



Modular Program Report

The following report(s) provides findings from an FDA-initiated query using its Mini-Sentinel pilot. While Mini-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 Mini-Sentinel, and seeking to better understand the capabilities of the Mini-Sentinel pilot.

Data obtained through Mini-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 the Mini-Sentinel pilot in the public domain as soon as possible. Any public health actions taken by FDA regarding products involved in Mini-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	
<u>Request Description</u>	<p>FDA requested execution of Modular Program #3 (MP3), version 4.0, to investigate use of several anti-epileptic drug products (AEDs) and diagnosis of kidney stones (see Appendix A). Due to the large list of exposure codes, a code list for AEDs is not provided in this report. Please contact the Mini-Sentinel Operations Center (MSOC_Requests@harvardpilgrim.org) for a list of exposure codes. Each product was analyzed by two unique incidence definitions and two unique kidney stone definitions. Incidence was defined with respect to a specified list of AEDs as well as incidence with respect to the drug of interest, acetazolamide, topiramate, and zonisamide only. Kidney stone events were defined with the list of codes in Appendix A: one definition including ICD-9-CM diagnosis code 788.0, the other excluding ICD-9-CM diagnosis code 788.0. The query was run against the Mini-Sentinel Distributed Database (MSDD) for the time period of January 1, 2004 to December 31, 2012. This request was distributed to 18 Mini-Sentinel Data Partners on April 26, 2013.</p> <p>This report presents results for carbamazepine, oxcarbazepine, and zonisamide. Separate reports present results for lamotrigine, levetiracetam, and topiramate (MSY4_MPR29_V1, Report 1 of 3) and gabapentin and phenytoin (MSY4_MPR29_V1, Report 3 of 3).</p> <p>Results provide counts of new AED users, total dispensings, new episodes, days supplied, days at risk (days supplied + any episode gap days + any episode extension days), kidney stone events, eligible members, and member-days.</p>
<u>Request ID</u>	msy4_mpr29_v1 Report 2 of 3

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<u>Notes:</u>	Please contact the Mini-Sentinel Operations Center (MSOC_Requests@harvardpilgrim.org) for questions and to provide comments/suggestions for future enhancements to this document

Modular Program Specifications MSY4_MPR29_V1

Modular Program #3, version 4.0, was used to investigate exposure to antiepileptic drugs (AEDs) and kidney stone events. The query period was from January 1, 2004 to December 31, 2012. The enrollment gap was set at 45 days, and age groups were split as follows: 0-<2, 2-<5, 5-<10, 10-<17, 17-<40, 40-<65, 65+ years. In total, 12 different scenarios with differing exposures of interest, incidence definitions, and event definitions were examined in this report.

Drug/Exposure								Event/Outcome									
Incident exposure	Incident w/ respect to:	Washout (days)	Incidence Type	Episode Gap	Exposure Extension Period	Min. Episode Duration	Min. Days Supplied	Event/ Outcome	Care Setting	Principal Dx	Event incident w/ respect to:	Incident Only Care Setting	Washout (days)	Incidence Type	Incident Only Principal Dx	Blackout Period	
IVIG																	
1	carbamazepine	All AEDs	183	Single	10	10	0	0	Kidney stones	All	NO	Kidney stones	All	183	Multiple	NO	0
2	carbamazepine	All AEDs	183	Single	10	10	0	0	Kidney stones except 788.0	All	NO	Kidney stones except 788.0	All	183	Multiple	NO	0
3	carbamazepine	carbamazepine, topiramate, zonisamide, acetazolamide	183	Single	10	10	0	0	Kidney stones	All	NO	Kidney stones	All	183	Multiple	NO	0
4	carbamazepine	carbamazepine, topiramate, zonisamide, acetazolamide	183	Single	10	10	0	0	Kidney stones except 788.0	All	NO	Kidney stones except 788.0	All	183	Multiple	NO	0
5	oxcarbazepine	All AEDs	183	Single	10	10	0	0	Kidney stones	All	NO	Kidney stones	All	183	Multiple	NO	0
6	oxcarbazepine	All AEDs	183	Single	10	10	0	0	Kidney stones except 788.0	All	NO	Kidney stones except 788.0	All	183	Multiple	NO	0
7	oxcarbazepine	oxcarbazepine, topiramate, zonisamide, acetazolamide	183	Single	10	10	0	0	Kidney stones	All	NO	Kidney stones	All	183	Multiple	NO	0

Modular Program Specifications MSY4_MPR29_V1

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Drug/Exposure								Event/Outcome									
Incident exposure	Incident w/ respect to:	Washout (days)	Incidence Type	Episode Gap	Exposure Extension Period	Min. Episode Duration	Min. Days Supplied	Event/ Outcome	Care Setting	Principal Dx	Event incident w/ respect to:	Incident Only Care Setting	Washout (days)	Incidence Type	Incident Only Principal Dx	Blackout Period	
IVIG																	
8	oxcarbazepine	oxcarbazepine, topiramate, zonisamide, acetazolamide	183	Single	10	10	0	0	Kidney stones except 788.0	All	NO	Kidney stones except 788.0	All	183	Multiple	NO	0
9	zonisamide	All AEDs	183	Single	10	10	0	0	Kidney stones	All	NO	Kidney stones	All	183	Multiple	NO	0
10	zonisamide	All AEDs	183	Single	10	10	0	0	Kidney stones except 788.0	All	NO	Kidney stones except 788.0	All	183	Multiple	NO	0
11	zonisamide	topiramate, zonisamide, acetazolamide	183	Single	10	10	0	0	Kidney stones	All	NO	Kidney stones	All	183	Multiple	NO	0
12	zonisamide	topiramate, zonisamide, acetazolamide	183	Single	10	10	0	0	Kidney stones except 788.0	All	NO	Kidney stones except 788.0	All	183	Multiple	NO	0

NDC codes checked against First Data Bank's "National Drug Data File (NDDF®) Plus"
 ICD-9-CM diagnosis and procedure codes checked against "Ingenix 2012 ICD-9-CM Data File" provided by OptumInsight
 HCPCS codes checked against "Optum 2012 HCPCS Level II Data File" provided by OptumInsight
 CPT codes checked against "Optum 2012 Current Procedure Codes & Relative Values Data File" provided by OptumInsight

Glossary of Terms in Modular Program 3*

- 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).
- Days at Risk** - number of days supplied plus any episode gaps and exposure extension periods.
- 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.
- Episode Gap** - number of days allowed between two (or more) consecutive exposures (dispensings/procedures) to be considered the same treatment episode.
- Exposure Extension Period** - number of days post treatment period in which the outcomes/events are counted for a treatment episode.
- Incidence Type (drug/exposure)**- *Minimum incidence type* will consider the first treatment episode in the query period as long as it is the first treatment episode in the user's entire available history. *Single* and *Multiple incidence types* will use the washout period to establish incidence, however *Single* will only consider the first treatment episode whereas *Multiple* will consider all qualifying incident treatment episodes.
- Incidence Type (event/outcome)**- *Minimum incidence type* considers the first event in a valid episode as long as it is the first event in the user's entire available history. *Multiple incidence type* uses the washout period to establish incidence and considers all qualifying incident treatment episodes. The program will only consider one event per episode, but the *Multiple incidence type* will consider more than one event per user if a user has more than one incident 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-Days** - sum of all days of enrollment with medical and drug coverage** in the query period preceded by an exposure washout period.
- 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.
- New Episodes** - new treatment episodes; length of episode is determined by days supplied in one dispensing (or consecutive dispensings bridged by the episode gap).
- New Users** - number of members with incident 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.
- Principal Diagnosis** - diagnosis or condition established to be chiefly responsible for admission of the patient to the hospital. YES will only consider diagnoses flagged as Principal.
- Query Period** - period in which the modular program looks for exposures and outcomes of interest.
- Total Days Supplied** - number of days supplied for all dispensings in qualifying treatment episodes.
- 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.

*all terms may not be used in this report

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

Table 1: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, and Kidney Stone (Events) Definition

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/ 100K Days at Risk
carbamazepine													
Incident to All AEDs													
Events including code 788	64,847	64,847	162,562	5,981,739	6,264,442	229	91,178,399	75,005,507,431	0.71	92.24	2.51	36.80	3.66
Events excluding code 788	64,904	64,904	162,673	5,985,113	6,270,442	208	91,183,231	75,033,440,424	0.71	92.21	2.51	36.79	3.32
Incident to drug of interest, topiramate, zonisamide, acetazolamide													
Events including code 788	109,536	109,536	317,343	11,687,063	12,449,191	545	92,832,325	78,489,484,485	1.18	106.70	2.90	36.83	4.38
Events excluding code 788	109,657	109,657	317,596	11,694,855	12,466,859	487	92,837,055	78,520,974,427	1.18	106.65	2.90	36.82	3.91
oxcarbazepine													
Incident to All AEDs													
Events including code 788	67,416	67,416	220,430	7,095,836	7,496,452	201	91,178,402	75,005,901,263	0.74	105.25	3.27	32.19	2.68
Events excluding code 788	67,481	67,481	220,592	7,100,587	7,502,775	188	91,183,234	75,033,821,570	0.74	105.22	3.27	32.19	2.51
Incident to drug of interest, topiramate, zonisamide, acetazolamide													
Events including code 788	117,177	117,177	425,904	13,992,925	14,838,619	556	92,863,184	78,528,647,596	1.26	119.42	3.63	32.85	3.75
Events excluding code 788	117,320	117,320	426,323	14,005,255	14,858,733	515	92,867,913	78,560,122,605	1.26	119.38	3.63	32.85	3.47
Zonisamide													
Incident to All AEDs													
Events including code 788	18,841	18,841	48,315	1,561,713	1,672,744	141	91,178,405	75,023,465,487	0.21	82.89	2.56	32.32	8.43
Events excluding code 788	18,862	18,862	48,359	1,563,512	1,675,872	129	91,183,237	75,051,422,162	0.21	82.89	2.56	32.33	7.70
Incident to topiramate, zonisamide, acetazolamide													
Events including code 788	37,917	37,917	129,102	4,277,585	4,521,701	364	92,909,351	78,649,407,824	0.41	112.81	3.40	33.13	8.05
Events excluding code 788	37,964	37,964	129,241	4,282,138	4,530,379	339	92,914,080	78,681,042,204	0.41	112.79	3.40	33.13	7.48

Table 2: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Age Group

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/ 100K Days at Risk
Carbamazepine													
Incident to All AEDs													
Events including code 788													
00 to 01 year	234	234	1,088	40,798	40,579	0	3,797,546	1,270,226,756	0.06	174.35	4.65	37.50	0.00
02 to 04 years	725	725	3,573	128,385	130,321	0	5,799,260	2,878,311,781	0.13	177.08	4.93	35.93	0.00
05 to 09 years	1,694	1,694	8,323	296,110	303,971	2	8,390,256	5,107,432,221	0.20	174.80	4.91	35.58	0.66
10 to 16 years	3,861	3,861	14,832	511,843	535,541	4	11,198,021	7,716,362,186	0.34	132.57	3.84	34.51	0.75
17 to 39 years	18,360	18,360	43,409	1,465,481	1,564,286	55	35,690,496	23,054,700,840	0.51	79.82	2.36	33.76	3.52
40 to 64 years	27,657	27,657	64,392	2,404,166	2,517,411	106	33,176,472	27,539,523,248	0.83	86.93	2.33	37.34	4.21
65+ years	12,316	12,316	26,945	1,134,956	1,172,333	62	8,000,545	7,365,137,124	1.54	92.15	2.19	42.12	5.29
Events excluding code 788													
00 to 01 year	234	234	1,088	40,798	40,579	0	3,797,628	1,270,320,213	0.06	174.35	4.65	37.50	0.00
02 to 04 years	725	725	3,573	128,385	130,321	0	5,799,314	2,878,569,343	0.13	177.08	4.93	35.93	0.00
05 to 09 years	1,695	1,695	8,324	296,140	304,011	2	8,390,345	5,107,793,734	0.20	174.71	4.91	35.58	0.66
10 to 16 years	3,861	3,861	14,832	511,843	536,035	2	11,198,175	7,717,026,779	0.34	132.57	3.84	34.51	0.37
17 to 39 years	18,386	18,386	43,460	1,467,223	1,566,504	49	35,693,002	23,064,065,794	0.52	79.80	2.36	33.76	3.13
40 to 64 years	27,679	27,679	64,426	2,405,160	2,519,398	96	33,178,613	27,552,836,800	0.83	86.89	2.33	37.33	3.81
65+ years	12,324	12,324	26,970	1,135,564	1,173,594	59	8,001,259	7,369,008,498	1.54	92.14	2.19	42.10	5.03

Table 2: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Age Group

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/ 100K Days at Risk
Carbamazepine (continued)													
Incident to drug of interest, topiramate, zonisamide, acetazolamide													
Events including code 788													
00 to 01 year	327	327	1,809	66,170	67,735	1	3,800,648	1,272,442,327	0.09	202.35	5.53	36.58	1.48
02 to 04 years	916	916	5,346	195,200	201,405	1	5,805,590	2,884,830,970	0.16	213.10	5.84	36.51	0.50
05 to 09 years	2,122	2,122	11,764	416,737	432,602	4	8,406,176	5,128,822,029	0.25	196.39	5.54	35.42	0.92
10 to 16 years	5,019	5,019	21,600	750,984	793,461	9	11,235,655	7,778,719,783	0.45	149.63	4.30	34.77	1.13
17 to 39 years	30,767	30,767	86,470	2,905,694	3,135,124	152	36,095,389	23,780,475,520	0.85	94.44	2.81	33.60	4.85
40 to 64 years	50,127	50,127	139,148	5,201,238	5,539,451	263	34,196,586	29,465,883,807	1.47	103.76	2.78	37.38	4.75
65+ years	20,258	20,258	51,206	2,151,040	2,279,413	115	8,391,913	8,104,361,808	2.41	106.18	2.53	42.01	5.05
Events excluding code 788													
00 to 01 year	327	327	1,809	66,170	67,735	1	3,800,731	1,272,536,382	0.09	202.35	5.53	36.58	1.48
02 to 04 years	916	916	5,346	195,200	201,405	1	5,805,644	2,885,089,695	0.16	213.10	5.84	36.51	0.50
05 to 09 years	2,123	2,123	11,765	416,767	433,278	3	8,406,267	5,129,188,830	0.25	196.31	5.54	35.42	0.69
10 to 16 years	5,019	5,019	21,600	750,984	793,955	7	11,235,807	7,779,406,028	0.45	149.63	4.30	34.77	0.88
17 to 39 years	30,819	30,819	86,587	2,909,423	3,141,897	125	36,097,870	23,790,725,801	0.85	94.40	2.81	33.60	3.98
40 to 64 years	50,176	50,176	139,245	5,204,133	5,544,710	241	34,198,707	29,481,147,431	1.47	103.72	2.78	37.37	4.35
65+ years	20,277	20,277	51,244	2,152,178	2,283,879	109	8,392,607	8,108,926,031	2.42	106.14	2.53	42.00	4.77

Table 2: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Age Group

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/ 100K Days at Risk
Oxcarbazepine													
Incident to All AEDs													
Events including code 788													
00 to 01 year	552	552	2,180	71,290	72,827	0	3,797,546	1,270,223,514	0.15	129.15	3.95	32.70	0.00
02 to 04 years	1,843	1,843	8,968	289,626	297,809	1	5,799,169	2,878,224,062	0.32	157.15	4.87	32.30	0.34
05 to 09 years	7,107	7,107	35,603	1,145,141	1,191,559	4	8,389,889	5,106,591,000	0.85	161.13	5.01	32.16	0.34
10 to 16 years	15,487	15,487	60,701	1,926,479	2,044,231	21	11,196,180	7,712,661,682	1.38	124.39	3.92	31.74	1.03
17 to 39 years	23,322	23,322	59,778	1,867,762	2,013,888	74	35,686,280	23,049,957,114	0.65	80.09	2.56	31.24	3.67
40 to 64 years	15,901	15,901	44,256	1,469,699	1,543,083	83	33,176,613	27,544,506,475	0.48	92.43	2.78	33.21	5.38
65+ years	3,204	3,204	8,944	325,839	333,055	18	8,001,493	7,369,929,928	0.40	101.70	2.79	36.43	5.40
Events excluding code 788													
00 to 01 year	552	552	2,180	71,290	72,827	0	3,797,628	1,270,316,971	0.15	129.15	3.95	32.70	0.00
02 to 04 years	1,843	1,843	8,968	289,626	297,809	1	5,799,223	2,878,481,624	0.32	157.15	4.87	32.30	0.34
05 to 09 years	7,109	7,109	35,606	1,145,207	1,191,652		8,389,978	5,106,952,513	0.85	161.09	5.01	32.16	0.34
10 to 16 years	15,489	15,489	60,720	1,927,039	2,044,913	2	11,196,335	7,713,325,206	1.38	124.41	3.92	31.74	0.98
17 to 39 years	23,345	23,345	59,827	1,869,147	2,016,052	3	35,688,785	23,059,319,845	0.65	80.07	2.56	31.24	3.32
40 to 64 years	15,935	15,935	44,334	1,472,029	1,545,990		33,178,754	27,557,807,777	0.48	92.38	2.78	33.20	5.05
65+ years	3,208	3,208	8,957	326,249	333,532	4	8,002,207	7,373,804,158	0.40	101.70	2.79	36.42	5.40

Table 2: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Age Group

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/ 100K Days at Risk
Oxcarbazepine (continued)													
Incident to drug of interest, topiramate, zonisamide, acetazolamide													
Events including code 788													
00 to 01 year	985	985	4,441	149,500	154,448	3	3,800,362	1,272,250,593	0.26	151.78	4.51	33.66	1.94
02 to 04 years	2,611	2,611	14,862	483,826	500,256	3	5,804,345	2,883,708,321	0.45	185.30	5.69	32.55	0.60
05 to 09 years	8,686	8,686	48,469	1,567,750	1,634,997	5	8,402,550	5,123,745,210	1.03	180.49	5.58	32.35	0.31
10 to 16 years	18,894	18,894	82,692	2,675,657	2,836,450	27	11,227,650	7,765,234,992	1.68	141.61	4.38	32.36	0.95
17 to 39 years	41,353	41,353	126,692	4,004,141	4,321,898	201	36,095,998	23,775,566,511	1.15	96.83	3.06	31.61	4.65
40 to 64 years	37,270	37,270	125,065	4,246,236	4,484,550	255	34,219,789	29,504,017,855	1.09	113.93	3.36	33.95	5.69
65+ years	7,378	7,378	23,683	865,815	906,020	62	8,403,750	8,130,213,553	0.88	117.35	3.21	36.56	6.84
Events excluding code 788													
00 to 01 year	985	985	4,441	149,500	154,535	2	3,800,445	1,272,344,648	0.26	151.78	4.51	33.66	1.29
02 to 04 years	2,611	2,611	14,862	483,826	500,256	3	5,804,399	2,883,966,852	0.45	185.30	5.69	32.55	0.60
05 to 09 years	8,688	8,688	48,472	1,567,816	1,635,090	5	8,402,640	5,124,109,800	1.03	180.46	5.58	32.34	0.31
10 to 16 years	18,897	18,897	82,712	2,676,247	2,838,057	25	11,227,802	7,765,916,615	1.68	141.62	4.38	32.36	0.88
17 to 39 years	41,421	41,421	126,853	4,008,862	4,328,644	183	36,098,472	23,785,796,139	1.15	96.78	3.06	31.60	4.23
40 to 64 years	37,332	37,332	125,243	4,251,489	4,494,230	237	34,221,912	29,519,277,335	1.09	113.88	3.35	33.95	5.27
65+ years	7,386	7,386	23,740	867,515	907,921	60	8,404,445	8,134,794,667	0.88	117.45	3.21	36.54	6.61

Table 2: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Age Group

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/ 100K Days at Risk
Zonisamide													
Incident to All AEDs													
Events including code 788													
00 to 01 year	95	95	450	13,704	13,366	0	3,797,546	1,270,229,181	0.03	144.25	4.74	30.45	0.00
02 to 04 years	144	144	836	29,196	29,272	0	5,799,349	2,878,420,038	0.02	202.75	5.81	34.92	0.00
05 to 09 years	336	336	1,311	42,896	43,112	3	8,390,649	5,107,966,032	0.04	127.67	3.90	32.72	6.96
10 to 16 years	1,243	1,243	4,544	146,433	154,298	4	11,198,669	7,717,437,876	0.11	117.81	3.66	32.23	2.59
17 to 39 years	7,429	7,429	17,397	543,135	589,908	59	35,691,453	23,058,326,909	0.21	73.11	2.34	31.22	10.00
40 to 64 years	8,602	8,602	20,883	682,056	735,003	63	33,177,423	27,546,774,110	0.26	79.29	2.43	32.66	8.57
65+ years	992	992	2,894	104,293	107,785	12	8,001,693	7,370,496,287	0.12	105.13	2.92	36.04	11.13
Events excluding code 788													
00 to 01 year	95	95	450	13,704	13,366	0	3,797,628	1,270,322,638	0.03	144.25	4.74	30.45	0.00
02 to 04 years	144	144	836	29,196	29,272	0	5,799,403	2,878,677,600	0.02	202.75	5.81	34.92	0.00
05 to 09 years	336	336	1,311	42,896	43,112	3	8,390,738	5,108,327,545	0.04	127.67	3.90	32.72	6.96
10 to 16 years	1,243	1,243	4,544	146,433	154,299	4	11,198,824	7,718,102,875	0.11	117.81	3.66	32.23	2.59
17 to 39 years	7,441	7,441	17,413	543,602	590,882	52	35,693,959	23,067,701,997	0.21	73.05	2.34	31.22	8.80
40 to 64 years	8,610	8,610	20,910	683,358	736,794	59	33,179,566	27,560,095,663	0.26	79.37	2.43	32.68	8.01
65+ years	993	993	2,895	104,323	108,147	11	8,002,408	7,374,372,802	0.12	105.06	2.92	36.04	10.17

Table 2: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Age Group

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/ 100K Days at Risk
Zonisamide (continued)													
Incident to topiramate, zonisamide, acetazolamide													
Events including code 788													
00 to 01 year	296	296	1,810	57,452	58,537	2	3,800,778	1,272,551,686	0.08	194.09	6.11	31.74	3.42
02 to 04 years	515	515	3,844	127,105	129,079	1	5,806,186	2,885,531,254	0.09	246.81	7.46	33.07	0.77
05 to 09 years	997	997	6,261	205,297	209,316	6	8,408,504	5,131,675,548	0.12	205.91	6.28	32.79	2.87
10 to 16 years	2,447	2,447	12,927	420,371	434,833	16	11,240,830	7,786,028,489	0.22	171.79	5.28	32.52	3.68
17 to 39 years	13,612	13,612	41,818	1,342,988	1,433,693	142	36,121,400	23,818,491,668	0.38	98.66	3.07	32.12	9.90
40 to 64 years	17,695	17,695	54,201	1,813,098	1,935,407	167	34,241,277	29,543,136,980	0.52	102.46	3.06	33.45	8.63
65+ years	2,355	2,355	8,241	311,274	320,836	30	8,408,325	8,138,040,274	0.28	132.18	3.50	37.77	9.35
Events excluding code 788													
00 to 01 year	297	297	1,820	57,729	58,790	2	3,800,861	1,272,645,741	0.08	194.37	6.13	31.72	3.40
02 to 04 years	515	515	3,844	127,105	129,079	1	5,806,240	2,885,789,979	0.09	246.81	7.46	33.07	0.77
05 to 09 years	997	997	6,261	205,297	209,316	6	8,408,594	5,132,042,748	0.12	205.91	6.28	32.79	2.87
10 to 16 years	2,447	2,447	12,927	420,371	434,917	15	11,240,983	7,786,716,456	0.22	171.79	5.28	32.52	3.45
17 to 39 years	13,640	13,640	41,883	1,344,822	1,437,442	131	36,123,876	23,828,789,981	0.38	98.59	3.07	32.11	9.11
40 to 64 years	17,712	17,712	54,264	1,815,510	1,939,600	155	34,243,404	29,558,467,291	0.52	102.50	3.06	33.46	7.99
65+ years	2,356	2,356	8,242	311,304	321,235	29	8,409,019	8,142,632,095	0.28	132.13	3.50	37.77	9.03

Table 3: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Sex

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/ 100K Days at Risk
Carbamazepine													
Incident to All AEDs													
Events including code 788													
Female	37,580	37,580	87,055	3,214,178	3,364,105	118	46,243,069	38,132,678,730	0.81	85.53	2.32	36.92	3.51
Male	27,208	27,208	75,343	2,762,616	2,894,955	110	44,826,648	36,763,352,307	0.61	101.54	2.77	36.67	3.80
Unknown	59	59	164	4,945	5,382	1	108,682	109,476,394	0.54	83.81	2.78	30.15	18.58
Events excluding code 788													
Female	37,617	37,617	87,137	3,216,752	3,368,305	105	46,245,903	38,148,010,156	0.81	85.51	2.32	36.92	3.12
Male	27,228	27,228	75,372	2,763,416	2,896,755	102	44,828,644	36,775,923,629	0.61	101.49	2.77	36.66	3.52
Unknown	59	59	164	4,945	5,382	1	108,684	109,506,639	0.54	83.81	2.78	30.15	18.58
Incident to drug of interest, topiramate, zonisamide, acetazolamide													
Events including code 788													
Female	65,861	65,861	178,713	6,577,328	7,042,645	298	47,275,904	40,336,053,549	1.39	99.87	2.71	36.80	4.23
Male	43,572	43,572	138,155	5,095,109	5,393,594	243	45,447,142	38,041,515,177	0.96	116.94	3.17	36.88	4.51
Unknown	103	103	475	14,626	12,952	4	109,279	111,915,759	0.94	142.00	4.61	30.79	30.88
Events excluding code 788													
Female	65,944	65,944	178,895	6,583,087	7,052,968	260	47,278,696	40,353,739,672	1.39	99.83	2.71	36.80	3.69
Male	43,610	43,610	138,226	5,097,142	5,398,513	224	45,449,080	38,055,286,324	0.96	116.88	3.17	36.88	4.15
Unknown	103	103	475	14,626	15,378	3	109,279	111,948,431	0.94	142.00	4.61	30.79	19.51

Table 3: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Sex

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/ 100K Days at Risk
Oxcarbazepine													
Incident to All AEDs													
Events including code 788													
Female	35,362	35,362	104,455	3,368,324	3,569,031	108	46,243,068	38,134,605,981	0.76	95.25	2.95	32.25	3.03
Male	31,942	31,942	115,576	3,715,142	3,914,336	93	44,826,652	36,761,831,712	0.71	116.31	3.62	32.14	2.38
Unknown	112	112	399	12,370	13,085	0	108,682	109,463,570	1.03	110.45	3.56	31.00	0.00
Events excluding code 788													
Female	35,407	35,407	104,576	3,371,878	3,573,141	101	46,245,902	38,149,928,405	0.77	95.23	2.95	32.24	2.83
Male	31,962	31,962	115,617	3,716,339	3,916,549	87	44,828,648	36,774,399,350	0.71	116.27	3.62	32.14	2.22
Unknown	112	112	399	12,370	13,085	0	108,684	109,493,815	1.03	110.45	3.56	31.00	0.00
Incident to drug of interest, topiramate, zonisamide, acetazolamide													
Events including code 788													
Female	66,799	66,799	221,951	7,306,381	7,798,479	312	47,293,074	40,361,648,738	1.41	109.38	3.32	32.92	4.00
Male	50,201	50,201	203,312	6,666,286	7,018,384	244	45,460,828	38,055,127,041	1.10	132.79	4.05	32.79	3.48
Unknown	177	177	641	20,258	21,756	0	109,282	111,871,817	1.62	114.45	3.62	31.60	0.00
Events excluding code 788													
Female	66,902	66,902	222,248	7,314,992	7,810,405	290	47,295,862	40,379,321,737	1.41	109.34	3.32	32.91	3.71
Male	50,241	50,241	203,434	6,670,005	7,026,572	225	45,462,769	38,068,896,125	1.11	132.76	4.05	32.79	3.20
Unknown	177	177	641	20,258	21,756	0	109,282	111,904,743	1.62	114.45	3.62	31.60	0.00

Table 3: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Sex

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings/ User	Days Supplied/ Dispensing	Events/ 100K Days at Risk
Zonisamide													
Incident to All AEDs													
Events including code 788													
Female	13,786	13,786	33,935	1,096,124	1,182,231	91	46,243,072	38,142,366,715	0.30	79.51	2.46	32.30	7.70
Male	5,032	5,032	14,332	464,143	488,898	50	44,826,651	36,771,606,354	0.11	92.24	2.85	32.39	10.23
Unknown	23	23	48	1,446	1,615	0	108,682	109,492,418	0.21	62.87	2.09	30.13	0.00
Events excluding code 788													
Female	13,802	13,802	33,960	1,097,041	1,184,387	82	46,245,906	38,157,713,818	0.30	79.48	2.46	32.30	6.92
Male	5,037	5,037	14,351	465,025	489,870	47	44,828,647	36,784,185,681	0.11	92.32	2.85	32.40	9.59
Unknown	23	23	48	1,446	1,615	0	108,684	109,522,663	0.21	62.87	2.09	30.13	0.00
Incident to topiramate, zonisamide, acetazolamide													
Events including code 788													
Female	26,629	26,629	85,325	2,809,739	2,990,018	225	47,317,642	40,426,443,548	0.56	105.51	3.20	32.93	7.53
Male	11,246	11,246	43,671	1,464,644	1,528,298	139	45,482,404	38,110,914,582	0.25	130.24	3.88	33.54	9.10
Unknown	42	42	106	3,202	3,385	0	109,305	112,049,694	0.38	76.24	2.52	30.21	0.00
Events excluding code 788													
Female	26,666	26,666	85,417	2,812,636	2,996,681	207	47,320,428	40,444,224,525	0.56	105.48	3.20	32.93	6.91
Male	11,256	11,256	43,718	1,466,300	1,530,313	132	45,484,347	38,124,735,015	0.25	130.27	3.88	33.54	8.63
Unknown	42	42	106	3,202	3,385	0	109,305	112,082,664	0.38	76.24	2.52	30.21	0.00

Table 4: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Year

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	Events/100K Days at Risk
Carbamazepine													
Incident to All AEDs													
Events including code 788													
2004	6,300	6,300	19,041	771,076	801,882	17	18,956,673	4,111,075,501	0.33	122.39	3.02	40.50	2.12
2005	6,865	6,865	18,670	724,784	755,626	24	20,901,267	5,876,992,116	0.33	105.58	2.72	38.82	3.18
2006	6,466	6,466	19,676	745,056	777,505	22	22,347,186	6,164,506,842	0.29	115.23	3.04	37.87	2.83
2007	6,240	6,240	16,569	638,289	663,523	23	24,903,949	6,562,899,009	0.25	102.29	2.66	38.52	3.47
2008	8,527	8,527	21,728	783,384	827,793	33	45,488,962	10,105,934,842	0.19	91.87	2.55	36.05	3.99
2009	10,097	10,097	24,608	852,423	907,935	36	46,514,917	12,993,638,063	0.22	84.42	2.44	34.64	3.97
2010	9,220	9,220	21,344	740,881	784,656	32	44,707,455	12,540,713,669	0.21	80.36	2.31	34.71	4.08
2011	7,748	7,748	15,655	543,201	573,784	37	43,164,726	12,065,022,509	0.18	70.11	2.02	34.70	6.45
2012	3,384	3,384	5,271	182,645	171,738	5	24,808,839	4,584,724,880	0.14	53.97	1.56	34.65	2.91
Events excluding code 788													
2004	6,307	6,307	19,053	771,486	802,608	15	18,958,374	4,112,723,055	0.33	122.32	3.02	40.49	1.87
2005	6,873	6,873	18,679	725,024	755,992	22	20,902,833	5,879,276,995	0.33	105.49	2.72	38.81	2.91
2006	6,468	6,468	19,698	745,866	778,846	20	22,348,755	6,166,808,669	0.29	115.32	3.05	37.87	2.57
2007	6,244	6,244	16,574	638,429	663,726	21	24,906,534	6,565,281,850	0.25	102.25	2.65	38.52	3.16
2008	8,534	8,534	21,748	783,984	828,974	26	45,493,221	10,109,891,751	0.19	91.87	2.55	36.05	3.14
2009	10,103	10,103	24,618	852,699	908,332	36	46,518,092	12,998,672,581	0.22	84.40	2.44	34.64	3.96
2010	9,234	9,234	21,364	741,531	786,039	28	44,710,416	12,545,299,329	0.21	80.30	2.31	34.71	3.56
2011	7,754	7,754	15,662	543,258	573,954	36	43,167,302	12,069,172,666	0.18	70.06	2.02	34.69	6.27
2012	3,387	3,387	5,277	182,836	171,971	4	24,810,928	4,586,313,528	0.14	53.98	1.56	34.65	2.33

Table 4: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Year

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	Events/100K Days at Risk
Carbamazepine (continued)													
Incident to drug of interest, topiramate, zonisamide, acetazolamide													
Events including code 788													
2004	10,325	10,325	37,898	1,509,407	1,588,022	41	19,450,543	4,298,657,744	0.53	146.19	3.67	39.83	2.58
2005	11,694	11,694	37,739	1,469,876	1,554,224	61	21,411,726	6,138,645,488	0.55	125.69	3.23	38.95	3.92
2006	10,453	10,453	37,351	1,419,552	1,499,791	49	22,828,892	6,416,204,841	0.46	135.80	3.57	38.01	3.27
2007	10,215	10,215	31,743	1,217,139	1,294,538	53	25,555,197	6,848,746,579	0.40	119.15	3.11	38.34	4.09
2008	14,636	14,636	42,913	1,557,393	1,673,946	71	46,696,193	10,571,878,754	0.31	106.41	2.93	36.29	4.24
2009	17,130	17,130	48,065	1,673,190	1,808,152	91	47,709,311	13,598,073,192	0.36	97.68	2.81	34.81	5.03
2010	15,879	15,879	42,035	1,475,802	1,588,133	87	45,916,185	13,136,569,249	0.35	92.94	2.65	35.11	5.48
2011	13,301	13,301	29,873	1,032,611	1,117,756	78	44,357,424	12,647,566,238	0.30	77.63	2.25	34.57	6.98
2012	5,903	5,903	9,726	332,093	324,629	14	25,707,849	4,833,142,400	0.23	56.26	1.65	34.14	4.31
Events excluding code 788													
2004	10,341	10,341	37,923	1,510,184	1,589,408	37	19,452,202	4,300,542,820	0.53	146.04	3.67	39.82	2.33
2005	11,708	11,708	37,772	1,470,836	1,558,101	55	21,413,235	6,141,221,240	0.55	125.63	3.23	38.94	3.53
2006	10,460	10,460	37,381	1,420,602	1,502,612	43	22,830,372	6,418,751,914	0.46	135.81	3.57	38.00	2.86
2007	10,220	10,220	31,749	1,217,309	1,295,091	47	25,557,886	6,851,395,328	0.40	119.11	3.11	38.34	3.63
2008	14,651	14,651	42,947	1,558,317	1,675,908	62	46,700,361	10,576,327,677	0.31	106.36	2.93	36.28	3.70
2009	17,150	17,150	48,092	1,673,998	1,810,328	81	47,712,397	13,603,752,395	0.36	97.61	2.80	34.81	4.47
2010	15,902	15,902	42,097	1,477,849	1,591,231	81	45,919,014	13,141,747,611	0.35	92.93	2.65	35.11	5.09
2011	13,317	13,317	29,898	1,033,326	1,119,131	69	44,359,936	12,652,266,646	0.30	77.59	2.25	34.56	6.17
2012	5,908	5,908	9,737	332,434	325,049	12	25,709,918	4,834,968,796	0.23	56.27	1.65	34.14	3.69

Table 4: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Year

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	Events/100K Days at Risk
Oxcarbazepine													
Incident to All AEDs													
Events including code 788													
2004	7,855	7,855	28,148	877,354	932,907	27	18,956,673	4,111,073,093	0.41	111.69	3.58	31.17	2.89
2005	7,928	7,928	26,698	861,803	917,737	27	20,900,541	5,876,890,065	0.38	108.70	3.37	32.28	2.94
2006	6,579	6,579	24,565	796,038	843,410	22	22,346,224	6,164,309,468	0.29	121.00	3.73	32.41	2.61
2007	6,108	6,108	22,414	730,375	768,767	25	24,902,968	6,562,694,390	0.25	119.58	3.67	32.59	3.25
2008	8,448	8,448	29,982	980,041	1,032,846	28	45,488,082	10,105,743,099	0.19	116.01	3.55	32.69	2.71
2009	10,158	10,158	33,658	1,084,002	1,145,435	25	46,514,488	12,993,630,106	0.22	106.71	3.31	32.21	2.18
2010	9,532	9,532	29,442	948,700	1,009,509	24	44,707,400	12,540,793,544	0.21	99.53	3.09	32.22	2.38
2011	8,047	8,047	20,536	655,868	690,191	21	43,164,460	12,065,061,167	0.19	81.50	2.55	31.94	3.04
2012	2,761	2,761	4,987	161,655	155,650	2	24,814,180	4,585,706,331	0.11	58.55	1.81	32.42	1.28
Events excluding code 788													
2004	7,862	7,862	28,175	878,075	934,313	25	18,958,374	4,112,720,603	0.41	111.69	3.58	31.17	2.68
2005	7,940	7,940	26,742	863,005	919,159	26	20,902,104	5,879,174,499	0.38	108.69	3.37	32.27	2.83
2006	6,586	6,586	24,574	796,304	843,770	21	22,347,787	6,166,610,064	0.29	120.91	3.73	32.40	2.49
2007	6,112	6,112	22,419	730,525	768,929	25	24,905,551	6,565,074,680	0.25	119.52	3.67	32.59	3.25
2008	8,456	8,456	29,994	980,396	1,033,351	25	45,492,332	10,109,698,782	0.19	115.94	3.55	32.69	2.42
2009	10,169	10,169	33,689	1,084,909	1,146,488	25	46,517,655	12,998,663,426	0.22	106.69	3.31	32.20	2.18
2010	9,539	9,539	29,464	949,480	1,010,404	22	44,710,350	12,545,376,013	0.21	99.54	3.09	32.23	2.18
2011	8,051	8,051	20,540	655,978	690,439	17	43,167,033	12,069,208,670	0.19	81.48	2.55	31.94	2.46
2012	2,766	2,766	4,995	161,915	155,922	2	24,816,266	4,587,294,833	0.11	58.54	1.81	32.42	1.28

Table 4: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Year

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	Events/100K Days at Risk
Oxcarbazepine (continued)													
Incident to drug of interest, topiramate, zonisamide, acetazolamide													
Events including code 788													
2004	13,762	13,762	58,045	1,843,178	1,961,046	77	19,466,850	4,302,581,677	0.71	133.93	4.22	31.75	3.93
2005	13,493	13,493	51,512	1,685,730	1,796,702	59	21,424,601	6,142,521,786	0.63	124.93	3.82	32.72	3.28
2006	10,651	10,651	45,251	1,509,958	1,597,121	51	22,841,259	6,420,258,699	0.47	141.77	4.25	33.37	3.19
2007	10,050	10,050	40,475	1,353,908	1,430,394	48	25,569,781	6,852,700,756	0.39	134.72	4.03	33.45	3.36
2008	14,587	14,587	57,103	1,898,386	2,013,576	86	46,712,776	10,576,961,972	0.31	130.14	3.91	33.24	4.27
2009	17,998	17,998	66,221	2,182,728	2,320,535	79	47,725,064	13,603,378,816	0.38	121.28	3.68	32.96	3.40
2010	16,900	16,900	57,186	1,885,474	2,011,771	91	45,930,569	13,141,424,008	0.37	111.57	3.38	32.97	4.52
2011	14,272	14,272	39,686	1,295,474	1,377,519	56	44,369,665	12,651,772,865	0.32	90.77	2.78	32.64	4.07
2012	5,464	5,464	10,425	338,089	329,955	9	25,726,906	4,837,047,017	0.21	61.88	1.91	32.43	2.73
Events excluding code 788													
2004	13,779	13,779	58,122	1,845,544	1,964,975	67	19,468,509	4,304,463,699	0.71	133.94	4.22	31.75	3.41
2005	13,516	13,516	51,581	1,687,596	1,799,723	58	21,426,112	6,145,093,037	0.63	124.86	3.82	32.72	3.22
2006	10,667	10,667	45,294	1,511,182	1,599,033	47	22,842,741	6,422,804,581	0.47	141.67	4.25	33.36	2.94
2007	10,062	10,062	40,514	1,354,948	1,432,402	46	25,572,471	6,855,346,608	0.39	134.66	4.03	33.44	3.21
2008	14,603	14,603	57,171	1,900,343	2,016,962	76	46,716,941	10,581,410,956	0.31	130.13	3.92	33.24	3.77
2009	18,020	18,020	66,272	2,184,235	2,322,391	77	47,728,118	13,609,058,078	0.38	121.21	3.68	32.96	3.32
2010	16,916	16,916	57,220	1,886,734	2,013,791	85	45,933,384	13,146,598,150	0.37	111.54	3.38	32.97	4.22
2011	14,282	14,282	39,704	1,295,964	1,378,889	50	44,372,170	12,656,472,619	0.32	90.74	2.78	32.64	3.63
2012	5,475	5,475	10,445	338,709	330,567	9	25,728,979	4,838,874,877	0.21	61.86	1.91	32.43	2.72

Table 4: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Year

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	Events/100K Days at Risk
Zonisamide													
Incident to All AEDs													
Events including code 788													
2004	1,812	1,812	5,301	164,499	176,515	15	18,956,673	4,111,111,260	0.10	90.78	2.93	31.03	8.50
2005	1,834	1,834	4,872	155,253	167,435	14	20,903,566	5,877,513,332	0.09	84.65	2.66	31.87	8.36
2006	1,563	1,563	4,852	155,285	166,659	14	22,351,851	6,165,677,674	0.07	99.35	3.10	32.00	8.40
2007	1,584	1,584	4,427	145,030	155,129	11	24,910,794	6,564,689,778	0.06	91.56	2.79	32.76	7.09
2008	2,542	2,542	6,747	220,397	237,248	15	45,497,554	10,108,211,554	0.06	86.70	2.65	32.67	6.32
2009	3,302	3,302	7,901	254,244	274,308	20	46,525,884	12,996,556,055	0.07	77.00	2.39	32.18	7.29
2010	2,936	2,936	7,392	241,600	258,361	27	44,720,328	12,544,222,451	0.07	82.29	2.52	32.68	10.45
2011	2,324	2,324	5,247	173,414	185,081	22	43,179,526	12,069,040,129	0.05	74.62	2.26	33.05	11.89
2012	944	944	1,576	51,991	52,008	3	24,818,673	4,586,443,254	0.04	55.08	1.67	32.99	5.77
Events excluding code 788													
2004	1,812	1,812	5,301	164,499	177,051	11	18,958,374	4,112,758,818	0.10	90.78	2.93	31.03	6.21
2005	1,836	1,836	4,880	155,842	168,082	12	20,905,133	5,879,798,625	0.09	84.88	2.66	31.93	7.14
2006	1,564	1,564	4,853	155,313	166,667	14	22,353,427	6,167,981,472	0.07	99.30	3.10	32.00	8.40
2007	1,591	1,591	4,440	145,372	155,538	11	24,913,389	6,567,075,226	0.06	91.37	2.79	32.74	7.07
2008	2,542	2,542	6,747	220,397	237,457	14	45,501,816	10,112,170,320	0.06	86.70	2.65	32.67	5.90
2009	3,303	3,303	7,903	254,304	274,761	18	46,529,069	13,001,594,882	0.07	76.99	2.39	32.18	6.55
2010	2,941	2,941	7,402	242,080	258,854	26	44,723,296	12,548,812,539	0.07	82.31	2.52	32.70	10.04
2011	2,328	2,328	5,256	173,684	185,424	20	43,182,117	12,073,196,573	0.05	74.61	2.26	33.04	10.79
2012	945	945	1,577	52,021	52,038	3	24,820,768	4,588,033,707	0.04	55.05	1.67	32.99	5.77

Table 4: Summary of Incident AED Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by AED Product, Exposure Incidence Definition, Kidney Stone (Events) Definition, and Year

	New Users	New Episodes	Dispensings	Total Days Supplied	Days at Risk	New Events	Eligible Members	Member-Days	New Users/ 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	Events/100K Days at Risk
Zonisamide (continued)													
Incident to topiramate, zonisamide, acetazolamide													
Events including code 788													
2004	4,199	4,199	17,438	541,734	577,810	47	19,483,927	4,309,472,004	0.22	129.02	4.15	31.07	8.13
2005	4,083	4,083	15,227	498,978	527,063	43	21,448,821	6,152,683,365	0.19	122.21	3.73	32.77	8.16
2006	2,976	2,976	12,711	426,599	443,424	42	22,867,233	6,430,169,131	0.13	143.35	4.27	33.56	9.47
2007	3,051	3,051	11,389	388,378	409,553	28	25,602,016	6,863,932,447	0.12	127.30	3.73	34.10	6.84
2008	4,922	4,922	17,212	590,904	628,396	41	46,764,595	10,592,777,339	0.11	120.05	3.50	34.33	6.52
2009	6,220	6,220	20,114	664,853	706,492	53	47,779,279	13,623,147,705	0.13	106.89	3.23	33.05	7.50
2010	5,643	5,643	18,475	614,026	652,688	51	45,986,567	13,161,514,107	0.12	108.81	3.27	33.24	7.81
2011	4,852	4,852	12,844	428,685	454,734	51	44,427,908	12,672,210,140	0.11	88.35	2.65	33.38	11.22
2012	1,971	1,971	3,692	123,428	121,541	8	25,756,859	4,843,501,586	0.08	62.62	1.87	33.43	6.58
Events excluding code 788													
2004	4,203	4,203	17,444	541,914	578,813	41	19,485,585	4,311,364,832	0.22	128.94	4.15	31.07	7.08
2005	4,089	4,089	15,241	499,747	528,341	38	21,450,335	6,155,270,501	0.19	122.22	3.73	32.79	7.19
2006	2,978	2,978	12,714	426,674	443,540	42	22,868,729	6,432,727,268	0.13	143.28	4.27	33.56	9.47
2007	3,060	3,060	11,417	389,170	410,993	26	25,604,729	6,866,595,853	0.12	127.18	3.73	34.09	6.33
2008	4,926	4,926	17,216	591,024	629,702	37	46,768,776	10,597,245,006	0.11	119.98	3.49	34.33	5.88
2009	6,224	6,224	20,146	665,723	707,832	51	47,782,378	13,628,852,085	0.13	106.96	3.24	33.04	7.21
2010	5,651	5,651	18,501	614,956	654,003	48	45,989,422	13,166,712,762	0.12	108.82	3.27	33.24	7.34
2011	4,860	4,860	12,868	429,442	455,582	48	44,430,451	12,676,936,268	0.11	88.36	2.65	33.37	10.54
2012	1,973	1,973	3,694	123,488	121,573	8	25,758,945	4,845,337,629	0.08	62.59	1.87	33.43	6.58

Appendix A. Diagnosis and procedure codes used to define kidney stone events

ICD-9 diagnosis codes

592.0	Calculus of kidney (excludes uric acid stone)
592.1	Calculus of ureter
592.9	Urinary calculus, unspecified
274.11	Uric acid nephrolithiasis
788.0	Renal colic
594	Calculus of lower urinary tract

ICD-9 procedure codes

55.04	Percutaneous fragmentation with fragmentation
55.92	Repeat nephroscopic removal during current episode
56.2	Ureterotomy for removal of calculus or exploration
59.8	Transurethral ureteral stent placement for passage of calculus
59.95	Ultrasonic fragmentation of urinary stones
98.51	ESWL
55.04	percutaneous nephrostomy with fragmentation
98.51	Extracorporeal shockwave lithotripsy of the kidney, ureter, or bladder
59.95	ultrasonic fragmentation of urinary stones

CPT codes

50060	Nephrolithotomy; removal of calculus
50065	Secondary surgical operation for calculus
50070	Nephrolithotomy complicated by congenital kidney abnormality
50075	Removal of large staghorn calculus filling renal pelvis (includes anatomic pyelolithotomy)
50080	Percutaneous nephrostolithotomy with or without lithotripsy, up to 2 cm
50081	PCNL, over 2 cm
50130	Pyelotomy, with removal of calculus
50590	ESWL
50610	Ureterolithotomy; upper one third of ureter
50620	Ureterolithotomy, middle one third of ureter
50630	Ureterolithotomy, lower one third of ureter
52320	Cysto, ureteral cath, removal of calculus

Appendix A. Diagnosis and procedure codes used to define kidney stone events

CPT codes (continued)

52325	With fragmentation of calculus (ultrasound or EHL)
52330	With manipulation, but not removal of stone
52336	With removal of stone
52337	With lithotripsy
50945	Laproscopy, surgical; ureterolithotomy
50561	Renal endoscopy through established nephrostomy or pyelostomy; with removal for foreign body or calculus
50580	Renal endoscopy through nephrotomy or pyelotomy, with or without irrigation, instillation or ureteropyelography, exclusive of radiologic service; with removal of foreign body or calculus
51060	transvesical ureterolithotomy
51065	Cystotomy, with calculus basket extraction and/or ultrasonic or electrohydraulic fragmentation of urethral calculus
50080	Percutaneous nephrostolithotomy or pyelostolithotomy, with or without dilation, endoscopy, lithotripsy, stenting: up to 2cm
50081	Percutaneous nephrostolithotomy or pyelostolithotomy, with or without dilation, endoscopy, lithotripsy, stenting: over 2cm
50060	Nephrolithotomy; removal of calculus
50070	Nephrolithotomy; complicated by congenital kidney abnormality
50075	Nephrolithotomy; removal of large staghorn calculus filling renal pelvis and calyces
50610	Ureterolithotomy; upper one-third of ureter
50620	Ureterolithotomy; middle one-third of ureter
50630	Ureterolithotomy; lower one-third of ureter
50590	Lithotripsy, extracorporeal shock wave
52320	Cystourethroscopy with removal of ureteral calculus
52325	cystourethroscopy with fragmentation of ureteral calculus
52352	Cystourethroscopy with ureteroscopy; with removal or manipulation of calculus
52353	Cystourethroscopy with ureteroscopy; with lithotripsy
