Disclaimer

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 for Request msy4_mpr58, Report 1 of 2

Request ID: msy4_mpr58

Request Description: This report examined angioedema among new users of dipeptidyl peptidase IV (DPP IV) inhibitors and/or angiotensin converting enzyme (ACE) inhibitors in the Mini-Sentinel Distributed Database (MSDD). This is report 1 of 2. Report 2 examined angioedema among individuals with concomitant exposures to both DPP IV inhibitors and ACE inhibitors.

Mini-Sentinel Modular Program Tool Used: Modular Program #3 (MP3)

Data Source: We included data from October 16, 2006 to December 31, 2012 from 18 Data Partners contributing to the MSDD. We distributed this request to Data Partners on December 20, 2013. See Appendix A for the dates of available data for each Data Partner.

Study Design: We designed this request to investigate angioedema following incident use of DPP IV Inhibitors and ACE Inhibitors. In total, four scenarios were examined in one run of MP3 with differing exposures of interest and event primary diagnosis (PDX) indicators: (1) scenario one examined incident DPP IV inhibitors use with no PDX indicator on angioedema, (2) scenario examined incident ACE inhibitors use with no PDX indicator on angioedema, (3) scenario 3 examined incident DPP IV inhibitor use with a PDX indicator on angioedema, and (4) scenario 4 examined incident ACE inhibitors use with a PDX indicator on angioedema. Data were further stratified by sex, age group, and year.

Exposure of Interest: The exposures of interest were DPP IV Inhibitors and ACE Inhibitors. We defined exposures using National Drug Codes (NDCs). Please see Appendix B for a list of generic names of medical products used to define exposures in this request.

Outcome of Interest: The outcome of interest in this request was angioedema among incident users of DPP IV inhibitors and ACE inhibitors. We defined angioedema using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes. Please see Appendix C for a list of ICD-9-CM diagnosis codes used to define angioedema in this request.

Cohort Eligibility Criteria: We required members included in the cohort to be continuously enrolled in health plans with medical and drug coverage for at least 183 days prior to their first qualifying (index) DPP IV Inhibitor or ACE Inhibitor dispensing date, during which gaps in coverage of up to 45 days were allowed. We included individuals aged 20 years or older in the cohort.

Please see Appendix D for the specifications of parameters used in this request.

Limitations: Algorithms used to define the exposure, outcomes, exclusions, and covariates are imperfect; thus, it is possible that there may be misclassification. Therefore, data should be interpreted with this limitation in mind.

Note: Please contact the Sentinel Operations Center (info@sentinelsystem.org) for questions and to provide comments/suggestions for future enhancements to this document.

Mini-Sentinel

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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 Angioedema following Incident Angiotensin Converting Enzyme (ACE) Inhibitor and Dipeptidyl Peptidase IV (DPP IV) Inhibitor Use in the Mini-Sentinel Distributed Database (MSDD) between October 16, 2006 and December 31, 2012, by Exposure and Diagnosis Position

Diagnosis Position	New Users	New Episodes	Dispensings	Total Days Supplied	Total Amount Supplied	Years at Risk*	New Episodes with Events	Total Number of Events	Eligible Members	Member-Years	New Users per 1,000 Eligible Members	Days Supplied per User	Dispensings per User	Days Supplied per Dispensing	New Episodes with Events per 10,000 Years at Risk*
ACE Inhibitors															
Any	3,821,489	3,821,489	17,414,569	748,393,942	803,461,069	2,069,362.0	5,130	5,734	61,461,220	123,592,698.1	62.18	195.84	4.56	42.98	24.79
Primary	3,822,212	3,822,212	17,417,369	748,500,022	803,574,928	2,070,392.9	1,145	1,164	61,462,327	123,607,742.2	62.19	195.83	4.56	42.97	5.53
DPP IV Inhibitors															
Any	231,641	231,641	1,004,723	37,305,937	45,470,066	104,101.0	46	50	61,461,220	125,674,624.1	3.77	161.05	4.34	37.13	4.42
Primary	231,723	231,723	1,004,959	37,314,052	45,480,470	104,142.4	9	9	61,462,327	125,690,895.8	3.77	161.03	4.34	37.13	0.86

* Years at Risk stop accumulating when first event during episode is encountered

Table 2. Summary of Angioedema following Incident Angiotensin Converting Enzyme (ACE) Inhibitor and Dipeptidyl Peptidase IV (DPP IV) Inhibitor Use in the Mini-Sentinel Distributed Database (MSDD) between October 16, 2006 and December 31, 2012, by Exposure, Diagnosis Position, and Age Group

Age Group (years)	Diagnosis Position	New Users	New Episodes	Dispensings	Total Days Supplied	Total Amount Supplied	Years at Risk*	New Episodes with Events	Total Number of Events	Eligible Members	Member-Years	New Users per 1,000 Eligible Members	Days Supplied per User	Dispensings per User	Days Supplied per Dispensing	New Episodes with Events per 10,000 Years at Risk*
ACE Inhibitors																
20-44	Any	782,499	782,499	2,891,509	106,533,004	112,014,276	297,137.7	820	872	35,724,764	62,078,845.8	21.90	136.14	3.70	36.84	27.60
45-64	Any	2,015,310	2,015,310	9,445,559	390,186,177	416,101,494	1,080,786.7	2,476	2,731	22,967,340	47,393,763.8	87.75	193.61	4.69	41.31	22.91
65+	Any	1,023,680	1,023,680	5,077,501	251,674,761	275,345,298	691,437.6	1,834	2,131	6,380,083	14,120,088.5	160.45	245.85	4.96	49.57	26.52
20-44	Primary	782,682	782,682	2,892,033	106,551,041	112,033,421	297,295.2	150	152	35,725,376	62,085,412.1	21.91	136.14	3.70	36.84	5.05
45-64	Primary	2,015,641	2,015,641	9,447,035	390,240,491	416,159,903	1,081,283.2	536	549	22,967,750	47,399,620.2	87.76	193.61	4.69	41.31	4.96
65+	Primary	1,023,889	1,023,889	5,078,301	251,708,490	275,381,604	691,814.5	459	463	6,380,260	14,122,709.9	160.48	245.84	4.96	49.57	6.63
DPP IV Inhibitors																
20-44	Any	36,881	36,881	120,334	4,025,726	5,234,116	11,330.7	2	2	35,724,764	62,424,278.9	1.03	109.15	3.26	33.45	1.77
45-64	Any	138,560	138,560	634,284	23,107,662	28,712,130	64,544.4	29	30	23,043,781	48,451,847.0	6.01	166.77	4.58	36.43	4.49
65+	Any	56,200	56,200	250,105	10,172,549	11,523,820	28,226.0	15	18	6,449,811	14,798,498.2	8.71	181.01	4.45	40.67	5.31
20-44	Primary	36,893	36,893	120,383	4,027,467	5,236,457	11,336.4	0	0	35,725,376	62,431,096.7	1.03	109.17	3.26	33.46	0.00
45-64	Primary	138,610	138,610	634,428	23,112,478	28,718,328	64,572.8	5	5	23,044,212	48,458,292.4	6.01	166.74	4.58	36.43	0.77
65+	Primary	56,220	56,220	250,148	10,174,107	11,525,685	28,233.3	4	4	6,450,010	14,801,506.7	8.72	180.97	4.45	40.67	1.42

* Years at Risk stop accumulating when first event during episode is encountered

Table 3. Summary of Angioedema following Incident Angiotensin Converting Enzyme (ACE) Inhibitor and Dipeptidyl Peptidase IV (DPP IV) Inhibitor Use in the Mini-Sentinel Distributed Database (MSDD) between October 16, 2006 and December 31, 2012, by Exposure, Diagnosis Position, and Sex

Sex	Diagnosis Position	New Users	New Episodes	Dispensings	Total Days Supplied	Total Amount Supplied	Years at Risk*	New Episodes with Events	Total Number of Events	Eligible Members	Member-Years	New Users per 1,000 Eligible Members	Days Supplied per User	Dispensings per User	Days Supplied per Dispensing	New Episodes with Events per 10,000 Years at
ACE Inhibitors																
Female	Any	1,770,690	1,770,690	7,921,304	341,538,251	366,722,448	943,037.3	2,931	3,278	31,972,768	65,833,832.4	55.38	192.88	4.47	43.12	31.08
Male	Any	2,050,671	2,050,671	9,492,806	406,835,960	436,718,116	1,126,270.0	2,199	2,456	29,485,912	57,754,795.1	69.55	198.39	4.63	42.86	19.52
Unknown	Any	128	128	459	19,731	20,505	54.6	0	0	2,540	4,070.5	50.39	154.15	3.59	42.99	0.00
Female	Primary	1,771,073	1,771,073	7,922,669	341,590,186	366,777,401	943,588.9	621	631	31,973,414	65,842,917.7	55.39	192.87	4.47	43.12	6.58
Male	Primary	2,051,011	2,051,011	9,494,241	406,890,105	436,777,023	1,126,749.4	524	533	29,486,373	57,760,753.6	69.56	198.39	4.63	42.86	4.65
Unknown	Primary	128	128	459	19,731	20,505	54.6	0	0	2,540	4,070.8	50.39	154.15	3.59	42.99	0.00
DPP IV Inhibitors																
Female	Any	110,457	110,457	463,240	17,130,008	20,758,103	47,784.5	18	21	31,972,768	66,901,977.1	3.45	155.08	4.19	36.98	3.77
Male	Any	121,176	121,176	541,463	20,174,909	24,710,193	56,313.7	28	29	29,485,912	58,768,499.1	4.11	166.49	4.47	37.26	4.97
Unknown	Any	8	8	20	1,020	1,770	2.9	0	0	2,540	4,147.9	3.15	127.50	2.50	51.00	0.00
Female	Primary	110,505	110,505	463,366	17,134,094	20,763,181	47,801.1	5	5	31,973,414	66,911,787.4	3.46	155.05	4.19	36.98	1.05
Male	Primary	121,210	121,210	541,573	20,178,938	24,715,519	56,338.4	4	4	29,486,373	58,774,960.1	4.11	166.48	4.47	37.26	0.71
Unknown	Primary	8	8	20	1,020	1,770	2.9	0	0	2,540	4,148.2	3.15	127.50	2.50	51.00	0.00

* Years at Risk stop accumulating when first event during episode is encountered

Table 4. Summary of Angioedema following Incident Angiotensin Converting Enzyme (ACE) Inhibitor and Dipeptidyl Peptidase IV (DPP IV) Inhibitor Use in the Mini-Sentinel Distributed Database (MSDD) between October 16, 2006 and December 31, 2012, by Exposure, Diagnosis Position, and Year

Year	Diagnosis Position	New Users	New Episodes	Dispensings	Total Days Supplied	Total Amount Supplied	Years at Risk*	New Episodes with Events	Total Number of Events	Eligible Members	Member-Years	New Users per 1,000 Eligible Members	Days Supplied per User	Dispensings per User	Days Supplied per Dispensing	New Episodes with Events per 10,000 Years at Risk*
ACE Inhibitors																
2006	Any	87,169	87,169	507,269	25,838,111	27,984,534	71,017.1	116	121	11,978,403	2,371,793.2	7.28	296.41	5.82	50.94	16.33
2007	Any	375,477	375,477	2,177,178	105,919,860	114,366,688	291,743.6	542	576	15,857,183	11,251,114.7	23.68	282.09	5.80	48.65	18.58
2008	Any	629,324	629,324	3,301,886	143,142,018	154,504,205	395,627.2	878	996	30,316,278	18,677,114.0	20.76	227.45	5.25	43.35	22.19
2009	Any	809,432	809,432	3,925,892	165,110,987	177,505,911	457,033.8	1,132	1,270	31,558,353	23,945,789.3	25.65	203.98	4.85	42.06	24.77
2010	Any	716,311	716,311	3,255,246	137,323,686	146,931,521	380,166.0	1,025	1,131	30,127,038	22,934,140.1	23.78	191.71	4.54	42.19	26.96
2011	Any	628,287	628,287	2,507,367	103,829,962	110,613,151	287,512.5	838	967	29,353,023	22,545,814.4	21.40	165.26	3.99	41.41	29.15
2012	Any	575,489	575,489	1,739,731	67,229,318	71,555,059	186,261.8	599	673	28,698,590	21,866,932.5	20.05	116.82	3.02	38.64	32.16
2006	Primary	87,183	87,183	507,309	25,840,882	27,987,353	71,051.7	31	31	11,979,428	2,372,107.3	7.28	296.40	5.82	50.94	4.36
2007	Primary	375,541	375,541	2,177,546	105,935,353	114,383,077	291,905.4	142	146	15,857,627	11,252,421.3	23.68	282.09	5.80	48.65	4.86
2008	Primary	629,459	629,459	3,302,411	143,163,641	154,527,589	395,818.6	210	212	30,316,927	18,679,438.3	20.76	227.44	5.25	43.35	5.31
2009	Primary	809,589	809,589	3,926,441	165,130,963	177,527,510	457,272.7	248	251	31,558,930	23,948,681.1	25.65	203.97	4.85	42.06	5.42
2010	Primary	716,442	716,442	3,255,831	137,344,589	146,953,242	380,350.7	218	223	30,127,462	22,936,915.3	23.78	191.70	4.54	42.18	5.73
2011	Primary	628,400	628,400	2,507,779	103,844,257	110,628,821	287,648.8	185	190	29,353,386	22,548,539.6	21.41	165.25	3.99	41.41	6.43
2012	Primary	575,598	575,598	1,740,052	67,240,337	71,567,335	186,344.9	111	111	28,698,948	21,869,639.2	20.06	116.82	3.02	38.64	5.96
DPP IV Inhibitors																
2006	Any	1,545	1,545	9,524	373,200	390,776	1,035.4	0	0	11,978,403	2,371,793.2	0.13	241.55	6.16	39.19	0.00
2007	Any	16,760	16,760	105,305	4,125,550	4,735,687	11,479.9	3	3	15,881,738	11,264,053.0	1.06	246.15	6.28	39.18	2.61
2008	Any	32,188	32,188	163,602	6,241,354	7,858,919	17,415.7	6	6	30,480,764	18,776,275.4	1.06	193.90	5.08	38.15	3.45
2009	Any	37,373	37,373	171,403	6,576,030	8,215,491	18,349.7	6	6	31,946,614	24,190,812.3	1.17	175.96	4.59	38.37	3.27
2010	Any	39,013	39,013	173,928	6,472,436	7,881,152	18,059.1	14	14	30,775,453	23,365,596.8	1.27	165.90	4.46	37.21	7.75
2011	Any	51,842	51,842	213,500	7,710,118	9,383,496	21,526.7	9	12	30,201,058	23,137,256.0	1.72	148.72	4.12	36.11	4.18
2012	Any	52,920	52,920	167,461	5,807,249	7,004,546	16,234.5	8	9	29,683,144	22,568,837.3	1.78	109.74	3.16	34.68	4.93
2006	Primary	1,546	1,546	9,525	373,206	390,782	1,035.5	0	0	11,979,428	2,372,107.3	0.13	241.40	6.16	39.18	0.00
2007	Primary	16,765	16,765	105,321	4,125,998	4,736,202	11,484.4	0	0	15,882,193	11,265,369.1	1.06	246.11	6.28	39.18	0.00

Table 4. Summary of Angioedema following Incident Angiotensin Converting Enzyme (ACE) Inhibitor and Dipeptidyl Peptidase IV (DPP IV) Inhibitor Use in the Mini-Sentinel Distributed Database (MSDD) between October 16, 2006 and December 31, 2012, by Exposure, Diagnosis Position, and Year

Year	Diagnosis Position	New Users	New Episodes	Dispensings	Total Days Supplied	Total Amount Supplied	Years at Risk*	New Episodes with Events	Total Number of Events	Eligible Members	Member-Years	New Users per 1,000 Eligible Members	Days Supplied per User	Dispensings per User	Days Supplied per Dispensing	New Episodes with Events per 10,000 Years at Risk*
2008	Primary	32,194	32,194	163,627	6,242,164	7,860,089	17,422.6	0	0	30,481,470	18,778,661.2	1.06	193.89	5.08	38.15	0.00
2009	Primary	37,386	37,386	171,454	6,577,610	8,217,641	18,357.1	0	0	31,947,330	24,193,864.2	1.17	175.94	4.59	38.36	0.00
2010	Primary	39,028	39,028	173,971	6,473,893	7,882,881	18,067.3	5	5	30,776,069	23,368,617.8	1.27	165.88	4.46	37.21	2.77
2011	Primary	51,865	51,865	213,550	7,712,047	9,386,265	21,534.6	4	4	30,201,667	23,140,311.9	1.72	148.69	4.12	36.11	1.86
2012	Primary	52,939	52,939	167,511	5,809,134	7,006,611	16,241.0	0	0	29,683,785	22,571,964.3	1.78	109.73	3.16	34.68	0.00

* Years at Risk stop accumulating when first event during episode is encountered

Appendix A. Dates of Available Data for Each Data Partner (DP) in the Mini-Sentinel Distributed Database (MSDD) as of Request Distribution Date (December 20, 2013)

DPID	DP Start Date	DP End Date
DP001	1/2/2008	12/31/2012
DP002	10/16/2006	12/31/2012
DP003	10/16/2006	6/30/2012
DP004	10/16/2006	12/31/2012
DP005	10/16/2006	4/30/2012
DP006	6/2/2007	12/31/2012
DP007	10/16/2006	12/31/2012
DP008	1/2/2008	12/31/2012
DP009	10/16/2006	12/31/2012
DP010	10/16/2006	12/31/2012
DP011	10/16/2006	12/31/2012
DP012	10/16/2006	12/31/2012
DP013	10/16/2006	6/30/2012
DP014	10/16/2006	12/31/2012
DP015	10/16/2006	12/31/2012
DP016	10/16/2006	12/31/2011
DP017	10/16/2006	12/31/2012
DP018	10/16/2006	12/31/2012

Appendix B. Generic Names of Medical Products Used to Define Exposures in this Request

Generic Name
Amlodipine besylate/benazepril
Benazepril HCl
Benazepril/hydrochlorothiazide
Captopril
Captopril/hydrochlorothiazide
Enalapril mal/diltiazem mal
Enalapril maleate
Enalapril maleate/felodipine
Enalapril/hydrochlorothiazide
Fosinopril sodium
Fosinopril/hydrochlorothiazide
Lisinopril
Lisinopril/dietary sup.cmb10
Lisinopril/hydrochlorothiazide
Moexipril HCl
Moexipril/hydrochlorothiazide
Perindopril erbumine
Quinapril HCl
Quinapril/hydrochlorothiazide
Ramipril
Trandolapril
Trandolapril/verapamil HCl
Alogliptin benz/metformin HCl
Alogliptin benz/pioglitzone
Alogliptin benzoate
Linagliptin
Linagliptin/metformin HCl
Saxagliptin HCl
Saxagliptin HCl/metformin HCl
Sitagliptin phos/metformin HCl
Sitagliptin phosphate
Sitagliptin/simvastatin

Appendix C. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) Codes Used to Define Outcomes in this Request

Code	Description	Code Type
995.1	Angioneurotic edema, not elsewhere classified	ICD-9-CM

Appendix D. Specifications of Parameters Used in this Request

This request utilized the Mini-Sentinel Modular Program #3 (MP3) to examine angioedema among new users of dipeptidyl peptidase IV (DPP IV) inhibitors and/or angiotensin converting enzyme (ACE) inhibitors in the Mini-Sentinel Distributed Database (MSDD). In total, four different scenarios will be examined in this report with differing exposures of interest and event PDX indicators. See below for a description of each of these scenarios.

Query Period: October 16, 2006 to December 31, 2012
Enrollment Gap: 45 days
Age Groups: 20-44, 45-64, 65+ years
Coverage Requirement: Medical and Drug Coverage
Enrollment Requirement: 183 days

	Drug/Exposure								Event/Outcome							
Scenario	Incident Exposure	Incident with Respect to:	Washout (days)	Incidence Type[1]	Episode Gap (days)	Episode Extension Period (days)	Minimum Episode Duration (days)	Minimum Days Supplied (days)	Event/ Outcome	Care Setting	Primary Diagnosis (PDX) Indicator	Incident with Respect to:	Incident Only Care Setting	Incident Only PDX Indicator	Washout (days)	Incidence Type[1]	Blackout Period (days)
1	DPP IV Inhibitors	DPP IV Inhibitors or ACE Inhibitors	183	Single	10	0	0	0	Angioedema	Inpatient (IP), Emergency Department (ED)	NO	Angioedema	IP, ED	NO	183	Multiple	0
2	ACE Inhibitors	DPP IV Inhibitors or ACE Inhibitors	183	Single	10	0	0	0	Angioedema	IP, ED	NO	Angioedema	IP, ED	NO	183	Multiple	0
3	DPP IV Inhibitors	DPP IV Inhibitors or ACE Inhibitors	183	Single	10	0	0	0	Angioedema	IP, ED	YES	Angioedema	IP, ED	YES	183	Multiple	0
4	ACE Inhibitors	DPP IV Inhibitors or ACE Inhibitors	183	Single	10	0	0	0	Angioedema	IP, ED	YES	Angioedema	IP, ED	YES	183	Multiple	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

[1]"Single" incidence type indicates that only the first valid episode is captured while "Multiple" incidence type indicates that all valid episodes are captured

Note: When we have an incident exposure of DPP IV inhibitors, we look for a new DPP IV inhibitor episode with respect to both DPP IV inhibitors and ACE inhibitors (Scenarios 1 and 3 above). This means that an incident DPP IV inhibitor user does not have a prior dispensing of DPP IV inhibitors or ACE inhibitors in the prior 183 days. Once we have a DPP IV inhibitor treatment episode, if the user begins an ACE inhibitor regimen, the initial DPP IV inhibitor treatment episode will be truncated even if DPP IV inhibitor use continues along with ACE inhibitor use. The same logic can be applied when we have an incident exposure of ACE inhibitors and we look for incident episodes with respect to both DPP IV and ACE inhibitors (Scenarios 2 and 4 above).