,887.1	257	25,089,931	75,935,899.2	2.50	1256.17	34.79	36.11	27.67
Male	78,950	78,950	2,862,041	105,218,089	154,601,581	127,703.6	369	23,665,255	68,872,219.1	3.34	1332.72	36.25	36.76	28.90
Unknown	3	3	129	4,314	6,792	6.9	0	1,893	5,876.3	1.58	1438.00	43.00	33.44	0.00
<b>1,095-Day Blackout Period</b>														
Female	30,527	30,527	1,383,689	51,589,260	82,755,144	48,818.5	122	17,741,954	54,256,313.6	1.72	1689.96	45.33	37.28	24.99
Male	40,506	40,506	1,901,784	72,222,910	106,843,751	70,834.0	196	16,532,714	48,666,642.7	2.45	1783.02	46.95	37.98	27.67
Unknown	2	2	110	3,441	5,485	4.7	0	1,319	4,233.8	1.52	1720.50	55.00	31.28	0.00
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
Female	897,388	897,388	7,286,381	243,284,471	375,817,978	909,803.7	3,172	56,071,570	157,855,915.2	16.00	271.10	8.12	33.39	34.86
Male	1,115,480	1,115,480	9,228,503	312,938,337	460,449,513	1,159,952.1	3,445	54,201,402	146,435,798.6	20.58	280.54	8.27	33.91	29.70
Unknown	80	80	543	17,637	22,778	65.0	0	5,710	12,681.4	14.01	220.46	6.79	32.48	0.00
<b>90-Day Blackout Period</b>														
Female	800,516	800,516	7,136,522	239,848,186	370,788,876	701,632.2	2,100	51,321,976	142,932,471.9	15.60	299.62	8.91	33.61	29.93
Male	1,000,699	1,000,699	9,049,845	308,817,495	454,669,828	900,324.6	2,334	49,468,191	132,139,658.1	20.23	308.60	9.04	34.12	25.92
Unknown	69	69	523	17,152	22,187	46.5	0	4,827	11,273.6	14.29	248.58	7.58	32.80	0.00

**Table 3a: Summary of Attention Deficit and Hyperactivity Disorder (ADHD) Medications and Subsequent Heart Failures in the Sentinel Distributed Database (SDD) between January 1, 2000 and March 3, 2016 by Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>180-Day Blackout Period</b>														
Female	517,549	517,549	6,871,453	233,292,443	359,826,679	571,423.8	1,556	47,747,038	129,842,949.4	10.84	450.76	13.28	33.95	27.23
Male	656,133	656,133	8,785,099	302,775,053	438,959,804	740,096.4	1,824	45,877,871	119,739,413.6	14.30	461.45	13.39	34.46	24.65
Unknown	36	36	440	15,006	19,805	34.4	0	4,160	10,108.2	8.65	416.83	12.22	34.10	0.00
<b>270-Day Blackout Period</b>														
Female	384,010	384,010	6,421,054	219,818,506	339,933,005	472,177.2	1,249	40,898,956	118,644,855.2	9.39	572.43	16.72	34.23	26.45
Male	485,079	485,079	8,235,072	286,116,465	415,662,286	615,494.1	1,477	39,180,162	109,129,676.7	12.38	589.83	16.98	34.74	24.00
Unknown	22	22	387	13,274	17,155	27.4	0	3,301	9,197.5	6.66	603.36	17.59	34.30	0.00
<b>365-Day Blackout Period</b>														
Female	292,362	292,362	5,891,188	203,240,618	315,384,258	390,260.6	1,031	36,882,874	107,927,152.1	7.93	695.17	20.15	34.50	26.42
Male	366,907	366,907	7,573,176	265,157,089	386,041,422	512,540.8	1,261	35,195,207	98,990,474.8	10.42	722.68	20.64	35.01	24.60
Unknown	13	13	331	11,506	15,085	22.9	0	2,916	8,340.8	4.46	885.08	25.46	34.76	0.00
<b>730-Day Blackout Period</b>														
Female	130,127	130,127	4,078,421	144,471,682	227,640,381	199,032.1	523	25,089,931	75,922,162.6	5.19	1110.24	31.34	35.42	26.28
Male	165,617	165,617	5,363,752	192,616,723	282,337,539	270,799.5	678	23,665,254	68,848,357.8	7.00	1163.03	32.39	35.91	25.04
Unknown	9	9	259	9,216	12,154	11.8	0	1,893	5,865.9	4.75	1024.00	28.78	35.58	0.00
<b>1,095-Day Blackout Period</b>														
Female	65,647	65,647	2,713,558	98,730,013	157,823,354	106,226.2	268	17,741,954	54,252,719.6	3.70	1503.95	41.34	36.38	25.23
Male	86,375	86,375	3,699,993	136,348,702	201,143,157	150,984.1	373	16,532,714	48,659,734.3	5.22	1578.57	42.84	36.85	24.70
Unknown	3	3	166	5,113	7,187	6.6	0	1,319	4,233.8	2.27	1704.33	55.33	30.80	0.00

**Table 3b: Rate of Heart Failure Outcomes at Different Stages of Attention Deficit and Hyperactivity Disorder (ADHD) Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>30-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
Female	904	171,450	52.7
Male	905	211,564	42.8
Unknown	0	16	0.0
<b>Days 91-180</b>			
Female	372	90,835	41.0
Male	329	113,112	29.1
Unknown	0	7	0.0
<b>Days 181-270</b>			
Female	199	60,133	33.1
Male	230	74,095	31.0
Unknown	0	3	0.0
<b>Days 271-365</b>			
Female	133	45,608	29.2
Male	128	55,216	23.2
Unknown	0	2	0.0
<b>Days 366-730</b>			
Female	279	97,731	28.5
Male	314	120,174	26.1
Unknown	0	5	0.0
<b>Days 731-1,095</b>			
Female	135	44,069	30.6
Male	173	56,870	30.4
Unknown	0	2	0.0
<b>90-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
Female	1,072	208,172	51.5
Male	1,111	259,627	42.8
Unknown	0	18	0.0

**Table 3b: Rate of Heart Failure Outcomes at Different Stages of Attention Deficit and Hyperactivity Disorder (ADHD) Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>Days 91-180</b>			
Female	544	130,208	41.8
Male	510	160,228	31.8
Unknown	0	12	0.0
<b>Days 181-270</b>			
Female	307	99,247	30.9
Male	347	124,602	27.8
Unknown	0	7	0.0
<b>Days 271-365</b>			
Female	218	81,917	26.6
Male	216	102,953	21.0
Unknown	0	4	0.0
<b>Days 366-730</b>			
Female	508	191,228	26.6
Male	583	241,741	24.1
Unknown	0	11	0.0
<b>Days 731-1,095</b>			
Female	255	92,806	27.5
Male	305	119,815	25.5
Unknown	0	5	0.0

**Table 4a: Summary of Attention Deficit and Hyperactivity Disorder (ADHD) Medications and Subsequent Heart Failures in the Sentinel Distributed Database (SDD) between January 1, 2000 and March 3, 2016 by Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>30-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
2000	10,073	10,073	46,881	2,232,971	4,818,086	6,867.5	55	6,528,505	2,996,063.5	1.54	221.68	4.65	47.63	80.09
2001	23,781	23,781	117,849	5,214,146	10,393,469	16,071.0	122	7,124,941	5,951,031.9	3.34	219.26	4.96	44.24	75.91
2002	22,030	22,030	125,545	5,669,327	10,344,964	16,902.7	140	7,268,912	6,044,597.6	3.03	257.35	5.70	45.16	82.83
2003	39,557	39,557	356,513	13,550,731	28,021,376	38,727.1	246	7,256,450	6,013,488.8	5.45	342.56	9.01	38.01	63.52
2004	36,743	36,743	279,313	10,941,569	25,962,137	32,025.5	265	7,684,048	6,252,434.1	4.78	297.79	7.60	39.17	82.75
2005	32,185	32,185	227,843	9,117,595	15,015,893	26,904.9	224	7,914,335	6,533,766.8	4.07	283.29	7.08	40.02	83.26
2006	64,172	64,172	444,992	16,283,744	24,980,455	49,568.2	276	19,377,486	11,560,151.7	3.31	253.75	6.93	36.59	55.68
2007	101,120	101,120	708,421	24,761,682	36,723,656	76,047.6	406	23,558,641	17,103,857.2	4.29	244.87	7.01	34.95	53.39
2008	185,170	185,170	1,202,030	40,414,284	65,126,469	126,608.4	418	44,233,171	27,926,872.3	4.19	218.26	6.49	33.62	33.02
2009	252,256	252,256	1,635,005	54,111,194	76,946,563	170,229.2	502	45,583,547	35,375,937.5	5.53	214.51	6.48	33.10	29.49
2010	248,418	248,418	1,626,636	53,237,767	74,621,591	168,116.1	426	43,399,441	33,837,684.3	5.72	214.31	6.55	32.73	25.34
2011	243,313	243,313	1,557,620	50,518,863	70,151,577	160,541.4	374	41,957,157	33,010,289.8	5.80	207.63	6.40	32.43	23.30
2012	232,052	232,052	1,406,048	45,446,610	62,736,316	145,723.0	307	40,906,211	32,312,504.6	5.67	195.85	6.06	32.32	21.07
2013	220,759	220,759	1,167,482	37,150,024	52,212,407	121,207.4	354	40,739,384	31,970,797.5	5.42	168.28	5.29	31.82	29.21
2014	208,694	208,694	828,345	25,518,623	35,589,657	85,557.5	252	41,657,540	31,834,173.8	5.01	122.28	3.97	30.81	29.45
2015	92,625	92,625	205,880	5,780,049	8,104,410	19,453.5	52	34,274,854	15,580,743.3	2.70	62.40	2.22	28.07	26.73
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>90-Day Blackout Period</b>														
2000	5,612	5,612	41,738	2,072,486	4,470,001	4,723.8	33	6,271,124	2,822,037.9	0.89	369.30	7.44	49.65	69.86
2001	12,779	12,779	106,166	4,871,775	9,686,429	11,185.8	79	6,792,835	5,668,922.3	1.88	381.23	8.31	45.89	70.63
2002	12,941	12,941	118,928	5,526,485	10,148,243	12,665.4	103	6,954,734	5,740,234.3	1.86	427.05	9.19	46.47	81.32
2003	26,090	26,090	376,047	14,343,740	30,415,372	33,383.7	191	6,902,033	5,720,069.3	3.78	549.78	14.41	38.14	57.21
2004	23,960	23,960	277,251	11,004,949	22,902,523	25,378.4	182	7,419,221	5,966,400.0	3.23	459.31	11.57	39.69	71.71
2005	20,302	20,302	223,485	9,090,082	14,848,858	20,976.5	169	7,567,408	6,181,224.8	2.68	447.74	11.01	40.67	80.57
2006	37,857	37,857	425,138	15,839,432	24,228,289	37,200.5	189	18,277,819	10,858,946.7	2.07	418.40	11.23	37.26	50.81
2007	59,382	59,382	674,346	23,955,548	35,467,985	56,409.2	230	22,110,220	16,065,156.2	2.69	403.41	11.36	35.52	40.77
2008	106,249	106,249	1,132,811	38,708,895	55,531,211	90,523.2	232	41,827,414	25,705,878.0	2.54	364.32	10.66	34.17	25.63
2009	148,023	148,023	1,545,392	51,913,079	73,685,996	120,908.4	286	42,459,607	32,580,742.8	3.49	350.71	10.44	33.59	23.65
2010	152,104	152,104	1,560,339	51,776,549	72,450,830	120,508.1	220	40,671,676	31,302,280.8	3.74	340.40	10.26	33.18	18.26
2011	151,328	151,328	1,498,894	49,288,044	68,222,044	114,116.1	199	39,547,056	30,660,003.8	3.83	325.70	9.90	32.88	17.44
2012	147,424	147,424	1,359,381	44,541,339	61,319,779	101,652.9	177	39,120,462	30,146,502.5	3.77	302.13	9.22	32.77	17.41
2013	139,266	139,266	1,114,133	35,991,721	50,503,949	78,677.4	191	38,400,778	29,675,580.7	3.63	258.44	8.00	32.30	24.28
2014	129,123	129,123	760,470	23,878,502	33,192,212	44,413.5	120	38,992,459	29,132,269.5	3.31	184.93	5.89	31.40	27.02
2015	27,744	27,744	113,647	3,640,916	5,125,216	4,797.2	9	22,916,189	7,666,195.9	1.21	131.23	4.10	32.04	18.76
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>180-Day Blackout Period</b>														
2000	2,879	2,879	35,938	1,809,717	3,941,651	3,713.6	29	6,000,861	2,668,686.9	0.48	628.59	12.48	50.36	78.09
2001	6,639	6,639	92,087	4,302,703	8,581,717	8,924.5	59	6,564,344	5,409,180.9	1.01	648.10	13.87	46.72	66.11
2002	7,222	7,222	106,776	5,079,919	9,378,133	10,520.4	87	6,681,565	5,451,185.7	1.08	703.40	14.78	47.58	82.70
2003	16,363	16,363	358,263	13,748,103	29,780,842	29,140.4	161	6,653,960	5,454,419.3	2.46	840.19	21.89	38.37	55.25
2004	14,869	14,869	257,352	10,338,145	19,955,823	21,248.8	152	7,089,660	5,701,356.7	2.10	695.28	17.31	40.17	71.53
2005	12,144	12,144	205,745	8,503,090	13,899,943	17,625.9	130	7,308,360	5,852,082.1	1.66	700.19	16.94	41.33	73.76
2006	22,806	22,806	389,620	14,706,772	22,512,269	30,713.1	153	17,569,273	10,218,513.9	1.30	644.86	17.08	37.75	49.82
2007	35,165	35,165	614,331	22,075,630	32,743,830	46,193.2	171	21,016,855	15,118,273.8	1.67	627.77	17.47	35.93	37.02
2008	61,933	61,933	1,016,781	35,146,665	50,630,382	72,027.6	158	39,154,581	23,690,789.5	1.58	567.49	16.42	34.57	21.94
2009	85,565	85,565	1,381,096	46,914,075	66,900,897	95,271.7	216	40,435,968	30,022,398.8	2.12	548.29	16.14	33.97	22.67
2010	89,606	89,606	1,398,709	46,896,599	65,837,269	94,288.1	156	38,792,742	28,983,870.6	2.31	523.36	15.61	33.53	16.55
2011	89,707	89,707	1,344,485	44,676,183	62,002,560	88,473.0	131	37,811,776	28,465,324.8	2.37	498.02	14.99	33.23	14.81
2012	88,653	88,653	1,213,362	40,163,640	55,459,132	76,513.1	126	36,944,969	28,110,149.9	2.40	453.04	13.69	33.10	16.47
2013	82,278	82,278	969,547	31,650,758	44,634,162	54,946.9	124	36,793,275	27,506,858.5	2.24	384.68	11.78	32.64	22.57
2014	65,008	65,008	565,739	18,108,580	25,330,037	22,860.3	56	36,337,891	23,777,910.7	1.79	278.56	8.70	32.01	24.50

**Table 4a: Summary of Attention Deficit and Hyperactivity Disorder (ADHD) Medications and Subsequent Heart Failures in the Sentinel Distributed Database (SDD) between January 1, 2000 and March 3, 2016 by Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2015	7,755	7,755	47,078	1,637,539	2,340,624	1,104.8	0	13,573,031	3,594,374.6	0.57	211.16	6.07	34.78	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>270-Day Blackout Period</b>														
2000	1,827	1,827	31,813	1,620,336	3,558,287	3,134.2	26	5,556,700	2,575,583.1	0.33	886.88	17.41	50.93	82.95
2001	4,336	4,336	82,545	3,895,867	7,824,460	7,604.6	48	6,239,294	5,172,487.9	0.69	898.49	19.04	47.20	63.12
2002	4,881	4,881	97,211	4,685,665	8,710,060	9,122.8	73	6,327,865	5,194,819.8	0.77	959.98	19.92	48.20	80.02
2003	12,452	12,452	341,147	13,127,209	28,612,607	25,854.1	143	6,271,884	5,218,684.5	1.99	1054.22	27.40	38.48	55.31
2004	10,689	10,689	237,726	9,640,380	17,918,050	18,317.3	129	6,682,289	5,463,654.5	1.60	901.90	22.24	40.55	70.43
2005	8,391	8,391	189,114	7,911,770	12,983,445	15,387.6	106	6,841,074	5,561,451.0	1.23	942.89	22.54	41.84	68.89
2006	15,909	15,909	356,477	13,583,230	20,892,181	26,230.9	136	16,117,223	9,726,886.4	0.99	853.81	22.41	38.10	51.85
2007	24,646	24,646	560,223	20,312,086	30,260,803	39,198.7	117	19,507,389	14,302,985.3	1.26	824.15	22.73	36.26	29.85
2008	43,088	43,088	917,502	31,989,023	46,302,651	59,676.7	122	34,980,373	22,225,652.4	1.23	742.41	21.29	34.87	20.44
2009	59,684	59,684	1,243,344	42,555,645	60,930,056	78,216.2	166	36,915,935	27,856,447.6	1.62	713.02	20.83	34.23	21.22
2010	62,891	62,891	1,258,991	42,515,305	59,941,708	76,663.9	110	35,491,114	27,016,037.5	1.77	676.02	20.02	33.77	14.35
2011	62,925	62,925	1,205,307	40,337,297	56,111,328	70,915.0	101	34,681,882	26,573,418.0	1.81	641.04	19.15	33.47	14.24
2012	62,925	62,925	1,079,521	35,992,235	49,839,726	59,014.9	89	33,840,673	26,403,912.2	1.86	571.99	17.16	33.34	15.08
2013	57,574	57,574	838,746	27,577,442	39,079,709	38,774.6	86	33,808,952	25,586,376.1	1.70	478.99	14.57	32.88	22.18
2014	35,858	35,858	390,064	12,761,814	17,954,964	11,098.6	28	31,963,743	18,138,805.0	1.12	355.90	10.88	32.72	25.23
2015	1,133	1,133	7,220	332,034	500,607	7.2	0	9,117,746	1,031,405.7	0.12	293.06	6.37	45.99	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>365-Day Blackout Period</b>														
2000	1,294	1,294	28,713	1,477,356	3,272,297	2,728.7	25	5,308,553	2,486,852.0	0.24	1141.70	22.19	51.45	91.62
2001	3,164	3,164	75,007	3,580,376	7,227,757	6,640.7	40	5,774,591	4,927,903.9	0.55	1131.60	23.71	47.73	60.23
2002	3,654	3,654	90,023	4,369,841	8,167,513	8,069.6	65	5,830,948	4,954,985.4	0.63	1195.91	24.64	48.54	80.55
2003	9,786	9,786	322,065	12,462,805	27,137,464	23,117.1	132	5,852,369	4,989,967.4	1.67	1273.53	32.91	38.70	57.10
2004	8,061	8,061	218,657	8,959,569	16,429,652	15,976.3	117	6,393,943	5,221,951.4	1.26	1111.47	27.13	40.98	73.23
2005	6,370	6,370	175,733	7,403,779	12,202,855	13,606.5	93	6,232,444	5,288,536.5	1.02	1162.29	27.59	42.13	68.35
2006	11,824	11,824	326,613	12,551,245	19,367,335	22,805.6	118	14,950,192	9,249,652.2	0.79	1061.51	27.62	38.43	51.74
2007	18,860	18,860	516,820	18,875,826	28,239,133	33,840.8	94	17,876,690	13,520,744.5	1.06	1000.84	27.40	36.52	27.78
2008	31,962	31,962	829,903	29,156,697	42,381,478	50,281.7	101	32,588,109	20,825,408.0	0.98	912.23	25.97	35.13	20.09
2009	44,044	44,044	1,118,090	38,554,006	55,346,913	65,216.2	135	32,127,034	25,751,386.4	1.37	875.35	25.39	34.48	20.70
2010	46,718	46,718	1,129,178	38,396,279	54,292,829	62,976.8	92	31,148,239	25,143,032.5	1.50	821.87	24.17	34.00	14.61
2011	46,773	46,773	1,075,923	36,249,746	50,522,480	57,294.5	76	30,515,011	24,724,891.2	1.53	775.01	23.00	33.69	13.26
2012	46,956	46,956	952,210	31,962,319	44,369,523	45,346.5	66	32,107,957	24,731,403.3	1.46	680.69	20.28	33.57	14.55
2013	42,344	42,344	714,334	23,649,435	33,587,273	26,264.7	56	29,540,364	23,697,188.5	1.43	558.51	16.87	33.11	21.32
2014	17,531	17,531	222,360	7,556,807	10,750,901	4,341.3	9	24,777,704	11,575,934.2	0.71	431.05	12.68	33.98	20.73
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>730-Day Blackout Period</b>														
2000	651	651	22,355	1,172,496	2,603,703	1,823.5	17	4,472,253	2,102,706.0	0.15	1801.07	34.34	52.45	93.23
2001	1,530	1,530	56,898	2,810,134	5,734,392	4,444.7	27	4,798,130	4,155,884.0	0.32	1836.69	37.19	49.39	60.75
2002	1,918	1,918	70,820	3,538,078	6,714,957	5,479.8	41	4,865,966	4,226,363.7	0.39	1844.67	36.92	49.96	74.82
2003	5,815	5,815	270,018	10,586,560	22,081,355	15,730.8	98	5,026,184	4,274,333.0	1.16	1820.56	46.43	39.21	62.30
2004	3,781	3,781	162,964	6,932,634	12,278,591	10,544.6	72	5,309,479	4,319,411.4	0.71	1833.55	43.10	42.54	68.28
2005	3,331	3,331	139,611	6,009,116	9,907,605	9,171.7	46	5,224,568	4,518,528.6	0.64	1804.00	41.91	43.04	50.15
2006	5,976	5,976	250,959	9,850,234	15,252,604	14,649.4	34	12,088,301	7,672,762.5	0.49	1648.30	41.99	39.25	23.21
2007	9,427	9,427	390,206	14,552,131	21,869,996	20,774.3	45	14,481,828	10,817,986.4	0.65	1543.67	41.39	37.29	21.66
2008	15,233	15,233	600,063	21,543,056	31,519,050	28,671.2	60	24,134,456	16,017,982.3	0.63	1414.24	39.39	35.90	20.93
2009	20,662	20,662	792,422	27,881,609	40,135,616	35,447.7	71	23,892,209	19,741,754.9	0.86	1349.41	38.35	35.19	20.03
2010	21,366	21,366	773,280	26,827,833	37,893,303	31,734.6	43	23,490,633	19,385,046.4	0.91	1255.63	36.19	34.69	13.55
2011	22,546	22,546	736,854	25,297,759	35,387,828	25,463.3	40	24,765,799	19,568,112.3	0.91	1122.05	32.68	34.33	15.71
2012	20,735	20,735	580,578	19,940,647	27,718,488	14,254.3	25	24,547,471	18,839,968.6	0.84	961.69	28.00	34.35	17.54



**Table 4a: Summary of Attention Deficit and Hyperactivity Disorder (ADHD) Medications and Subsequent Heart Failures in the Sentinel Distributed Database (SDD) between January 1, 2000 and March 3, 2016 by Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2013	8,710	8,710	197,230	7,077,356	10,265,152	2,407.7	7	18,912,052	9,173,154.4	0.46	812.56	22.64	35.88	29.07
2014	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>1,095-Day Blackout Period</b>														
2000	414	414	17,903	965,680	2,150,312	1,305.2	12	3,815,304	1,806,471.1	0.11	2332.56	43.24	53.94	91.94
2001	984	984	46,099	2,333,320	4,763,651	3,218.3	16	4,106,384	3,609,920.6	0.24	2371.26	46.85	50.62	49.72
2002	1,246	1,246	56,932	2,926,608	5,605,681	3,936.2	20	4,274,287	3,683,668.1	0.29	2348.80	45.69	51.41	50.81
2003	3,557	3,557	213,633	8,592,318	17,051,420	11,249.6	61	4,276,056	3,584,235.5	0.83	2415.61	60.06	40.22	54.22
2004	2,420	2,420	131,949	5,718,185	9,555,261	7,519.7	39	4,485,118	3,756,821.1	0.54	2362.89	54.52	43.34	51.86
2005	2,151	2,151	113,411	4,962,746	8,206,101	6,509.7	16	4,514,953	3,941,019.8	0.48	2307.18	52.72	43.76	24.58
2006	3,802	3,802	201,259	8,008,144	12,426,383	9,932.7	20	9,874,826	6,410,292.0	0.39	2106.30	52.94	39.79	20.14
2007	5,830	5,830	303,214	11,521,897	17,336,334	13,415.0	30	11,685,705	8,935,099.5	0.50	1976.31	52.01	38.00	22.36
2008	8,970	8,970	445,726	16,295,062	23,909,483	17,131.1	32	18,691,666	12,886,922.3	0.48	1816.62	49.69	36.56	18.68
2009	11,853	11,853	570,406	20,429,039	29,327,767	19,807.2	42	18,566,893	15,598,244.7	0.64	1723.53	48.12	35.81	21.20
2010	12,512	12,512	549,570	19,384,503	27,359,438	15,396.9	20	19,670,338	15,781,071.0	0.64	1549.27	43.92	35.27	12.99
2011	12,188	12,188	473,097	16,574,085	23,286,501	8,821.7	9	19,624,130	15,302,221.9	0.62	1359.87	38.82	35.03	10.20
2012	5,108	5,108	162,384	6,104,024	8,626,048	1,414.0	1	17,015,021	7,631,202.7	0.30	1194.99	31.79	37.59	7.07
2013	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2014	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
2000	10,073	10,073	73,754	3,520,359	7,383,599	12,709.7	83	6,528,505	2,996,063.5	1.54	349.48	7.32	47.73	65.30
2001	23,781	23,781	189,239	8,321,905	16,294,881	30,262.2	186	7,124,941	5,951,031.9	3.34	349.94	7.96	43.98	61.46
2002	22,030	22,030	204,830	9,054,989	16,910,000	31,341.2	207	7,268,912	6,044,597.6	3.03	411.03	9.30	44.21	66.05
2003	39,557	39,557	574,401	21,580,833	44,683,703	69,689.4	413	7,256,450	6,013,488.8	5.45	545.56	14.52	37.57	59.26
2004	36,743	36,743	409,366	16,068,313	34,381,235	54,349.5	385	7,684,048	6,252,434.1	4.78	437.32	11.14	39.25	70.84
2005	32,185	32,185	341,536	13,646,139	22,014,281	46,632.6	321	7,914,335	6,533,766.8	4.07	423.99	10.61	39.96	68.84
2006	64,172	64,172	651,087	23,798,845	36,320,005	85,050.1	394	19,377,486	11,560,151.7	3.31	370.86	10.15	36.55	46.33
2007	101,120	101,120	1,021,044	35,672,426	53,125,662	129,014.5	568	23,558,641	17,103,857.2	4.29	352.77	10.10	34.94	44.03
2008	185,170	185,170	1,707,222	57,537,400	89,863,608	213,370.8	625	44,233,171	27,926,872.3	4.19	310.73	9.22	33.70	29.29
2009	252,255	252,255	2,315,290	76,751,013	109,346,180	285,730.3	772	45,583,547	35,375,937.5	5.53	304.26	9.18	33.15	27.02
2010	248,418	248,418	2,278,762	74,793,546	105,053,548	279,600.0	688	43,399,441	33,837,684.3	5.72	301.08	9.17	32.82	24.61
2011	243,313	243,313	2,148,632	69,880,424	97,486,616	263,672.5	571	41,957,157	33,010,289.8	5.80	287.20	8.83	32.52	21.66
2012	232,053	232,053	1,888,527	61,135,574	84,675,893	234,332.1	474	40,906,212	32,312,505.0	5.67	263.46	8.14	32.37	20.23
2013	220,759	220,759	1,507,494	47,993,099	67,642,390	188,199.5	529	40,739,384	31,970,797.5	5.42	217.40	6.83	31.84	28.11
2014	208,694	208,694	984,820	30,319,963	42,436,377	122,044.2	339	41,657,540	31,834,173.8	5.01	145.28	4.72	30.79	27.78
2015	92,625	92,625	219,423	6,165,617	8,672,292	23,822.2	62	34,274,854	15,580,743.3	2.70	66.57	2.37	28.10	26.03
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>90-Day Blackout Period</b>														
2000	9,445	9,445	72,760	3,494,588	7,331,191	10,304.4	61	6,271,124	2,822,037.9	1.51	369.99	7.70	48.03	59.20
2001	22,799	22,799	187,426	8,272,635	16,202,177	24,528.4	137	6,790,396	5,667,396.1	3.36	362.85	8.22	44.14	55.85
2002	21,034	21,034	203,143	9,009,043	16,815,309	26,051.6	161	6,945,424	5,733,970.3	3.03	428.31	9.66	44.35	61.80
2003	38,086	38,086	572,088	21,520,542	44,619,173	60,187.9	338	6,888,450	5,710,901.7	5.53	565.05	15.02	37.62	56.16
2004	35,061	35,061	406,287	15,989,625	34,079,126	45,531.9	281	7,400,902	5,953,512.6	4.74	456.05	11.59	39.36	61.72
2005	30,527	30,527	339,244	13,595,688	21,932,085	38,994.6	247	7,541,979	6,162,713.5	4.05	445.37	11.11	40.08	63.34
2006	59,966	59,966	644,459	23,642,083	36,088,286	69,835.8	290	18,247,972	10,836,107.0	3.29	394.26	10.75	36.69	41.53
2007	94,439	94,439	1,009,471	35,386,748	52,702,492	105,004.4	358	22,068,451	16,033,988.7	4.28	374.70	10.69	35.05	34.09
2008	168,111	168,111	1,680,551	56,916,060	88,983,108	169,927.8	403	41,766,612	25,661,336.2	4.03	338.56	10.00	33.87	23.72
2009	230,285	230,285	2,281,344	75,960,085	108,238,917	226,448.0	519	42,370,820	32,517,771.4	5.43	329.85	9.91	33.30	22.92

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	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2010	227,048	227,048	2,245,599	74,034,853	103,975,564	221,207.2	429	40,550,260	31,215,942.0	5.60	326.08	9.89	32.97	19.39
2011	222,786	222,786	2,117,268	69,173,394	96,502,045	206,524.4	366	39,400,576	30,554,699.3	5.65	310.49	9.50	32.67	17.72
2012	213,580	213,580	1,861,390	60,524,622	83,838,215	179,769.3	319	38,955,830	30,026,864.8	5.48	283.38	8.72	32.52	17.74
2013	201,729	201,729	1,478,966	47,347,438	66,746,134	136,452.1	334	38,223,298	29,545,106.0	5.28	234.71	7.33	32.01	24.48
2014	186,169	186,169	949,952	29,524,402	41,322,116	73,581.1	177	38,811,968	29,002,879.0	4.80	158.59	5.10	31.08	24.06
2015	40,219	40,219	136,942	4,291,027	6,104,953	7,654.5	14	22,818,967	7,638,176.9	1.76	106.69	3.40	31.33	18.29
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>180-Day Blackout Period</b>														
2000	5,968	5,968	67,591	3,321,370	6,962,901	8,433.6	52	6,000,861	2,668,686.9	0.99	556.53	11.33	49.14	61.66
2001	13,959	13,959	177,087	7,962,647	15,551,684	20,406.9	106	6,563,113	5,408,787.0	2.13	570.43	12.69	44.96	51.94
2002	13,951	13,951	202,252	9,068,071	16,969,162	23,013.9	144	6,676,775	5,448,740.8	2.09	649.99	14.50	44.84	62.57
2003	28,001	28,001	612,788	23,004,761	48,557,518	57,841.3	313	6,646,256	5,450,109.1	4.21	821.57	21.88	37.54	54.11
2004	24,341	24,341	408,958	16,213,658	30,932,895	40,577.9	240	7,078,319	5,694,835.2	3.44	666.10	16.80	39.65	59.15
2005	20,547	20,547	338,393	13,670,712	21,929,572	34,579.6	199	7,291,548	5,841,750.3	2.82	665.34	16.47	40.40	57.55
2006	38,853	38,853	630,316	23,349,417	35,591,310	60,146.4	247	17,548,140	10,204,397.5	2.21	600.97	16.22	37.04	41.07
2007	60,672	60,672	982,875	34,775,996	51,762,735	89,589.0	261	20,989,745	15,100,381.1	2.89	573.18	16.20	35.38	29.13
2008	106,964	106,964	1,620,918	55,372,900	79,741,662	141,778.9	283	39,117,424	23,666,658.4	2.73	517.68	15.15	34.16	19.96
2009	148,506	148,506	2,205,808	74,016,002	105,520,600	188,039.7	396	40,385,164	29,991,035.0	3.68	498.40	14.85	33.56	21.06
2010	152,078	152,078	2,198,132	73,005,630	102,566,428	184,944.7	321	38,722,262	28,940,549.9	3.93	480.05	14.45	33.21	17.36
2011	151,288	151,288	2,076,410	68,343,594	95,340,330	171,034.6	262	37,722,559	28,409,789.5	4.01	451.74	13.72	32.91	15.32
2012	147,793	147,793	1,829,357	59,921,446	83,012,963	145,474.6	235	36,840,642	28,043,118.6	4.01	405.44	12.38	32.76	16.15
2013	138,073	138,073	1,429,208	46,133,170	65,083,706	102,467.8	230	36,675,179	27,430,653.8	3.76	334.12	10.35	32.28	22.45
2014	109,395	109,395	808,810	25,611,565	35,978,446	41,295.6	90	36,218,366	23,709,337.9	3.02	234.12	7.39	31.67	21.79
2015	13,329	13,329	68,089	2,311,563	3,304,375	1,930.1	1	13,535,979	3,583,640.2	0.98	173.42	5.11	33.95	5.18
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>270-Day Blackout Period</b>														
2000	4,153	4,153	63,238	3,117,974	6,552,274	7,227.2	47	5,556,700	2,575,583.1	0.75	750.78	15.23	49.31	65.03
2001	9,744	9,744	166,173	7,523,119	14,700,955	17,677.3	88	6,238,865	5,172,422.3	1.56	772.08	17.05	45.27	49.78
2002	10,225	10,225	194,342	8,796,269	16,676,956	20,558.6	128	6,325,629	5,193,923.6	1.62	860.27	19.01	45.26	62.26
2003	22,864	22,864	609,568	22,897,434	48,731,354	53,089.7	289	6,267,844	5,216,714.2	3.65	1001.46	26.66	37.56	54.44
2004	18,787	18,787	397,644	15,858,288	28,905,294	36,259.4	210	6,675,697	5,460,344.0	2.81	844.11	21.17	39.88	57.92
2005	15,547	15,547	327,950	13,338,509	21,393,785	31,043.6	169	6,830,575	5,555,531.6	2.28	857.95	21.09	40.67	54.44
2006	29,733	29,733	607,077	22,624,332	34,509,615	52,798.0	223	16,103,098	9,718,055.5	1.85	760.92	20.42	37.27	42.24
2007	45,857	45,857	938,483	33,413,894	49,781,423	77,854.8	187	19,489,352	14,291,588.8	2.35	728.65	20.47	35.60	24.02
2008	80,913	80,913	1,538,076	52,881,312	76,301,556	120,633.2	228	34,955,941	22,210,407.1	2.31	653.56	19.01	34.38	18.90
2009	111,550	111,550	2,084,278	70,365,633	100,485,138	158,850.7	326	36,883,498	27,836,870.0	3.02	630.80	18.68	33.76	20.52
2010	116,001	116,001	2,086,675	69,700,346	98,064,045	155,655.1	242	35,445,751	26,989,185.3	3.27	600.86	17.99	33.40	15.55
2011	115,762	115,762	1,969,188	65,206,525	91,062,614	142,121.5	203	34,622,834	26,538,046.5	3.34	563.28	17.01	33.11	14.28
2012	114,476	114,476	1,730,455	57,028,483	79,126,452	117,054.5	173	33,769,691	26,359,807.6	3.39	498.17	15.12	32.96	14.78
2013	105,616	105,616	1,325,506	43,052,893	60,879,819	75,501.6	166	33,726,911	25,535,281.4	3.13	407.64	12.55	32.48	21.99
2014	65,827	65,827	606,394	19,629,345	27,663,229	21,152.0	47	31,885,749	18,101,506.1	2.06	298.20	9.21	32.37	22.22
2015	2,056	2,056	11,466	513,889	777,939	221.4	0	9,097,168	1,028,462.2	0.23	249.95	5.58	44.82	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>365-Day Blackout Period</b>														
2000	2,965	2,965	58,466	2,906,674	6,137,886	6,317.7	45	5,308,553	2,486,852.0	0.56	980.33	19.72	49.72	71.23
2001	7,312	7,312	155,308	7,082,443	13,908,929	15,505.1	76	5,774,542	4,927,900.9	1.27	968.61	21.24	45.60	49.02
2002	7,901	7,901	185,248	8,425,136	16,042,070	18,423.1	115	5,830,030	4,954,680.7	1.36	1066.34	23.45	45.48	62.42
2003	19,018	19,018	595,226	22,400,619	47,363,895	48,322.8	276	5,850,344	4,989,040.2	3.25	1177.86	31.30	37.63	57.12
2004	14,992	14,992	380,210	15,256,004	27,077,363	32,318.6	190	6,390,319	5,220,218.3	2.35	1017.61	25.36	40.13	58.79
2005	12,368	12,368	315,034	12,890,148	20,654,335	27,952.3	151	6,226,057	5,285,085.2	1.99	1042.22	25.47	40.92	54.02
2006	22,992	22,992	574,638	21,560,892	32,986,450	46,554.4	199	14,940,792	9,243,953.3	1.54	937.76	24.99	37.52	42.75
2007	36,131	36,131	888,132	31,816,247	47,524,801	67,962.1	151	17,864,899	13,513,137.3	2.02	880.58	24.58	35.82	22.22

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	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2008	62,462	62,462	1,438,374	49,736,822	71,976,056	103,101.2	190	32,572,085	20,815,349.7	1.92	796.27	23.03	34.58	18.43
2009	85,915	85,915	1,939,715	65,840,539	94,181,590	134,570.8	270	32,106,665	25,738,513.2	2.68	766.35	22.58	33.94	20.06
2010	90,474	90,474	1,946,333	65,335,822	92,117,137	130,731.8	205	31,119,800	25,125,767.5	2.91	722.15	21.51	33.57	15.68
2011	90,497	90,497	1,831,812	60,976,175	85,245,172	117,521.0	160	30,477,633	24,701,986.6	2.97	673.79	20.24	33.29	13.61
2012	90,480	90,480	1,600,710	53,028,483	73,642,341	92,389.2	134	32,060,104	24,702,019.1	2.82	586.08	17.69	33.13	14.50
2013	81,962	81,962	1,189,327	38,846,160	55,070,794	52,526.2	115	29,486,808	23,662,577.8	2.78	473.95	14.51	32.66	21.89
2014	33,813	33,813	366,162	12,307,049	17,511,946	8,628.0	15	24,738,590	11,558,885.9	1.37	363.97	10.83	33.61	17.39
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>730-Day Blackout Period</b>														
2000	1,501	1,501	47,221	2,396,341	5,093,824	4,261.7	29	4,472,253	2,102,706.0	0.34	1596.50	31.46	50.75	68.05
2001	3,628	3,628	124,435	5,788,103	11,435,212	10,370.9	46	4,798,130	4,155,884.0	0.76	1595.40	34.30	46.52	44.35
2002	4,420	4,420	155,432	7,173,303	13,839,236	12,685.6	70	4,865,950	4,226,362.2	0.91	1622.92	35.17	46.15	55.18
2003	11,817	11,817	525,837	19,940,499	40,233,620	34,001.3	219	5,025,968	4,274,261.0	2.35	1687.44	44.50	37.92	64.41
2004	7,749	7,749	306,871	12,627,044	21,982,888	21,917.0	119	5,308,903	4,319,168.1	1.46	1629.51	39.60	41.15	54.30
2005	6,896	6,896	267,027	11,076,337	17,820,978	19,414.3	85	5,223,273	4,517,940.0	1.32	1606.20	38.72	41.48	43.78
2006	12,420	12,420	469,994	17,929,818	27,527,358	30,506.9	62	12,085,705	7,671,378.2	1.03	1443.62	37.84	38.15	20.32
2007	18,975	18,975	709,596	25,839,767	38,781,645	42,630.7	76	14,478,007	10,815,655.7	1.31	1361.78	37.40	36.41	17.83
2008	31,306	31,306	1,106,647	38,907,001	56,681,971	60,339.5	115	24,129,478	16,014,874.3	1.30	1242.80	35.35	35.16	19.06
2009	42,873	42,873	1,470,205	50,652,279	72,735,788	75,136.6	137	23,885,880	19,737,690.0	1.79	1181.45	34.29	34.45	18.23
2010	44,980	44,980	1,447,578	49,379,294	69,824,021	68,625.9	97	23,482,513	19,379,858.4	1.92	1097.81	32.18	34.11	14.13
2011	47,070	47,070	1,363,551	46,037,566	64,574,451	54,436.2	82	24,754,717	19,561,235.3	1.90	978.07	28.97	33.76	15.06
2012	44,040	44,040	1,086,309	36,604,241	50,980,725	30,541.1	50	24,533,150	18,830,938.6	1.80	831.16	24.67	33.70	16.37
2013	18,078	18,078	361,729	12,746,028	18,478,357	4,975.9	14	18,902,026	9,168,434.5	0.96	705.06	20.01	35.24	28.14
2014	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>1,095-Day Blackout Period</b>														
2000	939	939	38,414	1,991,437	4,267,731	3,073.8	22	3,815,304	1,806,471.1	0.25	2120.81	40.91	51.84	71.57
2001	2,329	2,329	103,239	4,888,176	9,703,758	7,483.7	27	4,106,384	3,609,920.6	0.57	2098.83	44.33	47.35	36.08
2002	2,933	2,933	129,642	6,082,255	11,789,411	9,064.4	41	4,274,287	3,683,668.1	0.69	2073.73	44.20	46.92	45.23
2003	7,665	7,665	437,952	16,859,241	32,330,517	24,475.6	141	4,276,054	3,584,235.2	1.79	2199.51	57.14	38.50	57.61
2004	5,057	5,057	256,606	10,698,453	17,995,850	15,736.1	75	4,485,036	3,756,795.8	1.13	2115.57	50.74	41.69	47.66
2005	4,508	4,508	222,888	9,362,575	15,060,847	13,918.9	31	4,514,682	3,940,899.3	1.00	2076.88	49.44	42.01	22.27
2006	7,914	7,914	384,979	14,848,236	22,830,034	20,803.8	39	9,874,131	6,409,980.4	0.80	1876.20	48.65	38.57	18.75
2007	12,022	12,022	570,072	21,054,511	31,696,546	27,705.2	48	11,684,374	8,934,399.2	1.03	1751.33	47.42	36.93	17.33
2008	18,680	18,680	847,973	30,240,924	44,125,979	36,491.5	64	18,689,668	12,885,731.9	1.00	1618.89	45.39	35.66	17.54
2009	25,237	25,237	1,100,969	38,453,536	55,301,517	42,421.6	82	18,564,415	15,596,636.0	1.36	1523.70	43.63	34.93	19.33
2010	27,214	27,214	1,077,124	37,183,139	52,649,342	33,875.0	47	19,666,995	15,778,969.6	1.38	1366.32	39.58	34.52	13.87
2011	26,495	26,495	926,246	31,754,100	44,713,896	19,061.7	22	19,619,778	15,299,363.9	1.35	1198.49	34.96	34.28	11.54
2012	11,032	11,032	317,613	11,667,245	16,508,270	3,105.6	2	17,010,746	7,629,616.6	0.65	1057.58	28.79	36.73	6.44
2013	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2014	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Attention Deficit and Hyperactivity Disorder (ADHD) Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>30-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
2000	22	2,144	102.6
2001	43	4,885	88.0
2002	37	4,237	87.3
2003	55	5,343	102.9
2004	83	6,647	124.9
2005	55	5,928	92.8
2006	87	12,368	70.3
2007	176	19,638	89.6
2008	186	36,085	51.5
2009	216	49,321	43.8
2010	206	47,608	43.3
2011	175	46,425	37.7
2012	130	44,070	29.5
2013	163	42,530	38.3
2014	132	41,144	32.1
2015	43	14,656	29.3
2016	0	0	---
<b>Days 91-180</b>			
2000	4	1,010	39.6
2001	20	2,261	88.4
2002	16	2,145	74.6
2003	30	4,243	70.7
2004	30	4,130	72.6
2005	39	3,351	116.4
2006	36	6,487	55.5
2007	59	10,216	57.8
2008	74	18,496	40.0
2009	70	25,637	27.3
2010	64	26,220	24.4
2011	68	25,643	26.5
2012	51	25,140	20.3
2013	67	23,731	28.2
2014	64	21,553	29.7
2015	9	3,692	24.4
2016	0	0	---
<b>Days 181-270</b>			
2000	3	579	51.8
2001	11	1,320	83.3
2002	14	1,398	100.2
2003	18	3,286	54.8
2004	23	2,932	78.5
2005	24	2,238	107.2
2006	17	4,482	37.9

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Attention Deficit and Hyperactivity Disorder (ADHD) Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
2007	54	6,995	77.2
2008	36	12,351	29.1
2009	50	17,056	29.3
2010	46	17,624	26.1
2011	30	17,558	17.1
2012	37	17,498	21.1
2013	38	16,172	23.5
2014	28	11,762	23.8
2015	0	982	0.0
2016	0	0	---
<b>Days 271-365</b>			
2000	1	406	24.7
2001	8	964	83.0
2002	8	1,053	76.0
2003	11	2,737	40.2
2004	12	2,341	51.3
2005	13	1,781	73.0
2006	18	3,425	52.6
2007	23	5,358	42.9
2008	21	9,395	22.4
2009	31	13,000	23.8
2010	18	13,687	13.2
2011	25	13,621	18.4
2012	23	13,668	16.8
2013	30	12,510	24.0
2014	19	6,757	28.1
2015	0	123	0.0
2016	0	0	---
<b>Days 366-730</b>			
2000	8	905	88.4
2001	13	2,196	59.2
2002	24	2,590	92.7
2003	34	7,386	46.0
2004	45	5,432	82.8
2005	47	4,435	106.0
2006	84	8,156	103.0
2007	49	13,067	37.5
2008	41	21,611	19.0
2009	64	29,769	21.5
2010	49	31,242	15.7
2011	36	31,831	11.3
2012	41	31,092	13.2
2013	49	23,857	20.5
2014	9	4,341	20.7

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Attention Deficit and Hyperactivity Disorder (ADHD) Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
2015	0	0	---
2016	0	0	---
<b>Days 731-1,095</b>			
2000	5	518	96.5
2001	11	1,226	89.7
2002	21	1,544	136.0
2003	37	4,481	82.6
2004	33	3,025	109.1
2005	30	2,662	112.7
2006	14	4,717	29.7
2007	15	7,359	20.4
2008	28	11,540	24.3
2009	29	15,640	18.5
2010	23	16,338	14.1
2011	31	16,642	18.6
2012	24	12,840	18.7
2013	7	2,408	29.1
2014	0	0	---
2015	0	0	---
2016	0	0	---
<b>90-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
2000	22	2,405	91.5
2001	49	5,734	85.5
2002	46	5,290	87.0
2003	75	9,501	78.9
2004	104	8,818	117.9
2005	74	7,638	96.9
2006	104	15,214	68.4
2007	210	24,010	87.5
2008	222	43,443	51.1
2009	253	59,282	42.7
2010	259	58,393	44.4
2011	205	57,148	35.9
2012	155	54,563	28.4
2013	195	51,747	37.7
2014	162	48,463	33.4
2015	48	16,168	29.7
2016	0	0	---
<b>Days 91-180</b>			
2000	9	1,871	48.1
2001	31	4,122	75.2
2002	17	3,038	56.0
2003	25	2,347	106.5
2004	41	4,954	82.8

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Attention Deficit and Hyperactivity Disorder (ADHD) Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
2005	48	4,415	108.7
2006	43	9,689	44.4
2007	97	15,415	62.9
2008	120	28,149	42.6
2009	123	38,408	32.0
2010	108	36,263	29.8
2011	104	35,490	29.3
2012	84	34,295	24.5
2013	104	33,984	30.6
2014	87	32,285	26.9
2015	13	5,724	22.7
2016	0	0	---
<b>Days 181-270</b>			
2000	5	1,206	41.4
2001	18	2,730	65.9
2002	16	2,455	65.2
2003	24	4,752	50.5
2004	30	4,319	69.5
2005	30	3,536	84.8
2006	24	7,348	32.7
2007	74	11,734	63.1
2008	55	21,146	26.0
2009	70	29,189	24.0
2010	79	29,290	27.0
2011	59	28,913	20.4
2012	62	28,420	21.8
2013	64	26,966	23.7
2014	43	20,144	21.3
2015	1	1,709	5.9
2016	0	0	---
<b>Days 271-365</b>			
2000	2	909	22.0
2001	12	2,172	55.2
2002	13	2,136	60.9
2003	13	4,767	27.3
2004	20	3,941	50.8
2005	18	3,091	58.2
2006	24	6,244	38.4
2007	36	9,893	36.4
2008	38	17,532	21.7
2009	56	24,280	23.1
2010	37	24,923	14.8
2011	43	24,601	17.5
2012	39	24,665	15.8

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Attention Deficit and Hyperactivity Disorder (ADHD) Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
2013	51	22,975	22.2
2014	32	12,524	25.6
2015	0	221	0.0
2016	0	0	---
<b>Days 366-730</b>			
2000	16	2,056	77.8
2001	30	5,134	58.4
2002	45	5,738	78.4
2003	57	14,322	39.8
2004	71	10,402	68.3
2005	66	8,538	77.3
2006	137	16,047	85.4
2007	75	25,331	29.6
2008	75	42,762	17.5
2009	133	59,434	22.4
2010	108	62,106	17.4
2011	78	63,085	12.4
2012	84	61,848	13.6
2013	101	47,550	21.2
2014	15	8,628	17.4
2015	0	0	---
2016	0	0	---
<b>Days 731-1,095</b>			
2000	7	1,188	58.9
2001	19	2,887	65.8
2002	29	3,621	80.1
2003	78	9,526	81.9
2004	44	6,181	71.2
2005	54	5,495	98.3
2006	23	9,703	23.7
2007	28	14,925	18.8
2008	51	23,848	21.4
2009	55	32,715	16.8
2010	50	34,751	14.4
2011	60	35,374	17.0
2012	48	27,436	17.5
2013	14	4,976	28.1
2014	0	0	---
2015	0	0	---
2016	0	0	---



**Appendix A: List of Generic and Brand Names Used To Define the Exposures and Exposure Incidence in this Request**

Generic Name	Brand Name
<b>Amphetamines</b>	
DEXTROAMPHETAMINE SULFATE	Dexedrine Spansule
DEXTROAMPHETAMINE SULFATE	dextroamphetamine
DEXTROAMPHETAMINE SULFATE	Dexedrine
DEXTROAMPHETAMINE SULFATE	DextroStat
DEXTROAMPHETAMINE SULFATE	Zenzedi
DEXTROAMPHETAMINE SULFATE	ProCentra
DEXTROAMPHETAMINE SULFATE	Liquadd
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	Amphetamine Salt Combo
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	Adderall XR
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	Adderall
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	dextroamphetamine-amphetamine
LISDEXAMFETAMINE DIMESYLATE	Vyvanse
METHAMPHETAMINE HCL	Desoxyn
AMPHETAMINE SULFATE	Evekeo
METHAMPHETAMINE HCL	methamphetamine
<b>Methylphenidates</b>	
DEXMETHYLPHENIDATE HCL	dexmethylphenidate
DEXMETHYLPHENIDATE HCL	Focalin XR
DEXMETHYLPHENIDATE HCL	Focalin
METHYLPHENIDATE HCL	Methylin
METHYLPHENIDATE HCL	Ritalin LA
METHYLPHENIDATE HCL	methylphenidate
METHYLPHENIDATE HCL	Concerta
METHYLPHENIDATE HCL	Metadate CD
METHYLPHENIDATE HCL	Aptensio XR
METHYLPHENIDATE HCL	Ritalin
METHYLPHENIDATE HCL	Ritalin SR
METHYLPHENIDATE HCL	Metadate ER
METHYLPHENIDATE HCL	Quillivant XR
METHYLPHENIDATE HCL	Methylin ER
<b>Strattera</b>	
ATOMOXETINE HCL	Strattera

**Appendix B: Codes used to define Heart Failure in this Request**

Code	Code Type	Description
398.91	ICD-9-CM Diagnosis	Rheumatic heart failure (congestive)
402.01	ICD-9-CM Diagnosis	Malignant hypertensive heart disease with heart failure
402.11	ICD-9-CM Diagnosis	Benign hypertensive heart disease with heart failure
402.91	ICD-9-CM Diagnosis	Unspecified hypertensive heart disease with heart failure
404.01	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.03	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic kidney disease stage V or end stage renal disease
404.11	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, benign, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.13	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, benign, with heart failure and chronic kidney disease stage V or end stage renal disease
404.91	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, unspecified, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.93	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, unspecified, with heart failure and chronic kidney disease stage V or end stage renal disease
422.90	ICD-9-CM Diagnosis	Acute myocarditis, unspecified
425.4	ICD-9-CM Diagnosis	Other primary cardiomyopathies
425.9	ICD-9-CM Diagnosis	Secondary cardiomyopathy, unspecified
428	ICD-9-CM Diagnosis	Heart Failure
428.0	ICD-9-CM Diagnosis	Congestive heart failure, unspecified
428.1	ICD-9-CM Diagnosis	Left heart failure
428.2	ICD-9-CM Diagnosis	Systolic heart failure
428.20	ICD-9-CM Diagnosis	Systolic heart failure, unspecified
428.21	ICD-9-CM Diagnosis	Acute systolic heart failure
428.22	ICD-9-CM Diagnosis	Chronic systolic heart failure
428.23	ICD-9-CM Diagnosis	Acute on chronic systolic heart failure
428.3	ICD-9-CM Diagnosis	Diastolic heart failure
428.30	ICD-9-CM Diagnosis	Diastolic heart failure, unspecified
428.31	ICD-9-CM Diagnosis	Acute diastolic heart failure
428.32	ICD-9-CM Diagnosis	Chronic diastolic heart failure
428.33	ICD-9-CM Diagnosis	Acute on chronic diastolic heart failure
428.4	ICD-9-CM Diagnosis	Combined systolic and diastolic heart failure
428.40	ICD-9-CM Diagnosis	Combined systolic and diastolic heart failure, unspecified
428.41	ICD-9-CM Diagnosis	Acute combined systolic and diastolic heart failure
428.42	ICD-9-CM Diagnosis	Chronic combined systolic and diastolic heart failure
428.43	ICD-9-CM Diagnosis	Acute on chronic combined systolic and diastolic heart failure
428.9	ICD-9-CM Diagnosis	Heart failure, unspecified

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Sentinel's Cohort Identification and Descriptive Analysis (CIDA) tool was used to investigate heart failure following treatment with select attention deficit and hyperactivity disorder (ADHD) medications. In total, 49 scenarios were examined with four different exposures, seven different blackout periods, and two different episod gaps/exposure extension periods. The four exposures are all amphetamines, all methylphenidates, strattera, and all stimulants (which include all amphetamines and all methylphenidates and strattera). **The outcome is heart failure, defined as any heart failure ICD-9-CM diagnosis code (398.91, 402.x1, 402.x3, 404.x1, 404.x3, 422.90, 425.4, 425.9, 428.xx) in any care setting with a primary discharge diagnosis (PDX) value of P (principal) for those diagnoses in the inpatient care setting.** See below for a description of each of these scenarios. The query period was from January 1, 2000 to March 3, 2016 and the enrollment gap was set at 45 days. Age groups were split as follows: 0-21, 22-44, 45-64, 65+.

Enrollment Gap	45 Days
Age Groups	0-21, 22-44, 45-64, 65+
Query Period	January 1, 2000 - Current
Coverage Requirement	Medical and Drug
Enrollment Requirement	183 Days

Scenario	Drug/Exposure										Event/Outcome					
	Incident exposure	Incident w/ respect to:	Episode Truncation at Incident Exposure	Episode Truncation at Death	Washout (days)	Cohort Definition	Episode Gap	Exposure Extension Period	Min Episode Duration	Min Days Supplied	Event/ Outcome	Care Setting/PDX	Incident with Respect to	Incident w/ respect to Care Setting/PDX	Washout (days)	Blackout Period
1	All Stimulants	All Stimulants	Yes	No	183	01	90	90	0	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	0
2	All Stimulants	All Stimulants	Yes	No	183	01	90	90	90	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	90
3	All Stimulants	All Stimulants	Yes	No	183	01	90	90	180	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	180
4	All Stimulants	All Stimulants	Yes	No	183	01	90	90	270	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	270
5	All Stimulants	All Stimulants	Yes	No	183	01	90	90	365	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	365
6	All Stimulants	All Stimulants	Yes	No	183	01	90	90	730	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	730
7	All Stimulants	All Stimulants	Yes	No	183	01	90	90	1095	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	1095
8	All Stimulants	All Stimulants	Yes	No	183	01	30	30	0	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	0
9	All Stimulants	All Stimulants	Yes	No	183	01	30	30	90	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	90
10	All Stimulants	All Stimulants	Yes	No	183	01	30	30	180	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	180
11	All Stimulants	All Stimulants	Yes	No	183	01	30	30	270	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	270
12	All Stimulants	All Stimulants	Yes	No	183	01	30	30	365	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	365
13	All Stimulants	All Stimulants	Yes	No	183	01	30	30	730	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	730
14	All Stimulants	All Stimulants	Yes	No	183	01	30	30	1095	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	1095

ICD-9, ICD-10, HCPCS, and CPT codes are provided by Optum360. NDC codes are checked against First Data Bank's "National Drug Data File (NDDF)" Plus."

Cohort Definition of 01 will only consider the first incident episode for each user during the query period that satisfies the washout period.

Note: Episodes are automatically truncated at outcome.

### Disclaimer

The following report(s) provides findings from an FDA-initiated query using Sentinel. While Sentinel queries may be undertaken to assess potential medical product safety risks, they may also be initiated for various other reasons. Some examples include determining a rate or count of an identified health outcome of interest, examining medical product use, exploring the feasibility of future, more detailed analyses within Sentinel, and seeking to better understand Sentinel capabilities.

Data obtained through Sentinel are intended to complement other types of evidence such as preclinical studies, clinical trials, postmarket studies, and adverse event reports, all of which are used by FDA to inform regulatory decisions regarding medical product safety. The information contained in this report is provided as part of FDA's commitment to place knowledge acquired from Sentinel in the public domain as soon as possible. Any public health actions taken by FDA regarding products involved in Sentinel queries will continue to be communicated through existing channels.

FDA wants to emphasize that the fact that FDA has initiated a query involving a medical product and is reporting findings related to that query does not mean that FDA is suggesting health care practitioners should change their prescribing practices for the medical product or that patients taking the medical product should stop using it. Patients who have questions about the use of an identified medical product should contact their health care practitioners.

The following report contains a description of the request, request specifications, and results from the modular program run(s).

If you are using a web page screen reader and are unable to access this document, please contact the Sentinel Operations Center for assistance at [info@sentinelssystem.org](mailto:info@sentinelssystem.org).

## Overview for Request cder\_mpl1r\_wp014\_nsdp\_v01, Report 4 of 8

**Request ID:** cder\_mpl1r\_wp014\_nsdp\_v01. This is report 4 of 8.

**Request Description:** FDA has requested execution of the Cohort Identification and Descriptive Analysis (CIDA) tool, version 2.1.1, to investigate heart failure diagnoses following new use of attention deficit hyperactivity disorder (ADHD) medications. This report presents results for strattera. Results for all methylphenidates, all amphetamines, and all stimulants are presented in separate reports.

**Data Source:** Data from January 1, 2000 to March 3, 2016 from 15 health plans contributing to the Sentinel Distributed Database (SDD) are included in this report.

**Study Design:** This request was designed to identify exposures and follow-up time. The exposure of interest and the occurrence of the health outcome of interest during exposed time were identified. The number of exposure episodes, number of individuals, number of events, and days at-risk in the SDD were calculated overall and were stratified by age group, sex, and year.

**Exposure of Interest:** The exposure of interest was strattera, which was defined using National Drug Codes (NDCs). Please refer to Appendix A for generic and brand names of strattera.

**Cohort Eligibility Criteria:** Patients were required to be continuously enrolled in plans with both medical and drug coverage for at least 6 months (183 days) before their dispensing date, during which gaps in coverage of up to 45 days were allowed. Members were excluded if they had any ADHD medication or the outcome of interest in the 6 months (183 days) prior to exposure initiation. The following age groups were included in the cohort: 0-21, 22-44, 45-64, 65+ years.

**Follow-Up Time:** Follow-up time for the outcome was determined by the length of the exposure episodes. Exposure episode lengths were defined using outpatient pharmacy dispensing days supplied to create a sequence of continuous exposure. Exposure episodes were considered continuous if gaps in days supply were less than 90 days. The end date of each exposure episode was extended by 90 additional days. Sensitivity analyses were performed using a 30-day episode gap and 30-day exposure extension period. Follow-up began on the day on which the first exposure of interest was dispensed and continued until the first occurrence of any of the following: 1) the outcome of interest; 2) any codes defining incidence criteria; 3) disenrollment; 4) the study end date (March, 2016); 5) the end date of the data provided by each Data Partner; or 6) the end of the exposure episode. Only the first valid incident exposure episode that occurred during the study period was included per patient.

This report examines different blackout periods which is a number of days at the beginning of the ADHD medication episode where if an outcome occurs, it is not attributed to the exposure and the person is omitted from the analysis. The blackout periods examined were 90 days, 180 days, 270 days, 365 days, 730 days, and 1,095 days. Episodes that were at least as long as the blackout period were required.

**Outcome of Interest:** Heart failure was defined using any of the ICD-9-CM diagnosis codes listed in Appendix B. This event had to be incident (no heart failure events in the 183 days prior to exposure initiation). The event could happen in any care setting. However, if the event happened in the inpatient or institutionalized care setting, the event had to be flagged as a principal diagnosis.

**Please refer to Appendix C for detailed specifications.**

**Limitations:** Algorithms to define exposures and outcomes are imperfect and, therefore, may be misclassified.

**Notes:** Please contact the Sentinel Operations Center Query Fulfillment Team ([production@mini-sentinel.org](mailto:production@mini-sentinel.org)) for questions and to provide comments/suggestions for future enhancements to this document.

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**Glossary of Terms for Analyses Using  
Cohort Identification and Descriptive Analysis (CIDA) Tool\***

**Amount Supplied** - number of units (pills, tablets, vials) dispensed. Net amount per NDC per dispensing. This is equivalent to the "RxAmt" value in the MSCDM.

**Blackout Period** - number of days at the beginning of a treatment episode that events are to be ignored. If an event occurs during the blackout period, the episode is excluded.

**Care Setting** - type of medical encounter or facility where the exposure, event, or condition code was recorded. Possible care settings include: Inpatient Hospital Stay (IP), Non-Acute Institutional Stay (IS), Emergency Department (ED), Ambulatory Visit (AV), and Other Ambulatory Visit (OA). For laboratory results, possible care settings include: Emergency department (E), Home (H), Inpatient (I), Outpatient (O), or Unknown or Missing (U). Along with the Principal Diagnosis Indicator, forms the Care Setting/PDX parameter.

**Cohort Definition (drug/exposure)** - indicates how the cohort will be defined: (1) 01: Cohort includes only the first valid incident treatment episode during the query period; (2) 02: Cohort includes all valid incident treatment episodes during the query period; (3) 03: Cohort includes all valid incident treatment episodes during the query period until an event

**Days Supplied** - number of days supplied for all dispensings in qualifying treatment episodes.

**Eligible Members** - number of members eligible for an incident treatment episode (defined by the drug/exposure and event washout periods) with drug and medical coverage during the query period.

**Enrollment Gap** - number of days allowed between two consecutive enrollment periods without breaking a "continuously enrolled" sequence.

**Episodes** - treatment episodes; length of episode is determined by days supplied in one dispensing or consecutive dispensings bridged by the episode gap.

**Episode Gap** - number of days allowed between two (or more) consecutive exposures (dispensings/procedures) to be considered the same treatment episode.

**Event Deduplication** - specifies how events are counted by the MP algorithm: (0) 0: Counts all occurrences of an HOI during an exposure episode; (1) 1: de-duplicates occurrences of the same HOI code and code type on the same day; (2) 2: de-duplicates occurrences of the same HOI group on the same day (e.g., de-duplicates at the group level).

**Exposure Episode Length** - number of days after exposure initiation that is considered "exposed time."

**Exposure Extension Period** - number of days post treatment period in which the outcomes/events are counted for a treatment episode.

**Lookback Period (pre-existing condition)** - number of days wherein a member is required to have evidence of pre-existing condition (diagnosis/procedure/drug dispensing).

**Member-Years** - sum of all days of enrollment with medical and drug coverage\*\* in the query period preceded by an exposure washout period all divided by **365.25**.

**Minimum Days Supplied** - specifies a minimum number of days in length of the days supplied for the episode to be considered.

**Minimum Episode Duration** - specifies a minimum number of days in length of the episode for it to be considered.

**Principal Diagnosis (PDX)** - diagnosis or condition established to be chiefly responsible for admission of the patient to the hospital. 'P' = principal diagnosis, 'S' = secondary diagnosis, 'X' = unspecified diagnosis, '.' = blank. Along with the Care Setting values, forms the Caresetting/PDX parameter.

**Query Period** - period in which the modular program looks for exposures and outcomes of interest.

**Treatment Episode Truncation Indicator** - indicates whether observation of the incident query code during follow-up requires truncation of valid treatment episodes. A value of Y indicates that the treatment episodes should be truncated at the first occurrence of an incident query code. A value of N indicates that the treatment episodes should not be truncated at the occurrence of the incident query code.

**Users** - number of members with exposure during the query period. Member must have no evidence of exposure(s) of interest (defined by incidence criteria) in the prior washout period. A user may only be counted once in a query period.

**Washout Period (drug/exposure)\*\*** - number of days a user is required to have no evidence of prior exposure (drug dispensing/procedure) and continuous drug and medical coverage prior to an incident treatment episode.

**Washout Period (event/outcome)\*\*** - number of days a user is required to have no evidence of a prior event (procedure/diagnosis) and continuous drug and medical coverage prior to an incident treatment episode.

**Years at Risk** - number of days supplied plus any episode gaps and exposure extension periods all divided by 365.25.

\*all terms may not be used in this report

\*\*incident treatment episodes must be incident to both the exposure and the event

**Table 1a: Summary of Incident Strattera Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, and Blackout Period**

New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>90-Day Episode Gap/Extension Period</b>													
<b>0-Day Blackout Period</b>													
163,171	163,171	722,438	23,698,374	34,557,134	100,675.8	404	110,278,922	305,937,613.4	1.48	145.24	4.43	32.80	40.13
<b>90-Day Blackout Period</b>													
128,189	128,189	675,259	22,594,173	33,024,164	65,272.4	251	100,795,207	276,545,200.6	1.27	176.26	5.27	33.46	38.45
<b>180-Day Blackout Period</b>													
59,453	59,453	568,356	19,461,174	27,751,663	44,184.2	166	93,629,252	250,298,369.6	0.63	327.34	9.56	34.24	37.57
<b>270-Day Blackout Period</b>													
36,865	36,865	482,741	16,779,528	23,708,194	32,951.2	121	80,082,582	228,191,331.4	0.46	455.16	13.09	34.76	36.72
<b>365-Day Blackout Period</b>													
24,711	24,711	409,224	14,401,326	19,854,502	25,225.3	103	72,081,132	207,171,542.8	0.34	582.79	16.56	35.19	40.83
<b>730-Day Blackout Period</b>													
8,250	8,250	229,790	8,393,667	11,321,208	10,820.9	42	48,757,177	144,831,855.5	0.17	1017.41	27.85	36.53	38.81
<b>1,095-Day Blackout Period</b>													
3,563	3,563	135,418	5,080,675	6,831,106	5,345.5	15	34,276,055	102,932,154.5	0.10	1425.95	38.01	37.52	28.06



**Table 1b: Rate of Heart Failure Outcomes at Different Stages of Strattera Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, and Blackout Period**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>90-Day Episode Gap/Extension Period</b>			
Days 0-90	153	35,403	43.2
Days 91-180	85	21,088	40.3
Days 181-270	45	11,233	40.1
Days 271-365	18	7,726	23.3
Days 366-730	61	14,404	42.3
Days 731-1,095	27	5,475	49.3

**Table 2a: Summary of Incident Strattera Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
00-21 Years	87,826	87,826	417,707	13,452,253	18,951,063	56,867.9	114	33,425,295	84,374,985.3	2.63	153.17	4.76	32.20	20.05
22-44 Years	51,258	51,258	186,074	5,975,959	9,363,960	26,782.3	85	45,805,062	96,123,905.2	1.12	116.59	3.63	32.12	31.74
45-64 Years	22,889	22,889	113,399	4,063,358	5,945,041	16,202.8	171	32,660,430	90,567,857.4	0.70	177.52	4.95	35.83	105.54
65+ Years	1,198	1,198	5,258	206,804	297,071	822.8	34	10,954,011	34,870,865.5	0.11	172.62	4.39	39.33	413.21
<b>90-Day Blackout Period</b>														
00-21 Years	70,155	70,155	393,692	12,899,136	18,193,010	37,654.1	81	30,664,764	76,605,430.0	2.29	183.87	5.61	32.76	21.51
22-44 Years	38,327	38,327	169,196	5,582,890	8,812,884	15,939.2	43	41,144,176	85,476,041.5	0.93	145.66	4.41	33.00	26.98
45-64 Years	18,676	18,676	107,387	3,913,766	5,732,605	11,129.0	109	30,239,050	82,574,303.4	0.62	209.56	5.75	36.45	97.94
65+ Years	1,031	1,031	4,984	198,381	285,665	550.0	18	9,847,413	31,889,425.8	0.10	192.42	4.83	39.80	327.27
<b>180-Day Blackout Period</b>														
00-21 Years	34,454	34,454	336,144	11,217,991	15,292,894	25,735.7	60	28,477,130	69,598,183.8	1.21	325.59	9.76	33.37	23.31
22-44 Years	15,433	15,433	134,786	4,575,042	7,192,951	10,022.5	20	37,559,359	76,134,143.0	0.41	296.45	8.73	33.94	19.96
45-64 Years	9,088	9,088	93,223	3,493,255	5,040,631	8,044.1	73	28,253,166	75,310,986.0	0.32	384.38	10.26	37.47	90.75
65+ Years	478	478	4,203	174,886	225,187	381.9	13	9,283,604	29,255,056.8	0.05	365.87	8.79	41.61	340.41
<b>270-Day Blackout Period</b>														
00-21 Years	21,533	21,533	287,092	9,693,252	13,173,458	19,181.4	39	24,382,853	63,673,138.3	0.88	450.16	13.33	33.76	20.33
22-44 Years	9,027	9,027	110,499	3,818,282	5,897,876	7,196.8	16	31,633,880	68,443,458.8	0.29	422.98	12.24	34.55	22.23
45-64 Years	6,008	6,008	81,691	3,120,188	4,448,753	6,283.6	60	24,594,403	69,095,877.5	0.24	519.34	13.60	38.20	95.49
65+ Years	297	297	3,459	147,806	188,106	289.5	6	8,263,459	26,978,856.8	0.04	497.66	11.65	42.73	207.26
<b>365-Day Blackout Period</b>														
00-21 Years	14,488	14,488	244,445	8,328,852	10,949,253	14,647.6	37	21,971,316	58,015,414.6	0.66	574.88	16.87	34.07	25.26
22-44 Years	5,801	5,801	90,802	3,184,730	4,834,397	5,350.4	12	27,915,415	61,263,849.8	0.21	549.00	15.65	35.07	22.43
45-64 Years	4,213	4,213	70,976	2,757,986	3,906,592	5,000.3	49	22,308,182	63,130,148.1	0.19	654.64	16.85	38.86	97.99
65+ Years	209	209	3,001	129,758	164,260	227.0	5	7,724,180	24,762,130.3	0.03	620.85	14.36	43.24	220.25
<b>730-Day Blackout Period</b>														
00-21 Years	4,823	4,823	138,119	4,826,352	6,212,962	6,144.1	19	14,939,259	40,913,741.1	0.32	1000.70	28.64	34.94	30.92
22-44 Years	1,746	1,746	46,797	1,717,246	2,567,234	2,131.8	6	17,764,039	40,909,165.2	0.10	983.53	26.80	36.70	28.15
45-64 Years	1,598	1,598	42,970	1,763,213	2,435,199	2,435.2	15	15,594,574	44,998,260.5	0.10	1103.39	26.89	41.03	61.60
65+ Years	83	83	1,904	86,856	105,812	109.8	2	5,590,312	18,010,688.7	0.01	1046.46	22.94	45.62	182.18
<b>1,095-Day Blackout Period</b>														
00-21 Years	2,065	2,065	81,246	2,889,368	3,804,279	2,948.0	5	10,527,068	29,229,576.4	0.20	1399.21	39.34	35.56	16.96
22-44 Years	688	688	25,456	972,541	1,326,421	1,022.2	3	11,867,600	28,140,076.7	0.06	1413.58	37.00	38.20	29.35
45-64 Years	763	763	27,396	1,158,359	1,625,617	1,327.0	5	11,226,189	32,398,475.6	0.07	1518.16	35.91	42.28	37.68
65+ Years	47	47	1,320	60,407	74,790	48.2	2	4,147,058	13,164,025.9	0.01	1285.26	28.09	45.76	414.54

**Table 2b: Rate of Heart Failure Outcomes at Different Stages of Strattera Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>90-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
00-21 Years	33	19,214	17.2
22-44 Years	42	10,843	38.7
45-64 Years	62	5,074	122.2
65+ Years	16	273	586.5
<b>Days 91-180</b>			
00-21 Years	21	11,918	17.6
22-44 Years	23	5,917	38.9
45-64 Years	36	3,085	116.7
65+ Years	5	168	297.4
<b>Days 181-270</b>			
00-21 Years	21	6,554	32.0
22-44 Years	4	2,826	14.2
45-64 Years	13	1,761	73.8
65+ Years	7	92	757.6
<b>Days 271-365</b>			
00-21 Years	2	4,534	4.4
22-44 Years	4	1,846	21.7
45-64 Years	11	1,283	85.7
65+ Years	1	62	160.0
<b>Days 366-730</b>			
00-21 Years	18	8,503	21.2
22-44 Years	6	3,219	18.6
45-64 Years	34	2,565	132.6
65+ Years	3	117	255.9
<b>Days 731-1,095</b>			
00-21 Years	14	3,196	43.8
22-44 Years	3	1,110	27.0
45-64 Years	10	1,108	90.2
65+ Years	0	62	0.0

**Table 3a: Summary of Incident Strattera Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
Female	69,984	69,984	304,526	10,044,922	14,794,849	42,765.0	184	56,071,659	158,543,963.5	1.25	143.53	4.35	32.99	43.03
Male	93,177	93,177	417,863	13,652,135	19,760,912	57,906.2	220	54,201,553	147,380,914.4	1.72	146.52	4.48	32.67	37.99
Unknown	10	10	49	1,317	1,374	4.6	0	5,710	12,735.5	1.75	131.70	4.90	26.88	0.00
<b>90-Day Blackout Period</b>														
Female	54,715	54,715	284,103	9,563,400	14,119,961	27,626.0	109	51,322,051	143,546,123.2	1.07	174.79	5.19	33.66	39.46
Male	73,470	73,470	391,115	13,029,587	18,902,992	37,643.1	142	49,468,329	132,987,755.2	1.49	177.35	5.32	33.31	37.72
Unknown	4	4	41	1,186	1,211	3.2	0	4,827	11,322.2	0.83	296.50	10.25	28.93	0.00
<b>180-Day Blackout Period</b>														
Female	25,214	25,214	238,590	8,230,138	11,840,984	18,674.9	62	47,747,103	130,123,549.1	0.53	326.41	9.46	34.49	33.20
Male	34,236	34,236	329,728	11,229,925	15,909,543	25,506.9	104	45,877,989	120,164,676.6	0.75	328.02	9.63	34.06	40.77
Unknown	3	3	38	1,111	1,136	2.4	0	4,160	10,143.8	0.72	370.33	12.67	29.24	0.00
<b>270-Day Blackout Period</b>														
Female	15,632	15,632	202,484	7,099,641	9,983,068	13,923.3	47	40,899,023	118,804,605.4	0.38	454.17	12.95	35.06	33.76
Male	21,231	21,231	280,225	9,678,932	13,724,146	19,026.1	74	39,180,258	109,377,513.2	0.54	455.89	13.20	34.54	38.89
Unknown	2	2	32	955	980	1.8	0	3,301	9,212.8	0.61	477.50	16.00	29.84	0.00
<b>365-Day Blackout Period</b>														
Female	10,452	10,452	171,429	6,087,125	8,412,422	10,657.6	41	36,882,927	108,022,216.2	0.28	582.39	16.40	35.51	38.47
Male	14,258	14,258	237,769	8,313,426	11,441,280	14,566.1	62	35,195,289	99,140,973.4	0.41	583.07	16.68	34.96	42.56
Unknown	1	1	26	775	800	1.6	0	2,916	8,353.3	0.34	775.00	26.00	29.81	0.00
<b>730-Day Blackout Period</b>														
Female	3,515	3,515	96,057	3,563,354	4,792,100	4,575.2	12	25,089,970	75,942,334.3	0.14	1013.76	27.33	37.10	26.23
Male	4,734	4,734	133,707	4,829,538	6,528,308	6,245.2	30	23,665,314	68,883,644.8	0.20	1020.18	28.24	36.12	48.04
Unknown	1	1	26	775	800	0.6	0	1,893	5,876.3	0.53	775.00	26.00	29.81	0.00
<b>1,095-Day Blackout Period</b>														
Female	1,533	1,533	56,295	2,164,768	2,911,750	2,246.8	5	17,741,982	54,257,865.0	0.09	1412.11	36.72	38.45	22.25
Male	2,030	2,030	79,123	2,915,907	3,919,356	3,098.7	10	16,532,754	48,670,055.7	0.12	1436.41	38.98	36.85	32.27
Unknown	0	0	0	0	0	0.0	0	1,319	4,233.8	0.00	---	---	---	---

**Table 3b: Rate of Heart Failure Outcomes at Different Stages of Strattera Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>90-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
Female	75	15,139	49.5
Male	78	20,263	38.5
Unknown	0	1	0.0
<b>Days 91-180</b>			
Female	47	8,951	52.5
Male	38	12,136	31.3
Unknown	0	1	0.0
<b>Days 181-270</b>			
Female	15	4,752	31.6
Male	30	6,481	46.3
Unknown	0	1	0.0
<b>Days 271-365</b>			
Female	6	3,266	18.4
Male	12	4,460	26.9
Unknown	0	0	0.0
<b>Days 366-730</b>			
Female	29	6,082	47.7
Male	32	8,321	38.5
Unknown	0	1	0.0
<b>Days 731-1,095</b>			
Female	7	2,328	30.1
Male	20	3,146	63.6
Unknown	0	1	0.0

**Table 4a: Summary of Incident Strattera Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
2000	0	0	0	0	0	0.0	0	6,528,534	2,996,066.8	0.00	---	---	---	---
2001	0	0	0	0	0	0.0	0	7,129,202	5,953,237.7	0.00	---	---	---	---
2002	2	2	2	60	60	0.7	0	7,285,378	6,054,653.0	0.00	30.00	1.00	30.00	0.00
2003	8,621	8,621	57,814	1,871,327	3,891,573	7,395.7	50	7,282,277	6,029,656.8	1.18	217.07	6.71	32.37	67.61
2004	10,232	10,232	56,640	1,913,645	5,948,965	7,798.0	51	7,717,803	6,274,442.3	1.33	187.03	5.54	33.79	65.40
2005	6,376	6,376	30,236	1,073,284	1,603,951	4,470.8	32	7,960,341	6,565,150.2	0.80	168.33	4.74	35.50	71.57
2006	8,538	8,538	41,441	1,418,493	1,989,633	5,980.6	25	19,434,246	11,600,400.6	0.44	166.14	4.85	34.23	41.80
2007	11,875	11,875	58,773	1,977,818	2,564,989	8,285.5	42	23,636,715	17,158,419.8	0.50	166.55	4.95	33.65	50.69
2008	17,422	17,422	77,355	2,552,917	3,207,412	10,971.3	25	44,345,486	28,004,627.8	0.39	146.53	4.44	33.00	22.79
2009	20,326	20,326	90,010	2,957,425	3,619,728	12,661.9	53	45,747,395	35,485,733.7	0.44	145.50	4.43	32.86	41.86
2010	17,401	17,401	76,974	2,527,664	3,002,623	10,806.4	33	43,630,024	33,991,412.0	0.40	145.26	4.42	32.84	30.54
2011	15,611	15,611	68,343	2,232,356	2,654,353	9,531.1	21	42,246,826	33,206,540.7	0.37	143.00	4.38	32.66	22.03
2012	14,452	14,452	60,963	1,974,077	2,324,769	8,572.9	25	41,244,007	32,545,413.4	0.35	136.60	4.22	32.38	29.16
2013	13,771	13,771	53,320	1,687,052	1,966,809	7,460.2	32	41,122,704	32,238,379.6	0.33	122.51	3.87	31.64	42.89
2014	13,341	13,341	40,653	1,240,807	1,446,471	5,613.4	15	42,067,394	32,123,148.1	0.32	93.01	3.05	30.52	26.72
2015	5,203	5,203	9,914	271,449	335,798	1,127.2	0	34,583,584	15,710,331.1	0.15	52.17	1.91	27.38	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>90-Day Blackout Period</b>														
2000	0	0	0	0	0	0.0	0	6,271,153	2,822,041.0	0.00	---	---	---	---
2001	0	0	0	0	0	0.0	0	6,794,445	5,669,482.3	0.00	---	---	---	---
2002	2	2	2	60	60	0.2	0	6,961,144	5,743,501.2	0.00	30.00	1.00	30.00	0.00
2003	7,346	7,346	55,843	1,824,315	3,828,499	5,431.8	35	6,912,962	5,726,169.8	1.06	248.34	7.60	32.67	64.44
2004	8,818	8,818	54,532	1,863,340	5,755,981	5,462.9	33	7,433,251	5,974,386.3	1.19	211.31	6.18	34.17	60.41
2005	5,439	5,439	28,957	1,042,928	1,558,072	3,032.8	24	7,586,085	6,192,374.9	0.72	191.75	5.32	36.02	79.13
2006	6,966	6,966	39,390	1,371,281	1,921,871	4,100.5	17	18,302,825	10,874,767.3	0.38	196.85	5.65	34.81	41.46
2007	9,768	9,768	55,949	1,911,766	2,477,162	5,661.1	21	22,143,526	16,086,200.7	0.44	195.72	5.73	34.17	37.10
2008	13,695	13,695	72,377	2,437,524	3,057,973	7,189.0	16	41,874,446	25,735,298.3	0.33	177.99	5.28	33.68	22.26
2009	16,051	16,051	84,298	2,822,300	3,447,874	8,240.2	30	42,525,956	32,620,907.5	0.38	175.83	5.25	33.48	36.41
2010	13,671	13,671	72,083	2,411,401	2,857,803	7,031.8	20	40,767,270	31,360,106.6	0.34	176.39	5.27	33.45	28.44
2011	12,211	12,211	63,933	2,128,261	2,523,598	6,158.8	13	39,673,962	30,738,320.4	0.31	174.29	5.24	33.29	21.11
2012	11,348	11,348	56,868	1,877,548	2,203,606	5,437.2	16	39,276,730	30,245,298.3	0.29	165.45	5.01	33.02	29.43
2013	10,832	10,832	49,497	1,598,595	1,857,346	4,479.3	17	38,583,392	29,793,680.5	0.28	147.58	4.57	32.30	37.95

**Table 4a: Summary of Incident Stratterra Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2014	10,159	10,159	36,323	1,140,771	1,327,447	2,759.3	9	39,192,799	29,261,157.0	0.26	112.29	3.58	31.41	32.62
2015	1,883	1,883	5,207	164,083	206,873	287.6	0	23,024,703	7,701,508.5	0.08	87.14	2.77	31.51	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>180-Day Blackout Period</b>														
2000	0	0	0	0	0	0.0	0	6,000,891	2,668,690.0	0.00	---	---	---	---
2001	0	0	0	0	0	0.0	0	6,564,683	5,409,255.6	0.00	---	---	---	---
2002	0	0	0	0	0	0.0	0	6,683,396	5,451,914.5	0.00	---	---	---	---
2003	4,025	4,025	50,484	1,672,116	3,609,521	4,101.6	27	6,657,686	5,456,280.0	0.60	415.43	12.54	33.12	65.83
2004	4,651	4,651	47,930	1,669,546	4,224,656	3,897.4	25	7,095,008	5,704,220.5	0.66	358.96	10.31	34.83	64.15
2005	2,634	2,634	25,111	930,445	1,390,784	2,150.8	21	7,316,134	5,856,450.3	0.36	353.24	9.53	37.05	97.64
2006	3,351	3,351	33,958	1,206,617	1,686,940	2,910.3	13	17,580,466	10,225,232.2	0.19	360.08	10.13	35.53	44.67
2007	4,672	4,672	48,012	1,677,861	2,168,096	4,012.2	11	21,031,857	15,127,496.1	0.22	359.13	10.28	34.95	27.42
2008	6,268	6,268	61,095	2,100,780	2,626,240	4,948.2	9	39,175,588	23,703,667.6	0.16	335.16	9.75	34.39	18.19
2009	7,395	7,395	71,050	2,428,323	2,953,399	5,580.2	20	40,464,903	30,039,834.2	0.18	328.37	9.61	34.18	35.84
2010	6,345	6,345	61,104	2,088,381	2,459,277	4,805.3	10	38,834,253	29,008,480.2	0.16	329.14	9.63	34.18	20.81
2011	5,633	5,633	54,107	1,842,289	2,170,287	4,190.8	8	37,868,215	28,499,251.7	0.15	327.05	9.61	34.05	19.09
2012	5,301	5,301	48,213	1,627,371	1,890,916	3,618.3	7	37,016,377	28,154,086.0	0.14	306.99	9.10	33.75	19.35
2013	4,897	4,897	40,667	1,345,493	1,553,293	2,747.6	13	36,879,084	27,560,537.8	0.13	274.76	8.30	33.09	47.31
2014	3,875	3,875	24,669	804,215	933,969	1,168.6	2	36,429,142	23,829,238.7	0.11	207.54	6.37	32.60	17.11
2015	406	406	1,956	67,737	84,285	53.1	0	13,603,450	3,603,734.0	0.03	166.84	4.82	34.63	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>270-Day Blackout Period</b>														
2000	0	0	0	0	0	0.0	0	5,556,728	2,575,586.1	0.00	---	---	---	---
2001	0	0	0	0	0	0.0	0	6,239,368	5,172,511.5	0.00	---	---	---	---
2002	0	0	0	0	0	0.0	0	6,328,503	5,195,042.0	0.00	---	---	---	---
2003	2,803	2,803	45,568	1,522,178	3,398,084	3,273.8	19	6,273,478	5,219,438.8	0.45	543.05	16.26	33.40	58.04
2004	3,053	3,053	41,834	1,476,415	3,285,386	2,978.7	19	6,684,780	5,464,988.8	0.46	483.59	13.70	35.29	63.79
2005	1,562	1,562	21,308	807,109	1,213,873	1,669.4	16	6,844,984	5,563,609.6	0.23	516.72	13.64	37.88	95.85
2006	2,126	2,126	29,612	1,070,726	1,499,184	2,272.5	11	16,123,323	9,730,469.8	0.13	503.63	13.93	36.16	48.40
2007	2,956	2,956	41,795	1,479,540	1,909,162	3,111.9	7	19,515,634	14,308,153.6	0.15	500.52	14.14	35.40	22.49
2008	3,895	3,895	52,264	1,826,461	2,278,269	3,752.4	8	34,991,840	22,232,838.0	0.11	468.92	13.42	34.95	21.32
2009	4,579	4,579	60,585	2,100,901	2,545,107	4,189.2	13	36,931,470	27,866,142.7	0.12	458.81	13.23	34.68	31.03
2010	4,013	4,013	52,477	1,817,545	2,132,471	3,609.3	6	35,513,434	27,029,550.9	0.11	452.91	13.08	34.64	16.62

**Table 4a: Summary of Incident Strattera Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2011	3,520	3,520	46,463	1,598,931	1,877,546	3,145.4	6	34,712,580	26,592,012.9	0.10	454.24	13.20	34.41	19.08
2012	3,350	3,350	41,026	1,404,649	1,627,429	2,622.3	6	33,880,355	26,428,502.7	0.10	419.30	12.25	34.24	22.88
2013	3,092	3,092	33,864	1,136,271	1,309,448	1,816.3	9	33,857,588	25,616,828.7	0.09	367.49	10.95	33.55	49.55
2014	1,873	1,873	15,708	528,323	617,611	505.4	1	32,012,586	18,162,035.8	0.06	282.07	8.39	33.63	19.79
2015	43	43	237	10,479	14,625	4.5	0	9,131,567	1,033,619.4	0.00	243.70	5.51	44.22	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>365-Day Blackout Period</b>														
2000	0	0	0	0	0	0.0	0	5,308,581	2,486,855.0	0.00	---	---	---	---
2001	0	0	0	0	0	0.0	0	5,774,614	4,927,922.5	0.00	---	---	---	---
2002	0	0	0	0	0	0.0	0	5,831,197	4,955,061.2	0.00	---	---	---	---
2003	2,044	2,044	40,872	1,375,008	2,850,363	2,648.2	18	5,853,147	4,990,324.4	0.35	672.70	20.00	33.64	67.97
2004	2,114	2,114	35,958	1,287,225	2,479,686	2,314.6	19	6,395,235	5,222,632.3	0.33	608.90	17.01	35.80	82.09
2005	993	993	17,930	696,189	1,052,474	1,346.1	14	6,234,524	5,289,693.2	0.16	701.10	18.06	38.83	104.00
2006	1,465	1,465	25,880	948,283	1,325,447	1,824.5	9	14,953,754	9,251,737.0	0.10	647.29	17.67	36.64	49.33
2007	2,065	2,065	36,649	1,311,788	1,693,398	2,485.0	4	17,881,692	13,523,922.7	0.12	635.25	17.75	35.79	16.10
2008	2,619	2,619	44,807	1,586,970	1,978,999	2,949.1	6	32,595,154	20,829,821.1	0.08	605.95	17.11	35.42	20.35
2009	3,076	3,076	51,736	1,811,229	2,192,411	3,230.6	10	32,136,415	25,757,376.6	0.10	588.83	16.82	35.01	30.95
2010	2,725	2,725	44,912	1,571,506	1,843,769	2,768.4	6	31,161,472	25,151,306.1	0.09	576.70	16.48	34.99	21.67
2011	2,420	2,420	39,972	1,386,798	1,624,860	2,403.7	5	30,533,150	24,736,197.1	0.08	573.06	16.52	34.69	20.80
2012	2,299	2,299	34,704	1,201,711	1,392,527	1,914.2	5	32,132,390	24,746,559.7	0.07	522.71	15.10	34.63	26.12
2013	2,096	2,096	27,803	941,975	1,084,477	1,165.8	6	29,569,680	23,716,319.0	0.07	449.42	13.26	33.88	51.47
2014	795	795	8,001	282,644	336,090	175.0	1	24,799,235	11,585,814.9	0.03	355.53	10.06	35.33	57.13
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>730-Day Blackout Period</b>														
2000	0	0	0	0	0	0.0	0	4,472,279	2,102,708.9	0.00	---	---	---	---
2001	0	0	0	0	0	0.0	0	4,798,149	4,155,900.9	0.00	---	---	---	---
2002	0	0	0	0	0	0.0	0	4,865,986	4,226,375.8	0.00	---	---	---	---
2003	830	830	26,571	918,736	1,543,449	1,315.4	8	5,026,254	4,274,354.5	0.17	1106.91	32.01	34.58	60.82
2004	654	654	19,502	747,690	1,404,151	1,091.7	9	5,309,678	4,319,501.9	0.12	1143.26	29.82	38.34	82.44
2005	368	368	11,424	469,310	705,936	743.0	8	5,224,964	4,518,735.9	0.07	1275.30	31.04	41.08	107.67
2006	554	554	16,532	628,301	883,000	931.6	2	12,089,198	7,673,245.5	0.05	1134.12	29.84	38.01	21.47
2007	770	770	22,976	850,173	1,103,987	1,229.9	1	14,483,413	10,818,909.2	0.05	1104.12	29.84	37.00	8.13



**Table 4a: Summary of Incident Stratterra Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2008	967	967	27,232	997,569	1,234,924	1,367.8	3	24,136,695	16,019,364.4	0.04	1031.61	28.16	36.63	21.93
2009	1,080	1,080	30,666	1,097,715	1,330,667	1,429.8	3	23,895,052	19,743,622.7	0.05	1016.40	28.39	35.80	20.98
2010	951	951	26,001	931,970	1,088,807	1,167.3	1	23,494,480	19,387,538.3	0.04	979.99	27.34	35.84	8.57
2011	909	909	23,592	840,900	966,564	924.2	1	24,770,948	19,571,464.6	0.04	925.08	25.95	35.64	10.82
2012	837	837	18,944	676,694	783,041	533.2	5	24,554,436	18,844,477.1	0.03	808.48	22.63	35.72	93.77
2013	330	330	6,350	234,609	276,682	87.1	1	18,916,971	9,175,655.8	0.02	710.94	19.24	36.95	114.78
2014	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>1,095-Day Blackout Period</b>														
2000	0	0	0	0	0	0.0	0	3,815,327	1,806,473.6	0.00	---	---	---	---
2001	0	0	0	0	0	0.0	0	4,106,403	3,609,935.8	0.00	---	---	---	---
2002	0	0	0	0	0	0.0	0	4,274,307	3,683,678.5	0.00	---	---	---	---
2003	384	384	17,081	610,059	1,018,801	752.4	1	4,276,082	3,584,244.3	0.09	1588.70	44.48	35.72	13.29
2004	320	320	12,830	506,854	808,255	627.6	5	4,485,167	3,756,840.5	0.07	1583.92	40.09	39.51	79.67
2005	192	192	7,948	340,265	498,638	478.4	3	4,515,077	3,941,075.0	0.04	1772.21	41.40	42.81	62.71
2006	278	278	11,300	438,978	616,986	544.4	2	9,875,053	6,410,412.8	0.03	1579.06	40.65	38.85	36.73
2007	397	397	15,590	592,717	770,011	686.4	1	11,686,202	8,935,372.5	0.03	1492.99	39.27	38.02	14.57
2008	447	447	16,983	634,426	783,339	707.0	1	18,692,524	12,887,415.9	0.02	1419.30	37.99	37.36	14.14
2009	490	490	19,201	691,905	853,981	709.2	1	18,568,006	15,598,991.5	0.03	1412.05	39.19	36.03	14.10
2010	456	456	16,208	589,767	696,929	505.6	1	19,671,862	15,782,079.7	0.02	1293.35	35.54	36.39	19.78
2011	428	428	13,827	499,753	573,195	289.1	0	19,626,173	15,303,601.7	0.02	1167.65	32.31	36.14	0.00
2012	171	171	4,450	175,951	210,972	45.3	0	17,017,117	7,632,032.6	0.01	1028.95	26.02	39.54	0.00
2013	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2014	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Strattera Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>90-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
2000	0	0	---
2001	0	0	---
2002	0	0	0.0
2003	15	1,964	76.4
2004	18	2,335	77.1
2005	8	1,438	55.6
2006	8	1,880	42.6
2007	21	2,624	80.0
2008	9	3,782	23.8
2009	23	4,422	52.0
2010	13	3,775	34.4
2011	8	3,372	23.7
2012	9	3,136	28.7
2013	15	2,981	50.3
2014	6	2,854	21.0
2015	0	840	0.0
2016	0	0	---
<b>Days 91-180</b>			
2000	0	0	---
2001	0	0	---
2002	0	0	0.0
2003	8	1,330	60.1
2004	8	1,565	51.1
2005	3	882	34.0
2006	4	1,190	33.6
2007	10	1,649	60.6
2008	7	2,241	31.2
2009	10	2,660	37.6
2010	10	2,226	44.9
2011	5	1,968	25.4
2012	9	1,819	49.5
2013	4	1,732	23.1
2014	7	1,591	44.0
2015	0	234	0.0
2016	0	0	---
<b>Days 181-270</b>			
2000	0	0	---

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Strattera Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
2001	0	0	---
2002	0	0	---
2003	8	828	96.6
2004	6	919	65.3
2005	5	481	103.9
2006	2	638	31.4
2007	4	900	44.4
2008	1	1,196	8.4
2009	7	1,391	50.3
2010	4	1,196	33.4
2011	2	1,045	19.1
2012	1	996	10.0
2013	4	931	43.0
2014	1	663	15.1
2015	0	49	0.0
2016	0	0	---
<b>Days 271-365</b>			
2000	0	0	---
2001	0	0	---
2002	0	0	---
2003	1	626	16.0
2004	0	664	0.0
2005	2	323	61.9
2006	2	448	44.6
2007	3	627	47.9
2008	2	803	24.9
2009	3	959	31.3
2010	0	841	0.0
2011	1	742	13.5
2012	1	708	14.1
2013	3	651	46.1
2014	0	330	0.0
2015	0	4	0.0
2016	0	0	---
<b>Days 366-730</b>			
2000	0	0	---
2001	0	0	---
2002	0	0	---

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Strattera Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
2003	10	1,333	75.0
2004	10	1,223	81.8
2005	6	603	99.5
2006	7	893	78.4
2007	3	1,255	23.9
2008	3	1,581	19.0
2009	7	1,801	38.9
2010	5	1,601	31.2
2011	4	1,479	27.0
2012	0	1,381	0.0
2013	5	1,079	46.4
2014	1	175	57.1
2015	0	0	---
2016	0	0	---
<b>Days 731-1,095</b>			
2000	0	0	---
2001	0	0	---
2002	0	0	---
2003	7	563	124.3
2004	4	464	86.2
2005	5	265	189.0
2006	0	387	0.0
2007	0	543	0.0
2008	2	661	30.3
2009	2	721	27.8
2010	0	662	0.0
2011	1	635	15.7
2012	5	488	102.5
2013	1	87	114.8
2014	0	0	---
2015	0	0	---
2016	0	0	---

**Appendix A: List of Generic and Brand Names Used To Define the Exposures and Exposure Incidence in this Request**

Generic Name	Brand Name
<b>Amphetamines</b>	
DEXTROAMPHETAMINE SULFATE	Dexedrine Spansule
DEXTROAMPHETAMINE SULFATE	dextroamphetamine
DEXTROAMPHETAMINE SULFATE	Dexedrine
DEXTROAMPHETAMINE SULFATE	DextroStat
DEXTROAMPHETAMINE SULFATE	Zenzedi
DEXTROAMPHETAMINE SULFATE	ProCentra
DEXTROAMPHETAMINE SULFATE	Liquadd
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	Amphetamine Salt Combo
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	Adderall XR
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	Adderall
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	dextroamphetamine-amphetamine
LISDEXAMFETAMINE DIMESYLATE	Vyvanse
METHAMPHETAMINE HCL	Desoxyn
AMPHETAMINE SULFATE	Evekeo
METHAMPHETAMINE HCL	methamphetamine
<b>Methylphenidates</b>	
DEXMETHYLPHENIDATE HCL	dexmethylphenidate
DEXMETHYLPHENIDATE HCL	Focalin XR
DEXMETHYLPHENIDATE HCL	Focalin
METHYLPHENIDATE HCL	Methylin
METHYLPHENIDATE HCL	Ritalin LA
METHYLPHENIDATE HCL	methylphenidate
METHYLPHENIDATE HCL	Concerta
METHYLPHENIDATE HCL	Metadate CD
METHYLPHENIDATE HCL	Aptensio XR
METHYLPHENIDATE HCL	Ritalin
METHYLPHENIDATE HCL	Ritalin SR
METHYLPHENIDATE HCL	Metadate ER
METHYLPHENIDATE HCL	Quillivant XR
METHYLPHENIDATE HCL	Methylin ER
<b>Strattera</b>	
ATOMOXETINE HCL	Strattera

**Appendix B: Codes Used to Define Heart Failure in this Request**


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<b>Code</b>	<b>Code Type</b>	<b>Description</b>
398.91	ICD-9-CM Diagnosis	Rheumatic heart failure (congestive)
402.01	ICD-9-CM Diagnosis	Malignant hypertensive heart disease with heart failure
402.11	ICD-9-CM Diagnosis	Benign hypertensive heart disease with heart failure
402.91	ICD-9-CM Diagnosis	Unspecified hypertensive heart disease with heart failure
404.01	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.03	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic kidney disease stage V or end stage renal disease
404.11	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, benign, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.13	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, benign, with heart failure and chronic kidney disease stage V or end stage renal disease
404.91	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, unspecified, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.93	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, unspecified, with heart failure and chronic kidney disease stage V or end stage renal disease
422.90	ICD-9-CM Diagnosis	Acute myocarditis, unspecified
425.4	ICD-9-CM Diagnosis	Other primary cardiomyopathies
425.9	ICD-9-CM Diagnosis	Secondary cardiomyopathy, unspecified
428	ICD-9-CM Diagnosis	Heart Failure
428.0	ICD-9-CM Diagnosis	Congestive heart failure, unspecified
428.1	ICD-9-CM Diagnosis	Left heart failure
428.2	ICD-9-CM Diagnosis	Systolic heart failure
428.20	ICD-9-CM Diagnosis	Systolic heart failure, unspecified
428.21	ICD-9-CM Diagnosis	Acute systolic heart failure
428.22	ICD-9-CM Diagnosis	Chronic systolic heart failure
428.23	ICD-9-CM Diagnosis	Acute on chronic systolic heart failure
428.3	ICD-9-CM Diagnosis	Diastolic heart failure
428.30	ICD-9-CM Diagnosis	Diastolic heart failure, unspecified
428.31	ICD-9-CM Diagnosis	Acute diastolic heart failure
428.32	ICD-9-CM Diagnosis	Chronic diastolic heart failure
428.33	ICD-9-CM Diagnosis	Acute on chronic diastolic heart failure
428.4	ICD-9-CM Diagnosis	Combined systolic and diastolic heart failure
428.40	ICD-9-CM Diagnosis	Combined systolic and diastolic heart failure, unspecified
428.41	ICD-9-CM Diagnosis	Acute combined systolic and diastolic heart failure
428.42	ICD-9-CM Diagnosis	Chronic combined systolic and diastolic heart failure
428.43	ICD-9-CM Diagnosis	Acute on chronic combined systolic and diastolic heart failure
428.9	ICD-9-CM Diagnosis	Heart failure, unspecified

**Modular Program Specifications for cder\_mpl1r\_wp014\_nsdp\_v01 Report 4 of 8**

Sentinel's Cohort Identification and Descriptive Analysis (CIDA) tool was used to investigate heart failure following treatment with select attention deficit and hyperactivity disorder (ADHD) medications. In total, 49 scenarios were examined with four different exposures, seven different blackout periods, and two different episode gaps/exposure extension periods. The four exposures are all amphetamines, all methylphenidates, strattera, and all stimulants (which include all amphetamines and all methylphenidates and strattera). **The outcome is heart failure, defined as any heart failure ICD-9-CM diagnosis code (398.91, 402.x1, 402.x3, 404.x1, 404.x3, 422.90, 425.4, 425.9, 428.xx) in any care setting with a primary discharge diagnosis (PDX) value of P (principal) for those diagnoses in the inpatient care setting.** See below for a description of each of these scenarios. The query period was from January 1, 2000 to March 3, 2016 and the enrollment gap was set at 45 days. Age groups were split as follows: 0-21, 22-44, 45-64, 65+.

Enrollment Gap	45 Days
Age Groups	0-21, 22-44, 45-64, 65+
Query Period	January 1, 2000 - Current
Coverage Requirement	Medical and Drug
Enrollment Requirement	183 Days

Scenario	Drug/Exposure										Event/Outcome					
	Incident exposure	Incident w/ respect to:	Episode Truncation at Incident	Episode Truncation at Death	Washout (days)	Cohort Definition	Exposure Episode Gap	Exposure Extension Period	Exposure Episode Duration	Min Days Supplied	Event/ Outcome	Care Setting/PDX	Incident with Respect to Setting/PDX	Incident w/ respect to Care Setting/PDX	Washout (days)	Blackout Period
			Yes	No												
1	Stratera	All Stimulants	Yes	No	183	01	90	90	0	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	0
2	Stratera	All Stimulants	Yes	No	183	01	90	90	90	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	90
3	Stratera	All Stimulants	Yes	No	183	01	90	90	180	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	180
4	Stratera	All Stimulants	Yes	No	183	01	90	90	270	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	270
5	Stratera	All Stimulants	Yes	No	183	01	90	90	365	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	365
6	Stratera	All Stimulants	Yes	No	183	01	90	90	730	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	730
7	Stratera	All Stimulants	Yes	No	183	01	90	90	1095	0	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	Any Heart Failure Code	IPP, ISP AV*, AO* ED*	183	1095

ICD-9, ICD-10, HCPCS, and CPT codes are provided by Optum360. NDC codes are checked against First Data Bank's "National Drug Data File (NDDF\*) Plus."

Cohort Definition of 01 will only consider the first incident episode for each user during the query period that satisfies the washout period.

Note: Episodes are automatically truncated at outcome.

### Disclaimer

The following report(s) provides findings from an FDA-initiated query using Sentinel. While Sentinel queries may be undertaken to assess potential medical product safety risks, they may also be initiated for various other reasons. Some examples include determining a rate or count of an identified health outcome of interest, examining medical product use, exploring the feasibility of future, more detailed analyses within Sentinel, and seeking to better understand Sentinel capabilities.

Data obtained through Sentinel are intended to complement other types of evidence such as preclinical studies, clinical trials, postmarket studies, and adverse event reports, all of which are used by FDA to inform regulatory decisions regarding medical product safety. The information contained in this report is provided as part of FDA's commitment to place knowledge acquired from Sentinel in the public domain as soon as possible. Any public health actions taken by FDA regarding products involved in Sentinel queries will continue to be communicated through existing channels.

FDA wants to emphasize that the fact that FDA has initiated a query involving a medical product and is reporting findings related to that query does not mean that FDA is suggesting health care practitioners should change their prescribing practices for the medical product or that patients taking the medical product should stop using it. Patients who have questions about the use of an identified medical product should contact their health care practitioners.

The following report contains a description of the request, request specifications, and results from the modular program run(s).

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## Overview for Request cder\_mpl1r\_wp014\_nsdp\_v01, Report 5 of 8

**Request ID:** cder\_mpl1r\_wp014\_nsdp\_v01. This is report 5 of 8.

**Request Description:** FDA has requested execution of the Cohort Identification and Descriptive Analysis (CIDA) tool, version 2.1.1, to investigate heart failure diagnoses following new use of attention deficit hyperactivity disorder (ADHD) medications. This report presents results for all amphetamines. Results for all methylphenidates, strattera, and all stimulants are presented in separate reports.

**Data Source:** Data from January 1, 2000 to March 3, 2016 from 15 health plans contributing to the Sentinel Distributed Database (SDD) are included in this report.

**Study Design:** This request was designed to identify exposures and follow-up time. The exposure of interest and the occurrence of the health outcome of interest during exposed time were identified. The number of exposure episodes, number of individuals, number of events, and days at-risk in the SDD were calculated overall and were stratified by age group, sex, and year.

**Exposure of Interest:** The exposures of interest were amphetamines, which were defined using National Drug Codes (NDCs). Please refer to Appendix A for a list of generic and brand names of amphetamines included in this request.

**Cohort Eligibility Criteria:** Patients were required to be continuously enrolled in plans with both medical and drug coverage for at least 6 months (183 days) before their dispensing date, during which gaps in coverage of up to 45 days were allowed. Members were excluded if they had any ADHD medication or the outcome of interest in the 6 months (183 days) prior to exposure initiation. The following age groups were included in the cohort: 0-21, 22-44, 45-64, 65+ years.

**Follow-Up Time:** Follow-up time for the outcome was determined by the length of the exposure episodes. Exposure episode lengths were defined using outpatient pharmacy dispensing days supplied to create a sequence of continuous exposure. Exposure episodes were considered continuous if gaps in days supply were less than 90 days. The end date of each exposure episode was extended by 90 additional days. Follow-up began on the day on which the first exposure of interest was dispensed and continued until the first occurrence of any of the following: 1) the outcome of interest; 2) any codes defining incidence criteria; 3) disenrollment; 4) the study end date (March, 2016); 5) the end date of the data provided by each Data Partner; or 6) the end of the exposure episode. Only the first valid incident exposure episode that occurred during the study period was included per patient.

This report examines different blackout periods which is a number of days at the beginning of the ADHD medication episode where if an outcome occurs, it is not attributed to the exposure and the person is omitted from the analysis. The blackout periods examined were 90 days, 180 days, 270 days, 365 days, 730 days, and 1,095 days. Episodes that were at least as long as the blackout period were required.

**Outcome of Interest:** Heart failure was defined using the ICD-9-CM diagnosis codes listed in Appendix B. The event needed to meet one of the following criteria: (1) at least one code in the inpatient setting with primary diagnosis flag = Primary, OR (2) at least three codes in the inpatient setting with primary diagnosis flag = Secondary, OR (3) at least two codes in the outpatient setting with any primary diagnosis flag value, OR (4) at least three codes in the emergency department setting with any primary diagnosis flag value, OR (5) at least two codes in the inpatient setting with primary diagnosis flag = Secondary and at least one code in the outpatient with any primary diagnosis flag value. The temporal relationship between codes was 365 days. This event had to be incident (no heart failure events in the 183 days prior to exposure initiation).

**Please refer to Appendix C for detailed specifications.**

**Limitations:** Algorithms to define exposures and outcomes are imperfect and, therefore, may be misclassified.

**Notes:** Please contact the Sentinel Operations Center Query Fulfillment Team ([production@mini-sentinel.org](mailto:production@mini-sentinel.org)) for questions and to provide comments/suggestions for future enhancements to this document.

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**Glossary of Terms for Analyses Using  
Cohort Identification and Descriptive Analysis (CIDA) Tool\***

**Amount Supplied** - number of units (pills, tablets, vials) dispensed. Net amount per NDC per dispensing. This is equivalent to the "RxAmt" value in the MSCDM.

**Blackout Period** - number of days at the beginning of a treatment episode that events are to be ignored. If an event occurs during the blackout period, the episode is excluded.

**Care Setting** - type of medical encounter or facility where the exposure, event, or condition code was recorded. Possible care settings include: Inpatient Hospital Stay (IP), Non-Acute Institutional Stay (IS), Emergency Department (ED), Ambulatory Visit (AV), and Other Ambulatory Visit (OA). For laboratory results, possible care settings include: Emergency department (E), Home (H), Inpatient (I), Outpatient (O), or Unknown or Missing (U). Along with the Principal Diagnosis Indicator, forms the Care Setting/PDX parameter.

**Cohort Definition (drug/exposure)** - indicates how the cohort will be defined: (1) 01: Cohort includes only the first valid incident treatment episode during the query period; (2) 02: Cohort includes all valid incident treatment episodes during the query period; (3) 03: Cohort includes all valid incident treatment episodes during the query period until an event

**Days Supplied** - number of days supplied for all dispensings in qualifying treatment episodes.

**Eligible Members** - number of members eligible for an incident treatment episode (defined by the drug/exposure and event washout periods) with drug and medical coverage during the query period.

**Enrollment Gap** - number of days allowed between two consecutive enrollment periods without breaking a "continuously enrolled" sequence.

**Episodes** - treatment episodes; length of episode is determined by days supplied in one dispensing or consecutive dispensings bridged by the episode gap.

**Episode Gap** - number of days allowed between two (or more) consecutive exposures (dispensings/procedures) to be considered the same treatment episode.

**Event Deduplication** - specifies how events are counted by the MP algorithm: (0) 0: Counts all occurrences of an HOI during an exposure episode; (1) 1: de-duplicates occurrences of the same HOI code and code type on the same day; (2) 2: de-duplicates occurrences of the same HOI group on the same day (e.g., de-duplicates at the group level).

**Exposure Episode Length** - number of days after exposure initiation that is considered "exposed time."

**Exposure Extension Period** - number of days post treatment period in which the outcomes/events are counted for a treatment episode.

**Lookback Period (pre-existing condition)** - number of days wherein a member is required to have evidence of pre-existing condition (diagnosis/procedure/drug dispensing).

**Member-Years** - sum of all days of enrollment with medical and drug coverage\*\* in the query period preceded by an exposure washout period all divided by **365.25**.

**Minimum Days Supplied** - specifies a minimum number of days in length of the days supplied for the episode to be considered.

**Minimum Episode Duration** - specifies a minimum number of days in length of the episode for it to be considered.

**Principal Diagnosis (PDX)** - diagnosis or condition established to be chiefly responsible for admission of the patient to the hospital. 'P' = principal diagnosis, 'S' = secondary diagnosis, 'X' = unspecified diagnosis, '.' = blank. Along with the Care Setting values, forms the Caresetting/PDX parameter.

**Query Period** - period in which the modular program looks for exposures and outcomes of interest.

**Treatment Episode Truncation Indicator** - indicates whether observation of the incident query code during follow-up requires truncation of valid treatment episodes. A value of Y indicates that the treatment episodes should be truncated at the first occurrence of an incident query code. A value of N indicates that the treatment episodes should not be truncated at the occurrence of the incident query code.

**Users** - number of members with exposure during the query period. Member must have no evidence of exposure(s) of interest (defined by incidence criteria) in the prior washout period. A user may only be counted once in a query period.

**Washout Period (drug/exposure)\*\*** - number of days a user is required to have no evidence of prior exposure (drug dispensing/procedure) and continuous drug and medical coverage prior to an incident treatment episode.

**Washout Period (event/outcome)\*\*** - number of days a user is required to have no evidence of a prior event (procedure/diagnosis) and continuous drug and medical coverage prior to an incident treatment episode.

**Years at Risk** - number of days supplied plus any episode gaps and exposure extension periods all divided by 365.25.

\*all terms may not be used in this report

\*\*incident treatment episodes must be incident to both the exposure and the event

**Table 1a: Summary of Incident Amphetamine Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, and Blackout Period**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>30-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
	1,170,671	1,170,671	6,161,718	198,454,634	297,843,439	645,693.3	747	110,296,636	305,858,034.4	10.61	169.52	5.26	32.21	11.57
<b>90-Day Blackout Period</b>														
	650,990	650,990	5,657,312	186,030,011	272,812,063	421,604.5	446	100,830,396	277,151,093.2	6.46	285.76	8.69	32.88	10.58
<b>180-Day Blackout Period</b>														
	363,368	363,368	4,856,149	161,518,389	239,337,671	308,466.5	331	93,687,938	251,138,015.2	3.88	444.50	13.36	33.26	10.73
<b>270-Day Blackout Period</b>														
	242,279	242,279	4,192,393	140,670,362	210,462,898	237,164.8	261	80,172,666	229,143,275.1	3.02	580.61	17.30	33.55	11.01
<b>365-Day Blackout Period</b>														
	170,544	170,544	3,601,985	121,897,803	183,889,187	185,184.6	194	72,200,029	208,176,014.6	2.36	714.76	21.12	33.84	10.48
<b>730-Day Blackout Period</b>														
	63,235	63,235	2,094,192	72,862,773	112,187,961	80,428.0	101	48,917,741	145,839,559.5	1.29	1152.25	33.12	34.79	12.56
<b>1,095-Day Blackout Period</b>														
	27,934	27,934	1,216,014	43,426,173	68,013,232	37,691.8	50	34,449,661	103,828,084.9	0.81	1554.60	43.53	35.71	13.27
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
	1,170,671	1,170,671	8,205,407	265,572,842	399,220,913	1,024,276.6	1,112	110,296,636	305,858,034.4	10.61	226.86	7.01	32.37	10.86
<b>90-Day Blackout Period</b>														
	989,549	989,549	7,956,593	260,104,476	391,803,951	762,846.4	766	100,830,396	276,763,173.9	9.81	262.85	8.04	32.69	10.04
<b>180-Day Blackout Period</b>														
	617,634	617,634	7,450,050	246,089,028	365,275,365	593,229.8	578	93,687,937	250,961,618.5	6.59	398.44	12.06	33.03	9.74
<b>270-Day Blackout Period</b>														
	443,831	443,831	6,802,454	226,356,716	338,252,532	472,239.1	465	80,172,665	229,044,080.2	5.54	510.01	15.33	33.28	9.85
<b>365-Day Blackout Period</b>														
	326,702	326,702	6,092,296	204,085,774	306,899,411	377,044.4	366	72,200,028	208,119,636.3	4.52	624.68	18.65	33.50	9.71
<b>730-Day Blackout Period</b>														
	130,549	130,549	3,863,322	132,261,545	202,702,618	170,648.7	181	48,917,741	145,830,027.2	2.67	1013.12	29.59	34.24	10.61
<b>1,095-Day Blackout Period</b>														
	59,509	59,509	2,350,767	82,244,846	128,417,565	81,225.5	96	34,449,661	103,826,015.4	1.73	1382.06	39.50	34.99	11.82

**Table 1b: Rate of Heart Failure Outcomes at Different Stages of Amphetamine Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, and Blackout Period**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>30-Day Episode Gap/Extension Period</b>			
Days 0-90	301	224,089	13.4
Days 91-180	115	113,138	10.2
Days 181-270	70	71,302	9.8
Days 271-365	67	51,980	12.9
Days 366-730	93	104,757	8.9
Days 731-1,095	51	42,736	11.9
<b>90-Day Episode Gap/Extension Period</b>			
Days 0-90	346	261,430	13.2
Days 91-180	188	169,617	11.1
Days 181-270	113	120,991	9.3
Days 271-365	99	95,195	10.4
Days 366-730	185	206,396	9.0
Days 731-1,095	85	89,423	9.5

**Table 2a: Summary of Incident Amphetamine Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>30-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
00-21 Years	558,945	558,945	2,592,503	84,174,276	107,108,936	280,725.6	85	33,426,038	84,089,330.6	16.72	150.59	4.64	32.47	3.03
22-44 Years	444,553	444,553	2,594,619	82,167,334	130,343,254	262,303.2	187	45,751,583	95,959,817.5	9.72	184.83	5.84	31.67	7.13
45-64 Years	157,358	157,358	935,208	30,733,898	57,959,156	98,059.3	359	32,658,948	90,679,017.8	4.82	195.31	5.94	32.86	36.61
65+ Years	9,815	9,815	39,388	1,379,126	2,432,093	4,605.2	116	10,956,784	35,129,868.5	0.90	140.51	4.01	35.01	251.89
<b>90-Day Blackout Period</b>														
00-21 Years	305,776	305,776	2,344,196	78,033,976	99,287,581	174,138.4	62	30,666,250	76,555,021.1	9.97	255.20	7.67	33.29	3.56
22-44 Years	254,637	254,637	2,409,137	77,619,445	123,168,597	176,492.6	121	41,129,883	85,494,398.2	6.19	304.82	9.46	32.22	6.86
45-64 Years	86,069	86,069	869,477	29,124,709	48,112,799	68,159.8	208	30,258,078	82,836,386.6	2.84	338.39	10.10	33.50	30.52
65+ Years	4,508	4,508	34,502	1,251,881	2,243,086	2,813.7	55	9,856,949	32,265,287.2	0.46	277.70	7.65	36.28	195.47
<b>180-Day Blackout Period</b>														
00-21 Years	155,699	155,699	1,933,733	65,312,824	83,658,098	122,891.9	41	28,479,454	69,606,645.9	5.47	419.48	12.42	33.78	3.34
22-44 Years	152,427	152,427	2,114,451	68,791,862	110,090,635	130,854.8	90	37,561,773	76,195,203.8	4.06	451.31	13.87	32.53	6.88
45-64 Years	52,799	52,799	778,562	26,327,755	43,628,749	52,644.4	160	28,285,285	75,627,541.2	1.87	498.64	14.75	33.82	30.39
65+ Years	2,443	2,443	29,403	1,085,948	1,960,189	2,075.4	40	9,304,714	29,708,624.4	0.26	444.51	12.04	36.93	192.73
<b>270-Day Blackout Period</b>														
00-21 Years	97,714	97,714	1,627,067	55,521,726	71,651,286	93,129.8	32	24,385,608	63,698,549.8	4.01	568.21	16.65	34.12	3.44
22-44 Years	105,357	105,357	1,845,092	60,520,564	97,582,902	100,463.5	72	31,643,077	68,524,569.0	3.33	574.43	17.51	32.80	7.17
45-64 Years	37,567	37,567	694,792	23,678,277	39,501,509	41,962.9	124	24,638,152	69,444,949.0	1.52	630.29	18.49	34.08	29.55
65+ Years	1,641	1,641	25,442	949,795	1,727,201	1,608.6	33	8,309,010	27,475,207.2	0.20	578.79	15.50	37.33	205.15
<b>365-Day Blackout Period</b>														
00-21 Years	66,076	66,076	1,375,789	47,400,549	61,533,148	72,577.4	22	21,974,522	58,048,537.7	3.01	717.36	20.82	34.45	3.03
22-44 Years	75,318	75,318	1,588,566	52,515,799	85,337,297	77,649.6	55	27,929,105	61,356,152.9	2.70	697.25	21.09	33.06	7.08
45-64 Years	27,967	27,967	615,511	21,149,983	35,488,359	33,697.1	92	22,361,860	63,496,158.8	1.25	756.25	22.01	34.36	27.30
65+ Years	1,183	1,183	22,119	831,472	1,530,383	1,260.5	25	7,789,636	25,275,165.2	0.15	702.85	18.70	37.59	198.33
<b>730-Day Blackout Period</b>														
00-21 Years	24,309	24,309	804,012	28,523,367	37,335,130	32,199.6	7	14,944,141	40,954,932.8	1.63	1173.37	33.07	35.48	2.17
22-44 Years	27,079	27,079	895,763	30,324,134	50,650,708	32,004.7	31	17,784,413	41,012,173.3	1.52	1119.84	33.08	33.85	9.69
45-64 Years	11,402	11,402	381,738	13,518,692	23,254,481	15,691.3	53	15,664,570	45,366,251.8	0.73	1185.64	33.48	35.41	33.78
65+ Years	445	445	12,679	496,580	947,643	532.4	10	5,678,206	18,506,201.5	0.08	1115.91	28.49	39.17	187.84
<b>1,095-Day Blackout Period</b>														
00-21 Years	11,061	11,061	479,500	17,481,937	23,209,926	15,534.7	5	10,532,871	29,272,169.6	1.05	1580.50	43.35	36.46	3.22
22-44 Years	11,388	11,388	498,367	17,215,780	29,229,983	14,083.0	17	11,889,809	28,238,072.8	0.96	1511.75	43.76	34.54	12.07
45-64 Years	5,318	5,318	231,900	8,460,136	15,039,414	7,815.0	25	11,300,263	32,726,086.8	0.47	1590.85	43.61	36.48	31.99
65+ Years	167	167	6,247	268,320	533,910	259.1	3	4,240,760	13,591,755.8	0.04	1606.71	37.41	42.95	115.79

**Table 2a: Summary of Incident Amphetamine Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
00-21 Years	558,945	558,945	3,642,049	118,815,194	152,222,168	477,166.4	127	33,426,038	84,089,330.6	16.72	212.57	6.52	32.62	2.66
22-44 Years	444,553	444,553	3,286,892	104,413,891	168,097,793	388,356.4	260	45,751,583	95,959,817.5	9.72	234.87	7.39	31.77	6.69
45-64 Years	157,358	157,358	1,224,207	40,495,607	75,569,393	151,185.1	547	32,658,948	90,679,017.8	4.82	257.35	7.78	33.08	36.18
65+ Years	9,815	9,815	52,259	1,848,150	3,331,559	7,568.6	178	10,956,784	35,129,868.5	0.90	188.30	5.32	35.37	235.18
<b>90-Day Blackout Period</b>														
00-21 Years	470,735	470,735	3,526,323	116,315,975	149,091,691	353,187.9	100	30,666,250	76,376,505.5	15.35	247.09	7.49	32.99	2.83
22-44 Years	374,025	374,025	3,185,420	102,154,265	164,860,862	288,817.2	193	41,103,093	85,367,165.5	9.10	273.12	8.52	32.07	6.68
45-64 Years	136,144	136,144	1,194,328	39,832,403	74,593,691	115,522.5	367	30,251,028	82,764,205.4	4.50	292.58	8.77	33.35	31.77
65+ Years	8,645	8,645	50,522	1,801,833	3,257,707	5,318.8	106	9,855,158	32,255,297.5	0.88	208.42	5.84	35.66	199.29
<b>180-Day Blackout Period</b>														
00-21 Years	294,238	294,238	3,293,930	109,854,345	141,283,956	272,272.5	77	28,479,453	69,513,661.0	10.33	373.35	11.19	33.35	2.83
22-44 Years	235,996	235,996	2,978,588	96,423,769	156,286,093	223,794.9	149	37,544,122	76,139,834.1	6.29	408.58	12.62	32.37	6.66
45-64 Years	83,058	83,058	1,131,446	38,125,399	64,614,250	93,098.6	281	28,281,991	75,602,881.2	2.94	459.02	13.62	33.70	30.18
65+ Years	4,342	4,342	46,086	1,685,515	3,091,066	4,063.9	71	9,303,909	29,705,242.1	0.47	388.19	10.61	36.57	174.71
<b>270-Day Blackout Period</b>														
00-21 Years	207,880	207,880	2,992,735	100,534,953	129,836,146	215,130.2	59	24,385,608	63,645,256.0	8.52	483.62	14.40	33.59	2.74
22-44 Years	171,004	171,004	2,715,394	88,534,609	144,593,453	177,225.0	124	31,632,119	68,494,875.2	5.41	517.73	15.88	32.60	7.00
45-64 Years	61,908	61,908	1,052,447	35,736,695	60,950,224	76,628.2	224	24,636,050	69,430,625.2	2.51	577.25	17.00	33.96	29.23
65+ Years	3,039	3,039	41,878	1,550,459	2,872,709	3,255.7	58	8,308,502	27,473,323.7	0.37	510.19	13.78	37.02	178.15
<b>365-Day Blackout Period</b>														
00-21 Years	149,401	149,401	2,662,272	90,013,267	116,637,263	170,955.9	45	21,974,521	58,017,988.6	6.80	602.49	17.82	33.81	2.63
22-44 Years	127,211	127,211	2,426,594	79,647,670	130,931,986	140,295.7	97	27,922,649	61,339,636.1	4.56	626.11	19.08	32.82	6.91
45-64 Years	47,840	47,840	965,668	33,011,675	56,679,520	63,148.7	178	22,360,439	63,487,929.1	2.14	690.04	20.19	34.19	28.19
65+ Years	2,250	2,250	37,762	1,413,162	2,650,641	2,644.2	46	7,789,320	25,274,082.4	0.29	628.07	16.78	37.42	173.97
<b>730-Day Blackout Period</b>														
00-21 Years	58,500	58,500	1,689,038	58,287,178	76,103,579	77,212.6	15	14,944,141	40,949,664.9	3.91	996.36	28.87	34.51	1.94
22-44 Years	49,475	49,475	1,491,173	49,933,671	84,229,947	60,925.4	51	17,783,336	41,009,827.8	2.78	1009.27	30.14	33.49	8.37
45-64 Years	21,601	21,601	658,476	23,085,182	40,534,487	31,304.3	96	15,664,243	45,364,626.2	1.38	1068.71	30.48	35.06	30.67
65+ Years	973	973	24,635	955,514	1,834,605	1,206.3	19	5,678,114	18,505,908.4	0.17	982.03	25.32	38.79	157.51
<b>1,095-Day Blackout Period</b>														
00-21 Years	26,833	26,833	1,043,016	36,756,296	48,526,532	37,015.6	12	10,532,871	29,270,933.9	2.55	1369.82	38.87	35.24	3.24
22-44 Years	21,622	21,622	871,904	29,709,395	51,216,163	27,640.0	28	11,889,627	28,237,700.4	1.82	1374.04	40.32	34.07	10.13
45-64 Years	10,676	10,676	422,838	15,229,580	27,568,240	15,945.7	47	11,300,196	32,725,687.8	0.94	1426.52	39.61	36.02	29.48

**Table 2a: Summary of Incident Amphetamine Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
65+ Years	378	378	13,009	549,575	1,106,630	624.3	9	4,240,731	13,591,693.3	0.09	1453.90	34.42	42.25	144.17



**Table 2b: Rate of Heart Failure Outcomes at Different Stages of Amphetamine Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>30-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
00-21 Years	23	106,587	2.2
22-44 Years	66	85,811	7.7
45-64 Years	151	29,900	50.5
65+ Years	61	1,791	340.5
<b>Days 91-180</b>			
00-21 Years	21	51,247	4.1
22-44 Years	31	45,638	6.8
45-64 Years	48	15,515	30.9
65+ Years	15	738	203.2
<b>Days 181-270</b>			
00-21 Years	9	29,762	3.0
22-44 Years	18	30,391	5.9
45-64 Years	36	10,681	33.7
65+ Years	7	467	150.0
<b>Days 271-365</b>			
00-21 Years	10	20,552	4.9
22-44 Years	17	22,814	7.5
45-64 Years	32	8,266	38.7
65+ Years	8	348	229.8
<b>Days 366-730</b>			
00-21 Years	15	40,378	3.7
22-44 Years	24	45,645	5.3
45-64 Years	39	18,006	21.7
65+ Years	15	728	206.0
<b>Days 731-1,095</b>			
00-21 Years	2	16,665	1.2
22-44 Years	14	17,922	7.8
45-64 Years	28	7,876	35.5
65+ Years	7	273	256.1

**Table 2b: Rate of Heart Failure Outcomes at Different Stages of Amphetamine Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>90-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
00-21 Years	27	123,979	2.2
22-44 Years	67	99,539	6.7
45-64 Years	180	35,663	50.5
65+ Years	72	2,250	320.0
<b>Days 91-180</b>			
00-21 Years	23	80,915	2.8
22-44 Years	44	65,022	6.8
45-64 Years	86	22,424	38.4
65+ Years	35	1,255	278.9
<b>Days 181-270</b>			
00-21 Years	18	57,142	3.2
22-44 Years	25	46,570	5.4
45-64 Years	57	16,470	34.6
65+ Years	13	808	160.9
<b>Days 271-365</b>			
00-21 Years	14	44,174	3.2
22-44 Years	27	36,929	7.3
45-64 Years	46	13,480	34.1
65+ Years	12	612	196.2
<b>Days 366-730</b>			
00-21 Years	30	93,743	3.2
22-44 Years	46	79,370	5.8
45-64 Years	82	31,844	25.8
65+ Years	27	1,438	187.8
<b>Days 731-1,095</b>			
00-21 Years	3	40,197	0.7
22-44 Years	23	33,285	6.9
45-64 Years	49	15,359	31.9
65+ Years	10	582	171.8

**Table 3a: Summary of Incident Amphetamine Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member-Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>30-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
Female	548,980	548,980	3,040,664	97,800,875	146,549,886	316,435.4	368	56,075,895	158,521,694.1	9.79	178.15	5.54	32.16	11.63
Male	621,643	621,643	3,120,846	100,647,087	151,283,649	329,235.5	379	54,215,032	147,323,588.4	11.47	161.90	5.02	32.25	11.51
Unknown	48	48	208	6,672	9,904	22.5	0	5,709	12,751.9	8.41	139.00	4.33	32.08	0.00
<b>90-Day Blackout Period</b>														
Female	309,654	309,654	2,810,179	92,135,579	138,088,282	210,933.2	208	51,333,654	143,840,092.4	6.03	297.54	9.08	32.79	9.86
Male	341,315	341,315	2,846,960	93,888,701	134,714,674	210,658.1	238	49,491,914	133,299,637.5	6.90	275.08	8.34	32.98	11.30
Unknown	21	21	173	5,731	9,107	13.2	0	4,828	11,363.2	4.35	272.90	8.24	33.13	0.00
<b>180-Day Blackout Period</b>														
Female	178,414	178,414	2,445,169	81,042,711	122,514,322	156,566.2	158	47,769,583	130,527,196.0	3.73	454.24	13.71	33.14	10.09
Male	184,944	184,944	2,410,850	80,471,215	116,815,928	151,891.0	173	45,914,193	120,600,620.3	4.03	435.11	13.04	33.38	11.39
Unknown	10	10	130	4,463	7,422	9.3	0	4,162	10,198.9	2.40	446.30	13.00	34.33	0.00
<b>270-Day Blackout Period</b>														
Female	121,639	121,639	2,133,297	71,310,115	108,612,099	121,352.3	126	40,935,510	119,266,511.3	2.97	586.24	17.54	33.43	10.38
Male	120,635	120,635	2,058,988	69,356,587	101,844,415	115,804.9	135	39,233,851	109,867,483.5	3.07	574.93	17.07	33.68	11.66
Unknown	5	5	108	3,660	6,384	7.7	0	3,305	9,280.2	1.51	732.00	21.60	33.89	0.00
<b>365-Day Blackout Period</b>														
Female	86,879	86,879	1,846,307	62,240,691	95,484,326	95,127.2	89	36,934,046	108,514,513.8	2.35	716.41	21.25	33.71	9.36
Male	83,662	83,662	1,755,584	59,654,105	88,399,309	90,051.0	105	35,263,062	99,653,075.9	2.37	713.04	20.98	33.98	11.66
Unknown	3	3	94	3,007	5,551	6.5	0	2,921	8,424.9	1.03	1002.33	31.33	31.99	0.00
<b>730-Day Blackout Period</b>														
Female	32,692	32,692	1,082,750	37,497,221	58,861,893	41,413.1	41	25,164,106	76,451,048.1	1.30	1146.98	33.12	34.63	9.90
Male	30,542	30,542	1,011,375	35,363,568	53,322,101	39,009.9	60	23,751,735	69,382,556.9	1.29	1157.87	33.11	34.97	15.38
Unknown	1	1	67	1,984	3,968	5.0	0	1,900	5,954.5	0.53	1984.00	67.00	29.61	0.00
<b>1,095-Day Blackout Period</b>														
Female	14,491	14,491	630,589	22,359,215	35,635,519	19,284.4	18	17,825,659	54,718,493.7	0.81	1542.97	43.52	35.46	9.33
Male	13,442	13,442	585,358	21,064,974	32,373,745	18,403.5	32	16,622,676	49,105,282.9	0.81	1567.10	43.55	35.99	17.39
Unknown	1	1	67	1,984	3,968	4.0	0	1,326	4,308.3	0.75	1984.00	67.00	29.61	0.00
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
Female	548,980	548,980	4,041,626	130,591,533	197,666,607	497,464.9	561	56,075,895	158,521,694.1	9.79	237.88	7.36	32.31	11.28
Male	621,643	621,643	4,163,483	134,971,541	201,540,839	526,774.2	551	54,215,032	147,323,588.4	11.47	217.12	6.70	32.42	10.46
Unknown	48	48	298	9,768	13,467	37.4	0	5,709	12,751.9	8.41	203.50	6.21	32.78	0.00
<b>90-Day Blackout Period</b>														
Female	466,207	466,207	3,927,450	128,086,198	194,227,124	374,519.1	374	51,333,654	143,667,823.5	9.08	274.74	8.42	32.61	9.99
Male	523,303	523,303	4,028,863	132,008,946	197,563,796	388,300.8	392	49,491,914	133,083,996.0	10.57	252.26	7.70	32.77	10.10

**Table 3a: Summary of Incident Amphetamine Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
Unknown	39	39	280	9,332	13,031	26.5	0	4,828	11,354.4	8.08	239.28	7.18	33.33	0.00
<b>180-Day Blackout Period</b>														
Female	294,857	294,857	3,694,461	121,654,908	184,862,967	294,137.6	284	47,769,582	130,454,646.9	6.17	412.59	12.53	32.93	9.66
Male	322,758	322,758	3,755,353	124,426,046	180,400,664	299,072.6	294	45,914,193	120,496,782.4	7.03	385.51	11.64	33.13	9.83
Unknown	19	19	236	8,074	11,735	19.6	0	4,162	10,189.2	4.57	424.95	12.42	34.21	0.00
<b>270-Day Blackout Period</b>														
Female	215,279	215,279	3,395,113	112,602,085	172,233,970	236,037.1	226	40,935,510	119,225,628.7	5.26	523.05	15.77	33.17	9.57
Male	228,541	228,541	3,407,140	113,747,662	166,008,432	236,186.0	239	39,233,850	109,809,180.2	5.83	497.71	14.91	33.39	10.12
Unknown	11	11	201	6,969	10,130	16.0	0	3,305	9,271.3	3.33	633.55	18.27	34.67	0.00
<b>365-Day Blackout Period</b>														
Female	160,855	160,855	3,060,722	102,188,140	157,071,376	189,627.4	172	36,934,046	108,491,547.0	4.36	635.28	19.03	33.39	9.07
Male	165,841	165,841	3,031,406	101,891,770	149,819,191	187,403.4	194	35,263,061	99,619,671.2	4.70	614.39	18.28	33.61	10.35
Unknown	6	6	168	5,864	8,843	13.6	0	2,921	8,418.1	2.05	977.33	28.00	34.90	0.00
<b>730-Day Blackout Period</b>														
Female	66,009	66,009	1,970,263	67,222,416	105,367,141	86,895.1	79	25,164,106	76,447,054.8	2.62	1018.38	29.85	34.12	9.09
Male	64,536	64,536	1,892,918	65,034,288	97,328,217	83,744.5	102	23,751,735	69,377,023.7	2.72	1007.72	29.33	34.36	12.18
Unknown	4	4	141	4,841	7,260	9.1	0	1,900	5,948.7	2.11	1210.25	35.25	34.33	0.00
<b>1,095-Day Blackout Period</b>														
Female	30,483	30,483	1,207,706	42,088,540	67,147,568	41,422.5	41	17,825,659	54,717,705.0	1.71	1380.72	39.62	34.85	9.90
Male	29,024	29,024	1,142,938	40,152,650	61,264,327	39,797.0	55	16,622,676	49,104,002.1	1.75	1383.43	39.38	35.13	13.82
Unknown	2	2	123	3,656	5,670	5.9	0	1,326	4,308.3	1.51	1828.00	61.50	29.72	0.00

**Table 3b: Rate of Heart Failure Outcomes at Different Stages of Amphetamine Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>30-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
Female	160	105,502	15.2
Male	141	118,577	11.9
Unknown	0	9	0.0
<b>Days 91-180</b>			
Female	50	54,367	9.2
Male	65	58,767	11.1
Unknown	0	4	0.0
<b>Days 181-270</b>			
Female	32	35,214	9.1
Male	38	36,086	10.5
Unknown	0	2	0.0
<b>Days 271-365</b>			
Female	37	26,225	14.1
Male	30	25,754	11.6
Unknown	0	1	0.0
<b>Days 366-730</b>			
Female	48	53,714	8.9
Male	45	51,041	8.8
Unknown	0	1	0.0
<b>Days 731-1,095</b>			
Female	23	22,129	10.4
Male	28	20,606	13.6
Unknown	0	1	0.0
<b>90-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
Female	187	122,946	15.2
Male	159	138,473	11.5
Unknown	0	11	0.0
<b>Days 91-180</b>			
Female	90	80,382	11.2

**Table 3b: Rate of Heart Failure Outcomes at Different Stages of Amphetamine Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
Male	98	89,228	11.0
Unknown	0	7	0.0
<b>Days 181-270</b>			
Female	58	58,100	10.0
Male	55	62,887	8.7
Unknown	0	4	0.0
<b>Days 271-365</b>			
Female	54	46,410	11.6
Male	45	48,783	9.2
Unknown	0	2	0.0
<b>Days 366-730</b>			
Female	93	102,732	9.1
Male	92	103,659	8.9
Unknown	0	4	0.0
<b>Days 731-1,095</b>			
Female	38	45,473	8.4
Male	47	43,947	10.7
Unknown	0	3	0.0

**Table 4a: Summary of Incident Amphetamine Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>30-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
2000	4,448	4,448	16,890	770,008	1,688,606	2,489.4	11	6,530,503	3,002,268.1	0.68	173.11	3.80	45.59	44.19
2001	10,032	10,032	35,433	1,490,942	3,002,950	5,017.4	12	7,127,951	5,964,717.2	1.41	148.62	3.53	42.08	23.92
2002	9,496	9,496	38,481	1,601,546	2,948,229	5,232.4	15	7,278,506	6,063,178.3	1.30	168.65	4.05	41.62	28.67
2003	14,609	14,609	87,143	3,226,498	8,056,017	10,148.8	24	7,271,380	6,036,501.0	2.01	220.86	5.97	37.03	23.65
2004	12,022	12,022	67,876	2,555,499	6,709,412	8,059.6	21	7,706,753	6,282,301.6	1.56	212.57	5.65	37.65	26.06
2005	11,547	11,547	63,964	2,386,184	3,914,152	7,535.3	22	7,949,367	6,571,646.2	1.45	206.65	5.54	37.31	29.20
2006	27,079	27,079	158,162	5,519,540	8,627,322	17,675.2	36	19,418,578	11,609,746.0	1.39	203.83	5.84	34.90	20.37
2007	44,928	44,928	271,692	9,140,047	14,165,462	29,310.0	51	23,622,477	17,174,878.6	1.90	203.44	6.05	33.64	17.40
2008	97,256	97,256	570,802	18,603,426	34,166,516	59,928.3	83	44,315,343	28,041,631.4	2.19	191.28	5.87	32.59	13.85
2009	143,662	143,662	855,772	27,536,993	39,610,075	88,763.8	83	45,691,347	35,514,584.3	3.14	191.68	5.96	32.18	9.35
2010	149,920	149,920	897,613	28,647,981	40,512,503	92,481.0	83	43,537,676	33,993,319.1	3.44	191.09	5.99	31.92	8.97
2011	150,907	150,907	878,927	27,890,609	38,896,923	90,497.2	82	42,117,644	33,184,599.5	3.58	184.82	5.82	31.73	9.06
2012	148,538	148,538	834,724	26,515,235	36,805,495	86,435.3	69	41,082,652	32,498,484.5	3.62	178.51	5.62	31.77	7.98
2013	143,930	143,930	715,656	22,536,370	31,386,487	74,430.0	86	40,932,837	32,169,921.5	3.52	156.58	4.97	31.49	11.55
2014	139,343	139,343	533,649	16,275,890	22,206,116	54,956.8	64	41,863,933	32,044,427.5	3.33	116.80	3.83	30.50	11.65
2015	62,954	62,954	134,934	3,757,866	5,147,174	12,733.0	5	34,482,260	15,705,829.6	1.83	59.69	2.14	27.85	3.93
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>90-Day Blackout Period</b>														
2000	2,326	2,326	14,437	696,155	1,543,467	1,569.5	6	6,279,504	2,830,510.6	0.37	299.29	6.21	48.22	38.23
2001	4,951	4,951	29,996	1,329,558	2,693,653	2,990.4	9	6,796,802	5,686,405.9	0.73	268.54	6.06	44.32	30.10
2002	4,999	4,999	34,397	1,490,159	2,855,059	3,397.1	10	6,961,458	5,760,031.5	0.72	298.09	6.88	43.32	29.44
2003	8,437	8,437	86,633	3,270,550	8,666,310	7,813.4	16	6,911,809	5,743,251.7	1.22	387.64	10.27	37.75	20.48
2004	6,860	6,860	63,588	2,457,899	5,461,870	5,803.5	15	7,433,723	5,993,523.4	0.92	358.29	9.27	38.65	25.85
2005	6,354	6,354	59,304	2,272,715	3,719,326	5,346.6	14	7,588,702	6,210,655.9	0.84	357.68	9.33	38.32	26.18
2006	14,618	14,618	146,054	5,212,886	8,147,774	12,424.2	25	18,312,667	10,901,551.8	0.80	356.61	9.99	35.69	20.12
2007	24,261	24,261	250,917	8,604,607	13,328,944	20,559.3	34	22,158,799	16,130,193.7	1.09	354.67	10.34	34.29	16.54
2008	52,203	52,203	523,378	17,385,132	25,377,841	40,950.5	49	41,899,630	25,813,443.4	1.25	333.03	10.03	33.22	11.97
2009	79,888	79,888	789,690	25,837,153	37,206,856	60,512.0	55	42,531,731	32,702,790.4	1.88	323.42	9.88	32.72	9.09
2010	86,262	86,262	837,921	27,168,206	38,500,959	63,381.2	42	40,758,995	31,430,818.1	2.12	314.95	9.71	32.42	6.63
2011	87,393	87,393	822,450	26,530,890	36,993,322	61,525.4	49	39,649,136	30,799,478.9	2.20	303.58	9.41	32.26	7.96
2012	88,147	88,147	785,475	25,341,780	35,206,317	58,006.5	42	39,236,862	30,292,629.3	2.25	287.49	8.91	32.26	7.24
2013	85,017	85,017	664,424	21,290,550	29,668,020	46,656.0	52	38,528,318	29,830,951.6	2.21	250.43	7.82	32.04	11.15
2014	81,669	81,669	477,724	14,877,704	20,306,268	27,713.4	26	39,139,987	29,297,160.3	2.09	182.17	5.85	31.14	9.38
2015	17,605	17,605	70,924	2,264,067	3,136,076	2,955.6	2	23,065,690	7,727,696.7	0.76	128.60	4.03	31.92	6.77
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>180-Day Blackout Period</b>														
2000	1,152	1,152	11,899	584,370	1,339,944	1,158.5	6	6,014,580	2,679,165.4	0.19	507.27	10.33	49.11	51.79
2001	2,382	2,382	24,164	1,093,833	2,261,620	2,134.4	4	6,570,971	5,430,470.5	0.36	459.21	10.14	45.27	18.74
2002	2,528	2,528	28,793	1,278,033	2,515,759	2,568.3	5	6,689,455	5,473,831.9	0.38	505.55	11.39	44.39	19.47
2003	4,802	4,802	78,420	2,985,836	8,391,536	6,387.8	14	6,663,681	5,480,124.7	0.72	621.79	16.33	38.07	21.92
2004	3,971	3,971	56,910	2,224,101	4,588,928	4,628.1	12	7,101,428	5,729,027.3	0.56	560.09	14.33	39.08	25.93
2005	3,617	3,617	52,720	2,048,581	3,390,913	4,255.8	14	7,326,117	5,877,407.8	0.49	566.38	14.58	38.86	32.90

**Table 4a: Summary of Incident Amphetamine Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2006	8,435	8,435	130,051	4,698,555	7,391,894	9,843.4	22	17,604,222	10,258,500.7	0.48	557.03	15.42	36.13	22.35
2007	14,106	14,106	223,645	7,749,713	12,104,151	16,231.7	25	21,063,201	15,183,773.4	0.67	549.39	15.85	34.65	15.40
2008	29,943	29,943	461,132	15,471,566	22,780,914	31,614.1	37	39,228,820	23,798,252.6	0.76	516.70	15.40	33.55	11.70
2009	45,738	45,738	693,536	22,912,272	33,294,756	46,265.3	45	40,500,316	30,140,171.7	1.13	500.95	15.16	33.04	9.73
2010	50,177	50,177	737,493	24,128,046	34,463,149	48,038.4	29	38,862,579	29,103,105.9	1.29	480.86	14.70	32.72	6.04
2011	50,425	50,425	722,136	23,509,093	32,999,431	46,302.9	34	37,887,177	28,588,710.1	1.33	466.22	14.32	32.55	7.34
2012	51,802	51,802	688,499	22,405,326	31,353,068	42,574.8	33	37,026,914	28,234,863.1	1.40	432.52	13.29	32.54	7.75
2013	49,074	49,074	568,066	18,366,574	25,772,715	31,884.8	37	36,884,605	27,636,432.9	1.33	374.26	11.58	32.33	11.60
2014	40,513	40,513	350,512	11,090,852	15,315,163	13,938.5	14	36,454,062	23,905,349.3	1.11	273.76	8.65	31.64	10.04
2015	4,703	4,703	28,173	971,638	1,373,730	639.7	0	13,682,094	3,618,827.9	0.34	206.60	5.99	34.49	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>270-Day Blackout Period</b>														
2000	718	718	10,143	506,907	1,199,525	929.0	6	5,575,360	2,587,781.7	0.13	706.00	14.13	49.98	64.58
2001	1,478	1,478	20,542	936,389	1,982,104	1,672.2	3	6,252,827	5,197,077.9	0.24	633.55	13.90	45.58	17.94
2002	1,578	1,578	24,785	1,112,029	2,238,861	2,082.5	5	6,343,185	5,220,677.7	0.25	704.71	15.71	44.87	24.01
2003	3,412	3,412	71,854	2,749,389	7,947,527	5,423.0	10	6,289,298	5,247,587.5	0.54	805.80	21.06	38.26	18.44
2004	2,787	2,787	51,352	2,022,499	4,084,885	3,838.8	11	6,701,207	5,493,550.3	0.42	725.69	18.43	39.39	28.65
2005	2,416	2,416	47,155	1,853,361	3,086,481	3,575.0	14	6,863,488	5,585,947.7	0.35	767.12	19.52	39.30	39.16
2006	5,824	5,824	116,868	4,256,103	6,752,546	8,144.2	20	16,162,051	9,769,038.7	0.36	730.79	20.07	36.42	24.56
2007	9,726	9,726	200,436	7,004,855	11,042,261	13,400.4	15	19,574,009	14,373,677.4	0.50	720.22	20.61	34.95	11.19
2008	20,601	20,601	410,603	13,884,255	20,614,767	25,595.8	32	35,082,617	22,338,686.9	0.59	673.96	19.93	33.81	12.50
2009	31,627	31,627	616,328	20,497,102	29,982,878	37,079.3	39	37,007,586	27,978,511.3	0.85	648.09	19.49	33.26	10.52
2010	34,621	34,621	652,512	21,491,834	30,929,831	38,024.8	24	35,587,039	27,138,070.1	0.97	620.77	18.85	32.94	6.31
2011	34,766	34,766	637,483	20,886,080	29,445,334	36,315.6	26	34,777,592	26,696,570.2	1.00	600.76	18.34	32.76	7.16
2012	36,347	36,347	605,648	19,834,589	27,912,083	32,258.8	23	33,939,602	26,526,384.0	1.07	545.70	16.66	32.75	7.13
2013	33,817	33,817	485,096	15,791,307	22,318,852	22,175.8	24	33,917,177	25,710,744.7	1.00	466.96	14.34	32.55	10.82
2014	21,991	21,991	238,132	7,681,127	10,667,942	6,590.4	9	32,093,640	18,241,659.6	0.69	349.29	10.83	32.26	13.66
2015	570	570	3,456	162,536	257,023	59.0	0	9,164,434	1,037,309.5	0.06	285.15	6.06	47.03	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>365-Day Blackout Period</b>														
2000	473	473	8,740	442,203	1,076,617	775.1	6	5,330,912	2,500,414.1	0.09	934.89	18.48	50.60	77.40
2001	1,034	1,034	17,837	820,985	1,759,017	1,350.9	3	5,792,403	4,955,275.2	0.18	793.99	17.25	46.03	22.21
2002	1,096	1,096	21,869	987,755	2,036,416	1,758.2	4	5,850,396	4,983,663.8	0.19	901.24	19.95	45.17	22.75
2003	2,552	2,552	65,621	2,529,701	7,318,723	4,671.0	9	5,874,831	5,021,564.8	0.43	991.26	25.71	38.55	19.27
2004	1,996	1,996	45,476	1,819,252	3,630,352	3,245.1	7	6,418,233	5,253,527.5	0.31	911.45	22.78	40.00	21.57
2005	1,767	1,767	42,539	1,683,576	2,828,278	3,054.4	9	6,250,912	5,312,348.1	0.28	952.79	24.07	39.58	29.47
2006	4,253	4,253	105,043	3,855,780	6,166,922	6,870.6	15	15,001,621	9,294,997.3	0.28	906.60	24.70	36.71	21.83
2007	7,272	7,272	180,934	6,377,501	10,153,026	11,253.9	13	17,955,872	13,596,175.5	0.40	876.99	24.88	35.25	11.55
2008	15,020	15,020	365,661	12,447,078	18,624,758	21,085.7	26	32,710,159	20,942,397.3	0.46	828.70	24.34	34.04	12.33
2009	22,949	22,949	545,326	18,252,941	26,866,140	30,172.2	34	32,223,197	25,877,240.2	0.71	795.37	23.76	33.47	11.27
2010	25,154	25,154	574,606	19,046,470	27,528,494	30,484.5	21	31,247,789	25,268,361.2	0.80	757.19	22.84	33.15	6.89
2011	25,345	25,345	560,823	18,488,025	26,171,129	28,819.7	18	30,613,408	24,849,787.5	0.83	729.45	22.13	32.97	6.25
2012	26,712	26,712	527,177	17,368,764	24,542,138	24,341.0	16	32,219,732	24,854,572.9	0.83	650.22	19.74	32.95	6.57



**Table 4a: Summary of Incident Amphetamine Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2013	24,491	24,491	407,689	13,357,376	18,965,300	14,813.9	12	29,645,949	23,820,276.5	0.83	545.40	16.65	32.76	8.10
2014	10,430	10,430	132,644	4,420,396	6,221,878	2,488.3	1	24,898,676	11,645,412.7	0.42	423.82	12.72	33.33	4.02
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>730-Day Blackout Period</b>														
2000	219	219	6,238	324,889	833,332	461.2	4	4,503,593	2,119,747.1	0.05	1483.51	28.48	52.08	86.72
2001	378	378	10,599	516,353	1,153,989	700.5	2	4,827,583	4,189,894.8	0.08	1366.01	28.04	48.72	28.55
2002	455	455	15,118	698,472	1,519,522	1,066.2	4	4,898,157	4,262,794.9	0.09	1535.10	33.23	46.20	37.52
2003	1,302	1,302	49,807	1,956,791	5,375,440	2,881.1	8	5,060,570	4,310,545.3	0.26	1502.91	38.25	39.29	27.77
2004	816	816	30,795	1,280,985	2,376,805	1,984.4	2	5,343,190	4,345,805.0	0.15	1569.83	37.74	41.60	10.08
2005	822	822	30,594	1,246,356	2,135,549	1,854.0	5	5,249,025	4,547,043.5	0.16	1516.25	37.22	40.74	26.97
2006	1,943	1,943	75,152	2,814,270	4,555,922	4,045.2	7	12,162,163	7,729,541.5	0.16	1448.41	38.68	37.45	17.30
2007	3,329	3,329	127,905	4,596,950	7,460,398	6,385.9	10	14,587,412	10,897,785.1	0.23	1380.88	38.42	35.94	15.66
2008	6,695	6,695	249,300	8,661,970	13,164,494	11,126.1	14	24,273,547	16,138,116.1	0.28	1293.80	37.24	34.75	12.58
2009	9,889	9,889	360,989	12,296,921	18,215,462	15,092.4	17	24,014,706	19,877,720.2	0.41	1243.49	36.50	34.06	11.26
2010	10,454	10,454	366,347	12,369,356	17,960,204	14,263.0	15	23,615,311	19,518,743.7	0.44	1183.22	35.04	33.76	10.52
2011	11,370	11,370	363,292	12,198,076	17,459,608	12,037.3	9	24,895,235	19,699,299.1	0.46	1072.83	31.95	33.58	7.48
2012	10,813	10,813	300,949	10,125,262	14,407,697	7,259.9	3	24,676,982	18,964,995.1	0.44	936.40	27.83	33.64	4.13
2013	4,750	4,750	107,107	3,776,122	5,569,541	1,270.8	1	19,031,404	9,237,528.2	0.25	794.97	22.55	35.26	7.87
2014	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>1,095-Day Blackout Period</b>														
2000	106	106	4,185	227,366	605,512	303.5	3	3,851,156	1,825,130.7	0.03	2144.96	39.48	54.33	98.86
2001	180	180	7,169	350,823	829,474	440.5	1	4,142,586	3,648,176.4	0.04	1949.02	39.83	48.94	22.70
2002	259	259	11,286	536,522	1,244,494	722.8	1	4,312,739	3,721,868.4	0.06	2071.51	43.58	47.54	13.83
2003	713	713	36,432	1,473,280	3,680,307	1,932.3	6	4,312,579	3,611,202.4	0.17	2066.31	51.10	40.44	31.05
2004	492	492	23,691	1,007,069	1,767,397	1,340.3	2	4,514,009	3,786,085.9	0.11	2046.89	48.15	42.51	14.92
2005	464	464	22,616	945,924	1,636,630	1,229.7	3	4,547,506	3,975,630.2	0.10	2038.63	48.74	41.83	24.40
2006	1,142	1,142	56,648	2,150,563	3,526,908	2,568.6	3	9,956,594	6,466,149.8	0.11	1883.15	49.60	37.96	11.68
2007	1,896	1,896	93,587	3,416,499	5,620,995	3,881.4	4	11,789,364	9,011,716.3	0.16	1801.95	49.36	36.51	10.31
2008	3,662	3,662	173,963	6,146,923	9,413,985	6,194.8	9	18,836,543	13,007,592.0	0.19	1678.57	47.50	35.33	14.53
2009	5,158	5,158	241,760	8,358,196	12,341,856	7,921.2	9	18,699,442	15,734,944.5	0.28	1620.43	46.87	34.57	11.36
2010	5,677	5,677	245,537	8,412,668	12,299,381	6,554.0	6	19,812,057	15,915,682.5	0.29	1481.89	43.25	34.26	9.15
2011	5,651	5,651	217,568	7,450,173	10,736,482	3,942.3	3	19,762,518	15,429,930.4	0.29	1318.38	38.50	34.24	7.61
2012	2,534	2,534	81,572	2,950,167	4,309,812	660.5	0	17,150,082	7,693,975.4	0.15	1164.23	32.19	36.17	0.00
2013	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2014	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
2000	4,448	4,448	25,051	1,153,741	2,510,045	4,464.3	13	6,530,503	3,002,268.1	0.68	259.38	5.63	46.06	29.12
2001	10,032	10,032	55,284	2,336,089	4,643,138	9,498.8	15	7,127,951	5,964,717.2	1.41	232.86	5.51	42.26	15.79

**Table 4a: Summary of Incident Amphetamine Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2002	9,496	9,496	57,945	2,402,214	4,757,505	9,386.9	21	7,278,506	6,063,178.3	1.30	252.97	6.10	41.46	22.37
2003	14,609	14,609	131,735	4,859,116	12,185,340	17,543.1	35	7,271,380	6,036,501.0	2.01	332.61	9.02	36.89	19.95
2004	12,022	12,022	94,177	3,586,803	8,694,141	13,189.8	28	7,706,753	6,282,301.6	1.56	298.35	7.83	38.09	21.23
2005	11,547	11,547	92,316	3,466,975	5,690,054	12,785.2	27	7,949,367	6,571,646.2	1.45	300.25	7.99	37.56	21.12
2006	27,079	27,079	222,918	7,796,431	12,277,655	29,451.7	48	19,418,578	11,609,746.0	1.39	287.91	8.23	34.97	16.30
2007	44,928	44,928	380,529	12,815,450	20,105,702	48,467.5	75	23,622,477	17,174,878.6	1.90	285.24	8.47	33.68	15.47
2008	97,256	97,256	783,224	25,625,735	44,638,938	97,779.7	120	44,315,343	28,041,631.4	2.19	263.49	8.05	32.72	12.27
2009	143,662	143,662	1,174,481	37,892,165	54,756,980	144,379.7	133	45,691,347	35,514,584.3	3.14	263.76	8.18	32.26	9.21
2010	149,920	149,920	1,223,008	39,136,528	55,622,396	149,607.1	141	43,537,676	33,993,319.1	3.44	261.05	8.16	32.00	9.42
2011	150,907	150,907	1,182,936	37,641,465	52,758,166	145,040.2	117	42,117,644	33,184,599.5	3.58	249.43	7.84	31.82	8.07
2012	148,538	148,538	1,101,958	35,090,668	48,897,041	136,534.0	108	41,082,652	32,498,484.5	3.62	236.24	7.42	31.84	7.91
2013	143,930	143,930	908,425	28,623,280	39,956,367	113,362.6	138	40,932,837	32,169,921.5	3.52	198.87	6.31	31.51	12.17
2014	139,343	139,343	628,091	19,149,634	26,233,935	77,305.4	86	41,863,933	32,044,427.5	3.33	137.43	4.51	30.49	11.12
2015	62,954	62,954	143,329	3,996,548	5,493,511	15,480.7	7	34,482,260	15,705,829.6	1.83	63.48	2.28	27.88	4.52
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>90-Day Blackout Period</b>														
2000	3,979	3,979	24,382	1,136,945	2,478,691	3,427.0	8	6,279,504	2,830,510.6	0.63	285.74	6.13	46.63	23.34
2001	9,192	9,192	54,159	2,306,216	4,588,040	7,130.6	12	6,795,743	5,685,748.9	1.35	250.89	5.89	42.58	16.83
2002	8,604	8,604	56,731	2,370,219	4,705,018	7,170.3	16	6,957,497	5,757,355.3	1.24	275.48	6.59	41.78	22.31
2003	12,956	12,956	129,632	4,811,332	12,130,352	14,195.8	27	6,905,937	5,739,410.0	1.88	371.36	10.01	37.12	19.02
2004	10,433	10,433	91,971	3,536,238	8,492,662	10,463.9	22	7,426,584	5,988,624.9	1.40	338.95	8.82	38.45	21.02
2005	10,104	10,104	90,518	3,428,821	5,631,656	10,186.0	19	7,579,449	6,203,993.3	1.33	339.35	8.96	37.88	18.65
2006	23,793	23,793	219,028	7,715,616	12,155,317	23,313.9	35	18,301,520	10,893,144.3	1.30	324.28	9.21	35.23	15.01
2007	39,508	39,508	373,074	12,647,188	19,857,286	38,195.4	55	22,142,528	16,118,217.9	1.78	320.12	9.44	33.90	14.40
2008	83,576	83,576	764,092	25,201,600	44,073,102	75,776.0	79	41,875,197	25,795,855.1	2.00	301.54	9.14	32.98	10.43
2009	124,183	124,183	1,147,947	37,307,238	53,989,413	111,822.5	102	42,492,808	32,676,076.9	2.92	300.42	9.24	32.50	9.12
2010	130,239	130,239	1,196,719	38,562,027	54,848,225	115,648.1	94	40,702,115	31,391,514.4	3.20	296.09	9.19	32.22	8.13
2011	131,108	131,108	1,157,435	37,101,217	52,065,252	111,032.5	76	39,576,020	30,748,405.8	3.31	282.98	8.83	32.05	6.84
2012	130,498	130,498	1,079,146	34,612,809	48,280,083	102,952.8	78	39,150,905	30,231,743.5	3.33	265.24	8.27	32.07	7.58
2013	125,770	125,770	884,708	28,113,659	39,290,105	80,837.4	97	38,431,981	29,762,162.0	3.27	223.53	7.03	31.78	12.00
2014	119,636	119,636	600,579	18,543,847	25,436,536	45,921.2	43	39,039,797	29,227,224.8	3.06	155.00	5.02	30.88	9.36
2015	25,970	25,970	86,472	2,709,504	3,782,212	4,773.0	3	23,013,136	7,713,186.2	1.13	104.33	3.33	31.33	6.29
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>180-Day Blackout Period</b>														
2000	2,373	2,373	21,959	1,056,801	2,318,835	2,662.1	8	6,014,580	2,679,165.4	0.39	445.34	9.25	48.13	30.05
2001	5,307	5,307	49,161	2,147,285	4,282,111	5,463.9	6	6,570,481	5,430,314.0	0.81	404.61	9.26	43.68	10.98
2002	5,167	5,167	53,688	2,295,602	4,667,455	5,820.1	10	6,687,515	5,472,822.3	0.77	444.28	10.39	42.76	17.18
2003	8,561	8,561	131,908	4,924,032	12,890,531	12,662.2	23	6,660,564	5,478,392.8	1.29	575.17	15.41	37.33	18.16
2004	6,703	6,703	88,923	3,463,986	7,176,345	8,808.4	17	7,097,359	5,726,638.7	0.94	516.78	13.27	38.95	19.30
2005	6,277	6,277	87,025	3,339,670	5,491,377	8,563.5	19	7,320,568	5,873,985.1	0.86	532.05	13.86	38.38	22.19
2006	14,535	14,535	207,778	7,406,509	11,713,281	19,197.5	31	17,597,350	10,253,961.4	0.83	509.56	14.30	35.65	16.15
2007	24,231	24,231	354,160	12,128,423	19,076,943	31,393.1	43	21,054,264	15,177,968.1	1.15	500.53	14.62	34.25	13.70
2008	51,275	51,275	719,571	23,947,251	35,301,984	61,098.3	59	39,216,174	23,790,300.5	1.31	467.04	14.03	33.28	9.66

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	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2009	78,090	78,090	1,085,176	35,542,283	51,605,261	89,899.6	80	40,481,743	30,129,402.7	1.93	455.15	13.90	32.75	8.90
2010	84,321	84,321	1,141,783	37,064,778	52,929,080	93,226.3	66	38,834,221	29,086,822.6	2.17	439.57	13.54	32.46	7.08
2011	85,170	85,170	1,104,739	35,690,395	50,185,813	88,752.0	57	37,848,526	28,566,031.5	2.25	419.05	12.97	32.31	6.42
2012	87,001	87,001	1,033,798	33,395,951	46,721,542	80,710.3	60	36,979,093	28,205,652.7	2.35	383.86	11.88	32.30	7.43
2013	82,572	82,572	832,484	26,678,928	37,360,652	58,898.2	76	36,828,204	27,601,984.0	2.24	323.10	10.08	32.05	12.90
2014	67,946	67,946	497,352	15,631,003	21,606,781	24,950.1	23	36,396,149	23,873,775.4	1.87	230.05	7.32	31.43	9.22
2015	8,105	8,105	40,545	1,376,131	1,947,374	1,124.0	0	13,665,679	3,614,401.3	0.59	169.79	5.00	33.94	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>270-Day Blackout Period</b>														
2000	1,605	1,605	20,035	969,410	2,160,470	2,189.9	8	5,575,360	2,587,781.7	0.29	603.99	12.48	48.39	36.53
2001	3,515	3,515	44,429	1,956,143	3,934,405	4,441.0	6	6,252,664	5,197,053.0	0.56	556.51	12.64	44.03	13.51
2002	3,490	3,490	49,419	2,127,316	4,579,528	4,867.2	10	6,342,327	5,220,329.2	0.55	609.55	14.16	43.05	20.55
2003	6,473	6,473	126,511	4,738,721	12,768,740	11,098.8	20	6,287,791	5,246,859.2	1.03	732.07	19.54	37.46	18.02
2004	4,962	4,962	84,427	3,308,780	6,608,203	7,584.7	16	6,699,025	5,492,424.6	0.74	666.82	17.01	39.19	21.09
2005	4,577	4,577	82,131	3,168,084	5,228,757	7,372.0	19	6,860,247	5,584,095.1	0.67	692.17	17.94	38.57	25.77
2006	10,832	10,832	195,998	7,027,249	11,155,662	16,303.7	28	16,157,848	9,766,444.2	0.67	648.75	18.09	35.85	17.17
2007	17,926	17,926	332,540	11,450,195	18,095,934	26,531.4	28	19,568,620	14,370,357.8	0.92	638.75	18.55	34.43	10.55
2008	38,174	38,174	672,443	22,515,182	33,348,309	50,665.4	52	35,075,061	22,334,166.3	1.09	589.80	17.62	33.48	10.26
2009	57,704	57,704	1,010,075	33,266,396	48,485,463	74,132.8	71	36,996,761	27,972,439.2	1.56	576.50	17.50	32.93	9.58
2010	62,995	62,995	1,065,544	34,779,189	49,865,198	76,444.1	51	35,570,188	27,128,810.4	1.77	552.09	16.91	32.64	6.67
2011	63,334	63,334	1,028,250	33,398,556	47,123,268	71,989.4	42	34,753,720	26,683,229.7	1.82	527.34	16.24	32.48	5.83
2012	65,695	65,695	961,542	31,234,964	43,845,499	63,563.2	44	33,909,032	26,508,526.3	1.94	475.45	14.64	32.48	6.92
2013	61,593	61,593	758,641	24,453,362	34,374,753	42,545.7	56	33,880,468	25,689,266.2	1.82	397.02	12.32	32.23	13.16
2014	39,893	39,893	364,914	11,704,722	16,268,194	12,397.1	14	32,058,673	18,225,928.2	1.24	293.40	9.15	32.08	11.29
2015	1,063	1,063	5,555	258,447	410,147	112.6	0	9,156,382	1,036,369.4	0.12	243.13	5.23	46.53	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>365-Day Blackout Period</b>														
2000	1,099	1,099	17,926	879,128	2,002,451	1,843.9	8	5,330,912	2,500,414.1	0.21	799.93	16.31	49.04	43.39
2001	2,522	2,522	40,111	1,777,930	3,615,266	3,670.6	6	5,792,381	4,955,274.1	0.44	704.97	15.90	44.33	16.35
2002	2,502	2,502	45,066	1,949,370	4,292,209	4,145.4	9	5,850,056	4,983,547.7	0.43	779.12	18.01	43.26	21.71
2003	5,093	5,093	119,874	4,507,820	12,194,047	9,715.2	18	5,874,106	5,021,234.7	0.87	885.10	23.54	37.60	18.53
2004	3,750	3,750	78,138	3,092,205	5,966,656	6,534.9	12	6,416,997	5,252,927.7	0.58	824.59	20.84	39.57	18.36
2005	3,521	3,521	77,002	2,991,910	4,960,634	6,432.4	14	6,249,068	5,311,299.5	0.56	849.73	21.87	38.85	21.76
2006	8,141	8,141	181,807	6,558,912	10,468,228	13,970.0	23	14,999,024	9,293,428.2	0.54	805.66	22.33	36.08	16.46
2007	13,776	13,776	309,438	10,720,774	17,074,727	22,634.7	25	17,952,656	13,594,124.0	0.77	778.22	22.46	34.65	11.04
2008	28,916	28,916	619,689	20,853,287	31,068,448	42,328.2	41	32,705,643	20,939,684.7	0.88	721.17	21.43	33.65	9.69
2009	43,726	43,726	926,139	30,645,015	44,853,983	61,407.2	60	32,217,103	25,873,621.4	1.36	700.84	21.18	33.09	9.77
2010	47,980	47,980	976,792	32,024,668	46,096,290	62,748.1	46	31,238,143	25,262,951.7	1.54	667.46	20.36	32.79	7.33
2011	48,322	48,322	940,639	30,702,581	43,440,302	58,370.3	32	30,599,440	24,841,847.5	1.58	635.37	19.47	32.64	5.48
2012	50,890	50,890	876,693	28,613,239	40,293,474	49,263.5	34	32,200,387	24,843,505.7	1.58	562.26	17.23	32.64	6.90
2013	46,655	46,655	668,655	21,663,402	30,573,594	29,106.7	36	29,623,603	23,806,710.2	1.57	464.33	14.33	32.40	12.37
2014	19,809	19,809	214,327	7,105,533	9,999,104	4,873.3	2	24,882,474	11,639,065.0	0.80	358.70	10.82	33.15	4.10
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---

**Table 4a: Summary of Incident Amphetamine Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>730-Day Blackout Period</b>														
2000	499	499	13,242	668,320	1,593,675	1,116.4	5	4,503,593	2,119,747.1	0.11	1339.32	26.54	50.47	44.79
2001	1,043	1,043	27,407	1,253,163	2,620,700	2,018.1	3	4,827,583	4,189,894.8	0.22	1201.50	26.28	45.72	14.87
2002	1,104	1,104	33,333	1,466,688	3,462,170	2,548.9	6	4,898,150	4,262,794.3	0.23	1328.52	30.19	44.00	23.54
2003	2,619	2,619	95,358	3,628,037	9,097,655	6,162.7	15	5,060,494	4,310,519.3	0.52	1385.28	36.41	38.05	24.34
2004	1,722	1,722	58,392	2,368,359	4,259,794	4,089.2	5	5,343,009	4,345,722.6	0.32	1375.35	33.91	40.56	12.23
2005	1,753	1,753	59,853	2,375,639	4,015,858	4,049.7	10	5,248,689	4,546,875.0	0.33	1355.18	34.14	39.69	24.69
2006	3,960	3,960	138,750	5,073,024	8,221,927	8,380.4	11	12,161,565	7,729,208.6	0.33	1281.07	35.04	36.56	13.13
2007	6,649	6,649	232,361	8,174,008	13,247,643	13,193.2	16	14,586,550	10,897,263.9	0.46	1229.36	34.95	35.18	12.13
2008	13,471	13,471	449,890	15,374,128	23,237,859	22,990.2	24	24,272,475	16,137,464.6	0.55	1141.28	33.40	34.17	10.44
2009	20,227	20,227	661,353	22,166,924	32,706,767	31,880.5	32	24,013,277	19,876,835.1	0.84	1095.91	32.70	33.52	10.04
2010	21,715	21,715	679,346	22,588,927	32,813,600	30,760.9	26	23,613,284	19,517,527.7	0.92	1040.25	31.28	33.25	8.45
2011	23,334	23,334	662,618	21,901,528	31,298,647	25,436.4	16	24,892,120	19,697,507.0	0.94	938.61	28.40	33.05	6.29
2012	22,830	22,830	559,249	18,540,142	26,311,940	15,461.7	8	24,672,526	18,962,427.8	0.93	812.10	24.50	33.15	5.17
2013	9,623	9,623	192,170	6,682,658	9,814,382	2,560.3	4	19,028,269	9,236,239.2	0.51	694.45	19.97	34.77	15.62
2014	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>1,095-Day Blackout Period</b>														
2000	263	263	9,543	496,827	1,252,832	744.7	4	3,851,156	1,825,130.7	0.07	1889.08	36.29	52.06	53.72
2001	515	515	19,377	897,501	1,959,973	1,301.0	2	4,142,586	3,648,176.4	0.12	1742.72	37.63	46.32	15.37
2002	657	657	25,788	1,156,213	2,643,050	1,682.3	2	4,312,739	3,721,868.4	0.15	1759.84	39.25	44.84	11.89
2003	1,529	1,529	73,437	2,854,738	6,710,212	4,155.6	10	4,312,578	3,611,202.3	0.35	1867.06	48.03	38.87	24.06
2004	1,037	1,037	45,773	1,890,781	3,275,098	2,755.3	5	4,513,988	3,786,080.0	0.23	1823.32	44.14	41.31	18.15
2005	1,029	1,029	46,062	1,873,339	3,199,474	2,734.1	7	4,547,446	3,975,603.6	0.23	1820.54	44.76	40.67	25.60
2006	2,308	2,308	106,219	3,931,137	6,463,533	5,370.9	7	9,956,444	6,466,079.1	0.23	1703.27	46.02	37.01	13.03
2007	3,920	3,920	177,131	6,300,380	10,364,546	8,113.5	7	11,789,106	9,011,584.3	0.33	1607.24	45.19	35.57	8.63
2008	7,499	7,499	325,455	11,260,259	17,182,836	13,007.4	15	18,836,173	13,007,369.9	0.40	1501.57	43.40	34.60	11.53
2009	10,889	10,889	463,190	15,699,587	23,233,945	16,999.7	18	18,698,975	15,734,646.9	0.58	1441.78	42.54	33.89	10.59
2010	12,302	12,302	479,986	16,135,998	23,623,490	14,437.7	11	19,811,399	15,915,279.6	0.62	1311.66	39.02	33.62	7.62
2011	12,134	12,134	421,793	14,141,573	20,370,447	8,466.7	8	19,761,597	15,429,348.6	0.61	1165.45	34.76	33.53	9.45
2012	5,427	5,427	157,013	5,606,513	8,138,130	1,456.7	0	17,149,150	7,693,645.7	0.32	1033.08	28.93	35.71	0.00
2013	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2014	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Amphetamine Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>30-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
2000	5	920	54.4
2001	3	2,027	14.8
2002	5	1,835	27.2
2003	8	2,335	34.3
2004	6	2,256	26.6
2005	8	2,189	36.6
2006	11	5,251	20.9
2007	17	8,751	19.4
2008	34	18,978	17.9
2009	28	28,252	9.9
2010	41	29,100	14.1
2011	33	28,972	11.4
2012	27	28,429	9.5
2013	34	27,774	12.2
2014	38	27,243	13.9
2015	3	9,777	3.1
2016	0	0	---
<b>Days 91-180</b>			
2000	0	411	0.0
2001	5	856	58.4
2002	5	829	60.3
2003	2	1,426	14.0
2004	3	1,175	25.5
2005	0	1,091	0.0
2006	3	2,581	11.6
2007	9	4,328	20.8
2008	12	9,336	12.9
2009	10	14,247	7.0
2010	13	15,343	8.5
2011	15	15,222	9.9
2012	9	15,432	5.8
2013	15	14,771	10.2
2014	12	13,775	8.7
2015	2	2,316	8.6
2016	0	0	---
<b>Days 181-270</b>			
2000	0	229	0.0
2001	1	462	21.6
2002	0	486	0.0
2003	4	965	41.5
2004	1	789	12.7
2005	0	681	0.0
2006	2	1,699	11.8

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Amphetamine Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
2007	10	2,831	35.3
2008	5	6,018	8.3
2009	6	9,186	6.5
2010	5	10,014	5.0
2011	8	9,987	8.0
2012	10	10,316	9.7
2013	13	9,709	13.4
2014	5	7,348	6.8
2015	0	581	0.0
2016	0	0	---
<b>Days 271-365</b>			
2000	0	154	0.0
2001	0	321	0.0
2002	1	324	30.8
2003	1	752	13.3
2004	4	594	67.4
2005	5	521	96.0
2006	5	1,274	39.3
2007	2	2,147	9.3
2008	6	4,510	13.3
2009	5	6,907	7.2
2010	3	7,540	4.0
2011	8	7,496	10.7
2012	7	7,918	8.8
2013	12	7,362	16.3
2014	8	4,102	19.5
2015	0	59	0.0
2016	0	0	---
<b>Days 366-730</b>			
2000	2	314	63.7
2001	1	650	15.4
2002	0	692	0.0
2003	1	1,790	5.6
2004	5	1,261	39.7
2005	4	1,200	33.3
2006	8	2,825	28.3
2007	3	4,868	6.2
2008	12	9,960	12.0
2009	17	15,080	11.3
2010	6	16,221	3.7
2011	9	16,782	5.4
2012	13	17,081	7.6
2013	11	13,543	8.1
2014	1	2,488	4.0

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Amphetamine Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
2015	0	0	---
2016	0	0	---
<b>Days 731-1,095</b>			
2000	1	158	63.4
2001	1	260	38.5
2002	3	343	87.4
2003	2	949	21.1
2004	0	644	0.0
2005	2	624	32.0
2006	4	1,477	27.1
2007	6	2,505	24.0
2008	5	4,931	10.1
2009	8	7,171	11.2
2010	9	7,709	11.7
2011	6	8,095	7.4
2012	3	6,599	4.5
2013	1	1,271	7.9
2014	0	0	---
2015	0	0	---
2016	0	0	---
<b>90-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
2000	5	1,037	48.2
2001	3	2,368	12.7
2002	5	2,217	22.6
2003	8	3,347	23.9
2004	6	2,726	22.0
2005	8	2,599	30.8
2006	13	6,138	21.2
2007	20	10,272	19.5
2008	41	22,004	18.6
2009	31	32,557	9.5
2010	47	33,959	13.8
2011	41	34,008	12.1
2012	30	33,581	8.9
2013	41	32,525	12.6
2014	43	31,384	13.7
2015	4	10,708	3.7
2016	0	0	---
<b>Days 91-180</b>			
2000	0	765	0.0
2001	6	1,667	36.0
2002	6	1,350	44.4
2003	4	1,534	26.1
2004	5	1,655	30.2

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Amphetamine Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
2005	0	1,622	0.0
2006	4	4,116	9.7
2007	12	6,802	17.6
2008	20	14,678	13.6
2009	22	21,923	10.0
2010	28	22,422	12.5
2011	19	22,281	8.5
2012	18	22,242	8.1
2013	21	21,939	9.6
2014	20	20,971	9.5
2015	3	3,649	8.2
2016	0	0	---
<b>Days 181-270</b>			
2000	0	472	0.0
2001	0	1,023	0.0
2002	0	953	0.0
2003	3	1,563	19.2
2004	1	1,224	8.2
2005	0	1,191	0.0
2006	3	2,894	10.4
2007	15	4,862	30.9
2008	7	10,433	6.7
2009	9	15,767	5.7
2010	15	16,782	8.9
2011	15	16,763	8.9
2012	16	17,147	9.3
2013	20	16,353	12.2
2014	9	12,553	7.2
2015	0	1,011	0.0
2016	0	0	---
<b>Days 271-365</b>			
2000	0	346	0.0
2001	0	770	0.0
2002	1	722	13.9
2003	2	1,384	14.5
2004	4	1,050	38.1
2005	5	940	53.2
2006	5	2,334	21.4
2007	3	3,897	7.7
2008	11	8,337	13.2
2009	11	12,726	8.6
2010	5	13,696	3.7
2011	10	13,619	7.3
2012	10	14,300	7.0



**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Amphetamine Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
2013	20	13,439	14.9
2014	12	7,524	15.9
2015	0	113	0.0
2016	0	0	---
<b>Days 366-730</b>			
2000	3	727	41.2
2001	3	1,652	18.2
2002	3	1,597	18.8
2003	3	3,552	8.4
2004	7	2,446	28.6
2005	4	2,383	16.8
2006	12	5,590	21.5
2007	9	9,441	9.5
2008	17	19,338	8.8
2009	28	29,527	9.5
2010	20	31,987	6.3
2011	16	32,934	4.9
2012	26	33,802	7.7
2013	32	26,546	12.1
2014	2	4,873	4.1
2015	0	0	---
2016	0	0	---
<b>Days 731-1,095</b>			
2000	1	372	26.9
2001	1	717	13.9
2002	4	867	46.2
2003	5	2,007	24.9
2004	0	1,334	0.0
2005	3	1,316	22.8
2006	4	3,009	13.3
2007	9	5,080	17.7
2008	9	9,983	9.0
2009	14	14,881	9.4
2010	15	16,323	9.2
2011	8	16,970	4.7
2012	8	14,005	5.7
2013	4	2,560	15.6
2014	0	0	---
2015	0	0	---
2016	0	0	---

**Appendix A: List of Generic and Brand Names Used To Define the Exposures and Exposure Incidence in this Request**

Generic Name	Brand Name
<b>Amphetamines</b>	
DEXTROAMPHETAMINE SULFATE	Dexedrine Spansule
DEXTROAMPHETAMINE SULFATE	dextroamphetamine
DEXTROAMPHETAMINE SULFATE	Dexedrine
DEXTROAMPHETAMINE SULFATE	DextroStat
DEXTROAMPHETAMINE SULFATE	Zenzedi
DEXTROAMPHETAMINE SULFATE	ProCentra
DEXTROAMPHETAMINE SULFATE	Liquadd
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	Amphetamine Salt Combo
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	Adderall XR
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	Adderall
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	dextroamphetamine-amphetamine
LISDEXAMFETAMINE DIMESYLATE	Vyvanse
METHAMPHETAMINE HCL	Desoxyn
AMPHETAMINE SULFATE	Evekeo
METHAMPHETAMINE HCL	methamphetamine
<b>Methylphenidates</b>	
DEXMETHYLPHENIDATE HCL	dexmethylphenidate
DEXMETHYLPHENIDATE HCL	Focalin XR
DEXMETHYLPHENIDATE HCL	Focalin
METHYLPHENIDATE HCL	Methylin
METHYLPHENIDATE HCL	Ritalin LA
METHYLPHENIDATE HCL	methylphenidate
METHYLPHENIDATE HCL	Concerta
METHYLPHENIDATE HCL	Metadate CD
METHYLPHENIDATE HCL	Aptensio XR
METHYLPHENIDATE HCL	Ritalin
METHYLPHENIDATE HCL	Ritalin SR
METHYLPHENIDATE HCL	Metadate ER
METHYLPHENIDATE HCL	Quillivant XR
METHYLPHENIDATE HCL	Methylin ER
<b>Strattera</b>	
ATOMOXETINE HCL	Strattera

**Appendix B: Codes Used to Define Heart Failure in this Request**

<b>Code</b>	<b>Code Type</b>	<b>Description</b>
398.91	ICD-9-CM Diagnosis	Rheumatic heart failure (congestive)
402.01	ICD-9-CM Diagnosis	Malignant hypertensive heart disease with heart failure
402.11	ICD-9-CM Diagnosis	Benign hypertensive heart disease with heart failure
402.91	ICD-9-CM Diagnosis	Unspecified hypertensive heart disease with heart failure
404.01	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.03	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic kidney disease stage V or end stage renal disease
404.11	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, benign, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.13	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, benign, with heart failure and chronic kidney disease stage V or end stage renal disease
404.91	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, unspecified, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.93	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, unspecified, with heart failure and chronic kidney disease stage V or end stage renal disease
422.90	ICD-9-CM Diagnosis	Acute myocarditis, unspecified
425.4	ICD-9-CM Diagnosis	Other primary cardiomyopathies
425.9	ICD-9-CM Diagnosis	Secondary cardiomyopathy, unspecified
428	ICD-9-CM Diagnosis	Heart Failure
428.0	ICD-9-CM Diagnosis	Congestive heart failure, unspecified
428.1	ICD-9-CM Diagnosis	Left heart failure
428.2	ICD-9-CM Diagnosis	Systolic heart failure
428.20	ICD-9-CM Diagnosis	Systolic heart failure, unspecified
428.21	ICD-9-CM Diagnosis	Acute systolic heart failure
428.22	ICD-9-CM Diagnosis	Chronic systolic heart failure
428.23	ICD-9-CM Diagnosis	Acute on chronic systolic heart failure
428.3	ICD-9-CM Diagnosis	Diastolic heart failure
428.30	ICD-9-CM Diagnosis	Diastolic heart failure, unspecified
428.31	ICD-9-CM Diagnosis	Acute diastolic heart failure
428.32	ICD-9-CM Diagnosis	Chronic diastolic heart failure
428.33	ICD-9-CM Diagnosis	Acute on chronic diastolic heart failure
428.4	ICD-9-CM Diagnosis	Combined systolic and diastolic heart failure
428.40	ICD-9-CM Diagnosis	Combined systolic and diastolic heart failure, unspecified
428.41	ICD-9-CM Diagnosis	Acute combined systolic and diastolic heart failure
428.42	ICD-9-CM Diagnosis	Chronic combined systolic and diastolic heart failure
428.43	ICD-9-CM Diagnosis	Acute on chronic combined systolic and diastolic heart failure
428.9	ICD-9-CM Diagnosis	Heart failure, unspecified

**Modular Program Specifications for cder\_mpl1r\_wp014\_nsdp\_v01 Report 5 of 8**

Sentinel's Cohort Identification and Descriptive Analysis (CIDA) tool was used to investigate heart failure following treatment with select attention deficit and hyperactivity disorder (ADHD) medications. In total, 49 scenarios were examined with four different exposures, seven different blackout periods, and two different episode gaps/exposure extension periods. The four exposures are all amphetamines, all methylphenidates, strattera, and all stimulants (which include all amphetamines and all methylphenidates, and strattera). **The outcome is heart failure, defined as any heart failure ICD-9-CM diagnosis code (398.91, 402.x1, 402.x3, 404.x1, 404.x3, 422.90, 425.4, 425.9, 428.xx) in any care setting with a primary discharge diagnosis (PDX) value of P (principal) for those diagnoses in the inpatient care setting.** See below for a description of each of these scenarios. The query period was from January 1, 2000 to March 3, 2016 and the enrollment gap was set at 45 days. Age groups were split as follows: 0-21, 22-44, 45-64, 65+.

Enrollment Gap	45 Days
Age Groups	0-21, 22-44, 45-64, 65+
Query Period	January 1, 2000 - Current
Coverage Requirement	Medical and Drug
Enrollment Requirement	183 Days

Scenario	Drug/Exposure										Event/Outcome					
	Incident exposure	Incident w/ respect to:	Episode Truncation at Incident Exposure	Episode Truncation at Death	Washout (days)	Cohort Definition	Episode Gap	Exposure Extension Period	Min Episode Duration	Min Days Supplied	Event/ Outcome	Care Setting/PDX	Incident with Respect to	Incident w/ respect to Care Setting/PDX	Washout (days)	Blackout Period
1	All Amphetamines	All Stimulants	Yes	No	183	01	90	90	90	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	0
2	All Amphetamines	All Stimulants	Yes	No	183	01	90	90	90	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	90
3	All Amphetamines	All Stimulants	Yes	No	183	01	90	90	180	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	180
4	All Amphetamines	All Stimulants	Yes	No	183	01	90	90	270	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	270
5	All Amphetamines	All Stimulants	Yes	No	183	01	90	90	365	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	365
6	All Amphetamines	All Stimulants	Yes	No	183	01	90	90	730	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	730
7	All Amphetamines	All Stimulants	Yes	No	183	01	90	90	1095	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	1095
8	All Amphetamines	All Stimulants	Yes	No	183	01	30	30	0	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	0
9	All Amphetamines	All Stimulants	Yes	No	183	01	30	30	90	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	90
10	All Amphetamines	All Stimulants	Yes	No	183	01	30	30	180	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	180
11	All Amphetamines	All Stimulants	Yes	No	183	01	30	30	270	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	270
12	All Amphetamines	All Stimulants	Yes	No	183	01	30	30	365	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	365
13	All Amphetamines	All Stimulants	Yes	No	183	01	30	30	730	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	730
14	All Amphetamines	All Stimulants	Yes	No	183	01	30	30	1095	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	1095

ICD-9, ICD-10, HCPCS, and CPT codes are provided by Optum360. NDC codes are checked against First Data Bank's "National Drug Data File (NDDF®) Plus."

Cohort Definition of 01 will only consider the first incident episode for each user during the query period that satisfies the washout period.

Note: Episodes are automatically truncated at outcome.

\*Codes in the algorithm include: 398.91, 402.x1, 402.x3, 404.x1, 404.x3, 422.90, 425.4, 425.9, 428.xx. Algorithm will look for at least one of five things: (1) at least one IP code with PDX flag = P, OR (2) at least three IP codes with PDX flag = S, OR (3) at least two AV\*/OA\* codes with any PDX flag value, OR (4) at least three ED\* codes with any PDX flag value, OR (5) at least two IP codes with PDX flag = S and at least one AV\*/OA\* code with any PDX flag value. The temporal relationship between codes will be 365 days. For example, for at least two AV\*/OA\* codes with any PDX flag value, we would find one code and then look for a second within 365 days of the first. For at least three IP codes with PDX flag = S, we would find one code, and then look for a second within 365 days of the first, and then look for a third within 365 days of the first. The date of the first of the one, two, or three codes will be used as the event date. This is important because episodes are truncated on occurrence of the event.

### Disclaimer

The following report(s) provides findings from an FDA-initiated query using Sentinel. While Sentinel queries may be undertaken to assess potential medical product safety risks, they may also be initiated for various other reasons. Some examples include determining a rate or count of an identified health outcome of interest, examining medical product use, exploring the feasibility of future, more detailed analyses within Sentinel, and seeking to better understand Sentinel capabilities.

Data obtained through Sentinel are intended to complement other types of evidence such as preclinical studies, clinical trials, postmarket studies, and adverse event reports, all of which are used by FDA to inform regulatory decisions regarding medical product safety. The information contained in this report is provided as part of FDA's commitment to place knowledge acquired from Sentinel in the public domain as soon as possible. Any public health actions taken by FDA regarding products involved in Sentinel queries will continue to be communicated through existing channels.

FDA wants to emphasize that the fact that FDA has initiated a query involving a medical product and is reporting findings related to that query does not mean that FDA is suggesting health care practitioners should change their prescribing practices for the medical product or that patients taking the medical product should stop using it. Patients who have questions about the use of an identified medical product should contact their health care practitioners.

The following report contains a description of the request, request specifications, and results from the modular program run(s).

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## Overview for Request cder\_mpl1r\_wp014\_nsdv\_v01, Report 6 of 8

**Request ID:** cder\_mpl1r\_wp014\_nsdv\_v01. This is report 6 of 8.

**Request Description:** FDA has requested execution of the Cohort Identification and Descriptive Analysis (CIDA) tool, version 2.1.1, to investigate heart failure diagnoses following new use of attention deficit hyperactivity disorder (ADHD) medications. This report presents results for all methylphenidates. Results for all amphetamines, strattera, and all stimulants are presented in separate reports.

**Data Source:** Data from January 1, 2000 to March 3, 2016 from 15 health plans contributing to the Sentinel Distributed Database (SDD) are included in this report.

**Study Design:** This request was designed to identify exposures and follow-up time. The exposure of interest and the occurrence of the health outcome of interest during exposed time were identified. The number of exposure episodes, number of individuals, number of events, and days at-risk in the SDD were calculated overall and were stratified by age group, sex, and year.

**Exposure of Interest:** The exposures of interest were methylphenidates, which were defined using National Drug Codes (NDCs). Please refer to Appendix A for a list of generic and brand names of methylphenidates included in this request.

**Cohort Eligibility Criteria:** Patients were required to be continuously enrolled in plans with both medical and drug coverage for at least 6 months (183 days) before their dispensing date, during which gaps in coverage of up to 45 days were allowed. Members were excluded if they had any ADHD medication or the outcome of interest in the 6 months (183 days) prior to exposure initiation. The following age groups were included in the cohort: 0-21, 22-44, 45-64, 65+ years.

**Follow-Up Time:** Follow-up time for the outcome was determined by the length of the exposure episodes. Exposure episode lengths were defined using outpatient pharmacy dispensing days supplied to create a sequence of continuous exposure. Exposure episodes were considered continuous if gaps in days supply were less than 90 days. The end date of each exposure episode was extended by 90 additional days. Follow-up began on the day on which the first exposure of interest was dispensed and continued until the first occurrence of any of the following: 1) the outcome of interest; 2) any codes defining incidence criteria; 3) disenrollment; 4) the study end date (March, 2016); 5) the end date of the data provided by each Data Partner; or 6) the end of the exposure episode. Only the first valid incident exposure episode that occurred during the study period was included per patient.

This report examines different blackout periods which is a number of days at the beginning of the ADHD medication episode where if an outcome occurs, it is not attributed to the exposure and the person is omitted from the analysis. The blackout periods examined were 90 days, 180 days, 270 days, 365 days, 730 days, and 1,095 days. Episodes that were at least as long as the blackout period were required.

**Outcome of Interest:** Heart failure was defined using the ICD-9-CM diagnosis codes listed in Appendix B. The event needed to meet one of the following criteria: (1) at least one code in the inpatient setting with primary diagnosis flag = Primary, OR (2) at least three codes in the inpatient setting with primary diagnosis flag = Secondary, OR (3) at least two codes in the outpatient setting with any primary diagnosis flag value, OR (4) at least three codes in the emergency department setting with any primary diagnosis flag value, OR (5) at least two codes in the inpatient setting with primary diagnosis flag = Secondary and at least one code in the outpatient with any primary diagnosis flag value. The temporal relationship between codes was 365 days. This event had to be incident (no heart failure events in the 183 days prior to exposure initiation).

**Please refer to Appendix C for detailed specifications.**

**Limitations:** Algorithms to define exposures and outcomes are imperfect and, therefore, may be misclassified.

**Notes:** Please contact the Sentinel Operations Center Query Fulfillment Team ([production@mini-sentinel.org](mailto:production@mini-sentinel.org)) for questions and to provide comments/suggestions for future enhancements to this document.

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**Glossary of Terms for Analyses Using  
Cohort Identification and Descriptive Analysis (CIDA) Tool\***

**Amount Supplied** - number of units (pills, tablets, vials) dispensed. Net amount per NDC per dispensing. This is equivalent to the "RxAmt" value in the MSCDM.

**Blackout Period** - number of days at the beginning of a treatment episode that events are to be ignored. If an event occurs during the blackout period, the episode is excluded.

**Care Setting** - type of medical encounter or facility where the exposure, event, or condition code was recorded. Possible care settings include: Inpatient Hospital Stay (IP), Non-Acute Institutional Stay (IS), Emergency Department (ED), Ambulatory Visit (AV), and Other Ambulatory Visit (OA). For laboratory results, possible care settings include: Emergency department (E), Home (H), Inpatient (I), Outpatient (O), or Unknown or Missing (U). Along with the Principal Diagnosis Indicator, forms the Care Setting/PDX parameter.

**Cohort Definition (drug/exposure)** - indicates how the cohort will be defined: (1) 01: Cohort includes only the first valid incident treatment episode during the query period; (2) 02: Cohort includes all valid incident treatment episodes during the query period; (3) 03: Cohort includes all valid incident treatment episodes during the query period until an event

**Days Supplied** - number of days supplied for all dispensings in qualifying treatment episodes.

**Eligible Members** - number of members eligible for an incident treatment episode (defined by the drug/exposure and event washout periods) with drug and medical coverage during the query period.

**Enrollment Gap** - number of days allowed between two consecutive enrollment periods without breaking a "continuously enrolled" sequence.

**Episodes** - treatment episodes; length of episode is determined by days supplied in one dispensing or consecutive dispensings bridged by the episode gap.

**Episode Gap** - number of days allowed between two (or more) consecutive exposures (dispensings/procedures) to be considered the same treatment episode.

**Event Deduplication** - specifies how events are counted by the MP algorithm: (0) 0: Counts all occurrences of an HOI during an exposure episode; (1) 1: de-duplicates occurrences of the same HOI code and code type on the same day; (2) 2: de-duplicates occurrences of the same HOI group on the same day (e.g., de-duplicates at the group level).

**Exposure Episode Length** - number of days after exposure initiation that is considered "exposed time."

**Exposure Extension Period** - number of days post treatment period in which the outcomes/events are counted for a treatment episode.

**Lookback Period (pre-existing condition)** - number of days wherein a member is required to have evidence of pre-existing condition (diagnosis/procedure/drug dispensing).

**Member-Years** - sum of all days of enrollment with medical and drug coverage\*\* in the query period preceded by an exposure washout period all divided by **365.25**.

**Minimum Days Supplied** - specifies a minimum number of days in length of the days supplied for the episode to be considered.

**Minimum Episode Duration** - specifies a minimum number of days in length of the episode for it to be considered.

**Principal Diagnosis (PDX)** - diagnosis or condition established to be chiefly responsible for admission of the patient to the hospital. 'P' = principal diagnosis, 'S' = secondary diagnosis, 'X' = unspecified diagnosis, '.' = blank. Along with the Care Setting values, forms the Caresetting/PDX parameter.

**Query Period** - period in which the modular program looks for exposures and outcomes of interest.

**Treatment Episode Truncation Indicator** - indicates whether observation of the incident query code during follow-up requires truncation of valid treatment episodes. A value of Y indicates that the treatment episodes should be truncated at the first occurrence of an incident query code. A value of N indicates that the treatment episodes should not be truncated at the occurrence of the incident query code.

**Users** - number of members with exposure during the query period. Member must have no evidence of exposure(s) of interest (defined by incidence criteria) in the prior washout period. A user may only be counted once in a query period.

**Washout Period (drug/exposure)\*\*** - number of days a user is required to have no evidence of prior exposure (drug dispensing/procedure) and continuous drug and medical coverage prior to an incident treatment episode.

**Washout Period (event/outcome)\*\*** - number of days a user is required to have no evidence of a prior event (procedure/diagnosis) and continuous drug and medical coverage prior to an incident treatment episode.

**Years at Risk** - number of days supplied plus any episode gaps and exposure extension periods all divided by 365.25.

\*all terms may not be used in this report

\*\*incident treatment episodes must be incident to both the exposure and the event





**Table 1a: Summary of Incident Methylphenidate Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, and Blackout Period**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>30-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
	789,333	789,333	3,408,749	117,755,806	178,791,747	391,123.2	987	110,296,640	305,859,192.9	7.16	149.18	4.32	34.55	25.24
<b>90-Day Blackout Period</b>														
	394,582	394,582	3,003,753	107,683,385	161,558,542	243,771.0	453	100,830,402	277,142,355.1	3.91	272.90	7.61	35.85	18.58
<b>180-Day Blackout Period</b>														
	203,849	203,849	2,491,655	91,339,713	137,282,740	177,101.0	314	93,687,940	251,132,527.3	2.18	448.08	12.22	36.66	17.73
<b>270-Day Blackout Period</b>														
	130,592	130,592	2,115,783	78,809,631	118,940,790	137,646.4	233	80,172,667	229,138,976.2	1.63	603.48	16.20	37.25	16.93
<b>365-Day Blackout Period</b>														
	90,778	90,778	1,811,690	68,512,851	103,880,107	109,782.1	189	72,200,029	208,171,971.5	1.26	754.73	19.96	37.82	17.22
<b>730-Day Blackout Period</b>														
	35,135	35,135	1,091,496	43,319,339	66,175,386	53,243.0	90	48,917,741	145,837,382.8	0.72	1232.94	31.07	39.69	16.90
<b>1,095-Day Blackout Period</b>														
	17,056	17,056	679,127	28,326,043	43,631,388	28,587.5	45	34,449,661	103,827,121.4	0.50	1660.77	39.82	41.71	15.74
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
	789,333	789,333	4,565,152	159,332,964	242,228,915	635,778.2	1,459	110,296,640	305,859,192.9	7.16	201.86	5.78	34.90	22.95
<b>90-Day Blackout Period</b>														
	646,667	646,667	4,378,395	155,203,078	235,808,325	462,921.7	812	100,830,402	276,759,710.9	6.41	240.00	6.77	35.45	17.54
<b>180-Day Blackout Period</b>														
	371,803	371,803	4,009,084	144,840,009	218,873,396	355,068.9	554	93,687,938	250,948,933.4	3.97	389.56	10.78	36.13	15.60
<b>270-Day Blackout Period</b>														
	258,558	258,558	3,613,531	132,252,413	200,049,142	283,160.1	408	80,172,665	229,033,398.7	3.23	511.50	13.98	36.60	14.41
<b>365-Day Blackout Period</b>														
	186,429	186,429	3,208,841	118,875,771	180,395,374	227,899.9	332	72,200,028	208,109,133.6	2.58	637.65	17.21	37.05	14.57
<b>730-Day Blackout Period</b>														
	74,464	74,464	2,049,818	79,063,362	121,096,175	110,410.9	152	48,917,741	145,824,436.9	1.52	1061.77	27.53	38.57	13.77
<b>1,095-Day Blackout Period</b>														
	35,846	35,846	1,301,875	52,442,827	81,559,757	58,362.6	82	34,449,661	103,823,696.4	1.04	1463.00	36.32	40.28	14.05

**Table 1b: Rate of Heart Failure Outcomes at Different Stages of Methylphenidate Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, and Blackout Period**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>30-Day Episode Gap/Extension Period</b>			
Days 0-90	534	147,352	36.2
Days 91-180	139	66,670	20.8
Days 181-270	81	39,455	20.5
Days 271-365	44	27,864	15.8
Days 366-730	99	56,539	17.5
Days 731-1,095	45	24,655	18.3
<b>90-Day Episode Gap/Extension Period</b>			
Days 0-90	647	172,857	37.4
Days 91-180	258	107,853	23.9
Days 181-270	146	71,909	20.3
Days 271-365	76	55,260	13.8
Days 366-730	180	117,489	15.3
Days 731-1,095	70	52,048	13.4

**Table 2a: Summary of Incident Methylphenidate Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>30-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
00-21 Years	516,348	516,348	2,340,201	81,413,160	107,588,412	268,675.4	63	33,426,040	83,999,134.4	15.45	157.67	4.53	34.79	2.34
22-44 Years	155,405	155,405	575,909	19,138,237	36,295,086	65,252.0	92	45,773,269	96,057,808.3	3.40	123.15	3.71	33.23	14.10
45-64 Years	96,132	96,132	414,527	14,583,417	29,890,181	48,375.3	338	32,663,858	90,691,214.4	2.94	151.70	4.31	35.18	69.87
65+ Years	21,448	21,448	78,112	2,620,992	5,018,069	8,820.6	494	10,955,715	35,111,035.7	1.96	122.20	3.64	33.55	560.06
<b>90-Day Blackout Period</b>														
00-21 Years	276,145	276,145	2,098,005	75,450,836	98,683,340	170,716.4	45	30,666,253	76,503,788.9	9.00	273.23	7.60	35.96	2.64
22-44 Years	66,515	66,515	480,203	16,708,606	31,472,633	37,240.6	50	41,141,728	85,538,040.2	1.62	251.20	7.22	34.79	13.43
45-64 Years	43,421	43,421	361,701	13,265,027	27,006,561	30,853.8	150	30,260,837	82,841,852.6	1.43	305.50	8.33	36.67	48.62
65+ Years	8,501	8,501	63,844	2,258,916	4,396,008	4,960.3	208	9,856,549	32,258,673.4	0.86	265.72	7.51	35.38	419.33
<b>180-Day Blackout Period</b>														
00-21 Years	142,554	142,554	1,739,875	63,961,437	83,231,076	123,712.6	37	28,479,455	69,581,872.3	5.01	448.68	12.21	36.76	2.99
22-44 Years	33,342	33,342	388,822	13,856,924	26,420,246	26,269.6	35	37,567,116	76,213,803.6	0.89	415.60	11.66	35.64	13.32
45-64 Years	23,564	23,564	310,300	11,619,956	23,884,505	23,561.8	113	28,286,717	75,630,897.9	0.83	493.12	13.17	37.45	47.96
65+ Years	4,389	4,389	52,658	1,901,396	3,746,913	3,557.1	129	9,304,555	29,705,953.6	0.47	433.22	12.00	36.11	362.66
<b>270-Day Blackout Period</b>														
00-21 Years	90,682	90,682	1,476,227	55,113,369	71,603,860	96,130.6	27	24,385,609	63,684,971.1	3.72	607.77	16.28	37.33	2.81
22-44 Years	21,079	21,079	323,814	11,740,854	22,688,606	19,868.8	24	31,645,777	68,533,812.3	0.67	556.99	15.36	36.26	12.08
45-64 Years	15,981	15,981	271,159	10,321,860	21,387,256	18,928.6	85	24,638,979	69,446,327.2	0.65	645.88	16.97	38.07	44.91
65+ Years	2,850	2,850	44,583	1,633,548	3,261,068	2,718.4	97	8,308,899	27,473,865.6	0.34	573.17	15.64	36.64	356.82
<b>365-Day Blackout Period</b>														
00-21 Years	62,696	62,696	1,264,025	47,876,826	62,114,569	76,777.8	25	21,974,522	58,040,042.3	2.85	763.63	20.16	37.88	3.26
22-44 Years	14,464	14,464	272,290	10,036,226	19,641,600	15,447.0	19	27,930,461	61,360,814.1	0.52	693.88	18.83	36.86	12.30
45-64 Years	11,622	11,622	237,724	9,194,487	19,280,421	15,452.0	72	22,362,303	63,496,596.9	0.52	791.13	20.45	38.68	46.60
65+ Years	1,996	1,996	37,651	1,405,312	2,843,517	2,105.3	73	7,789,566	25,274,518.2	0.26	704.06	18.86	37.32	346.75
<b>730-Day Blackout Period</b>														
00-21 Years	24,679	24,679	770,395	30,527,252	39,364,684	37,238.7	15	14,944,141	40,952,810.1	1.65	1236.97	31.22	39.63	4.03
22-44 Years	4,957	4,957	149,787	5,826,008	11,869,465	6,988.5	10	17,784,478	41,012,442.7	0.28	1175.31	30.22	38.90	14.31
45-64 Years	4,789	4,789	150,921	6,145,151	13,266,680	8,096.1	39	15,664,599	45,366,057.1	0.31	1283.18	31.51	40.72	48.17
65+ Years	710	710	20,393	820,928	1,674,557	919.6	26	5,678,180	18,506,072.9	0.13	1156.24	28.72	40.26	282.73
<b>1,095-Day Blackout Period</b>														
00-21 Years	12,118	12,118	481,406	20,040,836	25,939,387	19,783.3	8	10,532,871	29,271,392.2	1.15	1653.81	39.73	41.63	4.04
22-44 Years	2,219	2,219	88,145	3,605,148	7,409,443	3,659.4	5	11,889,764	28,238,033.7	0.19	1624.67	39.72	40.90	13.66
45-64 Years	2,443	2,443	98,988	4,218,878	9,320,978	4,669.9	21	11,300,251	32,725,968.3	0.22	1726.93	40.52	42.62	44.97
65+ Years	276	276	10,588	461,181	961,580	474.9	11	4,240,750	13,591,727.1	0.07	1670.95	38.36	43.56	231.61
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
00-21 Years	516,348	516,348	3,189,354	111,918,761	148,083,698	442,147.6	98	33,426,040	83,999,134.4	15.45	216.75	6.18	35.09	2.22

**Table 2a: Summary of Incident Methylphenidate Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
22-44 Years	155,405	155,405	729,607	24,591,054	47,110,836	102,112.5	128	45,773,269	96,057,808.3	3.40	158.24	4.69	33.70	12.54
45-64 Years	96,132	96,132	546,483	19,415,112	40,322,727	77,401.6	473	32,663,858	90,691,214.4	2.94	201.96	5.68	35.53	61.11
65+ Years	21,448	21,448	99,708	3,408,037	6,711,653	14,116.6	760	10,955,715	35,111,035.7	1.96	158.90	4.65	34.18	538.37
<b>90-Day Blackout Period</b>														
00-21 Years	428,968	428,968	3,077,386	109,510,000	144,745,372	328,680.2	72	30,666,253	76,296,780.4	13.99	255.29	7.17	35.59	2.19
22-44 Years	120,190	120,190	682,670	23,520,192	45,251,978	68,848.9	82	41,122,377	85,449,802.7	2.92	195.69	5.68	34.45	11.91
45-64 Years	79,966	79,966	524,674	18,915,361	39,377,220	56,052.8	255	30,255,136	82,774,159.6	2.64	236.54	6.56	36.05	45.49
65+ Years	17,543	17,543	93,665	3,257,525	6,433,756	9,339.8	403	9,854,222	32,238,968.3	1.78	185.69	5.34	34.78	431.49
<b>180-Day Blackout Period</b>														
00-21 Years	263,403	263,403	2,853,282	103,230,812	135,784,510	254,495.4	60	28,479,453	69,463,405.3	9.25	391.91	10.83	36.18	2.36
22-44 Years	59,642	59,642	596,457	21,058,267	40,486,893	49,908.4	57	37,555,763	76,177,743.8	1.59	353.08	10.00	35.31	11.42
45-64 Years	41,118	41,118	478,599	17,645,040	36,752,066	43,867.0	189	28,284,381	75,607,992.4	1.45	429.13	11.64	36.87	43.08
65+ Years	7,640	7,640	80,746	2,905,890	5,849,927	6,798.1	248	9,303,530	29,699,791.9	0.82	380.35	10.57	35.99	364.81
<b>270-Day Blackout Period</b>														
00-21 Years	185,573	185,573	2,582,063	94,530,276	123,970,744	202,914.8	46	24,385,607	63,613,022.8	7.61	509.40	13.91	36.61	2.27
22-44 Years	39,226	39,226	523,580	18,780,905	36,460,579	38,768.0	42	31,639,209	68,515,489.9	1.24	478.79	13.35	35.87	10.83
45-64 Years	28,700	28,700	436,156	16,319,249	34,260,297	36,071.6	141	24,637,608	69,434,256.2	1.16	568.61	15.20	37.42	39.09
65+ Years	5,059	5,059	71,732	2,621,983	5,357,521	5,405.7	179	8,308,270	27,470,629.8	0.61	518.28	14.18	36.55	331.13
<b>365-Day Blackout Period</b>														
00-21 Years	133,917	133,917	2,295,257	84,981,908	111,415,077	163,045.8	42	21,974,521	57,996,552.6	6.09	634.59	17.14	37.03	2.58
22-44 Years	27,429	27,429	454,689	16,548,908	32,445,036	30,537.1	35	27,926,616	61,350,675.2	0.98	603.34	16.58	36.40	11.46
45-64 Years	21,371	21,371	395,030	14,975,230	31,645,274	29,966.2	117	22,361,424	63,489,406.1	0.96	700.73	18.48	37.91	39.04
65+ Years	3,712	3,712	63,865	2,369,725	4,889,987	4,350.8	138	7,789,165	25,272,499.8	0.48	638.40	17.21	37.11	317.18
<b>730-Day Blackout Period</b>														
00-21 Years	53,637	53,637	1,468,547	56,451,304	73,593,004	77,933.3	23	14,944,141	40,943,607.3	3.59	1052.47	27.38	38.44	2.95
22-44 Years	9,894	9,894	270,044	10,324,611	20,924,841	14,250.2	15	17,783,743	41,010,843.9	0.56	1043.52	27.29	38.23	10.53
45-64 Years	9,435	9,435	271,602	10,731,865	23,302,243	16,167.4	56	15,664,371	45,364,417.3	0.60	1137.45	28.79	39.51	34.64
65+ Years	1,498	1,498	39,625	1,555,582	3,276,087	2,060.0	58	5,678,038	18,505,568.4	0.26	1038.44	26.45	39.26	281.56
<b>1,095-Day Blackout Period</b>														
00-21 Years	25,711	25,711	927,632	37,215,850	48,892,106	40,330.7	14	10,532,871	29,268,990.6	2.44	1447.47	36.08	40.12	3.47
22-44 Years	4,537	4,537	165,632	6,638,934	13,722,731	7,568.6	9	11,889,590	28,237,636.2	0.38	1463.29	36.51	40.08	11.89
45-64 Years	4,964	4,964	185,970	7,642,160	16,913,536	9,373.8	31	11,300,176	32,725,487.2	0.44	1539.52	37.46	41.09	33.07
65+ Years	634	634	22,641	945,883	2,031,384	1,089.4	28	4,240,695	13,591,582.3	0.15	1491.93	35.71	41.78	257.01

**Table 2b: Rate of Heart Failure Outcomes at Different Stages of Methylphenidate Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>30-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
00-21 Years	18	97,959	1.8
22-44 Years	42	28,011	15.0
45-64 Years	188	17,522	107.3
65+ Years	286	3,860	740.9
<b>Days 91-180</b>			
00-21 Years	8	47,004	1.7
22-44 Years	15	10,971	13.7
45-64 Years	37	7,292	50.7
65+ Years	79	1,403	563.0
<b>Days 181-270</b>			
00-21 Years	10	27,582	3.6
22-44 Years	11	6,401	17.2
45-64 Years	28	4,633	60.4
65+ Years	32	839	381.6
<b>Days 271-365</b>			
00-21 Years	2	19,353	1.0
22-44 Years	5	4,422	11.3
45-64 Years	13	3,477	37.4
65+ Years	24	613	391.4
<b>Days 366-730</b>			
00-21 Years	10	39,539	2.5
22-44 Years	9	8,459	10.6
45-64 Years	33	7,356	44.9
65+ Years	47	1,186	396.4
<b>Days 731-1,095</b>			
00-21 Years	7	17,455	4.0
22-44 Years	5	3,329	15.0
45-64 Years	18	3,426	52.5
65+ Years	15	445	337.3

**Table 2b: Rate of Heart Failure Outcomes at Different Stages of Methylphenidate Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>90-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
00-21 Years	26	113,467	2.3
22-44 Years	46	33,264	13.8
45-64 Years	218	21,349	102.1
65+ Years	357	4,777	747.4
<b>Days 91-180</b>			
00-21 Years	12	74,185	1.6
22-44 Years	25	18,940	13.2
45-64 Years	66	12,186	54.2
65+ Years	155	2,542	609.8
<b>Days 181-270</b>			
00-21 Years	14	51,581	2.7
22-44 Years	15	11,140	13.5
45-64 Years	48	7,795	61.6
65+ Years	69	1,392	495.6
<b>Days 271-365</b>			
00-21 Years	4	39,869	1.0
22-44 Years	7	8,231	8.5
45-64 Years	24	6,105	39.3
65+ Years	41	1,055	388.6
<b>Days 366-730</b>			
00-21 Years	19	85,112	2.2
22-44 Years	20	16,287	12.3
45-64 Years	61	13,799	44.2
65+ Years	80	2,291	349.2
<b>Days 731-1,095</b>			
00-21 Years	9	37,603	2.4
22-44 Years	6	6,682	9.0
45-64 Years	25	6,794	36.8

**Table 2b: Rate of Heart Failure Outcomes at Different Stages of Methylphenidate Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
65+ Years	30	971	309.1

**Table 3a: Summary of Incident Methylphenidate Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>30-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
Female	322,400	322,400	1,330,023	45,477,976	72,982,215	152,499.9	507	56,075,895	158,549,347.9	5.75	141.06	4.13	34.19	33.25
Male	466,909	466,909	2,078,665	72,275,861	105,807,013	238,615.7	480	54,215,036	147,297,105.3	8.61	154.80	4.45	34.77	20.12
Unknown	24	24	61	1,969	2,519	7.5	0	5,709	12,739.7	4.20	82.04	2.54	32.28	0.00
<b>90-Day Blackout Period</b>														
Female	154,371	154,371	1,154,071	41,069,897	64,828,643	92,769.4	231	51,333,656	143,851,581.5	3.01	266.05	7.48	35.59	24.90
Male	240,201	240,201	1,849,637	66,611,951	96,727,944	150,998.5	222	49,491,918	133,279,424.8	4.85	277.32	7.70	36.01	14.70
Unknown	10	10	45	1,537	1,955	3.1	0	4,828	11,348.9	2.07	153.70	4.50	34.16	0.00
<b>180-Day Blackout Period</b>														
Female	78,928	78,928	950,726	34,646,377	55,001,760	66,954.2	160	47,769,583	130,532,806.4	1.65	438.96	12.05	36.44	23.90
Male	124,916	124,916	1,540,898	56,692,214	82,279,590	110,145.3	154	45,914,195	120,589,537.5	2.72	453.84	12.34	36.79	13.98
Unknown	5	5	31	1,122	1,390	1.5	0	4,162	10,183.3	1.20	224.40	6.20	36.19	0.00
<b>270-Day Blackout Period</b>														
Female	50,406	50,406	803,900	29,789,423	47,637,040	51,771.8	115	40,935,510	119,269,278.0	1.23	590.99	15.95	37.06	22.21
Male	80,184	80,184	1,311,862	49,019,443	71,302,986	85,873.7	118	39,233,852	109,860,423.8	2.04	611.34	16.36	37.37	13.74
Unknown	2	2	21	765	765	0.9	0	3,305	9,274.4	0.61	382.50	10.50	36.43	0.00
<b>365-Day Blackout Period</b>														
Female	34,876	34,876	684,910	25,790,927	41,536,870	41,061.4	94	36,934,046	108,515,679.9	0.94	739.50	19.64	37.66	22.89
Male	55,901	55,901	1,126,763	42,721,419	62,342,731	68,720.1	95	35,263,062	99,647,866.6	1.59	764.23	20.16	37.92	13.82
Unknown	1	1	17	505	505	0.6	0	2,921	8,424.9	0.34	505.00	17.00	29.71	0.00
<b>730-Day Blackout Period</b>														
Female	13,135	13,135	404,422	16,048,654	26,344,489	19,702.5	42	25,164,106	76,450,793.7	0.52	1221.82	30.79	39.68	21.32
Male	22,000	22,000	687,074	27,270,685	39,830,897	33,540.5	48	23,751,735	69,380,634.6	0.93	1239.58	31.23	39.69	14.31
Unknown	0	0	0	0	0	0.0	0	1,900	5,954.5	0.00	---	---	---	---
<b>1,095-Day Blackout Period</b>														
Female	6,249	6,249	248,263	10,374,850	17,204,225	10,578.3	19	17,825,659	54,718,292.3	0.35	1660.24	39.73	41.79	17.96
Male	10,807	10,807	430,864	17,951,193	26,427,164	18,009.2	26	16,622,676	49,104,520.8	0.65	1661.07	39.87	41.66	14.44
Unknown	0	0	0	0	0	0.0	0	1,326	4,308.3	0.00	---	---	---	---
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
Female	322,400	322,400	1,775,265	61,448,091	98,720,791	248,816.1	731	56,075,895	158,549,347.9	5.75	190.60	5.51	34.61	29.38
Male	466,909	466,909	2,789,820	97,882,494	143,505,194	386,950.9	728	54,215,036	147,297,105.3	8.61	209.64	5.98	35.09	18.81
Unknown	24	24	67	2,379	2,929	11.2	0	5,709	12,739.7	4.20	99.13	2.79	35.51	0.00
<b>90-Day Blackout Period</b>														
Female	261,455	261,455	1,695,167	59,662,564	95,863,976	178,488.9	400	51,333,656	143,690,476.1	5.09	228.19	6.48	35.20	22.41
Male	385,195	385,195	2,683,170	95,538,363	139,941,733	284,426.7	412	49,491,918	133,057,893.9	7.78	248.03	6.97	35.61	14.49



**Table 3a: Summary of Incident Methylphenidate Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
Unknown	17	17	58	2,151	2,617	6.1	0	4,828	11,340.9	3.52	126.53	3.41	37.09	0.00
<b>180-Day Blackout Period</b>														
Female	144,757	144,757	1,536,509	55,198,185	87,990,673	135,473.6	272	47,769,583	130,463,388.4	3.03	381.32	10.61	35.92	20.08
Male	227,039	227,039	2,472,532	89,640,112	130,880,592	219,592.0	282	45,914,193	120,475,361.6	4.94	394.82	10.89	36.25	12.84
Unknown	7	7	43	1,712	2,130	3.4	0	4,162	10,183.3	1.68	244.57	6.14	39.81	0.00
<b>270-Day Blackout Period</b>														
Female	99,549	99,549	1,379,035	50,244,561	80,357,496	107,741.0	200	40,935,510	119,230,472.0	2.43	504.72	13.85	36.43	18.56
Male	159,007	159,007	2,234,469	82,006,677	119,690,471	175,416.8	208	39,233,850	109,793,652.3	4.05	515.74	14.05	36.70	11.86
Unknown	2	2	27	1,175	1,175	2.3	0	3,305	9,274.4	0.61	587.50	13.50	43.52	0.00
<b>365-Day Blackout Period</b>														
Female	71,585	71,585	1,221,472	45,074,161	72,501,163	86,532.0	167	36,934,046	108,492,757.0	1.94	629.66	17.06	36.90	19.30
Male	114,842	114,842	1,987,342	73,800,435	107,893,036	141,366.1	165	35,263,061	99,607,957.3	3.26	642.63	17.31	37.14	11.67
Unknown	2	2	27	1,175	1,175	1.8	0	2,921	8,419.3	0.68	587.50	13.50	43.52	0.00
<b>730-Day Blackout Period</b>														
Female	28,218	28,218	773,471	29,838,989	48,904,793	41,969.8	75	25,164,106	76,446,235.2	1.12	1057.45	27.41	38.58	17.87
Male	46,245	46,245	1,276,337	49,223,703	72,190,712	68,440.8	77	23,751,735	69,372,251.8	1.95	1064.41	27.60	38.57	11.25
Unknown	1	1	10	670	670	0.2	0	1,900	5,949.9	0.53	670.00	10.00	67.00	0.00
<b>1,095-Day Blackout Period</b>														
Female	13,481	13,481	489,130	19,728,309	32,895,297	22,329.0	38	17,825,659	54,717,106.8	0.76	1463.42	36.28	40.33	17.02
Male	22,365	22,365	812,745	32,714,518	48,664,461	36,033.6	44	16,622,676	49,102,281.3	1.35	1462.76	36.34	40.25	12.21
Unknown	0	0	0	0	0	0.0	0	1,326	4,308.3	0.00	---	---	---	---

**Table 3b: Rate of Heart Failure Outcomes at Different Stages of Methylphenidate Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Episodes with Events	Years at Risk	New Episodes with Events per 01,000 Years at Risk
<b>30-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
Female	276	59,730	46.2
Male	258	87,617	29.4
Unknown	0	4	0.0
<b>Days 91-180</b>			
Female	71	25,815	27.5
Male	68	40,853	16.6
Unknown	0	2	0.0
<b>Days 181-270</b>			
Female	45	15,182	29.6
Male	36	24,272	14.8
Unknown	0	1	0.0
<b>Days 271-365</b>			
Female	21	10,710	19.6
Male	23	17,154	13.4
Unknown	0	0	0.0
<b>Days 366-730</b>			
Female	52	21,359	24.3
Male	47	35,180	13.4
Unknown	0	1	0.0
<b>Days 731-1,095</b>			
Female	23	9,124	25.2
Male	22	15,531	14.2
Unknown	0	0	---
<b>90-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
Female	331	70,327	47.1
Male	316	102,524	30.8
Unknown	0	5	0.0
<b>Days 91-180</b>			
Female	128	43,015	29.8

**Table 3b: Rate of Heart Failure Outcomes at Different Stages of Methylphenidate Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Episodes with Events	Years at Risk	New Episodes with Events per 01,000 Years at Risk
Male	130	64,835	20.1
Unknown	0	3	0.0
<b>Days 181-270</b>			
Female	72	27,733	26.0
Male	74	44,175	16.8
Unknown	0	1	0.0
<b>Days 271-365</b>			
Female	33	21,209	15.6
Male	43	34,051	12.6
Unknown	0	1	0.0
<b>Days 366-730</b>			
Female	92	44,562	20.6
Male	88	72,925	12.1
Unknown	0	2	0.0
<b>Days 731-1,095</b>			
Female	37	19,641	18.8
Male	33	32,407	10.2
Unknown	0	0	0.0

**Table 4a: Summary of Incident Methylphenidate Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>30-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
2000	5,618	5,618	20,292	967,895	2,122,891	3,152.3	13	6,530,503	3,002,268.1	0.86	172.28	3.61	47.70	41.24
2001	13,958	13,958	55,793	2,418,698	4,721,266	7,900.3	31	7,127,364	5,964,403.0	1.96	173.28	4.00	43.35	39.24
2002	13,329	13,329	56,378	2,639,250	4,761,975	8,416.9	37	7,276,181	6,061,761.9	1.83	198.01	4.23	46.81	43.96
2003	18,690	18,690	105,135	4,305,974	8,492,355	13,367.5	46	7,267,492	6,033,883.2	2.57	230.39	5.63	40.96	34.41
2004	16,950	16,950	85,970	3,625,053	8,266,955	11,401.2	58	7,701,079	6,278,248.7	2.20	213.87	5.07	42.17	50.87
2005	17,104	17,104	81,933	3,502,744	5,988,729	11,116.4	39	7,941,270	6,565,824.4	2.15	204.79	4.79	42.75	35.08
2006	31,782	31,782	152,602	5,786,014	8,840,551	18,772.9	58	19,408,425	11,602,277.9	1.64	182.05	4.80	37.92	30.90
2007	48,572	48,572	235,994	8,458,219	12,405,216	27,657.9	72	23,609,439	17,165,207.4	2.06	174.14	4.86	35.84	26.03
2008	76,528	76,528	352,272	12,072,384	17,454,372	39,958.5	91	44,299,343	28,029,014.4	1.73	157.75	4.60	34.27	22.77
2009	96,931	96,931	436,703	14,711,652	21,030,931	49,075.1	115	45,679,002	35,502,667.1	2.12	151.77	4.51	33.69	23.43
2010	93,321	93,321	427,816	14,302,164	20,284,230	47,613.8	95	43,536,275	33,987,096.1	2.14	153.26	4.58	33.43	19.95
2011	91,211	91,211	418,318	13,793,930	19,309,577	46,011.6	98	42,130,515	33,186,784.8	2.16	151.23	4.59	32.97	21.30
2012	84,335	84,335	374,777	12,244,002	17,133,655	41,206.4	77	41,110,021	32,509,908.6	2.05	145.18	4.44	32.67	18.69
2013	78,760	78,760	317,830	10,174,674	14,915,132	34,750.6	91	40,974,287	32,190,439.3	1.92	129.19	4.04	32.01	26.19
2014	71,595	71,595	226,679	7,047,963	10,504,945	24,744.6	50	41,913,240	32,070,549.0	1.71	98.44	3.17	31.09	20.21
2015	30,649	30,649	60,257	1,705,190	2,558,965	5,977.1	16	34,513,929	15,708,858.8	0.89	55.64	1.97	28.30	26.77
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>90-Day Blackout Period</b>														
2000	2,918	2,918	17,169	870,508	1,898,208	1,983.4	7	6,279,504	2,830,510.6	0.46	298.32	5.88	50.70	35.29
2001	6,936	6,936	48,240	2,199,069	4,249,001	5,097.5	18	6,796,562	5,686,328.2	1.02	317.05	6.96	45.59	35.31
2002	7,065	7,065	50,148	2,477,316	4,437,255	5,814.4	21	6,960,697	5,759,643.7	1.01	350.65	7.10	49.40	36.12
2003	10,776	10,776	102,737	4,288,416	8,752,597	10,178.8	28	6,910,338	5,742,403.8	1.56	397.96	9.53	41.74	27.51
2004	9,519	9,519	78,858	3,449,099	6,462,082	8,136.8	33	7,431,292	5,991,979.2	1.28	362.34	8.28	43.74	40.56
2005	9,294	9,294	74,404	3,322,819	5,646,727	7,864.7	19	7,585,083	6,208,321.9	1.23	357.52	8.01	44.66	24.16
2006	16,438	16,438	136,826	5,385,677	8,159,298	12,667.1	33	18,307,845	10,898,216.2	0.90	327.64	8.32	39.36	26.05
2007	24,659	24,659	211,577	7,835,283	11,411,238	18,395.3	34	22,152,353	16,125,626.4	1.11	317.75	8.58	37.03	18.48
2008	37,444	37,444	311,225	11,015,310	15,861,600	25,499.3	32	41,891,691	25,807,390.5	0.89	294.18	8.31	35.39	12.55
2009	47,308	47,308	383,752	13,358,774	18,932,943	30,738.0	57	42,524,757	32,696,405.0	1.11	282.38	8.11	34.81	18.54
2010	46,793	46,793	380,438	13,133,337	18,448,270	30,191.9	39	40,757,315	31,426,636.1	1.15	280.67	8.13	34.52	12.92
2011	46,439	46,439	373,381	12,688,456	17,582,685	29,014.3	40	39,654,570	30,799,031.6	1.17	273.23	8.04	33.98	13.79
2012	44,034	44,034	336,102	11,313,994	15,700,629	25,550.8	33	39,250,644	30,296,813.0	1.12	256.94	7.63	33.66	12.92
2013	40,944	40,944	280,532	9,261,650	13,531,399	20,043.2	38	38,549,655	29,839,572.0	1.06	226.20	6.85	33.01	18.96
2014	36,191	36,191	188,860	6,099,747	9,027,480	11,265.2	18	39,165,456	29,308,509.5	0.92	168.54	5.22	32.30	15.98
2015	7,824	7,824	29,504	983,930	1,457,130	1,330.3	3	23,070,880	7,724,967.5	0.34	125.76	3.77	33.35	22.55
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>180-Day Blackout Period</b>														
2000	1,396	1,396	14,112	725,017	1,582,627	1,474.2	7	6,014,580	2,679,165.4	0.23	519.35	10.11	51.38	47.48
2001	3,438	3,438	40,343	1,872,742	3,594,282	3,882.7	13	6,570,901	5,430,458.2	0.52	544.72	11.73	46.42	33.48
2002	3,796	3,796	42,922	2,195,197	3,925,769	4,600.6	20	6,689,272	5,473,738.1	0.57	578.29	11.31	51.14	43.47
2003	6,130	6,130	92,459	3,913,660	8,203,089	8,359.2	21	6,663,189	5,479,855.6	0.92	638.44	15.08	42.33	25.12
2004	5,435	5,435	68,979	3,075,822	5,572,639	6,412.6	24	7,100,504	5,728,473.2	0.77	565.93	12.69	44.59	37.43
2005	5,150	5,150	64,648	2,972,119	5,063,332	6,260.9	13	7,324,722	5,876,611.7	0.70	577.11	12.55	45.97	20.76
2006	9,192	9,192	118,417	4,763,929	7,213,180	9,766.6	27	17,602,268	10,257,215.1	0.52	518.27	12.88	40.23	27.65
2007	13,335	13,335	181,793	6,862,624	9,983,226	14,081.6	28	21,060,515	15,181,955.5	0.63	514.63	13.63	37.75	19.88
2008	19,862	19,862	263,847	9,511,960	13,727,607	19,066.0	22	39,225,495	23,795,762.6	0.51	478.90	13.28	36.05	11.54
2009	24,252	24,252	321,249	11,401,878	16,144,623	22,747.1	36	40,497,008	30,137,332.9	0.60	470.14	13.25	35.49	15.83
2010	24,414	24,414	319,967	11,239,682	15,773,367	22,249.1	25	38,861,309	29,100,943.9	0.63	460.38	13.11	35.13	11.24
2011	24,550	24,550	314,207	10,867,797	15,017,780	21,192.4	26	37,889,331	28,588,162.7	0.65	442.68	12.80	34.59	12.27
2012	23,484	23,484	280,749	9,610,372	13,324,408	18,106.1	20	37,033,281	28,236,510.9	0.63	409.23	11.95	34.23	11.05
2013	21,536	21,536	228,196	7,650,600	11,254,010	13,154.7	23	36,894,766	27,640,207.7	0.58	355.25	10.60	33.53	17.48

**Table 4a: Summary of Incident Methylphenidate Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2014	15,874	15,874	128,297	4,258,814	6,286,954	5,445.8	8	36,465,327	23,908,781.2	0.44	268.29	8.08	33.19	14.69
2015	2,005	2,005	11,470	417,500	615,847	301.3	1	13,680,254	3,617,352.7	0.15	208.23	5.72	36.40	33.19
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>270-Day Blackout Period</b>														
2000	846	846	12,049	625,669	1,370,569	1,198.3	6	5,575,360	2,587,781.7	0.15	739.56	14.24	51.93	50.07
2001	2,209	2,209	35,296	1,653,178	3,175,568	3,196.9	10	6,252,822	5,197,077.3	0.35	748.38	15.98	46.84	31.28
2002	2,489	2,489	37,483	1,962,833	3,527,846	3,842.6	16	6,343,135	5,220,651.5	0.39	788.60	15.06	52.37	41.64
2003	4,332	4,332	84,643	3,605,726	7,692,866	7,135.4	17	6,289,096	5,247,498.0	0.69	832.35	19.54	42.60	23.83
2004	3,680	3,680	61,364	2,776,592	4,896,921	5,345.6	21	6,700,797	5,493,341.1	0.55	754.51	16.68	45.25	39.28
2005	3,431	3,431	57,103	2,681,463	4,593,739	5,262.9	11	6,862,817	5,585,589.5	0.50	781.54	16.64	46.96	20.90
2006	5,993	5,993	103,188	4,221,548	6,412,795	7,973.2	19	16,161,051	9,768,410.1	0.37	704.41	17.22	40.91	23.83
2007	8,754	8,754	158,501	6,074,610	8,887,521	11,452.5	20	19,572,682	14,372,756.7	0.45	693.92	18.11	38.33	17.46
2008	12,852	12,852	227,490	8,321,099	12,078,495	15,182.8	16	35,080,818	22,337,381.0	0.37	647.46	17.70	36.58	10.54
2009	15,687	15,687	276,507	9,935,156	14,099,001	17,989.7	27	37,005,621	27,976,940.0	0.42	633.34	17.63	35.93	15.01
2010	15,971	15,971	276,815	9,834,187	13,813,500	17,543.9	18	35,586,018	27,136,695.2	0.45	615.75	17.33	35.53	10.26
2011	15,988	15,988	269,296	9,421,606	13,008,924	16,392.7	18	34,778,422	26,696,052.0	0.46	589.29	16.84	34.99	10.98
2012	15,571	15,571	239,621	8,288,017	11,493,613	13,505.3	15	33,943,031	26,527,140.5	0.46	532.27	15.39	34.59	11.11
2013	14,158	14,158	189,516	6,411,949	9,456,302	8,959.0	16	33,922,669	25,712,649.9	0.42	452.89	13.39	33.83	17.86
2014	8,278	8,278	84,750	2,894,700	4,293,573	2,626.3	3	32,098,696	18,242,295.8	0.26	349.69	10.24	34.16	11.42
2015	353	353	2,161	101,298	139,558	39.2	0	9,163,008	1,036,715.9	0.04	286.96	6.12	46.88	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>365-Day Blackout Period</b>														
2000	587	587	10,568	555,903	1,221,518	1,012.1	5	5,330,912	2,500,414.1	0.11	947.02	18.00	52.60	49.40
2001	1,555	1,555	31,150	1,477,279	2,837,593	2,712.4	6	5,792,403	4,955,275.2	0.27	950.02	20.03	47.42	22.12
2002	1,783	1,783	33,429	1,778,428	3,207,755	3,308.4	13	5,850,375	4,983,651.4	0.30	997.44	18.75	53.20	39.29
2003	3,221	3,221	77,173	3,317,694	7,176,585	6,188.0	13	5,874,737	5,021,527.7	0.55	1030.02	23.96	42.99	21.03
2004	2,694	2,694	55,062	2,515,964	4,386,085	4,532.4	19	6,418,023	5,253,431.2	0.42	933.91	20.44	45.69	41.92
2005	2,528	2,528	51,439	2,452,064	4,255,703	4,529.5	8	6,250,587	5,312,186.4	0.40	969.96	20.35	47.67	17.66
2006	4,284	4,284	91,164	3,783,319	5,775,837	6,677.3	17	15,001,059	9,294,650.3	0.29	883.13	21.28	41.50	25.46
2007	6,332	6,332	140,778	5,459,789	8,030,484	9,576.0	17	17,955,119	13,595,636.3	0.35	862.25	22.23	38.78	17.75
2008	9,010	9,010	198,202	7,341,192	10,706,947	12,429.6	14	32,709,030	20,941,596.0	0.28	814.78	22.00	37.04	11.26
2009	11,048	11,048	240,677	8,755,444	12,431,038	14,637.4	22	32,221,922	25,876,252.7	0.34	792.49	21.78	36.38	15.03
2010	11,321	11,321	240,604	8,641,765	12,182,840	14,101.1	16	31,246,857	25,267,392.4	0.36	763.34	21.25	35.92	11.35
2011	11,317	11,317	232,535	8,223,127	11,339,461	12,945.5	12	30,613,493	24,849,238.7	0.37	726.62	20.55	35.36	9.27
2012	11,080	11,080	204,599	7,148,492	9,888,895	10,159.4	12	32,221,429	24,854,781.3	0.34	645.17	18.47	34.94	11.81
2013	9,917	9,917	155,773	5,324,261	7,855,772	5,925.8	13	29,648,647	23,821,154.3	0.33	536.88	15.71	34.18	21.94
2014	4,101	4,101	48,537	1,738,130	2,583,593	1,052.2	2	24,899,658	11,644,783.5	0.16	423.83	11.84	35.81	19.01
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>730-Day Blackout Period</b>														
2000	274	274	7,612	414,322	890,535	619.6	3	4,503,593	2,119,747.1	0.06	1512.12	27.78	54.43	48.42
2001	681	681	21,681	1,070,497	2,087,163	1,671.5	4	4,827,583	4,189,894.8	0.14	1571.95	31.84	49.37	23.93
2002	817	817	23,582	1,329,283	2,432,828	2,103.2	8	4,898,157	4,262,794.9	0.17	1627.03	28.86	56.37	38.04
2003	1,678	1,678	59,275	2,608,808	5,468,611	3,902.5	7	5,060,569	4,310,542.7	0.33	1554.71	35.32	44.01	17.94
2004	1,157	1,157	37,424	1,810,226	3,072,269	2,783.1	11	5,343,169	4,345,796.2	0.22	1564.59	32.35	48.37	39.52
2005	1,171	1,171	36,461	1,822,347	3,208,039	2,811.7	3	5,248,973	4,547,026.3	0.22	1556.23	31.14	49.98	10.67
2006	1,887	1,887	61,924	2,692,043	4,138,024	3,861.8	11	12,162,053	7,729,479.9	0.16	1426.63	32.82	43.47	28.48
2007	2,749	2,749	95,186	3,833,497	5,683,559	5,420.3	8	14,587,231	10,897,678.5	0.19	1394.51	34.63	40.27	14.76
2008	3,862	3,862	132,030	5,048,505	7,424,419	6,658.3	8	24,273,233	16,137,906.6	0.16	1307.23	34.19	38.24	12.02
2009	4,655	4,655	156,450	5,872,993	8,329,530	7,499.3	11	24,014,268	19,877,411.9	0.19	1261.65	33.61	37.54	14.67
2010	4,792	4,792	153,629	5,697,692	7,989,507	6,767.9	5	23,614,870	19,518,401.3	0.20	1189.00	32.06	37.09	7.39
2011	4,970	4,970	148,350	5,387,600	7,406,374	5,528.2	7	24,894,827	19,698,938.4	0.20	1084.02	29.85	36.32	12.66

**Table 4a: Summary of Incident Methylphenidate Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2012	4,519	4,519	117,214	4,201,537	5,790,888	3,070.8	4	24,676,810	18,964,678.7	0.18	929.75	25.94	35.85	13.03
2013	1,923	1,923	40,678	1,529,989	2,253,639	544.7	0	19,031,007	9,237,085.5	0.10	795.63	21.15	37.61	0.00
2014	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>1,095-Day Blackout Period</b>														
2000	159	159	5,756	318,563	701,501	413.6	3	3,851,156	1,825,130.7	0.04	2003.54	36.20	55.34	72.53
2001	408	408	16,516	840,153	1,627,744	1,140.4	2	4,142,586	3,648,176.4	0.10	2059.20	40.48	50.87	17.54
2002	490	490	18,101	1,054,485	1,959,655	1,475.1	6	4,312,739	3,721,868.4	0.11	2152.01	36.94	58.26	40.67
2003	939	939	42,974	1,990,525	3,810,989	2,666.8	4	4,312,579	3,611,202.4	0.22	2119.83	45.77	46.32	15.00
2004	725	725	29,186	1,441,686	2,429,274	1,863.6	4	4,514,008	3,786,085.9	0.16	1988.53	40.26	49.40	21.46
2005	729	729	28,418	1,454,057	2,605,047	1,894.2	2	4,547,485	3,975,628.1	0.16	1994.59	38.98	51.17	10.56
2006	1,061	1,061	44,390	2,000,506	3,110,816	2,439.5	5	9,956,554	6,466,131.4	0.11	1885.49	41.84	45.07	20.50
2007	1,587	1,587	68,900	2,876,812	4,276,745	3,346.3	5	11,789,285	9,011,673.1	0.13	1812.74	43.42	41.75	14.94
2008	2,102	2,102	91,840	3,610,055	5,342,404	3,847.4	6	18,836,394	13,007,504.8	0.11	1717.44	43.69	39.31	15.59
2009	2,522	2,522	106,723	4,118,546	5,809,215	4,070.4	8	18,699,242	15,734,802.6	0.13	1633.05	42.32	38.59	19.65
2010	2,633	2,633	102,754	3,909,147	5,439,251	3,187.2	0	19,811,788	15,915,493.0	0.13	1484.67	39.03	38.04	0.00
2011	2,605	2,605	91,998	3,435,700	4,713,368	1,923.3	0	19,762,182	15,429,694.8	0.13	1318.89	35.32	37.35	0.00
2012	1,096	1,096	31,571	1,275,808	1,805,379	319.7	0	17,149,705	7,693,729.7	0.06	1164.06	28.81	40.41	0.00
2013	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2014	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
2000	5,618	5,618	29,786	1,434,623	3,078,372	5,556.6	22	6,530,503	3,002,268.1	0.86	255.36	5.30	48.16	39.59
2001	13,958	13,958	80,634	3,528,057	6,904,771	13,807.8	57	7,127,364	5,964,403.0	1.96	252.76	5.78	43.75	41.28
2002	13,329	13,329	80,875	3,772,523	6,795,084	14,153.2	51	7,276,181	6,061,761.9	1.83	283.03	6.07	46.65	36.03
2003	18,690	18,690	153,189	6,240,947	12,187,024	22,252.7	64	7,267,492	6,033,883.2	2.57	333.92	8.20	40.74	28.76
2004	16,950	16,950	118,355	5,070,343	10,791,161	18,568.8	75	7,701,079	6,278,248.7	2.20	299.14	6.98	42.84	40.39
2005	17,104	17,104	115,497	4,984,430	8,386,756	18,521.1	51	7,941,270	6,565,824.4	2.15	291.42	6.75	43.16	27.54
2006	31,782	31,782	210,967	8,039,579	12,228,969	31,206.9	73	19,408,425	11,602,277.9	1.64	252.96	6.64	38.11	23.39
2007	48,572	48,572	324,396	11,685,530	17,264,390	45,817.8	115	23,609,439	17,165,207.4	2.06	240.58	6.68	36.02	25.10
2008	76,528	76,528	480,687	16,621,309	24,133,773	66,246.2	130	44,299,343	28,029,014.4	1.73	217.19	6.28	34.58	19.62
2009	96,931	96,931	596,265	20,248,515	29,053,517	81,629.6	179	45,679,002	35,502,667.1	2.12	208.90	6.15	33.96	21.93
2010	93,321	93,321	580,675	19,575,335	27,817,229	78,479.0	160	43,536,275	33,987,096.1	2.14	209.76	6.22	33.71	20.39
2011	91,211	91,211	558,597	18,563,437	26,134,569	74,849.5	151	42,130,515	33,186,784.8	2.16	203.52	6.12	33.23	20.17
2012	84,335	84,335	493,813	16,234,688	22,850,582	66,362.3	111	41,110,021	32,509,908.6	2.05	192.50	5.86	32.88	16.73
2013	78,760	78,760	407,755	13,123,122	19,322,092	54,835.2	128	40,974,287	32,190,439.3	1.92	166.62	5.18	32.18	23.34
2014	71,595	71,595	269,403	8,388,365	12,542,285	36,033.9	72	41,913,240	32,070,549.0	1.71	117.16	3.76	31.14	19.98
2015	30,649	30,649	64,258	1,822,161	2,738,341	7,457.5	20	34,513,929	15,708,858.8	0.89	59.45	2.10	28.36	26.82
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>90-Day Blackout Period</b>														
2000	5,011	5,011	28,903	1,411,586	3,027,771	4,246.8	16	6,279,504	2,830,510.6	0.80	281.70	5.77	48.84	37.68
2001	12,670	12,670	78,823	3,482,430	6,811,506	10,538.8	38	6,795,226	5,685,473.9	1.86	274.86	6.22	44.18	36.06
2002	11,922	11,922	79,060	3,730,411	6,703,990	11,075.7	32	6,955,406	5,756,072.7	1.71	312.90	6.63	47.18	28.89
2003	16,460	16,460	150,415	6,178,007	12,078,806	17,988.2	39	6,902,461	5,737,054.2	2.38	375.33	9.14	41.07	21.68
2004	14,717	14,717	115,407	4,999,540	10,607,362	14,728.6	45	7,421,440	5,984,944.1	1.98	339.71	7.84	43.32	30.55
2005	14,863	14,863	112,930	4,936,496	8,292,830	14,720.4	28	7,572,152	6,198,822.0	1.96	332.13	7.60	43.71	19.02
2006	27,434	27,434	205,536	7,924,961	12,035,765	24,076.6	43	18,292,375	10,886,466.1	1.50	288.87	7.49	38.56	17.86
2007	41,701	41,701	315,677	11,491,743	16,950,516	34,918.3	65	22,130,891	16,109,592.0	1.88	275.57	7.57	36.40	18.61
2008	63,550	63,550	463,135	16,218,874	23,533,915	49,231.6	60	41,860,850	25,784,560.9	1.52	255.21	7.29	35.02	12.19

**Table 4a: Summary of Incident Methylphenidate Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2009	80,663	80,663	574,579	19,760,476	28,317,062	60,120.3	106	42,481,930	32,665,371.3	1.90	244.98	7.12	34.39	17.63
2010	76,920	76,920	559,857	19,124,548	27,119,948	58,027.1	88	40,701,105	31,385,954.5	1.89	248.63	7.28	34.16	15.17
2011	75,203	75,203	538,374	18,133,845	25,499,736	54,943.1	85	39,588,340	30,750,556.9	1.90	241.13	7.16	33.68	15.47
2012	69,995	69,995	476,088	15,855,954	22,298,816	47,920.3	62	39,177,144	30,242,573.9	1.79	226.53	6.80	33.30	12.94
2013	65,333	65,333	390,855	12,757,362	18,781,967	37,608.0	69	38,471,214	29,780,772.5	1.70	195.27	5.98	32.64	18.35
2014	57,750	57,750	250,876	7,975,102	11,910,919	20,458.2	32	39,085,270	29,250,132.2	1.48	138.10	4.34	31.79	15.64
2015	12,475	12,475	37,880	1,221,743	1,837,416	2,319.6	4	23,025,841	7,710,852.9	0.54	97.94	3.04	32.25	17.24
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>180-Day Blackout Period</b>														
2000	2,983	2,983	26,067	1,311,537	2,799,503	3,282.4	14	6,014,580	2,679,165.4	0.50	439.67	8.74	50.31	42.65
2001	7,156	7,156	71,670	3,258,497	6,331,585	8,278.7	30	6,570,263	5,430,250.2	1.09	455.35	10.02	45.47	36.24
2002	7,264	7,264	74,156	3,595,832	6,434,593	9,076.2	27	6,686,836	5,472,509.4	1.09	495.02	10.21	48.49	29.75
2003	10,803	10,803	152,275	6,272,219	12,705,614	15,904.8	32	6,659,249	5,477,629.9	1.62	580.60	14.10	41.19	20.12
2004	9,336	9,336	109,323	4,832,881	8,774,429	12,224.5	31	7,095,061	5,725,212.3	1.32	517.66	11.71	44.21	25.36
2005	9,150	9,150	106,127	4,748,282	7,948,544	12,170.6	19	7,317,107	5,871,824.5	1.25	518.94	11.60	44.74	15.61
2006	16,303	16,303	191,722	7,549,491	11,409,920	19,388.9	34	17,592,563	10,250,754.1	0.93	463.07	11.76	39.38	17.54
2007	24,195	24,195	293,297	10,867,745	16,003,575	27,819.5	49	21,047,951	15,173,632.2	1.15	449.17	12.12	37.05	17.61
2008	36,044	36,044	425,582	15,144,860	21,971,872	38,458.1	38	39,208,509	23,784,566.6	0.92	420.18	11.81	35.59	9.88
2009	45,316	45,316	525,965	18,383,009	26,256,826	46,491.8	78	40,474,772	30,123,121.4	1.12	405.66	11.61	34.95	16.78
2010	44,578	44,578	518,016	17,967,435	25,382,450	45,291.2	55	38,832,263	29,082,376.3	1.15	403.06	11.62	34.69	12.14
2011	44,258	44,258	498,705	17,035,761	23,862,971	42,461.5	53	37,853,861	28,565,245.1	1.17	384.92	11.27	34.16	12.48
2012	41,911	41,911	441,950	14,923,446	20,938,287	36,338.1	38	36,992,930	28,209,637.7	1.13	356.07	10.54	33.77	10.46
2013	39,093	39,093	357,039	11,814,566	17,425,782	26,547.4	41	36,849,818	27,609,986.4	1.06	302.22	9.13	33.09	15.44
2014	29,550	29,550	198,892	6,489,452	9,671,616	10,752.5	15	36,419,517	23,881,115.6	0.81	219.61	6.73	32.63	13.95
2015	3,863	3,863	18,298	644,996	955,830	582.7	0	13,663,143	3,611,906.1	0.28	166.97	4.74	35.25	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>270-Day Blackout Period</b>														
2000	1,985	1,985	23,698	1,197,185	2,550,137	2,694.8	12	5,575,360	2,587,781.7	0.36	603.12	11.94	50.52	44.53
2001	4,799	4,799	65,425	2,995,396	5,827,518	6,885.7	22	6,252,613	5,197,046.3	0.77	624.17	13.63	45.78	31.95
2002	5,050	5,050	68,358	3,380,948	6,050,929	7,739.4	25	6,342,060	5,220,224.2	0.80	669.49	13.54	49.46	32.30
2003	8,118	8,118	145,487	6,017,221	12,377,406	13,867.3	27	6,287,126	5,246,518.9	1.29	741.22	17.92	41.36	19.47
2004	6,743	6,743	102,218	4,566,489	8,074,348	10,467.3	27	6,697,785	5,491,717.4	1.01	677.22	15.16	44.67	25.79
2005	6,534	6,534	98,994	4,496,772	7,530,436	10,485.8	14	6,858,424	5,583,039.6	0.95	688.21	15.15	45.42	13.35
2006	11,772	11,772	177,648	7,069,121	10,684,293	16,166.3	26	16,155,129	9,764,711.3	0.73	600.50	15.09	39.79	16.08
2007	17,178	17,178	269,584	10,096,429	14,873,640	23,042.3	34	19,565,018	14,367,887.4	0.88	587.75	15.69	37.45	14.76
2008	25,530	25,530	388,665	13,982,986	20,314,877	31,281.5	27	35,070,443	22,330,851.3	0.73	547.71	15.22	35.98	8.63
2009	31,734	31,734	477,945	16,880,541	24,100,104	37,552.1	59	36,992,256	27,968,626.2	0.86	531.94	15.06	35.32	15.71
2010	31,544	31,544	472,910	16,564,281	23,394,484	36,652.9	39	35,568,314	27,125,806.9	0.89	525.12	14.99	35.03	10.64
2011	31,624	31,624	454,655	15,688,011	21,952,545	33,838.9	36	34,756,297	26,682,240.7	0.91	496.08	14.38	34.51	10.64
2012	30,346	30,346	402,541	13,715,455	19,231,123	28,158.6	26	33,917,302	26,510,477.7	0.89	451.97	13.27	34.07	9.23
2013	28,181	28,181	318,818	10,642,467	15,719,333	18,842.6	28	33,893,431	25,693,652.5	0.83	377.65	11.31	33.38	14.86
2014	16,720	16,720	142,832	4,790,273	7,131,684	5,409.7	6	32,070,401	18,227,670.4	0.52	286.50	8.54	33.54	11.09
2015	700	700	3,753	168,838	236,286	74.8	0	9,153,714	1,035,146.2	0.08	241.20	5.36	44.99	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>365-Day Blackout Period</b>														
2000	1,350	1,350	21,181	1,080,007	2,299,721	2,270.8	10	5,330,912	2,500,414.1	0.25	800.01	15.69	50.99	44.04
2001	3,480	3,480	59,437	2,749,777	5,345,761	5,825.5	17	5,792,382	4,955,273.9	0.60	790.17	17.08	46.26	29.18
2002	3,687	3,687	62,540	3,133,708	5,626,320	6,671.4	21	5,849,963	4,983,512.2	0.63	849.93	16.96	50.11	31.48
2003	6,332	6,332	136,868	5,690,859	11,880,627	12,091.6	22	5,873,786	5,021,091.0	1.08	898.75	21.62	41.58	18.19
2004	5,166	5,166	94,988	4,284,583	7,496,283	9,022.0	24	6,416,433	5,252,612.7	0.81	829.38	18.39	45.11	26.60
2005	4,977	4,977	91,809	4,223,210	7,084,161	9,099.6	11	6,248,002	5,310,750.3	0.80	848.55	18.45	46.00	12.09
2006	8,656	8,656	162,158	6,526,706	9,898,620	13,648.1	24	14,997,355	9,292,392.0	0.58	754.01	18.73	40.25	17.58

**Table 4a: Summary of Incident Methylphenidate Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2007	12,786	12,786	245,812	9,299,169	13,751,728	19,309.9	29	17,950,401	13,592,578.0	0.71	727.29	19.23	37.83	15.02
2008	18,545	18,545	350,088	12,718,011	18,554,350	25,769.2	23	32,702,654	20,937,578.4	0.57	685.79	18.88	36.33	8.93
2009	22,991	22,991	428,848	15,292,252	21,844,492	30,702.0	50	32,213,931	25,871,108.2	0.71	665.14	18.65	35.66	16.29
2010	23,281	23,281	426,697	15,081,499	21,332,501	29,869.6	32	31,236,135	25,260,635.5	0.75	647.80	18.33	35.34	10.71
2011	23,235	23,235	407,236	14,164,933	19,783,049	27,050.0	25	30,599,941	24,840,579.5	0.76	609.64	17.53	34.78	9.24
2012	22,719	22,719	359,581	12,342,289	17,278,626	21,577.4	19	32,204,827	24,844,112.3	0.71	543.26	15.83	34.32	8.81
2013	20,698	20,698	275,962	9,283,309	13,738,683	12,769.4	21	29,630,234	23,808,765.1	0.70	448.51	13.33	33.64	16.45
2014	8,526	8,526	85,636	3,005,459	4,480,451	2,223.3	4	24,885,239	11,637,730.4	0.34	352.51	10.04	35.10	17.99
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>730-Day Blackout Period</b>														
2000	607	607	15,635	823,678	1,743,577	1,389.1	6	4,503,593	2,119,747.1	0.13	1356.97	25.76	52.68	43.19
2001	1,506	1,506	42,852	2,038,788	4,000,212	3,504.1	10	4,827,583	4,189,894.8	0.31	1353.78	28.45	47.58	28.54
2002	1,722	1,722	46,363	2,415,380	4,396,073	4,162.1	13	4,898,153	4,262,794.4	0.35	1402.66	26.92	52.10	31.23
2003	3,301	3,301	108,647	4,595,881	9,235,241	7,618.8	16	5,060,480	4,310,514.6	0.65	1392.27	32.91	42.30	21.00
2004	2,348	2,348	69,055	3,253,908	5,671,162	5,567.8	14	5,342,942	4,345,703.9	0.44	1385.82	29.41	47.12	25.14
2005	2,422	2,422	70,035	3,326,125	5,704,980	5,742.1	5	5,248,497	4,546,799.4	0.46	1373.30	28.92	47.49	8.71
2006	4,030	4,030	117,931	4,908,893	7,453,096	7,893.6	15	12,161,193	7,728,989.1	0.33	1218.09	29.26	41.63	19.00
2007	5,700	5,700	174,579	6,810,103	10,164,895	10,880.1	12	14,586,015	10,896,916.7	0.39	1194.75	30.63	39.01	11.03
2008	7,992	7,992	242,628	9,068,912	13,355,142	13,803.2	9	24,271,608	16,136,881.1	0.33	1134.75	30.36	37.38	6.52
2009	9,862	9,862	292,584	10,707,159	15,405,428	15,706.2	24	24,012,151	19,876,056.4	0.41	1085.70	29.67	36.60	15.28
2010	10,253	10,253	290,183	10,534,197	14,920,856	14,553.3	10	23,612,112	19,516,604.2	0.43	1027.43	28.30	36.30	6.87
2011	10,558	10,558	275,401	9,804,064	13,699,868	11,676.0	12	24,891,180	19,696,611.8	0.42	928.59	26.08	35.60	10.28
2012	9,847	9,847	223,878	7,845,913	10,968,418	6,706.0	6	24,672,271	18,961,718.5	0.40	796.78	22.74	35.05	8.95
2013	4,316	4,316	80,047	2,930,361	4,377,227	1,208.5	0	19,027,395	9,235,204.9	0.23	678.95	18.55	36.61	0.00
2014	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>1,095-Day Blackout Period</b>														
2000	330	330	11,541	627,671	1,332,474	936.7	6	3,851,156	1,825,130.7	0.09	1902.03	34.97	54.39	64.06
2001	862	862	32,590	1,594,115	3,153,604	2,357.1	8	4,142,586	3,648,176.4	0.21	1849.32	37.81	48.91	33.94
2002	1,019	1,019	35,853	1,917,114	3,543,023	2,832.0	8	4,312,739	3,721,868.4	0.24	1881.37	35.18	53.47	28.25
2003	1,890	1,890	81,810	3,582,545	6,993,051	5,111.2	11	4,312,578	3,611,202.2	0.44	1895.53	43.29	43.79	21.52
2004	1,443	1,443	54,679	2,625,175	4,621,982	3,752.6	7	4,513,979	3,786,075.3	0.32	1819.25	37.89	48.01	18.65
2005	1,470	1,470	54,889	2,667,619	4,676,759	3,868.5	4	4,547,382	3,975,579.7	0.32	1814.71	37.34	48.60	10.34
2006	2,231	2,231	85,511	3,677,504	5,671,019	4,914.4	7	9,956,318	6,466,013.6	0.22	1648.37	38.33	43.01	14.24
2007	3,221	3,221	127,725	5,135,764	7,741,084	6,618.2	7	11,788,885	9,011,450.4	0.27	1594.46	39.65	40.21	10.58
2008	4,331	4,331	172,041	6,595,939	9,737,215	7,931.9	7	18,835,799	13,007,136.8	0.23	1522.96	39.72	38.34	8.83
2009	5,399	5,399	205,000	7,700,122	11,058,718	8,431.2	14	18,698,484	15,734,307.5	0.29	1426.21	37.97	37.56	16.61
2010	5,706	5,706	201,290	7,451,974	10,548,278	6,904.3	2	19,810,745	15,914,832.2	0.29	1305.99	35.28	37.02	2.90
2011	5,533	5,533	175,583	6,398,909	8,970,177	3,999.0	1	19,760,854	15,428,817.7	0.28	1156.50	31.73	36.44	2.50
2012	2,411	2,411	63,363	2,468,376	3,512,374	705.7	0	17,148,343	7,693,105.5	0.14	1023.80	26.28	38.96	0.00
2013	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2014	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---



**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Methylphenidate Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>30-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
2000	6	1,169	51.3
2001	13	2,803	46.4
2002	16	2,603	61.5
2003	18	3,189	56.4
2004	25	3,264	76.6
2005	20	3,252	61.5
2006	25	6,106	40.9
2007	38	9,263	41.0
2008	59	14,459	40.8
2009	58	18,337	31.6
2010	56	17,422	32.1
2011	58	16,997	34.1
2012	44	15,656	28.1
2013	53	14,707	36.0
2014	32	13,479	23.7
2015	13	4,647	28.0
2016	0	0	---
<b>Days 91-180</b>			
2000	0	509	0.0
2001	5	1,215	41.2
2002	1	1,214	8.2
2003	7	1,820	38.5
2004	9	1,724	52.2
2005	6	1,604	37.4
2006	6	2,901	20.7
2007	6	4,314	13.9
2008	10	6,433	15.5
2009	21	7,991	26.3
2010	14	7,943	17.6
2011	14	7,822	17.9
2012	13	7,445	17.5
2013	15	6,888	21.8
2014	10	5,819	17.2
2015	2	1,029	19.4
2016	0	0	---
<b>Days 181-270</b>			
2000	1	276	36.2
2001	3	686	43.7
2002	4	758	52.8
2003	4	1,224	32.7
2004	3	1,067	28.1
2005	2	998	20.0
2006	8	1,793	44.6
2007	8	2,629	30.4

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Methylphenidate Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
2008	6	3,883	15.5
2009	9	4,757	18.9
2010	7	4,705	14.9
2011	8	4,800	16.7
2012	5	4,601	10.9
2013	7	4,196	16.7
2014	5	2,819	17.7
2015	1	262	38.2
2016	0	0	---
<b>Days 271-365</b>			
2000	1	186	53.7
2001	4	485	82.6
2002	3	534	56.2
2003	4	952	42.0
2004	2	813	24.6
2005	3	733	40.9
2006	2	1,296	15.4
2007	3	1,877	16.0
2008	2	2,753	7.3
2009	5	3,352	14.9
2010	2	3,443	5.8
2011	6	3,447	17.4
2012	3	3,346	9.0
2013	3	3,033	9.9
2014	1	1,574	6.4
2015	0	39	0.0
2016	0	0	---
<b>Days 366-730</b>			
2000	2	393	50.9
2001	2	1,041	19.2
2002	5	1,205	41.5
2003	6	2,281	26.3
2004	8	1,749	45.7
2005	5	1,718	29.1
2006	6	2,815	21.3
2007	9	4,156	21.7
2008	6	5,771	10.4
2009	11	7,138	15.4
2010	11	7,333	15.0
2011	5	7,417	6.7
2012	8	7,089	11.3
2013	13	5,381	24.2
2014	2	1,052	19.0
2015	0	0	---
2016	0	0	---

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Methylphenidate Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>Days 731-1,095</b>			
2000	0	206	0.0
2001	2	531	37.7
2002	2	628	31.8
2003	3	1,236	24.3
2004	7	920	76.1
2005	1	918	10.9
2006	6	1,422	42.2
2007	3	2,074	14.5
2008	2	2,811	7.1
2009	3	3,429	8.7
2010	5	3,581	14.0
2011	7	3,605	19.4
2012	4	2,751	14.5
2013	0	545	0.0
2014	0	0	---
2015	0	0	---
2016	0	0	---
<b>90-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
2000	6	1,310	45.8
2001	19	3,269	58.1
2002	19	3,077	61.7
2003	25	4,264	58.6
2004	30	3,840	78.1
2005	23	3,801	60.5
2006	30	7,130	42.1
2007	50	10,899	45.9
2008	70	17,015	41.1
2009	73	21,509	33.9
2010	72	20,452	35.2
2011	66	19,906	33.2
2012	49	18,442	26.6
2013	59	17,227	34.2
2014	40	15,576	25.7
2015	16	5,138	31.1
2016	0	0	---
<b>Days 91-180</b>			
2000	2	964	20.7
2001	8	2,260	35.4
2002	5	2,000	25.0
2003	7	2,083	33.6
2004	14	2,504	55.9
2005	9	2,550	35.3
2006	9	4,688	19.2

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Methylphenidate Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
2007	16	7,099	22.5
2008	22	10,774	20.4
2009	28	13,628	20.5
2010	33	12,736	25.9
2011	32	12,482	25.6
2012	24	11,582	20.7
2013	28	11,061	25.3
2014	17	9,706	17.5
2015	4	1,737	23.0
2016	0	0	---
<b>Days 181-270</b>			
2000	2	588	34.0
2001	8	1,393	57.4
2002	2	1,337	15.0
2003	5	2,038	24.5
2004	4	1,757	22.8
2005	5	1,685	29.7
2006	8	3,223	24.8
2007	15	4,777	31.4
2008	11	7,177	15.3
2009	19	8,940	21.3
2010	16	8,638	18.5
2011	17	8,623	19.7
2012	12	8,179	14.7
2013	13	7,705	16.9
2014	9	5,343	16.8
2015	0	508	0.0
2016	0	0	---
<b>Days 271-365</b>			
2000	2	424	47.2
2001	5	1,060	47.2
2002	4	1,068	37.5
2003	5	1,776	28.2
2004	3	1,445	20.8
2005	3	1,386	21.6
2006	2	2,518	7.9
2007	5	3,732	13.4
2008	4	5,512	7.3
2009	9	6,850	13.1
2010	7	6,783	10.3
2011	11	6,789	16.2
2012	7	6,581	10.6
2013	7	6,073	11.5
2014	2	3,186	6.3
2015	0	75	0.0

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Methylphenidate Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
2016	0	0	---
<b>Days 366-730</b>			
2000	4	882	45.4
2001	7	2,321	30.2
2002	8	2,509	31.9
2003	6	4,473	13.4
2004	10	3,454	28.9
2005	6	3,357	17.9
2006	9	5,754	15.6
2007	17	8,430	20.2
2008	14	11,966	11.7
2009	26	14,996	17.3
2010	22	15,316	14.4
2011	13	15,374	8.5
2012	13	14,871	8.7
2013	21	11,561	18.2
2014	4	2,223	18.0
2015	0	0	---
2016	0	0	---
<b>Days 731-1,095</b>			
2000	0	452	0.0
2001	2	1,147	17.4
2002	5	1,330	37.6
2003	5	2,508	19.9
2004	7	1,815	38.6
2005	1	1,874	5.3
2006	8	2,979	26.9
2007	5	4,262	11.7
2008	2	5,871	3.4
2009	10	7,275	13.7
2010	8	7,649	10.5
2011	11	7,677	14.3
2012	6	6,000	10.0
2013	0	1,208	0.0
2014	0	0	---
2015	0	0	---
2016	0	0	---

**Appendix A: List of Generic and Brand Names Used To Define the Exposures and Exposure Incidence in this Request**

Generic Name	Brand Name
<b>Amphetamines</b>	
DEXTROAMPHETAMINE SULFATE	Dexedrine Spansule
DEXTROAMPHETAMINE SULFATE	dextroamphetamine
DEXTROAMPHETAMINE SULFATE	Dexedrine
DEXTROAMPHETAMINE SULFATE	DextroStat
DEXTROAMPHETAMINE SULFATE	Zenzedi
DEXTROAMPHETAMINE SULFATE	ProCentra
DEXTROAMPHETAMINE SULFATE	Liquadd
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	Amphetamine Salt Combo
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	Adderall XR
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	Adderall
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	dextroamphetamine-amphetamine
LISDEXAMFETAMINE DIMESYLATE	Vyvanse
METHAMPHETAMINE HCL	Desoxyn
AMPHETAMINE SULFATE	Evekeo
METHAMPHETAMINE HCL	methamphetamine
<b>Methylphenidates</b>	
DEXMETHYLPHENIDATE HCL	dexmethylphenidate
DEXMETHYLPHENIDATE HCL	Focalin XR
DEXMETHYLPHENIDATE HCL	Focalin
METHYLPHENIDATE HCL	Methylin
METHYLPHENIDATE HCL	Ritalin LA
METHYLPHENIDATE HCL	methylphenidate
METHYLPHENIDATE HCL	Concerta
METHYLPHENIDATE HCL	Metadate CD
METHYLPHENIDATE HCL	Aptensio XR
METHYLPHENIDATE HCL	Ritalin
METHYLPHENIDATE HCL	Ritalin SR
METHYLPHENIDATE HCL	Metadate ER
METHYLPHENIDATE HCL	Quillivant XR
METHYLPHENIDATE HCL	Methylin ER
<b>Strattera</b>	
ATOMOXETINE HCL	Strattera

**Appendix B: Codes Used to Define Heart Failure in this Request**


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<b>Code</b>	<b>Code Type</b>	<b>Description</b>
398.91	ICD-9-CM Diagnosis	Rheumatic heart failure (congestive)
402.01	ICD-9-CM Diagnosis	Malignant hypertensive heart disease with heart failure
402.11	ICD-9-CM Diagnosis	Benign hypertensive heart disease with heart failure
402.91	ICD-9-CM Diagnosis	Unspecified hypertensive heart disease with heart failure
404.01	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.03	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic kidney disease stage V or end stage renal disease
404.11	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, benign, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.13	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, benign, with heart failure and chronic kidney disease stage V or end stage renal disease
404.91	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, unspecified, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.93	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, unspecified, with heart failure and chronic kidney disease stage V or end stage renal disease
422.90	ICD-9-CM Diagnosis	Acute myocarditis, unspecified
425.4	ICD-9-CM Diagnosis	Other primary cardiomyopathies
425.9	ICD-9-CM Diagnosis	Secondary cardiomyopathy, unspecified
428	ICD-9-CM Diagnosis	Heart Failure
428.0	ICD-9-CM Diagnosis	Congestive heart failure, unspecified
428.1	ICD-9-CM Diagnosis	Left heart failure
428.2	ICD-9-CM Diagnosis	Systolic heart failure
428.20	ICD-9-CM Diagnosis	Systolic heart failure, unspecified
428.21	ICD-9-CM Diagnosis	Acute systolic heart failure
428.22	ICD-9-CM Diagnosis	Chronic systolic heart failure
428.23	ICD-9-CM Diagnosis	Acute on chronic systolic heart failure
428.3	ICD-9-CM Diagnosis	Diastolic heart failure
428.30	ICD-9-CM Diagnosis	Diastolic heart failure, unspecified
428.31	ICD-9-CM Diagnosis	Acute diastolic heart failure
428.32	ICD-9-CM Diagnosis	Chronic diastolic heart failure
428.33	ICD-9-CM Diagnosis	Acute on chronic diastolic heart failure
428.4	ICD-9-CM Diagnosis	Combined systolic and diastolic heart failure
428.40	ICD-9-CM Diagnosis	Combined systolic and diastolic heart failure, unspecified
428.41	ICD-9-CM Diagnosis	Acute combined systolic and diastolic heart failure
428.42	ICD-9-CM Diagnosis	Chronic combined systolic and diastolic heart failure
428.43	ICD-9-CM Diagnosis	Acute on chronic combined systolic and diastolic heart failure
428.9	ICD-9-CM Diagnosis	Heart failure, unspecified

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Sentinel's Cohort Identification and Descriptive Analysis (CIDA) tool was used to investigate heart failure following treatment with select attention deficit and hyperactivity disorder (ADHD) medications. In total, 49 scenarios were examined with four different exposures, seven different blackout periods, and two different episode gaps/exposure extension periods. The four exposures are all amphetamines, all methylphenidates, strattera, and all stimulants (which include all amphetamines, all methylphenidates, and strattera). **The outcome is heart failure, defined as any heart failure ICD-9-CM diagnosis code (398.91, 402.x1, 402.x3, 404.x1, 404.x3, 422.90, 425.4, 425.9, 428.xx) in any care setting with a primary discharge diagnosis (PDX) value of P (principal) for those diagnoses in the inpatient care setting.** See below for a description of each of these scenarios. The query period was from January 1, 2000 to March 3, 2016 and the enrollment gap was set at 45 days. Age groups were split as follows: 0-21, 22-44, 45-64, 65+.

Enrollment Gap	45 Days
Age Groups	0-21, 22-44, 45-64, 65+
Query Period	January 1, 2000 - Current
Coverage Requirement	Medical and Drug
Enrollment Requirement	183 Days

Scenario	Drug/Exposure										Event/Outcome					
	Incident exposure	Incident w/ respect to:	Episode Truncation at Incident Exposure	Episode Truncation at Death	Washout (days)	Cohort Definition	Episode Gap	Exposure Extension Period	Min Episode Duration	Min Days Supplied	Event/ Outcome	Care Setting/PDX	Incident with Respect to	Incident w/ respect to Care Setting/PDX	Washout (days)	Blackout Period
8	All Methylphenidates	All Stimulants	Yes	No	183	01	90	90	0	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	0
9	All Methylphenidates	All Stimulants	Yes	No	183	01	90	90	90	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	90
10	All Methylphenidates	All Stimulants	Yes	No	183	01	90	90	180	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	180
11	All Methylphenidates	All Stimulants	Yes	No	183	01	90	90	270	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	270
12	All Methylphenidates	All Stimulants	Yes	No	183	01	90	90	365	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	365
13	All Methylphenidates	All Stimulants	Yes	No	183	01	90	90	730	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	730
14	All Methylphenidates	All Stimulants	Yes	No	183	01	90	90	1095	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	1095
29	All Methylphenidates	All Stimulants	Yes	No	183	01	30	30	0	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	0
30	All Methylphenidates	All Stimulants	Yes	No	183	01	30	30	90	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	90
31	All Methylphenidates	All Stimulants	Yes	No	183	01	30	30	180	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	180
32	All Methylphenidates	All Stimulants	Yes	No	183	01	30	30	270	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	270
33	All Methylphenidates	All Stimulants	Yes	No	183	01	30	30	365	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	365
34	All Methylphenidates	All Stimulants	Yes	No	183	01	30	30	730	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	730
35	All Methylphenidates	All Stimulants	Yes	No	183	01	30	30	1095	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	1095

ICD-9, ICD-10, HCPCS, and CPT codes are provided by Optum360. NDC codes are checked against First Data Bank's "National Drug Data File (NDDF\*) Plus."

Cohort Definition of 01 will only consider the first incident episode for each user during the query period that satisfies the washout period.

Note: Episodes are automatically truncated at outcome.

\*Codes in the algorithm include: 398.91, 402.x1, 402.x3, 404.x1, 404.x3, 422.90, 425.4, 425.9, 428.xx. Algorithm will look for at least one of five things: (1) at least one IP code with PDX flag = P, OR (2) at least three IP codes with PDX flag = S, OR (3) at least two AV\*/OA\* codes with any PDX flag value, OR (4) at least three ED\* codes with any PDX flag value, OR (5) at least two IP codes with PDX flag = S and at least one AV\*/OA\* code with any PDX flag value. The temporal relationship between codes will be 365 days. For example, for at least two AV\*/OA\* codes with any PDX flag value, we would find one code and then look for a second within 365 days of the first. For at least three IP codes with PDX flag = S, we would find one code, and then look for a second within 365 days of the first, and then look for a third within 365 days of the first. The date of the first of the one, two, or three codes will be used as the event date. This is important because episodes are truncated on occurrence of the event.



### Disclaimer

The following report(s) provides findings from an FDA-initiated query using Sentinel. While Sentinel queries may be undertaken to assess potential medical product safety risks, they may also be initiated for various other reasons. Some examples include determining a rate or count of an identified health outcome of interest, examining medical product use, exploring the feasibility of future, more detailed analyses within Sentinel, and seeking to better understand Sentinel capabilities.

Data obtained through Sentinel are intended to complement other types of evidence such as preclinical studies, clinical trials, postmarket studies, and adverse event reports, all of which are used by FDA to inform regulatory decisions regarding medical product safety. The information contained in this report is provided as part of FDA's commitment to place knowledge acquired from Sentinel in the public domain as soon as possible. Any public health actions taken by FDA regarding products involved in Sentinel queries will continue to be communicated through existing channels.

FDA wants to emphasize that the fact that FDA has initiated a query involving a medical product and is reporting findings related to that query does not mean that FDA is suggesting health care practitioners should change their prescribing practices for the medical product or that patients taking the medical product should stop using it. Patients who have questions about the use of an identified medical product should contact their health care practitioners.

The following report contains a description of the request, request specifications, and results from the modular program run(s).

If you are using a web page screen reader and are unable to access this document, please contact the Sentinel Operations Center for assistance at [info@sentinelssystem.org](mailto:info@sentinelssystem.org).

## Overview for Request cder\_mpl1r\_wp014\_nsdv\_v01, Report 7 of 8

**Request ID:** cder\_mpl1r\_wp014\_nsdv\_v01. This is report 7 of 8.

**Request Description:** FDA has requested execution of the Cohort Identification and Descriptive Analysis (CIDA) tool, version 2.1.1, to investigate heart failure diagnoses following new use of attention deficit hyperactivity disorder (ADHD) medications. This report presents results for all ADHD medications. Results for all methylphenidates, strattera, and amphetamines are presented in separate reports.

**Data Source:** Data from January 1, 2000 to March 3, 2016 from 15 health plans contributing to the Sentinel Distributed Database (SDD) are included in this report.

**Study Design:** This request was designed to identify exposures and follow-up time. The exposure of interest and the occurrence of the health outcome of interest during exposed time were identified. The number of exposure episodes, number of individuals, number of events, and days at-risk in the SDD were calculated overall and were stratified by age group, sex, and year.

**Exposure of Interest:** The exposures of interest were ADHD medications, which were defined using National Drug Codes (NDCs). Please refer to Appendix A for a list of generic and brand names of ADHD medications included in this request.

**Cohort Eligibility Criteria:** Patients were required to be continuously enrolled in plans with both medical and drug coverage for at least 6 months (183 days) before their dispensing date, during which gaps in coverage of up to 45 days were allowed. Members were excluded if they had any ADHD medication or the outcome of interest in the 6 months (183 days) prior to exposure initiation. The following age groups were included in the cohort: 0-21, 22-44, 45-64, 65+ years.

**Follow-Up Time:** Follow-up time for the outcome was determined by the length of the exposure episodes. Exposure episode lengths were defined using outpatient pharmacy dispensing days supplied to create a sequence of continuous exposure. Exposure episodes were considered continuous if gaps in days supply were less than 90 days. The end date of each exposure episode was extended by 90 additional days. Follow-up began on the day on which the first exposure of interest was dispensed and continued until the first occurrence of any of the following: 1) the outcome of interest; 2) any codes defining incidence criteria; 3) disenrollment; 4) the study end date (March, 2016); 5) the end date of the data provided by each Data Partner; or 6) the end of the exposure episode. Only the first valid incident exposure episode that occurred during the study period was included per patient.

This report examines different blackout periods which is a number of days at the beginning of the ADHD medication episode where if an outcome occurs, it is not attributed to the exposure and the person is omitted from the analysis. The blackout periods examined were 90 days, 180 days, 270 days, 365 days, 730 days, and 1,095 days. Episodes that were at least as long as the blackout period were required.

**Outcome of Interest:** Heart failure was defined using the ICD-9-CM diagnosis codes listed in Appendix B. The event needed to meet one of the following criteria: (1) at least one code in the inpatient setting with primary diagnosis flag = Primary, OR (2) at least three codes in the inpatient setting with primary diagnosis flag = Secondary, OR (3) at least two codes in the outpatient setting with any primary diagnosis flag value, OR (4) at least three codes in the emergency department setting with any primary diagnosis flag value, OR (5) at least two codes in the inpatient setting with primary diagnosis flag = Secondary and at least one code in the outpatient with any primary diagnosis flag value. The temporal relationship between codes was 365 days. This event had to be incident (no heart failure events in the 183 days prior to exposure initiation).

**Please refer to Appendix C for detailed specifications.**

**Limitations:** Algorithms to define exposures and outcomes are imperfect and, therefore, may be misclassified.

**Notes:** Please contact the Sentinel Operations Center Query Fulfillment Team (production@mini-sentinel.org) for questions and to provide comments/suggestions for future enhancements to this document.

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**Glossary of Terms for Analyses Using  
Cohort Identification and Descriptive Analysis (CIDA) Tool\***

**Amount Supplied** - number of units (pills, tablets, vials) dispensed. Net amount per NDC per dispensing. This is equivalent to the "RxAmt" value in the MSCDM.

**Blackout Period** - number of days at the beginning of a treatment episode that events are to be ignored. If an event occurs during the blackout period, the episode is excluded.

**Care Setting** - type of medical encounter or facility where the exposure, event, or condition code was recorded. Possible care settings include: Inpatient Hospital Stay (IP), Non-Acute Institutional Stay (IS), Emergency Department (ED), Ambulatory Visit (AV), and Other Ambulatory Visit (OA). For laboratory results, possible care settings include: Emergency department (E), Home (H), Inpatient (I), Outpatient (O), or Unknown or Missing (U). Along with the Principal Diagnosis Indicator, forms the Care Setting/PDX parameter.

**Cohort Definition (drug/exposure)** - indicates how the cohort will be defined: (1) 01: Cohort includes only the first valid incident treatment episode during the query period; (2) 02: Cohort includes all valid incident treatment episodes during the query period; (3) 03: Cohort includes all valid incident treatment episodes during the query period until an event

**Days Supplied** - number of days supplied for all dispensings in qualifying treatment episodes.

**Eligible Members** - number of members eligible for an incident treatment episode (defined by the drug/exposure and event washout periods) with drug and medical coverage during the query period.

**Enrollment Gap** - number of days allowed between two consecutive enrollment periods without breaking a "continuously enrolled" sequence.

**Episodes** - treatment episodes; length of episode is determined by days supplied in one dispensing or consecutive dispensings bridged by the episode gap.

**Episode Gap** - number of days allowed between two (or more) consecutive exposures (dispensings/procedures) to be considered the same treatment episode.

**Event Deduplication** - specifies how events are counted by the MP algorithm: (0) 0: Counts all occurrences of an HOI during an exposure episode; (1) 1: de-duplicates occurrences of the same HOI code and code type on the same day; (2) 2: de-duplicates occurrences of the same HOI group on the same day (e.g., de-duplicates at the group level).

**Exposure Episode Length** - number of days after exposure initiation that is considered "exposed time."

**Exposure Extension Period** - number of days post treatment period in which the outcomes/events are counted for a treatment episode.

**Lookback Period (pre-existing condition)** - number of days wherein a member is required to have evidence of pre-existing condition (diagnosis/procedure/drug dispensing).

**Member-Years** - sum of all days of enrollment with medical and drug coverage\*\* in the query period preceded by an exposure washout period all divided by 365.25.

**Minimum Days Supplied** - specifies a minimum number of days in length of the days supplied for the episode to be considered.

**Minimum Episode Duration** - specifies a minimum number of days in length of the episode for it to be considered.

**Principal Diagnosis (PDX)** - diagnosis or condition established to be chiefly responsible for admission of the patient to the hospital. 'P' = principal diagnosis, 'S' = secondary diagnosis, 'X' = unspecified diagnosis, '.' = blank. Along with the Care Setting values, forms the Caresetting/PDX parameter.

**Query Period** - period in which the modular program looks for exposures and outcomes of interest.

**Treatment Episode Truncation Indicator** - indicates whether observation of the incident query code during follow-up requires truncation of valid treatment episodes. A value of Y indicates that the treatment episodes should be truncated at the first occurrence of an incident query code. A value of N indicates that the treatment episodes should not be truncated at the occurrence of the incident query code.

**Users** - number of members with exposure during the query period. Member must have no evidence of exposure(s) of interest (defined by incidence criteria) in the prior washout period. A user may only be counted once in a query period.

**Washout Period (drug/exposure)\*\*** - number of days a user is required to have no evidence of prior exposure (drug dispensing/procedure) and continuous drug and medical coverage prior to an incident treatment episode.

**Washout Period (event/outcome)\*\*** - number of days a user is required to have no evidence of a prior event (procedure/diagnosis) and continuous drug and medical coverage prior to an incident treatment episode.

**Years at Risk** - number of days supplied plus any episode gaps and exposure extension periods all divided by 365.25.

\*all terms may not be used in this report

\*\*incident treatment episodes must be incident to both the exposure and the event

**Table 1a: Summary of Incident All Attention Deficit and Hyperactivity Disorder (ADHD) Medication Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, and Blackout Period**

New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>30-Day Episode Gap/Extension Period</b>													
<b>0-Day Blackout Period</b>													
2,014,623	2,014,623	11,947,187	400,292,053	602,237,864	1,264,221.4	2,006	110,296,405	304,867,413.2	18.27	198.69	5.93	33.51	15.87
<b>90-Day Blackout Period</b>													
1,201,741	1,201,741	11,346,063	387,027,951	573,096,142	880,980.7	1,141	100,830,201	276,646,571.6	11.92	322.06	9.44	34.11	12.95
<b>180-Day Blackout Period</b>													
689,919	689,919	10,019,929	346,515,131	515,028,590	676,759.9	854	93,687,770	250,917,726.7	7.36	502.25	14.52	34.58	12.62
<b>270-Day Blackout Period</b>													
470,378	470,378	8,862,641	309,687,775	462,643,957	542,246.9	676	80,172,511	229,023,392.2	5.87	658.38	18.84	34.94	12.47
<b>365-Day Blackout Period</b>													
340,357	340,357	7,822,314	276,087,226	414,566,097	441,170.1	549	72,199,899	208,104,657.7	4.71	811.17	22.98	35.29	12.44
<b>730-Day Blackout Period</b>													
142,361	142,361	5,071,989	184,959,909	280,783,531	222,478.8	282	48,917,643	145,822,892.2	2.91	1299.23	35.63	36.47	12.68
<b>1,095-Day Blackout Period</b>													
71,542	71,542	3,312,513	124,741,664	191,046,536	120,958.1	153	34,449,593	103,823,208.1	2.08	1743.61	46.30	37.66	12.65
<b>90-Day Episode Gap/Extension Period</b>													
<b>0-Day Blackout Period</b>													
2,014,623	2,014,623	16,529,398	556,684,470	836,943,990	2,076,018.3	3,032	110,296,405	304,867,413.5	18.27	276.32	8.20	33.68	14.60
<b>90-Day Blackout Period</b>													
1,803,644	1,803,644	16,209,078	549,400,993	826,543,499	1,607,647.3	1,976	100,830,192	275,834,553.3	17.89	304.61	8.99	33.89	12.29
<b>180-Day Blackout Period</b>													
1,175,669	1,175,669	15,688,490	537,111,431	800,350,938	1,317,064.9	1,495	93,687,757	250,483,380.7	12.55	456.86	13.34	34.24	11.35
<b>270-Day Blackout Period</b>													
870,928	870,928	14,693,458	507,159,970	757,420,078	1,092,883.6	1,210	80,172,504	228,757,468.3	10.86	582.32	16.87	34.52	11.07
<b>365-Day Blackout Period</b>													
660,927	660,927	13,504,384	469,710,239	703,379,731	907,637.6	1,009	72,199,893	207,940,005.5	9.15	710.68	20.43	34.78	11.12
<b>730-Day Blackout Period</b>													
296,974	296,974	9,488,981	338,643,319	512,310,715	473,357.8	510	48,917,642	145,785,017.5	6.07	1140.31	31.95	35.69	10.77
<b>1,095-Day Blackout Period</b>													
152,951	152,951	6,460,571	236,657,623	361,405,294	259,701.4	284	34,449,593	103,812,622.0	4.44	1547.28	42.24	36.63	10.94

**Table 1b: Rate of Heart Failure Outcomes at Different Stages of All Attention Deficit and Hyperactivity Disorder (ADHD) Medication Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, and Blackout Period**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>30-Day Episode Gap/Extension Period</b>			
Days 0-90	865	383,241	22.6
Days 91-180	287	204,221	14.1
Days 181-270	178	134,513	13.2
Days 271-365	127	101,077	12.6
Days 366-730	267	218,691	12.2
Days 731-1,095	129	101,521	12.7
<b>90-Day Episode Gap/Extension Period</b>			
Days 0-90	1,056	468,371	22.5
Days 91-180	481	290,582	16.6
Days 181-270	285	224,181	12.7
Days 271-365	201	185,246	10.9
Days 366-730	499	434,280	11.5
Days 731-1,095	226	213,656	10.6

**Table 2a: Summary of Incident All Attention Deficit and Hyperactivity Disorder (ADHD) Medication Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>30-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
00-21 Years	1,089,056	1,089,056	6,534,654	222,724,225	291,826,680	700,021.9	212	33,425,930	83,545,280.2	32.58	204.51	6.00	34.08	3.03
22-44 Years	628,795	628,795	3,697,580	119,182,859	198,389,814	378,703.1	352	45,699,071	95,718,085.8	13.76	189.54	5.88	32.23	9.29
45-64 Years	265,287	265,287	1,589,671	54,083,159	103,991,158	171,210.1	821	32,642,434	90,514,987.1	8.13	203.87	5.99	34.02	47.95
65+ Years	31,485	31,485	125,282	4,301,810	8,030,212	14,286.3	621	10,950,784	35,089,060.2	2.88	136.63	3.98	34.34	434.68
<b>90-Day Blackout Period</b>														
00-21 Years	675,867	675,867	6,267,535	217,275,300	284,154,592	492,109.7	171	30,666,158	76,247,800.6	22.04	321.48	9.27	34.67	3.47
22-44 Years	364,005	364,005	3,471,406	113,824,631	188,908,590	258,509.6	227	41,102,192	85,386,308.8	8.86	312.70	9.54	32.79	8.78
45-64 Years	148,024	148,024	1,499,042	52,052,023	92,732,992	121,730.5	467	30,249,879	82,763,584.0	4.89	351.65	10.13	34.72	38.36
65+ Years	13,845	13,845	108,080	3,875,997	7,299,967	8,631.0	276	9,854,040	32,248,878.2	1.41	279.96	7.81	35.86	319.78
<b>180-Day Blackout Period</b>														
00-21 Years	375,475	375,475	5,508,945	193,884,450	253,363,093	379,388.4	140	28,479,381	69,468,729.7	13.18	516.37	14.67	35.19	3.69
22-44 Years	216,783	216,783	3,067,292	101,735,194	170,159,051	194,961.9	171	37,549,690	76,152,081.4	5.77	469.30	14.15	33.17	8.77
45-64 Years	90,205	90,205	1,352,076	47,539,823	85,120,851	96,032.9	365	28,281,208	75,595,535.4	3.19	527.02	14.99	35.16	38.01
65+ Years	7,456	7,456	91,616	3,355,664	6,385,595	6,376.8	178	9,303,247	29,701,380.3	0.80	450.06	12.29	36.63	279.14
<b>270-Day Blackout Period</b>														
00-21 Years	250,461	250,461	4,869,777	173,247,024	226,855,307	307,040.9	105	24,385,545	63,623,096.3	10.27	691.71	19.44	35.58	3.42
22-44 Years	150,351	150,351	2,697,164	90,285,702	152,207,344	152,175.9	140	31,636,552	68,502,110.1	4.75	600.50	17.94	33.47	9.20
45-64 Years	64,609	64,609	1,216,872	43,224,098	77,945,349	78,064.0	293	24,635,676	69,426,978.5	2.62	669.01	18.83	35.52	37.53
65+ Years	4,957	4,957	78,828	2,930,951	5,635,956	4,966.1	138	8,308,100	27,471,207.3	0.60	591.28	15.90	37.18	277.88
<b>365-Day Blackout Period</b>														
00-21 Years	179,714	179,714	4,320,537	155,253,091	203,597,810	253,621.0	91	21,974,466	58,003,170.8	8.18	863.89	24.04	35.93	3.59
22-44 Years	108,604	108,604	2,346,246	79,250,897	134,922,763	119,748.1	113	27,925,315	61,343,584.3	3.89	729.72	21.60	33.78	9.44
45-64 Years	48,503	48,503	1,087,572	39,022,413	71,052,939	63,883.6	241	22,360,256	63,485,022.0	2.17	804.54	22.42	35.88	37.72
65+ Years	3,536	3,536	67,959	2,560,825	4,992,586	3,917.3	104	7,789,029	25,272,880.7	0.45	724.22	19.22	37.68	265.49
<b>730-Day Blackout Period</b>														
00-21 Years	79,336	79,336	2,944,866	109,057,153	143,635,368	135,410.0	50	14,944,097	40,943,485.8	5.31	1374.62	37.12	37.03	3.69
22-44 Years	40,931	40,931	1,381,758	48,031,476	84,727,920	52,916.9	62	17,783,487	41,009,793.5	2.30	1173.47	33.76	34.76	11.72
45-64 Years	20,763	20,763	706,327	26,305,476	49,278,735	32,375.3	129	15,664,153	45,363,905.9	1.33	1266.94	34.02	37.24	39.85
65+ Years	1,331	1,331	39,038	1,565,804	3,141,507	1,776.7	41	5,678,030	18,505,707.0	0.23	1176.41	29.33	40.11	230.77
<b>1,095-Day Blackout Period</b>														
00-21 Years	42,424	42,424	2,027,428	77,354,867	102,853,674	77,121.6	32	10,532,832	29,268,613.2	4.03	1823.38	47.79	38.15	4.15
22-44 Years	18,182	18,182	808,219	28,875,817	52,054,774	25,296.0	35	11,889,538	28,237,527.7	1.53	1588.15	44.45	35.73	13.84
45-64 Years	10,400	10,400	455,921	17,604,440	34,241,087	17,606.5	69	11,300,132	32,725,429.5	0.92	1692.73	43.84	38.61	39.19
65+ Years	536	536	20,945	906,540	1,897,001	933.9	17	4,240,704	13,591,637.6	0.13	1691.31	39.08	43.28	182.03
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														

**Table 2a: Summary of Incident All Attention Deficit and Hyperactivity Disorder (ADHD) Medication Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
00-21 Years	1,089,056	1,089,056	9,473,684	323,752,161	425,863,209	1,206,233.4	332	33,425,930	83,545,280.2	32.58	297.28	8.70	34.17	2.75
22-44 Years	628,795	628,795	4,766,474	154,365,471	260,162,423	575,662.6	496	45,699,071	95,718,086.1	13.76	245.49	7.58	32.39	8.62
45-64 Years	265,287	265,287	2,124,723	72,831,403	139,936,563	270,852.7	1,224	32,642,434	90,514,987.1	8.13	274.54	8.01	34.28	45.19
65+ Years	31,485	31,485	164,517	5,735,435	10,981,796	23,269.6	980	10,950,784	35,089,060.2	2.88	182.16	5.23	34.86	421.15
<b>90-Day Blackout Period</b>														
00-21 Years	991,411	991,411	9,325,546	320,413,121	421,546,666	950,911.4	275	30,666,151	75,856,193.4	32.33	323.19	9.41	34.36	2.89
22-44 Years	547,711	547,711	4,643,827	151,588,153	255,985,691	431,457.2	361	41,054,972	85,148,426.5	13.34	276.77	8.48	32.64	8.37
45-64 Years	237,548	237,548	2,082,505	71,853,680	138,363,375	209,197.9	795	30,235,708	82,611,496.2	7.86	302.48	8.77	34.50	38.00
65+ Years	26,974	26,974	157,200	5,546,039	10,647,766	16,080.8	545	9,849,824	32,218,437.1	2.74	205.61	5.83	35.28	338.91
<b>180-Day Blackout Period</b>														
00-21 Years	675,079	675,079	9,140,400	316,807,980	416,969,441	791,158.0	241	28,479,371	69,214,151.5	23.70	469.29	13.54	34.66	3.05
22-44 Years	342,893	342,893	4,401,748	145,159,786	245,623,998	340,993.3	282	37,517,063	76,041,969.0	9.14	423.34	12.84	32.98	8.27
45-64 Years	144,767	144,767	2,004,266	69,982,174	127,732,913	172,624.1	620	28,274,180	75,536,556.7	5.12	483.41	13.84	34.92	35.92
65+ Years	12,930	12,930	142,076	5,161,491	10,024,585	12,289.6	352	9,301,160	29,690,703.5	1.39	399.19	10.99	36.33	286.42
<b>270-Day Blackout Period</b>														
00-21 Years	504,298	504,298	8,626,495	301,198,434	396,510,309	662,865.9	196	24,385,538	63,458,273.0	20.68	597.26	17.11	34.92	2.96
22-44 Years	249,536	249,536	4,055,346	134,840,334	229,744,782	275,076.9	242	31,615,660	68,441,180.3	7.89	540.36	16.25	33.25	8.80
45-64 Years	108,221	108,221	1,882,862	66,370,848	121,824,179	144,969.8	507	24,631,122	69,392,724.9	4.39	613.29	17.40	35.25	34.97
65+ Years	8,873	8,873	128,755	4,750,354	9,340,808	9,971.0	265	8,306,738	27,465,290.0	1.07	535.37	14.51	36.89	265.77
<b>365-Day Blackout Period</b>														
00-21 Years	382,991	382,991	7,982,114	280,656,324	369,548,614	555,900.0	177	21,974,460	57,897,955.5	17.43	732.80	20.84	35.16	3.18
22-44 Years	187,064	187,064	3,661,717	122,691,403	210,557,637	221,764.3	196	27,912,374	61,308,473.5	6.70	655.88	19.57	33.51	8.84
45-64 Years	84,259	84,259	1,744,186	62,013,630	114,629,165	121,813.8	427	22,357,175	63,464,380.9	3.77	735.99	20.70	35.55	35.05
65+ Years	6,613	6,613	116,367	4,348,882	8,644,315	8,159.4	209	7,788,129	25,269,195.7	0.85	657.63	17.60	37.37	256.15
<b>730-Day Blackout Period</b>														
00-21 Years	177,767	177,767	5,810,958	209,009,074	276,383,302	300,183.3	95	14,944,096	40,917,333.8	11.90	1175.75	32.69	35.97	3.16
22-44 Years	76,473	76,473	2,356,280	80,960,009	143,172,128	103,613.2	98	17,780,894	41,003,962.2	4.30	1058.67	30.81	34.36	9.46
45-64 Years	39,879	39,879	1,245,322	45,676,207	86,643,737	65,558.9	226	15,663,335	45,359,055.8	2.55	1145.37	31.23	36.68	34.47
65+ Years	2,855	2,855	76,421	2,998,029	6,111,548	4,002.3	91	5,677,699	18,504,665.7	0.50	1050.10	26.77	39.23	227.37
<b>1,095-Day Blackout Period</b>														
00-21 Years	95,168	95,168	4,112,203	151,448,680	201,863,148	169,862.2	66	10,532,832	29,260,826.7	9.04	1591.38	43.21	36.83	3.89
22-44 Years	35,484	35,484	1,454,001	51,166,092	92,625,575	51,081.3	56	11,888,960	28,236,356.2	2.98	1441.95	40.98	35.19	10.96
45-64 Years	21,065	21,065	849,670	32,174,427	62,970,140	36,586.8	118	11,299,883	32,724,072.4	1.86	1527.39	40.34	37.87	32.25
65+ Years	1,234	1,234	44,697	1,868,424	3,946,430	2,171.1	44	4,240,586	13,591,366.7	0.29	1514.12	36.22	41.80	202.66



**Table 2b: Rate of Heart Failure Outcomes at Different Stages of All Attention Deficit and Hyperactivity Disorder (ADHD) Medication Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>30-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
00-21 Years	41	207,912	2.0
22-44 Years	125	120,193	10.4
45-64 Years	354	49,480	71.5
65+ Years	345	5,655	610.0
<b>Days 91-180</b>			
00-21 Years	31	112,721	2.8
22-44 Years	56	63,548	8.8
45-64 Years	102	25,698	39.7
65+ Years	98	2,254	434.7
<b>Days 181-270</b>			
00-21 Years	35	72,347	4.8
22-44 Years	31	42,786	7.2
45-64 Years	72	17,969	40.1
65+ Years	40	1,411	283.6
<b>Days 271-365</b>			
00-21 Years	14	53,420	2.6
22-44 Years	27	32,428	8.3
45-64 Years	52	14,180	36.7
65+ Years	34	1,049	324.2
<b>Days 366-730</b>			
00-21 Years	41	118,211	3.5
22-44 Years	51	66,831	7.6
45-64 Years	112	31,508	35.5
65+ Years	63	2,141	294.3
<b>Days 731-1,095</b>			
00-21 Years	18	58,288	3.1
22-44 Years	27	27,621	9.8
45-64 Years	60	14,769	40.6
65+ Years	24	843	284.8

**Table 2b: Rate of Heart Failure Outcomes at Different Stages of All Attention Deficit and Hyperactivity Disorder (ADHD) Medication Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>90-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
00-21 Years	57	255,322	2.2
22-44 Years	135	144,205	9.4
45-64 Years	429	61,655	69.6
65+ Years	435	7,189	605.1
<b>Days 91-180</b>			
00-21 Years	34	159,753	2.1
22-44 Years	79	90,464	8.7
45-64 Years	175	36,574	47.8
65+ Years	193	3,791	509.1
<b>Days 181-270</b>			
00-21 Years	45	128,292	3.5
22-44 Years	40	65,916	6.1
45-64 Years	113	27,654	40.9
65+ Years	87	2,319	375.2
<b>Days 271-365</b>			
00-21 Years	19	106,966	1.8
22-44 Years	46	53,313	8.6
45-64 Years	80	23,156	34.5
65+ Years	56	1,812	309.1
<b>Days 366-730</b>			
00-21 Years	82	255,717	3.2
22-44 Years	98	118,151	8.3
45-64 Years	201	56,255	35.7
65+ Years	118	4,157	283.9
<b>Days 731-1,095</b>			
00-21 Years	29	130,321	2.2
22-44 Years	42	52,532	8.0
45-64 Years	108	28,972	37.3
65+ Years	47	1,831	256.7

**Table 3a: Summary of Incident All Attention Deficit and Hyperactivity Disorder (ADHD) Medication Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>30-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
Female	898,248	898,248	5,314,846	176,442,745	271,579,313	560,381.3	998	56,075,808	158,112,869.7	16.02	196.43	5.92	33.20	17.81
Male	1,116,295	1,116,295	6,631,943	223,836,790	330,641,595	703,799.7	1,008	54,214,888	146,741,826.1	20.59	200.52	5.94	33.75	14.32
Unknown	80	80	398	12,518	16,957	40.4	0	5,709	12,717.5	14.01	156.48	4.98	31.45	0.00
<b>90-Day Blackout Period</b>														
Female	531,231	531,231	5,027,043	169,889,614	259,725,963	388,818.2	546	51,333,583	143,643,195.6	10.35	319.80	9.46	33.80	14.04
Male	670,467	670,467	6,318,666	217,126,918	313,354,356	492,137.8	595	49,491,790	132,992,037.1	13.55	323.84	9.42	34.36	12.09
Unknown	43	43	354	11,419	15,823	24.7	0	4,828	11,338.9	8.91	265.56	8.23	32.26	0.00
<b>180-Day Blackout Period</b>														
Female	308,771	308,771	4,443,645	152,190,535	233,797,727	297,845.0	404	47,769,519	130,443,170.6	6.46	492.89	14.39	34.25	13.56
Male	381,128	381,128	5,576,020	194,315,669	281,218,249	378,897.5	450	45,914,089	120,464,378.6	8.30	509.84	14.63	34.85	11.88
Unknown	20	20	264	8,927	12,614	17.4	0	4,162	10,177.5	4.81	446.35	13.20	33.81	0.00
<b>270-Day Blackout Period</b>														
Female	212,445	212,445	3,933,019	136,074,880	210,083,719	237,569.0	321	40,935,444	119,221,360.3	5.19	640.52	18.51	34.60	13.51
Male	257,922	257,922	4,929,396	173,605,308	252,549,467	304,663.8	355	39,233,762	109,792,757.9	6.57	673.09	19.11	35.22	11.65
Unknown	11	11	226	7,587	10,771	14.2	0	3,305	9,274.0	3.33	689.73	20.55	33.57	0.00
<b>365-Day Blackout Period</b>														
Female	154,140	154,140	3,463,336	121,007,043	187,950,019	191,835.2	255	36,933,992	108,487,842.0	4.17	785.05	22.47	34.94	13.29
Male	186,210	186,210	4,358,776	155,073,689	226,606,701	249,323.0	294	35,262,986	99,608,390.8	5.28	832.79	23.41	35.58	11.79
Unknown	7	7	202	6,494	9,378	11.9	0	2,921	8,424.9	2.40	927.71	28.86	32.15	0.00
<b>730-Day Blackout Period</b>														
Female	63,070	63,070	2,195,395	79,247,223	125,489,965	93,713.8	122	25,164,067	76,445,313.9	2.51	1256.50	34.81	36.10	13.02
Male	79,288	79,288	2,876,465	105,708,372	155,286,774	128,758.2	160	23,751,676	69,371,623.8	3.34	1333.22	36.28	36.75	12.43
Unknown	3	3	129	4,314	6,792	6.9	0	1,900	5,954.5	1.58	1438.00	43.00	33.44	0.00
<b>1,095-Day Blackout Period</b>														
Female	30,763	30,763	1,395,690	52,001,027	83,460,601	49,363.4	64	17,825,631	54,716,962.0	1.73	1690.38	45.37	37.26	12.97
Male	40,777	40,777	1,916,713	72,737,196	107,580,450	71,590.0	89	16,622,636	49,101,937.8	2.45	1783.78	47.00	37.95	12.43
Unknown	2	2	110	3,441	5,485	4.7	0	1,326	4,308.3	1.51	1720.50	55.00	31.28	0.00
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
Female	898,248	898,248	7,293,613	243,517,560	376,237,040	912,673.0	1,493	56,075,808	158,112,869.7	16.02	271.10	8.12	33.39	16.36
Male	1,116,295	1,116,295	9,235,242	313,149,273	460,684,172	1,163,280.4	1,539	54,214,888	146,741,826.4	20.59	280.53	8.27	33.91	13.23
Unknown	80	80	543	17,637	22,778	65.0	0	5,709	12,717.5	14.01	220.46	6.79	32.48	0.00
<b>90-Day Blackout Period</b>														
Female	801,669	801,669	7,147,364	240,198,930	371,395,832	704,231.0	944	51,333,581	143,286,318.3	15.62	299.62	8.92	33.61	13.40
Male	1,001,906	1,001,906	9,061,191	309,184,911	455,125,480	903,369.8	1,032	49,491,783	132,536,912.6	20.24	308.60	9.04	34.12	11.42

**Table 3a: Summary of Incident All Attention Deficit and Hyperactivity Disorder (ADHD) Medication Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
Unknown	69	69	523	17,152	22,187	46.5	0	4,828	11,322.4	14.29	248.58	7.58	32.80	0.00
<b>180-Day Blackout Period</b>														
Female	518,504	518,504	6,887,357	233,810,608	360,624,272	573,919.7	708	47,769,518	130,269,871.1	10.85	450.93	13.28	33.95	12.34
Male	657,129	657,129	8,800,693	303,285,817	439,706,861	743,110.9	787	45,914,077	120,203,341.7	14.31	461.53	13.39	34.46	10.59
Unknown	36	36	440	15,006	19,805	34.4	0	4,162	10,167.9	8.65	416.83	12.22	34.10	0.00
<b>270-Day Blackout Period</b>														
Female	384,903	384,903	6,439,269	220,415,408	340,850,946	474,487.4	577	40,935,443	119,117,591.6	9.40	572.65	16.73	34.23	12.16
Male	486,003	486,003	8,253,802	286,731,288	416,551,977	618,368.8	633	39,233,756	109,630,611.6	12.39	589.98	16.98	34.74	10.24
Unknown	22	22	387	13,274	17,155	27.4	0	3,305	9,265.0	6.66	603.36	17.59	34.30	0.00
<b>365-Day Blackout Period</b>														
Female	293,160	293,160	5,910,555	203,875,675	316,370,151	392,388.2	472	36,933,992	108,424,946.9	7.94	695.44	20.16	34.49	12.03
Male	367,754	367,754	7,593,498	265,823,058	386,994,496	515,226.4	537	35,262,980	99,506,646.1	10.43	722.83	20.65	35.01	10.42
Unknown	13	13	331	11,506	15,085	22.9	0	2,921	8,412.5	4.45	885.08	25.46	34.76	0.00
<b>730-Day Blackout Period</b>														
Female	130,706	130,706	4,099,583	145,171,214	228,764,087	200,522.6	232	25,164,067	76,431,453.6	5.19	1110.67	31.36	35.41	11.57
Male	166,259	166,259	5,389,139	193,462,889	283,534,474	272,823.3	278	23,751,675	69,347,619.8	7.00	1163.62	32.41	35.90	10.19
Unknown	9	9	259	9,216	12,154	11.8	0	1,900	5,944.1	4.74	1024.00	28.78	35.58	0.00
<b>1,095-Day Blackout Period</b>														
Female	66,068	66,068	2,733,846	99,407,319	158,982,095	107,237.4	128	17,825,631	54,713,327.6	3.71	1504.62	41.38	36.36	11.94
Male	86,880	86,880	3,726,559	137,245,191	202,416,012	152,457.4	156	16,622,636	49,094,986.1	5.23	1579.71	42.89	36.83	10.23
Unknown	3	3	166	5,113	7,187	6.6	0	1,326	4,308.3	2.26	1704.33	55.33	30.80	0.00

**Table 3b: Rate of Heart Failure Outcomes at Different Stages of All Attention Deficit and Hyperactivity Disorder (ADHD) Medication Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>30-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
Female	452	171,563	26.3
Male	413	211,662	19.5
Unknown	0	16	0.0
<b>Days 91-180</b>			
Female	142	90,973	15.6
Male	145	113,240	12.8
Unknown	0	7	0.0
<b>Days 181-270</b>			
Female	83	60,276	13.8
Male	95	74,234	12.8
Unknown	0	3	0.0
<b>Days 271-365</b>			
Female	66	45,734	14.4
Male	61	55,341	11.0
Unknown	0	2	0.0
<b>Days 366-730</b>			
Female	133	98,121	13.6
Male	134	120,565	11.1
Unknown	0	5	0.0
<b>Days 731-1,095</b>			
Female	58	44,350	13.1
Male	71	57,168	12.4
Unknown	0	2	0.0
<b>90-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
Female	549	208,442	26.3
Male	507	259,911	19.5
Unknown	0	18	0.0
<b>Days 91-180</b>			
Female	236	130,311	18.1

**Table 3b: Rate of Heart Failure Outcomes at Different Stages of All Attention Deficit and Hyperactivity Disorder (ADHD) Medication Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
Male	245	160,259	15.3
Unknown	0	12	0.0
<b>Days 181-270</b>			
Female	131	99,432	13.2
Male	154	124,742	12.3
Unknown	0	7	0.0
<b>Days 271-365</b>			
Female	105	82,099	12.8
Male	96	103,142	9.3
Unknown	0	4	0.0
<b>Days 366-730</b>			
Female	240	191,866	12.5
Male	259	242,403	10.7
Unknown	0	11	0.0
<b>Days 731-1,095</b>			
Female	104	93,285	11.1
Male	122	120,366	10.1
Unknown	0	5	0.0

**Table 4a: Summary of Incident All Attention Deficit and Hyperactivity Disorder (ADHD) Medication Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Eligible Members	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>30-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
2000	10,081	10,081	47,025	2,237,197	4,829,051	6,925.8	26	6,530,474	3,002,264.9	1.54	221.92	4.66	47.57	37.54
2001	23,815	23,815	118,039	5,221,711	10,407,714	16,215.1	51	7,125,509	5,963,443.2	3.34	219.26	4.96	44.24	31.45
2002	22,060	22,060	125,836	5,678,149	10,365,984	17,118.3	66	7,269,146	6,057,447.7	3.03	257.40	5.70	45.12	38.56
2003	39,593	39,593	356,680	13,557,629	28,032,266	38,997.9	103	7,256,728	6,027,105.0	5.46	342.42	9.01	38.01	26.41
2004	36,787	36,787	279,650	10,950,944	25,930,979	32,301.8	107	7,683,924	6,267,478.5	4.79	297.69	7.60	39.16	33.13
2005	32,232	32,232	228,086	9,126,162	15,028,995	27,138.9	76	7,913,620	6,547,366.0	4.07	283.14	7.08	40.01	28.00
2006	64,255	64,255	445,677	16,307,429	25,021,056	49,900.5	111	19,374,078	11,577,744.8	3.32	253.79	6.94	36.59	22.24
2007	101,230	101,230	709,388	24,792,319	36,771,848	76,467.1	145	23,562,766	17,132,264.3	4.30	244.91	7.01	34.95	18.96
2008	185,447	185,447	1,204,422	40,491,756	65,233,854	127,049.6	195	44,232,614	27,982,593.8	4.19	218.35	6.49	33.62	15.35
2009	252,479	252,479	1,636,061	54,145,148	77,007,341	170,598.8	233	45,579,872	35,436,831.4	5.54	214.45	6.48	33.09	13.66
2010	248,572	248,572	1,627,612	53,269,690	74,665,055	168,395.5	204	43,393,746	33,892,949.1	5.73	214.30	6.55	32.73	12.11
2011	243,452	243,452	1,558,672	50,549,966	70,195,472	160,740.7	202	41,949,646	33,065,186.9	5.80	207.64	6.40	32.43	12.57
2012	232,192	232,192	1,406,972	45,475,600	62,782,212	145,890.4	166	40,898,260	32,365,170.5	5.68	195.85	6.06	32.32	11.38
2013	220,913	220,913	1,168,200	37,170,777	52,247,563	121,353.9	185	40,733,081	32,023,780.6	5.42	168.26	5.29	31.82	15.24
2014	208,827	208,827	828,885	25,534,975	35,610,050	85,658.8	115	41,655,900	31,890,934.4	5.01	122.28	3.97	30.81	13.43
2015	92,688	92,688	205,982	5,782,601	8,108,424	19,468.3	21	34,324,966	15,634,852.2	2.70	62.39	2.22	28.07	10.79
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>90-Day Blackout Period</b>														
2000	5,620	5,620	41,884	2,076,818	4,481,231	4,779.0	15	6,279,475	2,830,507.5	0.89	369.54	7.45	49.58	31.39
2001	12,809	12,809	106,683	4,890,856	9,720,525	11,319.6	35	6,795,812	5,686,059.2	1.88	381.83	8.33	45.84	30.92
2002	12,969	12,969	119,491	5,545,135	10,194,588	12,887.5	45	6,957,651	5,758,084.9	1.86	427.57	9.21	46.41	34.92
2003	26,128	26,128	376,631	14,365,182	30,448,868	33,664.9	73	6,905,224	5,739,505.0	3.78	549.80	14.41	38.14	21.68
2004	24,020	24,020	278,130	11,033,274	22,957,241	25,665.6	74	7,422,481	5,987,140.9	3.24	459.34	11.58	39.67	28.83
2005	20,352	20,352	223,928	9,105,309	14,873,971	21,209.5	46	7,570,077	6,199,300.3	2.69	447.39	11.00	40.66	21.69
2006	37,945	37,945	426,598	15,888,883	24,296,959	37,533.5	74	18,287,665	10,884,818.2	2.07	418.73	11.24	37.25	19.72
2007	59,538	59,538	676,586	24,027,802	35,565,093	56,818.3	87	22,125,857	16,108,032.5	2.69	403.57	11.36	35.51	15.31
2008	106,474	106,474	1,136,027	38,812,102	55,675,074	90,938.7	100	41,854,839	25,783,362.6	2.54	364.52	10.67	34.16	11.00
2009	148,218	148,218	1,547,205	51,974,738	73,779,512	121,230.5	140	42,473,134	32,664,244.0	3.49	350.66	10.44	33.59	11.55
2010	152,259	152,259	1,561,955	51,829,510	72,528,191	120,761.6	99	40,683,179	31,380,703.0	3.74	340.40	10.26	33.18	8.20
2011	151,462	151,462	1,500,236	49,329,602	68,287,243	114,292.3	110	39,557,208	30,737,864.6	3.83	325.69	9.91	32.88	9.62
2012	147,542	147,542	1,360,548	44,579,169	61,376,591	101,797.7	95	39,132,037	30,221,102.9	3.77	302.15	9.22	32.77	9.33
2013	139,403	139,403	1,115,127	36,021,795	50,552,859	78,791.0	97	38,412,242	29,750,179.8	3.63	258.40	8.00	32.30	12.31
2014	129,238	129,238	761,299	33,904,134	33,228,700	44,488.9	46	39,016,173	29,212,528.4	3.31	184.96	5.89	31.40	10.34
2015	27,764	27,764	113,738	3,643,642	5,129,496	4,802.0	5	22,995,397	7,703,137.8	1.21	131.24	4.10	32.04	10.41
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>180-Day Blackout Period</b>														
2000	2,887	2,887	36,139	1,815,927	3,955,493	3,767.0	15	6,014,550	2,679,162.4	0.48	629.00	12.52	50.25	39.82
2001	6,664	6,664	92,876	4,330,862	8,632,286	9,052.2	25	6,570,735	5,430,412.8	1.01	649.89	13.94	46.63	27.62
2002	7,250	7,250	107,473	5,102,960	9,429,954	10,737.3	39	6,688,315	5,473,361.9	1.08	703.86	14.82	47.48	36.32
2003	16,396	16,396	359,073	13,779,222	29,779,764	29,417.3	59	6,661,315	5,478,933.6	2.46	840.40	21.90	38.37	20.06
2004	14,928	14,928	258,535	10,375,844	20,025,714	21,527.9	60	7,097,072	5,726,839.8	2.10	695.06	17.32	40.13	27.87
2005	12,203	12,203	206,701	8,537,294	13,950,561	17,857.6	35	7,318,231	5,873,079.5	1.67	699.61	16.94	41.30	19.60

**Table 4a: Summary of Incident All Attention Deficit and Hyperactivity Disorder (ADHD) Medication Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2006	22,901	22,901	391,628	14,775,316	22,601,684	31,036.8	64	17,592,647	10,251,223.3	1.30	645.18	17.10	37.73	20.62
2007	35,320	35,320	617,608	22,184,061	32,882,895	46,563.7	73	21,047,783	15,173,817.0	1.68	628.09	17.49	35.92	15.68
2008	62,116	62,116	1,020,604	35,268,982	50,801,046	72,410.4	74	39,208,063	23,784,770.5	1.58	567.79	16.43	34.56	10.22
2009	85,704	85,704	1,383,115	46,981,569	67,011,158	95,558.0	103	40,473,474	30,123,022.5	2.12	548.18	16.14	33.97	10.78
2010	89,735	89,735	1,400,863	46,965,414	65,939,274	94,516.9	68	38,827,847	29,080,898.8	2.31	523.38	15.61	33.53	7.19
2011	89,811	89,811	1,346,110	44,727,270	62,084,278	88,626.2	79	37,844,283	28,560,885.3	2.37	498.02	14.99	33.23	8.91
2012	88,750	88,750	1,214,668	40,207,012	55,526,379	76,637.0	70	36,976,930	28,201,746.2	2.40	453.04	13.69	33.10	9.13
2013	82,380	82,380	970,643	31,684,830	44,688,749	55,035.5	64	36,827,532	27,598,111.5	2.24	384.62	11.78	32.64	11.63
2014	65,109	65,109	566,752	18,139,161	25,376,144	22,910.6	25	36,394,568	23,869,857.5	1.79	278.60	8.70	32.01	10.91
2015	7,765	7,765	47,141	1,639,407	2,343,213	1,105.4	1	13,660,312	3,611,604.2	0.57	211.13	6.07	34.78	9.05
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>270-Day Blackout Period</b>														
2000	1,837	1,837	32,023	1,627,026	3,573,059	3,185.5	14	5,575,332	2,587,778.6	0.33	885.70	17.43	50.81	43.95
2001	4,363	4,363	83,350	3,924,823	7,877,911	7,725.8	21	6,252,772	5,197,055.8	0.70	899.57	19.10	47.09	27.18
2002	4,909	4,909	98,019	4,712,789	8,767,902	9,333.0	32	6,342,778	5,220,529.3	0.77	960.03	19.97	48.08	34.29
2003	12,485	12,485	342,061	13,161,691	28,616,563	26,123.0	48	6,288,261	5,247,100.9	1.99	1054.20	27.40	38.48	18.37
2004	10,745	10,745	239,173	9,687,162	17,998,377	18,582.5	51	6,699,208	5,492,588.3	1.60	901.55	22.26	40.50	27.45
2005	8,457	8,457	190,524	7,961,872	13,051,088	15,607.7	32	6,859,506	5,583,868.8	1.23	941.45	22.53	41.79	20.50
2006	15,981	15,981	358,431	13,650,651	20,978,721	26,537.7	52	16,155,554	9,765,110.2	0.99	854.18	22.43	38.08	19.59
2007	24,793	24,793	564,077	20,440,121	30,421,269	39,543.4	50	19,565,294	14,368,000.0	1.27	824.43	22.75	36.24	12.64
2008	43,261	43,261	921,848	32,128,088	46,503,158	60,022.9	63	35,070,877	22,331,026.6	1.23	742.66	21.31	34.85	10.50
2009	59,807	59,807	1,245,696	42,635,130	61,056,861	78,468.6	85	36,992,597	27,968,725.7	1.62	712.88	20.83	34.23	10.83
2010	63,011	63,011	1,261,481	42,596,433	60,060,831	76,860.4	55	35,567,451	27,125,414.3	1.77	676.02	20.02	33.77	7.16
2011	63,004	63,004	1,206,899	40,387,879	56,188,580	71,046.5	61	34,753,179	26,680,720.9	1.81	641.04	19.16	33.46	8.59
2012	63,008	63,008	1,080,967	36,039,674	49,913,282	59,117.6	54	33,910,748	26,507,118.7	1.86	571.99	17.16	33.34	9.13
2013	57,650	57,650	839,857	27,611,811	39,136,851	38,841.3	44	33,883,517	25,688,162.8	1.70	478.96	14.57	32.88	11.33
2014	35,934	35,934	391,015	12,790,591	17,998,896	11,127.8	14	32,060,039	18,224,774.0	1.12	355.95	10.88	32.71	12.58
2015	1,133	1,133	7,220	332,034	500,607	123.2	0	9,153,867	1,035,417.0	0.12	293.06	6.37	45.99	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>365-Day Blackout Period</b>														
2000	1,300	1,300	28,899	1,482,977	3,285,520	2,777.7	13	5,330,884	2,500,411.1	0.24	1140.75	22.23	51.32	46.80
2001	3,188	3,188	75,947	3,613,323	7,290,193	6,755.4	17	5,792,380	4,955,256.5	0.55	1133.41	23.82	47.58	25.17
2002	3,680	3,680	90,904	4,398,131	8,227,591	8,272.7	27	5,850,227	4,983,606.9	0.63	1195.14	24.70	48.38	32.64
2003	9,820	9,820	323,157	12,502,483	27,149,238	23,378.9	41	5,874,306	5,021,327.4	1.67	1273.17	32.91	38.69	17.54
2004	8,113	8,113	220,099	9,006,395	16,509,628	16,228.3	45	6,417,257	5,253,048.6	1.26	1110.12	27.13	40.92	27.73
2005	6,425	6,425	177,111	7,452,543	12,268,283	13,815.2	25	6,248,819	5,311,295.1	1.03	1159.93	27.57	42.08	18.10
2006	11,897	11,897	328,861	12,627,584	19,464,785	23,096.3	42	14,997,764	9,292,708.9	0.79	1061.41	27.64	38.40	18.18
2007	18,989	18,989	520,856	19,008,777	28,403,526	34,156.6	42	17,950,495	13,592,650.6	1.06	1001.04	27.43	36.50	12.30
2008	32,102	32,102	834,277	29,297,035	42,589,209	50,589.6	55	32,702,829	20,937,625.2	0.98	912.62	25.99	35.12	10.87
2009	44,148	44,148	1,120,573	38,639,110	55,480,713	65,444.0	72	32,213,937	25,871,071.9	1.37	875.22	25.38	34.48	11.00
2010	46,821	46,821	1,131,680	38,477,813	54,407,712	63,145.8	50	31,235,751	25,260,372.7	1.50	821.81	24.17	34.00	7.92
2011	46,847	46,847	1,077,691	36,305,589	50,609,589	57,407.7	46	30,598,420	24,839,797.0	1.53	774.98	23.00	33.69	8.01
2012	47,037	47,037	953,730	32,012,963	44,451,699	45,433.2	39	32,201,222	24,842,233.7	1.46	680.59	20.28	33.57	8.58



**Table 4a: Summary of Incident All Attention Deficit and Hyperactivity Disorder (ADHD) Medication Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2013	42,409	42,409	715,463	23,683,734	33,645,454	26,314.3	30	29,624,765	23,805,523.2	1.43	558.46	16.87	33.10	11.40
2014	17,581	17,581	223,066	7,578,769	10,782,960	4,354.4	5	24,883,193	11,637,728.8	0.71	431.08	12.69	33.98	11.48
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>730-Day Blackout Period</b>														
2000	658	658	22,717	1,184,141	2,624,049	1,865.9	9	4,503,567	2,119,744.2	0.15	1799.61	34.52	52.13	48.23
2001	1,549	1,549	57,853	2,845,337	5,799,230	4,537.9	13	4,827,564	4,189,878.0	0.32	1836.89	37.35	49.18	28.65
2002	1,953	1,953	72,622	3,600,858	6,833,715	5,652.5	19	4,898,137	4,262,782.8	0.40	1843.76	37.18	49.58	33.61
2003	5,861	5,861	271,841	10,649,368	22,196,185	15,950.9	33	5,060,516	4,310,526.8	1.16	1816.99	46.38	39.17	20.69
2004	3,820	3,820	164,818	6,996,934	12,367,240	10,755.0	25	5,343,040	4,345,739.0	0.71	1831.66	43.15	42.45	23.25
2005	3,379	3,379	141,377	6,074,707	10,004,931	9,341.0	13	5,248,706	4,546,896.2	0.64	1797.78	41.84	42.97	13.92
2006	6,058	6,058	254,538	9,974,947	15,406,164	14,852.2	21	12,161,305	7,729,105.3	0.50	1646.57	42.02	39.19	14.14
2007	9,516	9,516	394,249	14,685,468	22,055,958	20,989.1	23	14,585,827	10,896,870.3	0.65	1543.24	41.43	37.25	10.96
2008	15,325	15,325	604,012	21,672,640	31,707,516	28,880.5	29	24,271,336	16,136,731.8	0.63	1414.20	39.41	35.88	10.04
2009	20,724	20,724	794,712	27,960,892	40,264,639	35,599.4	37	24,011,886	19,875,849.7	0.86	1349.20	38.35	35.18	10.39
2010	21,430	21,430	775,551	26,903,573	37,997,827	31,829.4	25	23,611,682	19,516,324.6	0.91	1255.42	36.19	34.69	7.85
2011	22,588	22,588	738,330	25,343,589	35,460,263	25,523.8	22	24,890,577	19,696,158.8	0.91	1121.99	32.69	34.33	8.62
2012	20,767	20,767	581,564	19,971,217	27,768,759	14,286.9	12	24,671,052	18,960,955.4	0.84	961.68	28.00	34.34	8.40
2013	8,733	8,733	197,805	7,096,238	10,297,055	2,414.4	1	19,027,328	9,235,329.2	0.46	812.58	22.65	35.87	4.14
2014	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>1,095-Day Blackout Period</b>														
2000	422	422	18,433	981,816	2,192,746	1,339.4	7	3,851,133	1,825,128.1	0.11	2326.58	43.68	53.26	52.26
2001	1,003	1,003	47,150	2,372,859	4,849,882	3,291.6	9	4,142,567	3,648,161.1	0.24	2365.76	47.01	50.33	27.34
2002	1,277	1,277	59,134	3,004,138	5,745,062	4,075.6	10	4,312,719	3,721,858.0	0.30	2352.50	46.31	50.80	24.54
2003	3,603	3,603	216,138	8,677,814	17,200,594	11,429.9	23	4,312,553	3,611,193.5	0.84	2408.50	59.99	40.15	20.12
2004	2,463	2,463	134,242	5,799,302	9,657,986	7,689.9	14	4,513,966	3,786,068.7	0.55	2354.57	54.50	43.20	18.21
2005	2,194	2,194	115,817	5,051,702	8,332,537	6,636.2	8	4,547,399	3,975,587.3	0.48	2302.51	52.79	43.62	12.06
2006	3,856	3,856	204,450	8,118,779	12,570,937	10,070.2	10	9,956,398	6,466,047.2	0.39	2105.49	53.02	39.71	9.93
2007	5,890	5,890	306,640	11,634,374	17,494,570	13,557.0	15	11,788,879	9,011,459.8	0.50	1975.28	52.06	37.94	11.06
2008	9,043	9,043	449,379	16,417,228	24,087,223	17,256.7	19	18,835,681	13,007,096.9	0.48	1815.46	49.69	36.53	11.01
2009	11,899	11,899	572,651	20,507,038	29,486,037	19,908.3	24	18,698,335	15,734,199.9	0.64	1723.43	48.13	35.81	12.06
2010	12,551	12,551	551,334	19,442,373	27,441,863	15,443.8	8	19,810,546	15,914,672.9	0.63	1549.07	43.93	35.26	5.18
2011	12,220	12,220	474,311	16,615,097	23,337,232	8,842.9	5	19,760,526	15,428,565.6	0.62	1359.66	38.81	35.03	5.65
2012	5,121	5,121	162,834	6,119,144	8,649,868	1,416.5	1	17,148,058	7,693,169.0	0.30	1194.91	31.80	37.58	7.06
2013	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2014	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
2000	10,081	10,081	73,925	3,525,318	7,395,833	12,797.4	46	6,530,474	3,002,264.9	1.54	349.70	7.33	47.69	35.94

**Table 4a: Summary of Incident All Attention Deficit and Hyperactivity Disorder (ADHD) Medication Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2001	23,815	23,815	189,505	8,332,306	16,312,980	30,500.4	83	7,125,509	5,963,443.2	3.34	349.88	7.96	43.97	27.21
2002	22,060	22,060	205,165	9,065,254	16,936,128	31,678.9	88	7,269,146	6,057,447.7	3.03	410.94	9.30	44.19	27.78
2003	39,593	39,593	574,732	21,594,149	44,703,357	70,267.5	154	7,256,728	6,027,105.0	5.46	545.40	14.52	37.57	21.92
2004	36,787	36,787	409,808	16,080,902	34,351,292	54,822.1	151	7,683,924	6,267,478.5	4.79	437.14	11.14	39.24	27.54
2005	32,232	32,232	341,802	13,655,479	22,027,765	47,050.6	102	7,913,620	6,547,366.0	4.07	423.66	10.60	39.95	21.68
2006	64,255	64,255	651,869	23,825,210	36,363,492	85,570.0	146	19,374,078	11,577,744.8	3.32	370.79	10.15	36.55	17.06
2007	101,230	101,230	1,022,301	35,712,618	53,191,017	129,644.6	231	23,562,766	17,132,264.3	4.30	352.79	10.10	34.93	17.82
2008	185,447	185,447	1,710,428	57,641,015	90,005,280	214,089.4	287	44,232,614	27,982,593.8	4.19	310.82	9.22	33.70	13.41
2009	252,478	252,478	2,316,867	76,801,387	109,443,146	286,383.5	378	45,579,872	35,436,831.4	5.54	304.19	9.18	33.15	13.20
2010	248,572	248,572	2,280,093	74,836,913	105,115,526	280,101.3	344	43,393,746	33,892,949.1	5.73	301.07	9.17	32.82	12.28
2011	243,452	243,452	2,149,987	69,919,958	97,543,656	264,029.1	303	41,949,646	33,065,186.9	5.80	287.20	8.83	32.52	11.48
2012	232,193	232,193	1,889,557	61,168,090	84,729,895	234,608.4	249	40,898,261	32,365,170.8	5.68	263.44	8.14	32.37	10.61
2013	220,913	220,913	1,508,402	48,019,353	67,688,579	188,448.5	279	40,733,081	32,023,780.6	5.42	217.37	6.83	31.83	14.81
2014	208,827	208,827	985,429	30,338,294	42,459,849	122,185.2	164	41,655,900	31,890,934.4	5.01	145.28	4.72	30.79	13.42
2015	92,688	92,688	219,528	6,168,224	8,676,196	23,841.3	27	34,324,966	15,634,852.2	2.70	66.55	2.37	28.10	11.32
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>90-Day Blackout Period</b>														
2000	9,460	9,460	72,950	3,500,131	7,344,526	10,388.5	35	6,279,475	2,830,507.5	1.51	369.99	7.71	47.98	33.69
2001	22,857	22,857	188,072	8,296,584	16,243,275	24,754.6	61	6,793,365	5,684,525.9	3.36	362.98	8.23	44.11	24.64
2002	21,082	21,082	203,789	9,029,791	16,867,718	26,379.0	64	6,948,311	5,751,783.9	3.03	428.32	9.67	44.31	24.26
2003	38,149	38,149	573,045	21,554,741	44,669,917	60,748.9	114	6,891,587	5,730,279.6	5.54	565.01	15.02	37.61	18.77
2004	35,158	35,158	407,265	16,019,169	34,073,882	45,985.5	109	7,404,104	5,974,178.9	4.75	455.63	11.58	39.33	23.70
2005	30,607	30,607	339,819	13,615,199	21,962,942	39,393.7	68	7,544,555	6,180,685.0	4.06	444.84	11.10	40.07	17.26
2006	60,094	60,094	646,021	23,694,326	36,163,235	70,328.4	101	18,257,739	10,861,853.8	3.29	394.29	10.75	36.68	14.36
2007	94,657	94,657	1,012,230	35,476,502	52,831,185	105,588.5	155	22,083,969	16,076,655.9	4.29	374.79	10.69	35.05	14.68
2008	168,452	168,452	1,684,610	57,045,391	89,158,627	170,567.4	172	41,793,857	25,738,493.6	4.03	338.64	10.00	33.86	10.08
2009	230,593	230,593	2,283,717	76,040,810	108,374,989	227,020.5	265	42,384,134	32,601,031.5	5.44	329.76	9.90	33.30	11.67
2010	227,297	227,297	2,247,855	74,107,723	104,085,299	221,663.3	214	40,561,527	31,294,087.7	5.60	326.04	9.89	32.97	9.65
2011	222,977	222,977	2,118,951	69,224,998	96,583,870	206,836.5	192	39,410,476	30,632,222.3	5.66	310.46	9.50	32.67	9.28
2012	213,753	213,753	1,862,661	60,565,072	83,903,514	180,000.1	165	38,967,132	30,101,111.3	5.49	283.34	8.71	32.52	9.17
2013	201,920	201,920	1,480,229	47,385,320	66,810,325	136,650.1	175	38,234,525	29,619,331.4	5.28	234.67	7.33	32.01	12.81
2014	186,336	186,336	950,815	29,550,932	41,360,115	73,680.3	79	38,835,412	29,082,773.5	4.80	158.59	5.10	31.08	10.72
2015	40,252	40,252	137,049	4,294,304	6,110,082	7,662.0	7	22,897,921	7,675,031.5	1.76	106.69	3.40	31.33	9.14
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>180-Day Blackout Period</b>														
2000	5,983	5,983	68,027	3,334,541	6,988,592	8,514.4	33	6,014,550	2,679,162.4	0.99	557.34	11.37	49.02	38.76
2001	14,000	14,000	178,091	7,998,906	15,616,752	20,621.3	47	6,569,500	5,430,017.5	2.13	571.35	12.72	44.91	22.79
2002	13,989	13,989	203,160	9,096,838	17,034,383	23,356.2	53	6,683,520	5,470,912.2	2.09	650.29	14.52	44.78	22.69
2003	28,056	28,056	614,229	23,056,267	48,588,881	58,443.9	96	6,653,598	5,474,609.6	4.22	821.79	21.89	37.54	16.43
2004	24,424	24,424	410,562	16,264,956	31,020,815	41,046.7	89	7,085,707	5,720,298.3	3.45	665.94	16.81	39.62	21.68
2005	20,631	20,631	339,747	13,718,023	21,999,776	34,989.2	54	7,301,380	5,862,713.6	2.83	664.92	16.47	40.38	15.43
2006	38,980	38,980	632,941	23,438,207	35,706,137	60,650.9	85	17,571,452	10,237,034.8	2.22	601.29	16.24	37.03	14.01
2007	60,886	60,886	987,229	34,918,428	51,961,979	90,173.0	125	21,020,548	15,155,790.2	2.90	573.51	16.21	35.37	13.86

**Table 4a: Summary of Incident All Attention Deficit and Hyperactivity Disorder (ADHD) Medication Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2008	107,238	107,238	1,626,061	55,536,180	79,965,602	142,393.2	128	39,170,765	23,760,447.8	2.74	517.88	15.16	34.15	8.99
2009	148,726	148,726	2,208,662	74,112,245	105,689,455	188,568.3	205	40,422,530	30,091,554.3	3.68	498.31	14.85	33.56	10.87
2010	152,257	152,257	2,201,173	73,102,529	102,710,385	185,369.0	152	38,757,208	29,037,452.8	3.93	480.13	14.46	33.21	8.20
2011	151,453	151,453	2,078,651	68,414,495	95,461,823	171,319.6	142	37,754,911	28,505,195.3	4.01	451.72	13.72	32.91	8.29
2012	147,932	147,932	1,831,006	59,976,003	83,099,386	145,688.8	121	36,872,439	28,134,539.0	4.01	405.43	12.38	32.76	8.31
2013	138,236	138,236	1,430,808	46,182,938	65,166,670	102,632.1	122	36,709,240	27,521,698.6	3.77	334.09	10.35	32.28	11.89
2014	109,531	109,531	809,968	25,646,717	36,032,099	41,366.6	43	36,274,836	23,801,109.4	3.02	234.15	7.39	31.66	10.39
2015	13,347	13,347	68,175	2,314,158	3,308,204	1,931.5	0	13,623,153	3,600,844.8	0.98	173.38	5.11	33.94	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>270-Day Blackout Period</b>														
2000	4,166	4,166	63,671	3,131,493	6,578,452	7,304.9	31	5,575,332	2,587,778.6	0.75	751.68	15.28	49.18	42.44
2001	9,783	9,783	167,227	7,562,434	14,788,299	17,881.4	39	6,252,344	5,196,990.3	1.56	773.02	17.09	45.22	21.81
2002	10,266	10,266	195,493	8,833,218	16,755,709	20,892.5	48	6,340,537	5,219,630.7	1.62	860.43	19.04	45.18	22.97
2003	22,927	22,927	611,370	22,960,776	48,779,417	53,692.5	87	6,284,209	5,245,121.2	3.65	1001.47	26.67	37.56	16.20
2004	18,868	18,868	399,609	15,921,596	29,008,340	36,708.4	81	6,692,603	5,489,265.6	2.82	843.84	21.18	39.84	22.07
2005	15,642	15,642	330,101	13,412,617	21,495,252	31,457.6	48	6,848,968	5,577,924.7	2.28	857.47	21.10	40.63	15.26
2006	29,844	29,844	609,729	22,714,466	34,625,434	53,280.3	73	16,141,368	9,756,221.7	1.85	761.11	20.43	37.25	13.70
2007	46,071	46,071	943,606	33,581,801	50,010,445	78,399.0	90	19,547,125	14,356,490.3	2.36	728.91	20.48	35.59	11.48
2008	81,170	81,170	1,544,039	53,072,039	76,572,883	121,212.9	108	35,046,323	22,315,646.5	2.32	653.84	19.02	34.37	8.91
2009	111,739	111,739	2,087,796	70,484,635	100,682,596	159,337.5	171	36,960,065	27,949,078.4	3.02	630.80	18.68	33.76	10.73
2010	116,196	116,196	2,090,426	69,819,162	98,228,613	156,043.1	119	35,521,959	27,098,472.1	3.27	600.87	17.99	33.40	7.63
2011	115,903	115,903	1,971,582	65,282,944	91,191,805	142,380.9	108	34,693,981	26,645,228.4	3.34	563.25	17.01	33.11	7.59
2012	114,609	114,609	1,732,477	57,094,901	79,231,500	117,246.0	91	33,839,611	26,462,881.3	3.39	498.17	15.12	32.96	7.76
2013	105,753	105,753	1,327,286	43,108,700	60,974,452	75,630.0	91	33,801,285	25,636,909.8	3.13	407.64	12.55	32.48	12.03
2014	65,935	65,935	607,580	19,665,299	27,718,945	21,195.1	25	31,981,842	18,187,361.7	2.06	298.25	9.21	32.37	11.80
2015	2,056	2,056	11,466	513,889	777,939	221.4	0	9,133,234	1,032,467.0	0.23	249.95	5.58	44.82	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>365-Day Blackout Period</b>														
2000	2,977	2,977	58,895	2,920,073	6,163,944	6,392.2	29	5,330,884	2,500,411.1	0.56	980.88	19.78	49.58	45.37
2001	7,350	7,350	156,624	7,130,328	14,012,550	15,699.1	35	5,792,331	4,955,253.5	1.27	970.11	21.31	45.53	22.29
2002	7,941	7,941	186,569	8,467,297	16,127,374	18,746.3	42	5,849,306	4,983,299.7	1.36	1066.28	23.49	45.38	22.40
2003	19,084	19,084	597,255	22,470,807	47,424,615	48,924.0	78	5,872,273	5,020,395.0	3.25	1177.47	31.30	37.62	15.94
2004	15,065	15,065	382,445	15,327,785	27,191,010	32,748.2	73	6,413,621	5,251,307.5	2.35	1017.44	25.39	40.08	22.29
2005	12,451	12,451	317,315	12,968,372	20,761,375	28,354.1	39	6,242,402	5,307,825.5	1.99	1041.55	25.49	40.87	13.75
2006	23,100	23,100	577,622	21,661,183	33,116,078	47,015.9	63	14,988,314	9,286,962.4	1.54	937.71	25.01	37.50	13.40
2007	36,333	36,333	893,757	31,999,724	47,768,929	68,465.1	78	17,938,574	13,584,942.2	2.03	880.73	24.60	35.80	11.39
2008	62,687	62,687	1,444,598	49,937,034	72,267,020	103,625.5	93	32,686,695	20,927,464.1	1.92	796.61	23.04	34.57	8.97
2009	86,085	86,085	1,943,510	65,970,128	94,398,209	135,016.4	146	32,193,492	25,858,147.1	2.67	766.34	22.58	33.94	10.81
2010	90,646	90,646	1,950,239	65,459,046	92,285,139	131,077.2	103	31,207,219	25,243,043.6	2.90	722.14	21.51	33.56	7.86
2011	90,629	90,629	1,834,422	61,059,390	85,381,109	117,747.5	85	30,560,919	24,816,808.2	2.97	673.73	20.24	33.29	7.22
2012	90,605	90,605	1,602,811	53,097,402	73,754,106	92,549.5	70	32,153,208	24,812,735.2	2.82	586.03	17.69	33.13	7.56
2013	82,086	82,086	1,191,245	38,905,862	55,172,869	52,628.0	65	29,571,050	23,770,786.2	2.78	473.96	14.51	32.66	12.35
2014	33,888	33,888	367,077	12,335,808	17,555,405	8,648.5	10	24,843,958	11,620,624.3	1.36	364.02	10.83	33.61	11.56

**Table 4a: Summary of Incident All Attention Deficit and Hyperactivity Disorder (ADHD) Medication Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>730-Day Blackout Period</b>														
2000	1,511	1,511	47,841	2,416,015	5,127,020	4,324.9	19	4,503,567	2,119,744.2	0.34	1598.95	31.66	50.50	43.93
2001	3,661	3,661	125,860	5,840,862	11,541,668	10,528.6	23	4,827,564	4,189,878.0	0.76	1595.43	34.38	46.41	21.85
2002	4,477	4,477	158,222	7,266,859	14,013,769	12,961.0	28	4,898,121	4,262,781.3	0.91	1623.15	35.34	45.93	21.60
2003	11,898	11,898	529,353	20,054,227	40,425,054	34,535.0	61	5,060,297	4,310,452.8	2.35	1685.51	44.49	37.88	17.66
2004	7,821	7,821	310,262	12,740,432	22,134,648	22,276.0	41	5,342,458	4,345,493.8	1.46	1629.00	39.67	41.06	18.41
2005	6,980	6,980	270,321	11,193,403	17,987,707	19,744.2	23	5,247,400	4,546,302.0	1.33	1603.64	38.73	41.41	11.65
2006	12,553	12,553	475,697	18,124,547	27,760,335	30,849.6	32	12,158,654	7,727,692.0	1.03	1443.84	37.90	38.10	10.37
2007	19,126	19,126	715,873	26,043,706	39,060,478	42,991.6	42	14,581,927	10,894,493.2	1.31	1361.69	37.43	36.38	9.77
2008	31,448	31,448	1,112,413	39,096,731	56,950,460	60,705.9	50	24,266,326	16,133,586.6	1.30	1243.22	35.37	35.15	8.24
2009	42,995	42,995	1,474,364	50,792,039	72,967,925	75,442.4	75	24,005,530	19,871,765.4	1.79	1181.35	34.29	34.45	9.94
2010	45,101	45,101	1,451,435	49,505,580	69,998,538	68,830.1	49	23,603,520	19,511,110.9	1.91	1097.66	32.18	34.11	7.12
2011	47,156	47,156	1,366,113	46,118,878	64,709,022	54,566.3	40	24,879,438	19,689,245.6	1.90	978.01	28.97	33.76	7.33
2012	44,118	44,118	1,088,323	36,667,441	51,088,632	30,610.4	23	24,656,662	18,951,880.3	1.79	831.12	24.67	33.69	7.51
2013	18,129	18,129	362,904	12,782,599	18,545,460	4,991.6	4	19,017,258	9,230,591.5	0.95	705.09	20.02	35.22	8.01
2014	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>1,095-Day Blackout Period</b>														
2000	950	950	39,304	2,018,847	4,332,537	3,126.7	16	3,851,133	1,825,128.1	0.25	2125.10	41.37	51.36	51.17
2001	2,361	2,361	104,962	4,951,483	9,868,442	7,610.9	16	4,142,567	3,648,161.1	0.57	2097.20	44.46	47.17	21.02
2002	2,985	2,985	133,071	6,197,354	11,986,511	9,284.5	15	4,312,719	3,721,858.0	0.69	2076.17	44.58	46.57	16.16
2003	7,758	7,758	443,253	17,033,459	32,601,315	24,932.2	43	4,312,551	3,611,193.3	1.80	2195.60	57.13	38.43	17.25
2004	5,128	5,128	260,461	10,830,355	18,164,857	16,024.0	28	4,513,884	3,786,043.3	1.14	2112.00	50.79	41.58	17.47
2005	4,584	4,584	227,176	9,515,245	15,268,583	14,169.5	16	4,547,127	3,975,465.9	1.01	2075.75	49.56	41.88	11.29
2006	8,009	8,009	390,280	15,028,619	23,061,394	21,041.5	19	9,955,689	6,465,732.9	0.80	1876.47	48.73	38.51	9.03
2007	12,118	12,118	575,312	21,225,384	31,936,280	27,952.4	23	11,787,518	9,010,743.7	1.03	1751.56	47.48	36.89	8.23
2008	18,800	18,800	853,906	30,437,237	44,411,448	36,728.2	34	18,833,654	13,005,888.0	1.00	1619.00	45.42	35.64	9.26
2009	25,328	25,328	1,104,995	38,591,344	55,570,708	42,626.4	45	18,695,840	15,732,581.0	1.35	1523.66	43.63	34.92	10.56
2010	27,300	27,300	1,080,548	37,294,750	52,807,202	33,981.6	17	19,807,183	15,912,561.6	1.38	1366.11	39.58	34.51	5.00
2011	26,569	26,569	928,763	31,837,841	44,837,056	19,112.5	11	19,756,147	15,425,685.7	1.34	1198.31	34.96	34.28	5.76
2012	11,061	11,061	318,540	11,695,705	16,558,959	3,111.1	1	17,143,754	7,691,579.1	0.65	1057.38	28.80	36.72	3.21
2013	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2014	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of All Attention Deficit and Hyperactivity Disorder (ADHD) Medication Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>30-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
2000	11	2,147	51.2
2001	16	4,895	32.7
2002	21	4,231	49.6
2003	30	5,333	56.3
2004	33	6,636	49.7
2005	30	5,929	50.6
2006	37	12,367	29.9
2007	58	19,649	29.5
2008	95	36,111	26.3
2009	93	49,368	18.8
2010	105	47,634	22.0
2011	92	46,448	19.8
2012	71	44,093	16.1
2013	88	42,563	20.7
2014	69	41,170	16.8
2015	16	14,666	10.9
2016	0	0	---
<b>Days 91-180</b>			
2000	0	1,012	0.0
2001	10	2,267	44.1
2002	6	2,150	27.9
2003	14	4,248	33.0
2004	14	4,138	33.8
2005	11	3,352	32.8
2006	10	6,497	15.4
2007	14	10,255	13.7
2008	26	18,528	14.0
2009	37	25,673	14.4
2010	31	26,245	11.8
2011	31	25,666	12.1
2012	25	25,161	9.9
2013	33	23,756	13.9
2014	21	21,578	9.7
2015	4	3,697	10.8
2016	0	0	---
<b>Days 181-270</b>			
2000	1	582	17.2
2001	4	1,326	30.2
2002	7	1,404	49.8
2003	11	3,294	33.4
2004	9	2,945	30.6
2005	3	2,250	13.3
2006	12	4,499	26.7

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of All Attention Deficit and Hyperactivity Disorder (ADHD) Medication Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
2007	23	7,020	32.8
2008	11	12,388	8.9
2009	18	17,089	10.5
2010	13	17,656	7.4
2011	18	17,580	10.2
2012	16	17,519	9.1
2013	20	16,194	12.4
2014	11	11,783	9.3
2015	1	982	10.2
2016	0	0	---
<b>Days 271-365</b>			
2000	1	408	24.5
2001	4	970	41.2
2002	5	1,060	47.2
2003	7	2,744	25.5
2004	6	2,354	25.5
2005	7	1,793	39.1
2006	10	3,441	29.1
2007	8	5,387	14.9
2008	8	9,433	8.5
2009	13	13,025	10.0
2010	5	13,715	3.6
2011	15	13,639	11.0
2012	15	13,684	11.0
2013	14	12,527	11.2
2014	9	6,773	13.3
2015	0	123	0.0
2016	0	0	---
<b>Days 366-730</b>			
2000	4	912	43.9
2001	4	2,218	18.0
2002	8	2,620	30.5
2003	8	7,428	10.8
2004	20	5,473	36.5
2005	12	4,474	26.8
2006	21	8,244	25.5
2007	19	13,167	14.4
2008	26	21,709	12.0
2009	35	29,845	11.7
2010	25	31,316	8.0
2011	24	31,884	7.5
2012	27	31,146	8.7
2013	29	23,900	12.1
2014	5	4,354	11.5

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of All Attention Deficit and Hyperactivity Disorder (ADHD) Medication Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
2015	0	0	---
2016	0	0	---
<b>Days 731-1,095</b>			
2000	2	526	38.0
2001	4	1,246	32.1
2002	9	1,577	57.1
2003	10	4,521	22.1
2004	11	3,065	35.9
2005	5	2,705	18.5
2006	11	4,782	23.0
2007	8	7,432	10.8
2008	10	11,624	8.6
2009	13	15,691	8.3
2010	17	16,386	10.4
2011	17	16,681	10.2
2012	11	12,870	8.5
2013	1	2,414	4.1
2014	0	0	---
2015	0	0	---
2016	0	0	---
<b>90-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
2000	11	2,409	45.7
2001	22	5,746	38.3
2002	24	5,300	45.3
2003	40	9,519	42.0
2004	42	8,837	47.5
2005	34	7,657	44.4
2006	45	15,242	29.5
2007	76	24,056	31.6
2008	115	43,522	26.4
2009	113	59,363	19.0
2010	130	58,438	22.2
2011	111	57,193	19.4
2012	84	54,608	15.4
2013	104	51,798	20.1
2014	85	48,505	17.5
2015	20	16,179	12.4
2016	0	0	---
<b>Days 91-180</b>			
2000	2	1,874	10.7
2001	14	4,133	33.9
2002	11	3,023	36.4
2003	18	2,305	78.1
2004	20	4,939	40.5

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of All Attention Deficit and Hyperactivity Disorder (ADHD) Medication Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
2005	14	4,404	31.8
2006	16	9,677	16.5
2007	30	15,415	19.5
2008	44	28,174	15.6
2009	60	38,452	15.6
2010	62	36,294	17.1
2011	50	35,517	14.1
2012	44	34,311	12.8
2013	53	34,018	15.6
2014	36	32,314	11.1
2015	7	5,730	12.2
2016	0	0	---
<b>Days 181-270</b>			
2000	2	1,210	16.5
2001	8	2,740	29.2
2002	5	2,464	20.3
2003	9	4,751	18.9
2004	8	4,338	18.4
2005	6	3,532	17.0
2006	12	7,371	16.3
2007	35	11,774	29.7
2008	20	21,180	9.4
2009	34	29,231	11.6
2010	33	29,326	11.3
2011	34	28,939	11.7
2012	30	28,443	10.5
2013	31	27,002	11.5
2014	18	20,171	8.9
2015	0	1,710	0.0
2016	0	0	---
<b>Days 271-365</b>			
2000	2	913	21.9
2001	4	2,182	18.3
2002	6	2,146	28.0
2003	9	4,768	18.9
2004	8	3,960	20.2
2005	9	3,103	29.0
2006	10	6,264	16.0
2007	12	9,934	12.1
2008	15	17,587	8.5
2009	25	24,321	10.3
2010	16	24,966	6.4
2011	23	24,633	9.3
2012	21	24,696	8.5



**Table 4b: Rate of Heart Failure Outcomes at Different Stages of All Attention Deficit and Hyperactivity Disorder (ADHD) Medication Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
2013	26	23,002	11.3
2014	15	12,547	12.0
2015	0	221	0.0
2016	0	0	---
<b>Days 366-730</b>			
2000	10	2,067	48.4
2001	12	5,170	23.2
2002	14	5,785	24.2
2003	17	14,389	11.8
2004	32	10,472	30.6
2005	16	8,610	18.6
2006	31	16,166	19.2
2007	36	25,474	14.1
2008	43	42,920	10.0
2009	71	59,574	11.9
2010	54	62,247	8.7
2011	45	63,181	7.1
2012	47	61,939	7.6
2013	61	47,636	12.8
2014	10	8,649	11.6
2015	0	0	---
2016	0	0	---
<b>Days 731-1,095</b>			
2000	3	1,198	25.0
2001	7	2,918	24.0
2002	13	3,677	35.4
2003	18	9,603	18.7
2004	13	6,252	20.8
2005	7	5,575	12.6
2006	13	9,808	13.3
2007	19	15,039	12.6
2008	16	23,978	6.7
2009	30	32,816	9.1
2010	32	34,849	9.2
2011	29	35,454	8.2
2012	22	27,499	8.0
2013	4	4,992	8.0
2014	0	0	---
2015	0	0	---
2016	0	0	---

**Appendix A: List of Generic and Brand Names Used To Define the Exposures and Exposure Incidence in this Request**

Generic Name	Brand Name
<b>Amphetamines</b>	
DEXTROAMPHETAMINE SULFATE	Dexedrine Spansule
DEXTROAMPHETAMINE SULFATE	dextroamphetamine
DEXTROAMPHETAMINE SULFATE	Dexedrine
DEXTROAMPHETAMINE SULFATE	DextroStat
DEXTROAMPHETAMINE SULFATE	Zenzedi
DEXTROAMPHETAMINE SULFATE	ProCentra
DEXTROAMPHETAMINE SULFATE	Liquadd
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	Amphetamine Salt Combo
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	Adderall XR
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	Adderall
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	dextroamphetamine-amphetamine
LISDEXAMFETAMINE DIMESYLATE	Vyvanse
METHAMPHETAMINE HCL	Desoxyn
AMPHETAMINE SULFATE	Evekeo
METHAMPHETAMINE HCL	methamphetamine
<b>Methylphenidates</b>	
DEXMETHYLPHENIDATE HCL	dexmethylphenidate
DEXMETHYLPHENIDATE HCL	Focalin XR
DEXMETHYLPHENIDATE HCL	Focalin
METHYLPHENIDATE HCL	Methylin
METHYLPHENIDATE HCL	Ritalin LA
METHYLPHENIDATE HCL	methylphenidate
METHYLPHENIDATE HCL	Concerta
METHYLPHENIDATE HCL	Metadate CD
METHYLPHENIDATE HCL	Aptensio XR
METHYLPHENIDATE HCL	Ritalin
METHYLPHENIDATE HCL	Ritalin SR
METHYLPHENIDATE HCL	Metadate ER
METHYLPHENIDATE HCL	Quillivant XR
METHYLPHENIDATE HCL	Methylin ER
<b>Strattera</b>	
ATOMOXETINE HCL	Strattera

**Appendix B: Codes Used to Define Heart Failure in this Request**


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<b>Code</b>	<b>Code Type</b>	<b>Description</b>
398.91	ICD-9-CM Diagnosis	Rheumatic heart failure (congestive)
402.01	ICD-9-CM Diagnosis	Malignant hypertensive heart disease with heart failure
402.11	ICD-9-CM Diagnosis	Benign hypertensive heart disease with heart failure
402.91	ICD-9-CM Diagnosis	Unspecified hypertensive heart disease with heart failure
404.01	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.03	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic kidney disease stage V or end stage renal disease
404.11	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, benign, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.13	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, benign, with heart failure and chronic kidney disease stage V or end stage renal disease
404.91	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, unspecified, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.93	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, unspecified, with heart failure and chronic kidney disease stage V or end stage renal disease
422.90	ICD-9-CM Diagnosis	Acute myocarditis, unspecified
425.4	ICD-9-CM Diagnosis	Other primary cardiomyopathies
425.9	ICD-9-CM Diagnosis	Secondary cardiomyopathy, unspecified
428	ICD-9-CM Diagnosis	Heart Failure
428.0	ICD-9-CM Diagnosis	Congestive heart failure, unspecified
428.1	ICD-9-CM Diagnosis	Left heart failure
428.2	ICD-9-CM Diagnosis	Systolic heart failure
428.20	ICD-9-CM Diagnosis	Systolic heart failure, unspecified
428.21	ICD-9-CM Diagnosis	Acute systolic heart failure
428.22	ICD-9-CM Diagnosis	Chronic systolic heart failure
428.23	ICD-9-CM Diagnosis	Acute on chronic systolic heart failure
428.3	ICD-9-CM Diagnosis	Diastolic heart failure
428.30	ICD-9-CM Diagnosis	Diastolic heart failure, unspecified
428.31	ICD-9-CM Diagnosis	Acute diastolic heart failure
428.32	ICD-9-CM Diagnosis	Chronic diastolic heart failure
428.33	ICD-9-CM Diagnosis	Acute on chronic diastolic heart failure
428.4	ICD-9-CM Diagnosis	Combined systolic and diastolic heart failure
428.40	ICD-9-CM Diagnosis	Combined systolic and diastolic heart failure, unspecified
428.41	ICD-9-CM Diagnosis	Acute combined systolic and diastolic heart failure
428.42	ICD-9-CM Diagnosis	Chronic combined systolic and diastolic heart failure
428.43	ICD-9-CM Diagnosis	Acute on chronic combined systolic and diastolic heart failure
428.9	ICD-9-CM Diagnosis	Heart failure, unspecified

**Modular Program Specifications for cder\_mpl1r\_wp014\_nsdp\_v01 Report 7 of 8**

Sentinel's Cohort Identification and Descriptive Analysis (CIDA) tool was used to investigate heart failure following treatment with select attention deficit and hyperactivity disorder (ADHD) medications. In total, 49 scenarios were examined with four different exposures, seven different blackout periods, and two different episode gaps/exposure extension periods. The four exposures are all amphetamines, all methylphenidates, strattera, and all stimulants (which include all amphetamines, all methylphenidates, and strattera). **The outcome is heart failure, defined as any heart failure ICD-9-CM diagnosis code (398.91, 402.x1, 402.x3, 404.x1, 404.x3, 422.90, 425.4, 425.9, 428.xx) in any care setting with a primary discharge diagnosis (PDX) value of P (principal) for those diagnoses in the inpatient care setting.** See below for a description of each of these scenarios. The query period was from January 1, 2000 to March 3, 2016 and the enrollment gap was set at 45 days. Age groups were split as follows: 0-21, 22-44, 45-64, 65+.

Enrollment Gap	45 Days
Age Groups	0-21, 22-44, 45-64, 65+
Query Period	January 1, 2000 - Current
Coverage Requirement	Medical and Drug
Enrollment Requirement	183 Days

Scenario	Drug/Exposure										Event/Outcome					
	Incident exposure	Incident w/ respect to:	Episode Truncation at Incident Exposure	Episode Truncation at Death	Washout (days)	Cohort Definition	Episode Gap	Exposure Extension Period	Min Episode Duration	Min Days Supplied	Event/ Outcome	Care Setting/PDX	Incident with Respect to Setting/PDX	Incident w/ respect to Care Setting/PDX	Washout (days)	Blackout Period
15	All Stimulants	All Stimulants	Yes	No	183	01	90	90	0	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	0
16	All Stimulants	All Stimulants	Yes	No	183	01	90	90	90	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	90
17	All Stimulants	All Stimulants	Yes	No	183	01	90	90	180	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	180
18	All Stimulants	All Stimulants	Yes	No	183	01	90	90	270	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	270
19	All Stimulants	All Stimulants	Yes	No	183	01	90	90	365	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	365
20	All Stimulants	All Stimulants	Yes	No	183	01	90	90	730	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	730
21	All Stimulants	All Stimulants	Yes	No	183	01	90	90	1095	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	1095
36	All Stimulants	All Stimulants	Yes	No	183	01	30	30	0	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	0
37	All Stimulants	All Stimulants	Yes	No	183	01	30	30	90	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	90
38	All Stimulants	All Stimulants	Yes	No	183	01	30	30	180	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	180
39	All Stimulants	All Stimulants	Yes	No	183	01	30	30	270	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	270
40	All Stimulants	All Stimulants	Yes	No	183	01	30	30	365	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	365
41	All Stimulants	All Stimulants	Yes	No	183	01	30	30	730	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	730
42	All Stimulants	All Stimulants	Yes	No	183	01	30	30	1095	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	1095

ICD-9, ICD-10, HCPCS, and CPT codes are provided by Optum360. NDC codes are checked against First Data Bank's "National Drug Data File (NDDF®) Plus."

Cohort Definition of 01 will only consider the first incident episode for each user during the query period that satisfies the washout period.

Note: Episodes are automatically truncated at outcome.

\*Codes in the algorithm include: 398.91, 402.x1, 402.x3, 404.x1, 404.x3, 422.90, 425.4, 425.9, 428.xx. Algorithm will look for at least one of five things: (1) at least one IP code with PDX flag = P, OR (2) at least three IP codes with PDX flag = S, OR (3) at least two AV\*/OA\* codes with any PDX flag value, OR (4) at least three ED\* codes with any PDX flag value, OR (5) at least two IP codes with PDX flag = S and at least one AV\*/OA\* code with any PDX flag value. The temporal relationship between codes will be 365 days. For example, for at least two AV\*/OA\* codes with any PDX flag value, we would find one code and then look for a second within 365 days of the first. For at least three IP codes with PDX flag = S, we would find one code, and then look for a second within 365 days of the first, and then look for a third within 365 days of the first. The date of the first of the one, two, or three codes will be used as the event date. This is important because episodes are truncated on occurrence of the event.

## Disclaimer

The following report(s) provides findings from an FDA-initiated query using Sentinel. While Sentinel queries may be undertaken to assess potential medical product safety risks, they may also be initiated for various other reasons. Some examples include determining a rate or count of an identified health outcome of interest, examining medical product use, exploring the feasibility of future, more detailed analyses within Sentinel, and seeking to better understand Sentinel capabilities.

Data obtained through Sentinel are intended to complement other types of evidence such as preclinical studies, clinical trials, postmarket studies, and adverse event reports, all of which are used by FDA to inform regulatory decisions regarding medical product safety. The information contained in this report is provided as part of FDA's commitment to place knowledge acquired from Sentinel in the public domain as soon as possible. Any public health actions taken by FDA regarding products involved in Sentinel queries will continue to be communicated through existing channels.

FDA wants to emphasize that the fact that FDA has initiated a query involving a medical product and is reporting findings related to that query does not mean that FDA is suggesting health care practitioners should change their prescribing practices for the medical product or that patients taking the medical product should stop using it. Patients who have questions about the use of an identified medical product should contact their health care practitioners.

The following report contains a description of the request, request specifications, and results from the modular program run(s).

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## Overview for Request cder\_mpl1r\_wp014\_nsdp\_v01, Report 8 of 8

**Request ID:** cder\_mpl1r\_wp014\_nsdp\_v01. This is report 8 of 8.

**Request Description:** FDA has requested execution of the Cohort Identification and Descriptive Analysis (CIDA) tool, version 2.1.1, to investigate heart failure diagnoses following new use of attention deficit hyperactivity disorder (ADHD) medications. This report presents results for Strattera. Results for all methylphenidates, all amphetamines, and all stimulants are presented in separate reports.

**Data Source:** Data from January 1, 2000 to March 3, 2016 from 15 health plans contributing to the Sentinel Distributed Database (SDD) are included in this report.

**Study Design:** This request was designed to identify exposures and follow-up time. The exposure of interest and the occurrence of the health outcome of interest during exposed time were identified. The number of exposure episodes, number of individuals, number of events, and days at-risk in the SDD were calculated overall and were stratified by age group, sex, and year.

**Exposure of Interest:** The exposure of interest was Strattera, which was defined using National Drug Codes (NDCs). Please refer to Appendix A for generic and brand names of Strattera.

**Cohort Eligibility Criteria:** Patients were required to be continuously enrolled in plans with both medical and drug coverage for at least 6 months (183 days) before their dispensing date, during which gaps in coverage of up to 45 days were allowed. Members were excluded if they had any ADHD medication or the outcome of interest in the 6 months (183 days) prior to exposure initiation. The following age groups were included in the cohort: 0-21, 22-44, 45-64, 65+ years.

**Follow-Up Time:** Follow-up time for the outcome was determined by the length of the exposure episodes. Exposure episode lengths were defined using outpatient pharmacy dispensing days supplied to create a sequence of continuous exposure. Exposure episodes were considered continuous if gaps in days supply were less than 90 days. The end date of each exposure episode was extended by 90 additional days. Follow-up began on the day on which the first exposure of interest was dispensed and continued until the first occurrence of any of the following: 1) the outcome of interest; 2) any codes defining incidence criteria; 3) disenrollment; 4) the study end date (March, 2016); 5) the end date of the data provided by each Data Partner; or 6) the end of the exposure episode. Only the first valid incident exposure episode that occurred during the study period was included per patient.

This report examines different blackout periods which is a number of days at the beginning of the ADHD medication episode where if an outcome occurs, it is not attributed to the exposure and the person is omitted from the analysis. The blackout periods examined were 90 days, 180 days, 270 days, 365 days, 730 days, and 1,095 days. Episodes that were at least as long as the blackout period were required.

**Outcome of Interest:** Heart failure was defined using the ICD-9-CM diagnosis codes listed in Appendix B. The event needed to meet one of the following criteria: (1) at least one code in the inpatient setting with primary diagnosis flag = Primary, OR (2) at least three codes in the inpatient setting with primary diagnosis flag = Secondary, OR (3) at least two codes in the outpatient setting with any primary diagnosis flag value, OR (4) at least three codes in the emergency department setting with any primary diagnosis flag value, OR (5) at least two codes in the inpatient setting with primary diagnosis flag = Secondary and at least one code in the outpatient with any primary diagnosis flag value. The temporal relationship between codes will be 365 days. This event had to be incident (no heart failure events in the 183 days prior to exposure initiation).

**Please refer to Appendix C for detailed specifications.**

**Limitations:** Algorithms to define exposures and outcomes are imperfect and, therefore, may be misclassified.

**Notes:** Please contact the Sentinel Operations Center Query Fulfillment Team ([production@mini-sentinel.org](mailto:production@mini-sentinel.org)) for questions and to provide comments/suggestions for future enhancements to this document.

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**Glossary of Terms for Analyses Using  
Cohort Identification and Descriptive Analysis (CIDA) Tool\***

**Amount Supplied** - number of units (pills, tablets, vials) dispensed. Net amount per NDC per dispensing. This is equivalent to the "RxAmt" value in the MSCDM.

**Blackout Period** - number of days at the beginning of a treatment episode that events are to be ignored. If an event occurs during the blackout period, the episode is excluded.

**Care Setting** - type of medical encounter or facility where the exposure, event, or condition code was recorded. Possible care settings include: Inpatient Hospital Stay (IP), Non-Acute Institutional Stay (IS), Emergency Department (ED), Ambulatory Visit (AV), and Other Ambulatory Visit (OA). For laboratory results, possible care settings include: Emergency department (E), Home (H), Inpatient (I), Outpatient (O), or Unknown or Missing (U). Along with the Principal Diagnosis Indicator, forms the Care Setting/PDX parameter.

**Cohort Definition (drug/exposure)** - indicates how the cohort will be defined: (1) 01: Cohort includes only the first valid incident treatment episode during the query period; (2) 02: Cohort includes all valid incident treatment episodes during the query period; (3) 03: Cohort includes all valid incident treatment episodes during the query period until an event

**Days Supplied** - number of days supplied for all dispensings in qualifying treatment episodes.

**Eligible Members** - number of members eligible for an incident treatment episode (defined by the drug/exposure and event washout periods) with drug and medical coverage during the query period.

**Enrollment Gap** - number of days allowed between two consecutive enrollment periods without breaking a "continuously enrolled" sequence.

**Episodes** - treatment episodes; length of episode is determined by days supplied in one dispensing or consecutive dispensings bridged by the episode gap.

**Episode Gap** - number of days allowed between two (or more) consecutive exposures (dispensings/procedures) to be considered the same treatment episode.

**Event Deduplication** - specifies how events are counted by the MP algorithm: (0) 0: Counts all occurrences of an HOI during an exposure episode; (1) 1: de-duplicates occurrences of the same HOI code and code type on the same day; (2) 2: de-duplicates occurrences of the same HOI group on the same day (e.g., de-duplicates at the group level).

**Exposure Episode Length** - number of days after exposure initiation that is considered "exposed time."

**Exposure Extension Period** - number of days post treatment period in which the outcomes/events are counted for a treatment episode.

**Lookback Period (pre-existing condition)** - number of days wherein a member is required to have evidence of pre-existing condition (diagnosis/procedure/drug dispensing).

**Member-Years** - sum of all days of enrollment with medical and drug coverage\*\* in the query period preceded by an exposure washout period all divided by **365.25**.

**Minimum Days Supplied** - specifies a minimum number of days in length of the days supplied for the episode to be considered.

**Minimum Episode Duration** - specifies a minimum number of days in length of the episode for it to be considered.

**Principal Diagnosis (PDX)** - diagnosis or condition established to be chiefly responsible for admission of the patient to the hospital. 'P' = principal diagnosis, 'S' = secondary diagnosis, 'X' = unspecified diagnosis, '.' = blank. Along with the Care Setting values, forms the Caresetting/PDX parameter.

**Query Period** - period in which the modular program looks for exposures and outcomes of interest.

**Treatment Episode Truncation Indicator** - indicates whether observation of the incident query code during follow-up requires truncation of valid treatment episodes. A value of Y indicates that the treatment episodes should be truncated at the first occurrence of an incident query code. A value of N indicates that the treatment episodes should not be truncated at the occurrence of the incident query code.

**Users** - number of members with exposure during the query period. Member must have no evidence of exposure(s) of interest (defined by incidence criteria) in the prior washout period. A user may only be counted once in a query period.

**Washout Period (drug/exposure)\*\*** - number of days a user is required to have no evidence of prior exposure (drug dispensing/procedure) and continuous drug and medical coverage prior to an incident treatment episode.

**Washout Period (event/outcome)\*\*** - number of days a user is required to have no evidence of a prior event (procedure/diagnosis) and continuous drug and medical coverage prior to an incident treatment episode.

**Years at Risk** - number of days supplied plus any episode gaps and exposure extension periods all divided by 365.25.

\*all terms may not be used in this report

\*\*incident treatment episodes must be incident to both the exposure and the event



**Table 1a: Summary of Incident Stratterra Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, and Blackout Period**

New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>90-Day Episode Gap/Extension Period</b>													
<b>0-Day Blackout Period</b>													
163,371	163,371	723,434	23,730,387	34,596,810	100,972.7	196	110,296,645	306,504,103.2	1.48	145.25	4.43	32.80	70.81
<b>90-Day Blackout Period</b>													
128,426	128,426	676,623	22,639,144	33,081,562	65,509.8	130	100,830,405	277,301,011.3	1.27	176.28	5.27	33.46	83.35
<b>180-Day Blackout Period</b>													
59,595	59,595	569,710	19,506,042	27,809,625	44,379.5	84	93,687,940	251,191,772.4	0.64	327.31	9.56	34.24	86.98
<b>270-Day Blackout Period</b>													
36,965	36,965	484,282	16,829,777	23,770,112	33,118.4	62	80,172,667	229,166,908.1	0.46	455.29	13.10	34.75	84.55
<b>365-Day Blackout Period</b>													
24,796	24,796	410,722	14,450,230	19,914,724	25,370.5	52	72,200,029	208,186,931.2	0.34	582.76	16.56	35.18	86.32
<b>730-Day Blackout Period</b>													
8,295	8,295	231,240	8,440,014	11,387,425	10,907.4	18	48,917,741	145,840,941.8	0.17	1017.48	27.88	36.50	86.18
<b>1,095-Day Blackout Period</b>													
3,589	3,589	136,640	5,120,419	6,884,626	5,397.8	8	34,449,661	103,828,244.2	0.10	1426.70	38.07	37.47	42.61

**Table 1b: Rate of Heart Failure Outcomes at Different Stages of Strattera Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, and Blackout Period**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>90-Day Episode Gap/Extension Period</b>			
Days 0-90	66	35,463	18.6
Days 91-181	46	21,130	21.8
Days 181-271	22	11,261	19.5
Days 271-366	10	7,748	12.9
Days 366-731	34	14,463	23.5
Days 731-1,096	10	5,510	18.2

**Table 2a: Summary of Incident Strattera Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
00-21 Years	87,890	87,890	418,123	13,464,828	18,966,212	56,994.4	36	33,426,044	84,392,287.5	2.63	153.20	4.76	32.20	6.32
22-44 Years	51,320	51,320	186,251	5,981,965	9,372,105	26,837.3	37	45,809,227	96,181,197.9	1.12	116.56	3.63	32.12	13.79
45-64 Years	22,958	22,958	113,722	4,074,380	5,959,055	16,297.0	96	32,672,363	90,785,270.5	0.70	177.47	4.95	35.83	58.91
65+ Years	1,203	1,203	5,338	209,214	299,438	844.0	27	10,960,190	35,145,347.2	0.11	173.91	4.44	39.19	319.90
<b>90-Day Blackout Period</b>														
00-21 Years	70,226	70,226	394,230	12,915,297	18,212,337	37,759.6	29	30,666,256	76,628,630.2	2.29	183.91	5.61	32.76	7.68
22-44 Years	38,396	38,396	169,440	5,590,919	8,824,158	15,977.0	17	41,152,072	85,549,363.4	0.93	145.61	4.41	33.00	10.64
45-64 Years	18,760	18,760	107,819	3,928,810	5,752,380	11,203.6	64	30,262,221	82,854,341.2	0.62	209.42	5.75	36.44	57.12
65+ Years	1,044	1,044	5,134	204,118	292,687	569.5	20	9,857,924	32,268,676.5	0.11	195.52	4.92	39.76	351.17
<b>180-Day Blackout Period</b>														
00-21 Years	34,499	34,499	336,713	11,235,376	15,313,935	25,830.9	19	28,479,455	69,626,285.6	1.21	325.67	9.76	33.37	7.36
22-44 Years	15,467	15,467	135,002	4,582,247	7,202,984	10,047.7	9	37,571,026	76,219,201.1	0.41	296.26	8.73	33.94	8.96
45-64 Years	9,137	9,137	93,626	3,507,333	5,059,871	8,102.8	41	28,287,460	75,636,175.5	0.32	383.86	10.25	37.46	50.60
65+ Years	492	492	4,369	181,086	232,835	398.1	15	9,305,171	29,710,110.2	0.05	368.06	8.88	41.45	376.75
<b>270-Day Blackout Period</b>														
00-21 Years	21,577	21,577	287,873	9,716,507	13,200,529	19,266.8	10	24,385,609	63,705,042.8	0.88	450.32	13.34	33.75	5.19
22-44 Years	9,045	9,045	110,684	3,824,270	5,905,748	7,215.2	8	31,647,681	68,536,576.0	0.29	422.80	12.24	34.55	11.09
45-64 Years	6,032	6,032	82,075	3,133,474	4,465,822	6,333.9	34	24,639,416	69,449,291.3	0.24	519.48	13.61	38.18	53.68
65+ Years	311	311	3,650	155,526	198,012	302.5	10	8,309,234	27,475,998.0	0.04	500.08	11.74	42.61	330.62
<b>365-Day Blackout Period</b>														
00-21 Years	14,524	14,524	245,185	8,350,981	10,974,913	14,724.5	10	21,974,522	58,050,447.7	0.66	574.98	16.88	34.06	6.79
22-44 Years	5,815	5,815	90,981	3,190,607	4,842,277	5,364.8	7	27,931,467	61,362,198.7	0.21	548.69	15.65	35.07	13.05
45-64 Years	4,236	4,236	71,373	2,771,614	3,924,256	5,044.6	26	22,362,589	63,498,585.7	0.19	654.30	16.85	38.83	51.54
65+ Years	221	221	3,183	137,028	173,278	236.6	9	7,789,787	25,275,699.0	0.03	620.04	14.40	43.05	380.45
<b>730-Day Blackout Period</b>														
00-21 Years	4,841	4,841	138,785	4,846,843	6,235,979	6,195.5	3	14,944,141	40,955,219.6	0.32	1001.21	28.67	34.92	4.84
22-44 Years	1,750	1,750	46,930	1,721,081	2,573,884	2,138.8	4	17,784,743	41,012,880.0	0.10	983.47	26.82	36.67	18.70
45-64 Years	1,617	1,617	43,543	1,781,874	2,467,216	2,460.3	9	15,664,670	45,366,542.9	0.10	1101.96	26.93	40.92	36.58
65+ Years	87	87	1,982	90,216	110,345	112.8	2	5,678,231	18,506,299.4	0.02	1036.97	22.78	45.52	177.24
<b>1,095-Day Blackout Period</b>														
00-21 Years	2,083	2,083	82,093	2,916,677	3,835,919	2,983.2	1	10,532,871	29,272,185.6	0.20	1400.23	39.41	35.53	3.35
22-44 Years	690	690	25,548	975,518	1,331,043	1,026.1	2	11,889,840	28,238,152.8	0.06	1413.79	37.03	38.18	19.49
45-64 Years	768	768	27,657	1,166,257	1,640,745	1,338.7	3	11,300,287	32,726,142.8	0.07	1518.56	36.01	42.17	22.41
65+ Years	48	48	1,342	61,967	76,920	49.9	2	4,240,760	13,591,763.1	0.01	1290.98	27.96	46.18	400.69

**Table 2b: Rate of Heart Failure Outcomes at Different Stages of Strattera Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Age Group**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>90-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
00-21 Years	7	19,235	3.6
22-44 Years	20	10,860	18.4
45-64 Years	32	5,093	62.8
65+ Years	7	274	255.0
<b>Days 91-180</b>			
00-21 Years	10	11,929	8.4
22-44 Years	8	5,929	13.5
45-64 Years	23	3,101	74.2
65+ Years	5	171	291.7
<b>Days 181-270</b>			
00-21 Years	9	6,564	13.7
22-44 Years	1	2,833	3.5
45-64 Years	7	1,769	39.6
65+ Years	5	96	522.6
<b>Days 271-365</b>			
00-21 Years	0	4,542	0.0
22-44 Years	1	1,850	5.4
45-64 Years	8	1,289	62.1
65+ Years	1	66	151.7
<b>Days 366-730</b>			
00-21 Years	7	8,529	8.2
22-44 Years	3	3,226	9.3
45-64 Years	17	2,584	65.8
65+ Years	7	124	565.8
<b>Days 731-1,095</b>			
00-21 Years	2	3,212	6.2
22-44 Years	2	1,113	18.0
45-64 Years	6	1,122	53.5
65+ Years	0	63	0.0

**Table 3a: Summary of Incident Strattera Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
Female	70,083	70,083	304,932	10,057,904	14,810,505	42,891.0	88	56,075,897	158,802,680.1	1.25	143.51	4.35	32.98	20.52
Male	93,278	93,278	418,453	13,671,166	19,784,931	58,077.1	108	54,215,039	147,688,650.6	1.72	146.56	4.49	32.67	18.60
Unknown	10	10	49	1,317	1,374	4.6	0	5,709	12,772.5	1.75	131.70	4.90	26.88	0.00
<b>90-Day Blackout Period</b>														
Female	54,831	54,831	284,685	9,582,978	14,144,649	27,725.1	51	51,333,656	143,902,290.1	1.07	174.77	5.19	33.66	18.39
Male	73,591	73,591	391,897	13,054,980	18,935,702	37,781.5	79	49,491,921	133,387,348.9	1.49	177.40	5.33	33.31	20.91
Unknown	4	4	41	1,186	1,211	3.2	0	4,828	11,372.3	0.83	296.50	10.25	28.93	0.00
<b>180-Day Blackout Period</b>														
Female	25,289	25,289	239,203	8,250,685	11,867,032	18,750.7	30	47,769,583	130,551,681.5	0.53	326.26	9.46	34.49	16.00
Male	34,303	34,303	330,469	11,254,246	15,941,457	25,626.4	54	45,914,195	120,629,886.8	0.75	328.08	9.63	34.06	21.07
Unknown	3	3	38	1,111	1,136	2.4	0	4,162	10,204.0	0.72	370.33	12.67	29.24	0.00
<b>270-Day Blackout Period</b>														
Female	15,675	15,675	203,100	7,119,721	10,006,828	13,984.7	24	40,935,510	119,278,184.1	0.38	454.21	12.96	35.06	17.16
Male	21,288	21,288	281,150	9,709,101	13,762,304	19,131.8	38	39,233,852	109,879,443.8	0.54	456.08	13.21	34.53	19.86
Unknown	2	2	32	955	980	1.8	0	3,305	9,280.2	0.61	477.50	16.00	29.84	0.00
<b>365-Day Blackout Period</b>														
Female	10,487	10,487	172,008	6,105,981	8,434,509	10,709.1	20	36,934,046	108,520,625.8	0.28	582.24	16.40	35.50	18.68
Male	14,308	14,308	238,688	8,343,474	11,479,415	14,659.8	32	35,263,062	99,657,880.4	0.41	583.13	16.68	34.96	21.83
Unknown	1	1	26	775	800	1.6	0	2,921	8,424.9	0.34	775.00	26.00	29.81	0.00
<b>730-Day Blackout Period</b>														
Female	3,533	3,533	96,607	3,580,423	4,815,840	4,601.5	6	25,164,106	76,451,833.1	0.14	1013.42	27.34	37.06	13.04
Male	4,761	4,761	134,607	4,858,816	6,570,785	6,305.4	12	23,751,735	69,383,154.2	0.20	1020.55	28.27	36.10	19.03
Unknown	1	1	26	775	800	0.6	0	1,900	5,954.5	0.53	775.00	26.00	29.81	0.00
<b>1,095-Day Blackout Period</b>														
Female	1,542	1,542	56,683	2,176,544	2,927,755	2,260.3	3	17,825,659	54,718,539.4	0.09	1411.51	36.76	38.40	13.27
Male	2,047	2,047	79,957	2,943,875	3,956,871	3,137.5	5	16,622,676	49,105,396.6	0.12	1438.14	39.06	36.82	15.94
Unknown	0	0	0	0	0	0.0	0	1,326	4,308.3	0.00	---	---	---	---

**Table 3b: Rate of Heart Failure Outcomes at Different Stages of Strattera Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Sex**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>90-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
Female	37	15,166	24.4
Male	29	20,296	14.3
Unknown	0	1	0.0
<b>Days 91-180</b>			
Female	21	8,974	23.4
Male	25	12,155	20.6
Unknown	0	1	0.0
<b>Days 181-270</b>			
Female	6	4,766	12.6
Male	16	6,495	24.6
Unknown	0	1	0.0
<b>Days 271-365</b>			
Female	4	3,276	12.2
Male	6	4,472	13.4
Unknown	0	0	0.0
<b>Days 366-730</b>			
Female	14	6,108	22.9
Male	20	8,354	23.9
Unknown	0	1	0.0
<b>Days 731-1,095</b>			
Female	3	2,341	12.8
Male	7	3,168	22.1
Unknown	0	1	0.0

**Table 4a: Summary of Incident Strattera Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>90-Day Episode Gap/Extension Period</b>														
<b>0-Day Blackout Period</b>														
2000	0	0	0	0	0	0.0	0	6,530,503	3,002,268.1	0.00	---	---	---	---
2001	0	0	0	0	0	0.0	0	7,129,775	5,965,654.8	0.00	---	---	---	---
2002	2	2	2	60	60	0.7	0	7,285,626	6,067,534.3	0.00	30.00	1.00	30.00	0.00
2003	8,639	8,639	57,900	1,873,869	3,895,639	7,433.8	23	7,282,597	6,043,328.3	1.19	216.91	6.70	32.36	30.94
2004	10,255	10,255	56,772	1,917,703	5,954,980	7,855.5	25	7,717,732	6,289,558.1	1.33	187.00	5.54	33.78	31.82
2005	6,386	6,386	30,259	1,073,930	1,604,865	4,485.6	14	7,959,663	6,578,836.0	0.80	168.17	4.74	35.49	31.21
2006	8,555	8,555	41,548	1,421,455	1,993,317	6,002.9	7	19,430,902	11,618,115.6	0.44	166.15	4.86	34.21	11.66
2007	11,886	11,886	58,814	1,979,141	2,566,803	8,306.8	16	23,640,972	17,187,039.2	0.50	166.51	4.95	33.65	19.26
2008	17,448	17,448	77,535	2,558,230	3,213,104	10,997.7	12	44,345,118	28,060,734.2	0.39	146.62	4.44	32.99	10.91
2009	20,355	20,355	90,086	2,959,723	3,622,490	12,692.0	29	45,743,947	35,546,915.2	0.44	145.41	4.43	32.85	22.85
2010	17,410	17,410	77,002	2,528,723	3,004,314	10,824.9	18	43,624,605	34,046,972.6	0.40	145.25	4.42	32.84	16.63
2011	15,623	15,623	68,403	2,234,131	2,657,071	9,545.7	12	42,239,608	33,261,809.2	0.37	143.00	4.38	32.66	12.57
2012	14,473	14,473	61,113	1,980,312	2,331,294	8,599.4	18	41,236,346	32,598,487.7	0.35	136.83	4.22	32.40	20.93
2013	13,781	13,781	53,384	1,689,339	1,969,162	7,477.5	17	41,116,696	32,291,797.0	0.34	122.58	3.87	31.65	22.73
2014	13,354	13,354	40,699	1,242,179	1,447,962	5,622.6	5	42,066,072	32,180,374.6	0.32	93.02	3.05	30.52	8.89
2015	5,204	5,204	9,917	271,592	335,748	1,127.7	0	34,634,041	15,764,678.2	0.15	52.19	1.91	27.39	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>90-Day Blackout Period</b>														
2000	0	0	0	0	0	0.0	0	6,279,504	2,830,510.6	0.00	---	---	---	---
2001	0	0	0	0	0	0.0	0	6,797,427	5,686,620.7	0.00	---	---	---	---
2002	2	2	2	60	60	0.2	0	6,964,071	5,761,361.1	0.00	30.00	1.00	30.00	0.00
2003	7,368	7,368	55,993	1,829,618	3,836,795	5,464.7	15	6,916,170	5,745,623.8	1.07	248.32	7.60	32.68	27.45
2004	8,849	8,849	54,742	1,869,886	5,765,836	5,513.3	19	7,436,535	5,995,147.6	1.19	211.31	6.19	34.16	34.46
2005	5,448	5,448	28,980	1,043,593	1,559,065	3,044.7	9	7,588,772	6,210,468.8	0.72	191.56	5.32	36.01	29.56
2006	6,984	6,984	39,513	1,374,872	1,926,123	4,118.0	5	18,312,723	10,900,699.6	0.38	196.86	5.66	34.80	12.14
2007	9,791	9,791	56,087	1,915,953	2,482,363	5,678.0	10	22,159,284	16,129,190.6	0.44	195.69	5.73	34.16	17.61
2008	13,722	13,722	72,559	2,443,061	3,064,082	7,208.5	10	41,901,979	25,812,969.0	0.33	178.04	5.29	33.67	13.87
2009	16,086	16,086	84,394	2,825,148	3,451,622	8,260.2	20	42,539,619	32,704,522.1	0.38	175.63	5.25	33.48	24.21
2010	13,684	13,684	72,129	2,412,975	2,860,074	7,047.7	10	40,778,950	31,438,669.4	0.34	176.34	5.27	33.45	14.19
2011	12,224	12,224	64,003	2,130,833	2,527,193	6,169.5	9	39,684,320	30,816,372.4	0.31	174.32	5.24	33.29	14.59
2012	11,370	11,370	57,034	1,884,373	2,211,073	5,457.7	12	39,288,525	30,320,128.4	0.29	165.73	5.02	33.04	21.99
2013	10,844	10,844	49,597	1,601,927	1,860,710	4,493.5	8	38,595,111	29,868,530.1	0.28	147.72	4.57	32.30	17.80
2014	10,172	10,172	36,382	1,142,725	1,329,850	2,765.9	3	39,216,777	29,341,672.2	0.26	112.34	3.58	31.41	10.85
2015	1,882	1,882	5,208	164,120	206,717	287.9	0	23,104,096	7,738,524.7	0.08	87.21	2.77	31.51	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>180-Day Blackout Period</b>														
2000	0	0	0	0	0	0.0	0	6,014,580	2,679,165.4	0.00	---	---	---	---
2001	0	0	0	0	0	0.0	0	6,571,074	5,430,487.6	0.00	---	---	---	---
2002	0	0	0	0	0	0.0	0	6,690,149	5,474,093.9	0.00	---	---	---	---
2003	4,034	4,034	50,620	1,677,006	3,617,244	4,130.9	9	6,665,051	5,480,800.5	0.61	415.72	12.55	33.13	21.79
2004	4,673	4,673	48,140	1,676,140	4,235,086	3,941.6	16	7,102,431	5,729,712.9	0.66	358.69	10.30	34.82	40.59
2005	2,640	2,640	25,135	931,151	1,391,668	2,162.6	6	7,326,016	5,877,457.8	0.36	352.71	9.52	37.05	27.74
2006	3,359	3,359	34,069	1,209,880	1,690,758	2,925.1	2	17,603,868	10,257,974.3	0.19	360.19	10.14	35.51	6.84
2007	4,684	4,684	48,139	1,681,725	2,172,988	4,024.8	5	21,062,884	15,183,129.0	0.22	359.04	10.28	34.93	12.42

**Table 4a: Summary of Incident Strattera Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member- Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
2008	6,284	6,284	61,274	2,106,086	2,631,909	4,962.9	7	39,229,165	23,797,775.5	0.16	335.15	9.75	34.37	14.10
2009	7,411	7,411	71,131	2,430,585	2,956,997	5,593.5	15	40,502,501	30,140,522.5	0.18	327.97	9.60	34.17	26.82
2010	6,355	6,355	61,171	2,090,827	2,462,353	4,818.4	6	38,869,493	29,105,602.7	0.16	329.01	9.63	34.18	12.45
2011	5,644	5,644	54,191	1,845,376	2,174,410	4,199.2	7	37,900,900	28,594,936.4	0.15	326.96	9.60	34.05	16.67
2012	5,314	5,314	48,371	1,633,957	1,898,306	3,634.5	6	37,048,521	28,245,834.5	0.14	307.48	9.10	33.78	16.51
2013	4,906	4,906	40,774	1,349,063	1,556,998	2,759.9	5	36,913,549	27,651,961.4	0.13	274.98	8.31	33.09	18.12
2014	3,884	3,884	24,733	806,329	936,443	1,172.7	0	36,486,049	23,921,333.2	0.11	207.60	6.37	32.60	0.00
2015	407	407	1,962	67,917	84,465	53.3	0	13,690,820	3,620,984.8	0.03	166.87	4.82	34.62	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>270-Day Blackout Period</b>														
2000	0	0	0	0	0	0.0	0	5,575,360	2,587,781.7	0.00	---	---	---	---
2001	0	0	0	0	0	0.0	0	6,252,846	5,197,079.4	0.00	---	---	---	---
2002	0	0	0	0	0	0.0	0	6,343,417	5,220,753.5	0.00	---	---	---	---
2003	2,811	2,811	45,714	1,527,325	3,406,039	3,300.9	6	6,289,860	5,247,858.5	0.45	543.34	16.26	33.41	18.18
2004	3,069	3,069	42,167	1,486,541	3,298,411	3,018.2	14	6,701,713	5,493,931.1	0.46	484.37	13.74	35.25	46.39
2005	1,567	1,567	21,361	808,681	1,215,656	1,680.1	5	6,863,429	5,586,040.8	0.23	516.07	13.63	37.86	29.76
2006	2,131	2,131	29,709	1,073,570	1,502,489	2,285.5	1	16,161,693	9,768,723.8	0.13	503.79	13.94	36.14	4.38
2007	2,965	2,965	41,935	1,483,273	1,913,632	3,122.0	3	19,573,644	14,373,257.3	0.15	500.26	14.14	35.37	9.61
2008	3,904	3,904	52,421	1,831,045	2,282,945	3,764.4	6	35,082,434	22,338,316.8	0.11	469.02	13.43	34.93	15.94
2009	4,586	4,586	60,667	2,103,305	2,548,881	4,201.5	9	37,008,199	27,978,468.6	0.12	458.64	13.23	34.67	21.42
2010	4,022	4,022	52,601	1,822,563	2,138,509	3,620.1	5	35,589,884	27,139,004.6	0.11	453.15	13.08	34.65	13.81
2011	3,527	3,527	46,534	1,601,534	1,881,095	3,151.8	5	34,784,026	26,699,413.0	0.10	454.08	13.19	34.42	15.86
2012	3,361	3,361	41,184	1,411,121	1,634,531	2,635.9	5	33,950,589	26,531,827.9	0.10	419.85	12.25	34.26	18.97
2013	3,100	3,100	33,992	1,140,321	1,313,633	1,826.2	3	33,932,314	25,718,738.2	0.09	367.85	10.97	33.55	16.43
2014	1,879	1,879	15,760	530,019	619,667	507.5	0	32,109,032	18,248,077.1	0.06	282.08	8.39	33.63	0.00
2015	43	43	237	10,479	14,625	4.5	0	9,167,721	1,037,635.6	0.00	243.70	5.51	44.22	0.00
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>365-Day Blackout Period</b>														
2000	0	0	0	0	0	0.0	0	5,330,912	2,500,414.1	0.00	---	---	---	---
2001	0	0	0	0	0	0.0	0	5,792,403	4,955,275.2	0.00	---	---	---	---
2002	0	0	0	0	0	0.0	0	5,850,477	4,983,683.1	0.00	---	---	---	---
2003	2,050	2,050	41,006	1,379,795	2,857,730	2,673.7	5	5,875,089	5,021,687.7	0.35	673.07	20.00	33.65	18.70
2004	2,128	2,128	36,275	1,296,898	2,492,078	2,350.2	14	6,418,562	5,253,736.6	0.33	609.44	17.05	35.75	59.57
2005	999	999	17,995	698,075	1,054,571	1,356.7	4	6,250,912	5,312,459.8	0.16	698.77	18.01	38.79	29.48
2006	1,470	1,470	25,984	951,282	1,329,272	1,836.1	1	15,001,358	9,294,815.5	0.10	647.13	17.68	36.61	5.45
2007	2,073	2,073	36,793	1,315,725	1,697,938	2,493.0	1	17,955,608	13,595,906.9	0.12	634.70	17.75	35.76	4.01
2008	2,627	2,627	44,961	1,591,481	1,983,594	2,958.8	5	32,709,950	20,942,115.7	0.08	605.82	17.11	35.40	16.90
2009	3,082	3,082	51,811	1,813,460	2,196,012	3,241.2	6	32,223,368	25,877,095.6	0.10	588.40	16.81	35.00	18.51
2010	2,732	2,732	45,020	1,576,057	1,849,340	2,777.1	5	31,249,080	25,268,709.7	0.09	576.89	16.48	35.01	18.00
2011	2,424	2,424	40,028	1,388,942	1,627,569	2,408.8	4	30,616,661	24,851,175.7	0.08	573.00	16.51	34.70	16.61
2012	2,308	2,308	34,849	1,207,820	1,399,266	1,925.4	4	32,225,775	24,857,476.1	0.07	523.32	15.10	34.66	20.78
2013	2,105	2,105	27,961	946,955	1,090,077	1,173.6	3	29,654,200	23,824,742.1	0.07	449.86	13.28	33.87	25.56
2014	798	798	8,039	283,740	337,276	175.9	0	24,904,783	11,647,637.2	0.03	355.56	10.07	35.30	0.00
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---



**Table 4a: Summary of Incident Strattera Use and Heart Failure Outcomes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Users	New Episodes	Dispensings	Days Supplied	Amount Supplied	Years at Risk	New Episodes w/ Events	Eligible Members	Member-Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	New Episodes w/ Events / 10K Years at Risk
<b>730-Day Blackout Period</b>														
2000	0	0	0	0	0	0.0	0	4,503,593	2,119,747.1	0.00	---	---	---	---
2001	0	0	0	0	0	0.0	0	4,827,583	4,189,894.8	0.00	---	---	---	---
2002	0	0	0	0	0	0.0	0	4,898,157	4,262,794.9	0.00	---	---	---	---
2003	842	842	26,953	930,446	1,568,939	1,330.7	3	5,060,586	4,310,548.3	0.17	1105.04	32.01	34.52	22.54
2004	658	658	19,721	754,938	1,411,486	1,118.9	5	5,343,242	4,345,829.8	0.12	1147.32	29.97	38.28	44.69
2005	370	370	11,489	471,563	708,719	751.5	2	5,249,109	4,547,105.0	0.07	1274.49	31.05	41.04	26.61
2006	560	560	16,687	632,794	890,056	937.5	0	12,162,225	7,729,601.5	0.05	1129.99	29.80	37.92	0.00
2007	774	774	23,069	853,107	1,107,401	1,231.8	0	14,587,465	10,897,821.9	0.05	1102.21	29.80	36.98	0.00
2008	970	970	27,360	1,001,297	1,239,102	1,373.8	3	24,273,605	16,138,139.8	0.04	1032.26	28.21	36.60	21.84
2009	1,082	1,082	30,767	1,100,713	1,334,595	1,437.0	2	24,014,752	19,877,735.9	0.05	1017.29	28.44	35.78	13.92
2010	954	954	26,087	935,635	1,093,042	1,172.6	1	23,615,570	19,518,839.8	0.04	980.75	27.34	35.87	8.53
2011	911	911	23,650	842,635	968,419	927.2	0	24,895,778	19,699,545.5	0.04	924.96	25.96	35.63	0.00
2012	841	841	19,028	679,925	786,632	537.7	2	24,678,078	18,965,499.5	0.03	808.47	22.63	35.73	37.19
2013	333	333	6,429	236,961	279,034	88.6	0	19,032,258	9,237,838.0	0.02	711.59	19.31	36.86	0.00
2014	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
<b>1,095-Day Blackout Period</b>														
2000	0	0	0	0	0	0.0	0	3,851,156	1,825,130.7	0.00	---	---	---	---
2001	0	0	0	0	0	0.0	0	4,142,586	3,648,176.4	0.00	---	---	---	---
2002	0	0	0	0	0	0.0	0	4,312,739	3,721,868.4	0.00	---	---	---	---
2003	389	389	17,336	617,683	1,035,342	761.5	1	4,312,579	3,611,202.4	0.09	1587.87	44.57	35.63	13.13
2004	326	326	13,147	518,279	821,126	649.5	3	4,514,016	3,786,088.3	0.07	1589.81	40.33	39.42	46.19
2005	196	196	8,152	346,091	504,811	484.0	1	4,547,527	3,975,643.2	0.04	1765.77	41.59	42.45	20.66
2006	279	279	11,331	439,893	617,916	547.7	0	9,956,630	6,466,171.6	0.03	1576.68	40.61	38.82	0.00
2007	397	397	15,590	592,717	770,011	686.9	0	11,789,390	9,011,740.0	0.03	1492.99	39.27	38.02	0.00
2008	448	448	17,059	636,605	785,518	710.3	1	18,836,554	13,007,604.5	0.02	1420.99	38.08	37.32	14.08
2009	492	492	19,308	695,188	858,194	713.2	1	18,699,460	15,734,958.9	0.03	1412.98	39.24	36.01	14.02
2010	458	458	16,275	592,682	700,414	508.5	1	19,812,092	15,915,695.8	0.02	1294.07	35.53	36.42	19.67
2011	430	430	13,900	502,160	575,602	290.3	0	19,762,591	15,429,962.2	0.02	1167.81	32.33	36.13	0.00
2012	174	174	4,542	179,121	215,693	45.9	0	17,150,175	7,694,001.9	0.01	1029.43	26.10	39.44	0.00
2013	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2014	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2015	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---
2016	0	0	0	0	0	0.0	0	0	0.0	---	---	---	---	---

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Strattera Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
<b>90-Day Episode Gap/Extension Period</b>			
<b>Days 0-90</b>			
2000	0	0	---
2001	0	0	---
2002	0	0	0.0
2003	8	1,969	40.6
2004	6	2,342	25.6
2005	5	1,441	34.7
2006	2	1,885	10.6
2007	6	2,629	22.8
2008	2	3,789	5.3
2009	9	4,432	20.3
2010	8	3,777	21.2
2011	3	3,376	8.9
2012	6	3,142	19.1
2013	9	2,984	30.2
2014	2	2,857	7.0
2015	0	840	0.0
2016	0	0	---
<b>Days 91-180</b>			
2000	0	0	---
2001	0	0	---
2002	0	0	0.0
2003	6	1,334	45.0
2004	3	1,572	19.1
2005	3	882	34.0
2006	3	1,193	25.1
2007	5	1,653	30.2
2008	3	2,246	13.4
2009	5	2,667	18.7
2010	4	2,229	17.9
2011	2	1,970	10.2
2012	6	1,823	32.9
2013	3	1,734	17.3
2014	3	1,593	18.8
2015	0	235	0.0
2016	0	0	---
<b>Days 181-270</b>			

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Strattera Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
2000	0	0	---
2001	0	0	---
2002	0	0	---
2003	3	830	36.1
2004	2	923	21.7
2005	1	483	20.7
2006	1	640	15.6
2007	2	903	22.2
2008	1	1,199	8.3
2009	6	1,392	43.1
2010	1	1,198	8.3
2011	2	1,047	19.1
2012	1	999	10.0
2013	2	934	21.4
2014	0	665	0.0
2015	0	49	0.0
2016	0	0	---
<b>Days 271-365</b>			
2000	0	0	---
2001	0	0	---
2002	0	0	---
2003	1	627	15.9
2004	0	668	0.0
2005	1	323	30.9
2006	0	449	0.0
2007	2	629	31.8
2008	1	806	12.4
2009	3	960	31.2
2010	0	843	0.0
2011	1	743	13.5
2012	1	710	14.1
2013	0	653	0.0
2014	0	332	0.0
2015	0	4	0.0
2016	0	0	---
<b>Days 366-730</b>			
2000	0	0	---
2001	0	0	---

**Table 4b: Rate of Heart Failure Outcomes at Different Stages of Strattera Exposure Episodes in the Sentinel Distributed Database between January 1, 2000 and March 3, 2016, by Exposure, Episode Gap/Exposure Extension Period, Blackout Period, and Year**

	New Episodes with Events	Years at Risk	New Episodes with Events per 10,000 Years at Risk
2002	0	0	---
2003	2	1,343	14.9
2004	9	1,231	73.1
2005	2	605	33.0
2006	1	899	11.1
2007	1	1,261	7.9
2008	2	1,585	12.6
2009	4	1,804	22.2
2010	4	1,605	24.9
2011	4	1,482	27.0
2012	2	1,388	14.4
2013	3	1,085	27.6
2014	0	176	0.0
2015	0	0	---
2016	0	0	---
<b>Days 731-1,095</b>			
2000	0	0	---
2001	0	0	---
2002	0	0	---
2003	2	569	35.1
2004	2	469	42.6
2005	1	267	37.4
2006	0	390	0.0
2007	0	545	0.0
2008	2	664	30.1
2009	1	724	13.8
2010	0	664	0.0
2011	0	637	0.0
2012	2	492	40.7
2013	0	89	0.0
2014	0	0	---
2015	0	0	---
2016	0	0	---

**Appendix A: List of Generic and Brand Names Used To Define the Exposures and Exposure Incidence in this Request**

Generic Name	Brand Name
<b>Amphetamines</b>	
DEXTROAMPHETAMINE SULFATE	Dexedrine Spansule
DEXTROAMPHETAMINE SULFATE	dextroamphetamine
DEXTROAMPHETAMINE SULFATE	Dexedrine
DEXTROAMPHETAMINE SULFATE	DextroStat
DEXTROAMPHETAMINE SULFATE	Zenzedi
DEXTROAMPHETAMINE SULFATE	ProCentra
DEXTROAMPHETAMINE SULFATE	Liquadd
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	Amphetamine Salt Combo
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	Adderall XR
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	Adderall
DEXTROAMPHETAMINE SULF-SACCHARATE/AMPHETAMINE SULF-ASPARTATE	dextroamphetamine-amphetamine
LISDEXAMFETAMINE DIMESYLATE	Vyvanse
METHAMPHETAMINE HCL	Desoxyn
AMPHETAMINE SULFATE	Evekeo
METHAMPHETAMINE HCL	methamphetamine
<b>Methylphenidates</b>	
DEXMETHYLPHENIDATE HCL	dexmethylphenidate
DEXMETHYLPHENIDATE HCL	Focalin XR
DEXMETHYLPHENIDATE HCL	Focalin
METHYLPHENIDATE HCL	Methylin
METHYLPHENIDATE HCL	Ritalin LA
METHYLPHENIDATE HCL	methylphenidate
METHYLPHENIDATE HCL	Concerta
METHYLPHENIDATE HCL	Metadate CD
METHYLPHENIDATE HCL	Aptensio XR
METHYLPHENIDATE HCL	Ritalin
METHYLPHENIDATE HCL	Ritalin SR
METHYLPHENIDATE HCL	Metadate ER
METHYLPHENIDATE HCL	Quillivant XR
METHYLPHENIDATE HCL	Methylin ER
<b>Strattera</b>	
ATOMOXETINE HCL	Strattera

**Appendix B: Codes Used to Define Heart Failure in this Request**


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Code	Code Type	Description
398.91	ICD-9-CM Diagnosis	Rheumatic heart failure (congestive)
402.01	ICD-9-CM Diagnosis	Malignant hypertensive heart disease with heart failure
402.11	ICD-9-CM Diagnosis	Benign hypertensive heart disease with heart failure
402.91	ICD-9-CM Diagnosis	Unspecified hypertensive heart disease with heart failure
404.01	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.03	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic kidney disease stage V or end stage renal disease
404.11	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, benign, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.13	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, benign, with heart failure and chronic kidney disease stage V or end stage renal disease
404.91	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, unspecified, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified
404.93	ICD-9-CM Diagnosis	Hypertensive heart and chronic kidney disease, unspecified, with heart failure and chronic kidney disease stage V or end stage renal disease
422.90	ICD-9-CM Diagnosis	Acute myocarditis, unspecified
425.4	ICD-9-CM Diagnosis	Other primary cardiomyopathies
425.9	ICD-9-CM Diagnosis	Secondary cardiomyopathy, unspecified
428	ICD-9-CM Diagnosis	Heart Failure
428.0	ICD-9-CM Diagnosis	Congestive heart failure, unspecified
428.1	ICD-9-CM Diagnosis	Left heart failure
428.2	ICD-9-CM Diagnosis	Systolic heart failure
428.20	ICD-9-CM Diagnosis	Systolic heart failure, unspecified
428.21	ICD-9-CM Diagnosis	Acute systolic heart failure
428.22	ICD-9-CM Diagnosis	Chronic systolic heart failure
428.23	ICD-9-CM Diagnosis	Acute on chronic systolic heart failure
428.3	ICD-9-CM Diagnosis	Diastolic heart failure
428.30	ICD-9-CM Diagnosis	Diastolic heart failure, unspecified
428.31	ICD-9-CM Diagnosis	Acute diastolic heart failure
428.32	ICD-9-CM Diagnosis	Chronic diastolic heart failure
428.33	ICD-9-CM Diagnosis	Acute on chronic diastolic heart failure
428.4	ICD-9-CM Diagnosis	Combined systolic and diastolic heart failure
428.40	ICD-9-CM Diagnosis	Combined systolic and diastolic heart failure, unspecified
428.41	ICD-9-CM Diagnosis	Acute combined systolic and diastolic heart failure
428.42	ICD-9-CM Diagnosis	Chronic combined systolic and diastolic heart failure
428.43	ICD-9-CM Diagnosis	Acute on chronic combined systolic and diastolic heart failure
428.9	ICD-9-CM Diagnosis	Heart failure, unspecified

**Modular Program Specifications for cder\_mpl1r\_wp014\_nsdp\_v01 Report 8 of 8**

Sentinel's Cohort Identification and Descriptive Analysis (CIDA) tool was used to investigate heart failure following treatment with select attention deficit and hyperactivity disorder (ADHD) medications. In total, 49 scenarios were examined with four different exposures, seven different blackout periods, and two different episode gaps/exposure extension periods. The four exposures are all amphetamines, all methylphenidates, strattera, and all stimulants (which include all amphetamines, all methylphenidates, and strattera). **The outcome is heart failure, defined as any heart failure ICD-9-CM diagnosis code (398.91, 402.x1, 402.x3, 404.x1, 404.x3, 422.90, 425.4, 425.9, 428.xx) in any care setting with a primary discharge diagnosis (PDX) value of P (principal) for those diagnoses in the inpatient care setting.** See below for a description of each of these scenarios. The query period was from January 1, 2000 to March 3, 2016 and the enrollment gap was set at 45 days. Age groups were split as follows: 0-21, 22-44, 45-64, 65+.

Enrollment Gap	45 Days
Age Groups	0-21, 22-44, 45-64, 65+
Query Period	January 1, 2000 - Current
Coverage Requirement	Medical and Drug
Enrollment Requirement	183 Days

Scenario	Drug/Exposure										Event/Outcome					
	Incident exposure	Incident w/ respect to:	Episode Truncation at Incident Exposure	Episode Truncation at Death	Washout (days)	Cohort Definition	Episode Gap	Exposure Extension Period	Min Episode Duration	Min Days Supplied	Event/ Outcome	Care Setting/PDX	Incident with Respect to	Incident w/ respect to Care Setting/PDX	Washout (days)	Blackout Period
1	Stratera	All Stimulants	Yes	No	183	01	90	90	0	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	0
2	Stratera	All Stimulants	Yes	No	183	01	90	90	90	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	90
3	Stratera	All Stimulants	Yes	No	183	01	90	90	180	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	180
4	Stratera	All Stimulants	Yes	No	183	01	90	90	270	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	270
5	Stratera	All Stimulants	Yes	No	183	01	90	90	365	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	365
6	Stratera	All Stimulants	Yes	No	183	01	90	90	730	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	730
7	Stratera	All Stimulants	Yes	No	183	01	90	90	1095	0	Heart Failure Algorithm*	See algorithm*	Heart Failure Algorithm*	See algorithm*	183	1095

ICD-9, ICD-10, HCPCS, and CPT codes are provided by Optum360. NDC codes are checked against First Data Bank's "National Drug Data File (NDDF\*) Plus."

Cohort Definition of 01 will only consider the first incident episode for each user during the query period that satisfies the washout period.

Note: Episodes are automatically truncated at outcome.

\*Codes in the algorithm include: 398.91, 402.x1, 402.x3, 404.x1, 404.x3, 422.90, 425.4, 425.9, 428.xx. Algorithm will look for at least one of five things: (1) at least one IP code with PDX flag = P, OR (2) at least three IP codes with PDX flag = S, OR (3) at least two AV\*/OA\* codes with any PDX flag value, OR (4) at least three ED\* codes with any PDX flag value, OR (5) at least two IP codes with PDX flag = S and at least one AV\*/OA\* code with any PDX flag value. The temporal relationship between codes will be 365 days. For example, for at least two AV\*/OA\* codes with any PDX flag value, we would find one code and then look for a second within 365 days of the first. For at least three IP codes with PDX flag = S, we would find one code, and then look for a second within 365 days of the first, and then look for a third within 365 days of the first. The date of the first of the one, two, or three codes will be used as the event date. This is important because episodes are truncated on occurrence of the event.