



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

Request Description

FDA's Center for Drug Evaluation and Research requested execution of Modular Program #3 (MP3), version 5.0, to investigate kidney stones following new use of anti-epileptic medications among all exposed patients and among those with a pre-existing condition of epilepsy and those with an exclusion of pre-existing anti-diabetic agent exposure. This involved two runs of MP3. This report contains the results from the second run--kidney stones following new use of anti-epileptic medications among patients with a pre-existing condition of epilepsy or with an exclusion of pre-existing anti-diabetic agent use in the Mini-Sentinel Distributed Database (MSDD). A second report (MS_Brief_Report_MS4_MPR55_v1, Report 1 of 2) contains results from the first run--kidney stones following new use of anti-epileptic medications among all exposed patients. Please see the Specifications tab for details into the exact parameters used in this request.

The query was run against the Mini-Sentinel Distributed Database for the time period of January 1, 2004 – December 31, 2012. The package was distributed to 18 Data Partners on August 15, 2013.

Request ID

msy4_mpr55_v1, Report 2 of 2

Specifications

Program parameter inputs and scenarios

Glossary

List of terms found in this report and their definitions

Table 1

Table displaying the Number of New Users, New Episodes, Dispensings, Total Days Supplied, Years at Risk, New Events, Eligible Members, Member-Years, New Users per 1,000 Eligible Members, Days Supplied per User, Dispensings per User, Days Supplied per Dispensing, and New Events per 10,000 Years at Risk by Drug Product and Lookback Period - January 1, 2004 to December 31, 2012

Table 2

Table displaying the Number of New Users, New Episodes, Dispensings, Total Days Supplied, Years at Risk, New Events, Eligible Members, Member-Years, New Users per 1,000 Eligible Members, Days Supplied per User, Dispensings per User, Days Supplied per Dispensing, and New Events per 10,000 Years at Risk by Drug Product and Lookback Period and Age Group - January 1, 2004 to December 31, 2012

Table 3

Table displaying the Number of New Users, New Episodes, Dispensings, Total Days Supplied, Years at Risk, New Events, Eligible Members, Member-Years, New Users per 1,000 Eligible Members, Days Supplied per User, Dispensings per User, Days Supplied per Dispensing, and New Events per 10,000 Years at Risk by Drug Product and Lookback Period and Sex - January 1, 2004 to December 31, 2012

Table 4

Table displaying the Number of New Users, New Episodes, Dispensings, Total Days Supplied, Years at Risk, New Events, Eligible Members, Member-Years, New Users per 1,000 Eligible Members, Days Supplied per User, Dispensings per User, Days Supplied per Dispensing, and New Events per 10,000 Years at Risk by Drug Product and Lookback Period and Year - January 1, 2004 to December 31, 2012

Appendix A

Table displaying a list of epilepsy and kidney stone codes included in this request

Notes:

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_MPR55_v1

Modular Program #3, version 5.0, was used to investigate kidney stones following new use of anti-epileptic drugs (AEDs) among all patients and among those with a pre-existing condition of epilepsy and those with an exclusion of pre-existing anti-diabetic agent use. The query period was from January 1, 2004-December 31, 2012, and the enrollment gap was set at 45 days. Age groups were split as follows: 0-9, 10-16, 17-64, 65+. In total, 31 different scenarios were examined in this request with differing exposures of interest, blackout periods, and inclusion/exclusion criteria. This report contains information from Scenarios 23 through 31 outlined below. A second report (msy4_mpr55_v1, Report 1 of 2) contains results from Scenarios 1 through 22. See below for a description of each of these scenarios.

Enrollment Gap 45 Days
Age Groups 0-9, 10-16, 17-64, 65+
Query Period January 1, 2004 - December 31, 2012

Scenario	Drug/Exposure							Pre-Existing Condition					Event/Outcome							
	Incident exposure	Incident w/ respect to:	Wash out (days)	Incidence Type*	Episode Gap	Exposure Extension Period	Min Episode Duration	Min Days Supplied	Pre-Existing Condition	Include or Exclude	Lookback Start	Lookback End	Care Setting	Event/Outcome	Care Setting	Incident w/ respect to:	Incident Only Care Setting	Washout (days)	Incidence Type**	Blackout Period
1	Topiramate	All AEDs	183	SING	10	10	0	0	NA	NA	NA	NA	NA	Kidney Stones	Any	Kidney Stones	Any	183	MULT	0
2	Gabapentin	All AEDs	183	SING	10	10	0	0	NA	NA	NA	NA	NA	Kidney Stones	Any	Kidney Stones	Any	183	MULT	0
3	Zonisamide	All AEDs	183	SING	10	10	0	0	NA	NA	NA	NA	NA	Kidney Stones	Any	Kidney Stones	Any	183	MULT	0
4	Topiramate	All AEDs	183	SING	10	10	0	0	NA	NA	NA	NA	NA	Kidney Stones	Any	Kidney Stones	Any	183	MULT	90
5	Gabapentin	All AEDs	183	SING	10	10	0	0	NA	NA	NA	NA	NA	Kidney Stones	Any	Kidney Stones	Any	183	MULT	90
6	Zonisamide	All AEDs	183	SING	10	10	0	0	NA	NA	NA	NA	NA	Kidney Stones	Any	Kidney Stones	Any	183	MULT	90
7	Topiramate	All AEDs	183	SING	10	10	0	0	NA	NA	NA	NA	NA	Kidney Stones	Any	Kidney Stones	Any	183	MULT	183
8	Gabapentin	All AEDs	183	SING	10	10	0	0	NA	NA	NA	NA	NA	Kidney Stones	Any	Kidney Stones	Any	183	MULT	183
9	Zonisamide	All AEDs	183	SING	10	10	0	0	NA	NA	NA	NA	NA	Kidney Stones	Any	Kidney Stones	Any	183	MULT	183
10	Topiramate	All AEDs	183	SING	10	10	0	0	NA	NA	NA	NA	NA	Kidney Stones	Any	Kidney Stones	Any	183	MULT	365
11	Gabapentin	All AEDs	183	SING	10	10	0	0	NA	NA	NA	NA	NA	Kidney Stones	Any	Kidney Stones	Any	183	MULT	365
12	Zonisamide	All AEDs	183	SING	10	10	0	0	NA	NA	NA	NA	NA	Kidney Stones	Any	Kidney Stones	Any	183	MULT	365
13	Topiramate	All AEDs	183	SING	10	10	0	0	NA	NA	NA	NA	NA	Kidney Stones	Any	Kidney Stones	Any	183	MULT	730

Scenario	Drug/Exposure								Pre-Existing Condition					Event/Outcome						
	Incident exposure	Incident w/ respect to:	Wash out (days)	Incidence Type*	Episode Gap	Exposure Extension Period	Min Episode Duration	Min Days Supplied	Pre-Existing Condition	Include or Exclude	Lookback Start	Lookback End	Care Setting	Event/Outcome	Care Setting	Incident w/ respect to:	Incident Only Care Setting	Washout (days)	Incidence Type**	Blackout Period
14	<i>Gabapentin</i>	<i>All AEDs</i>	183	<i>SING</i>	10	10	0	0	NA	NA	NA	NA	NA	<i>Kidney Stones</i>	<i>Any</i>	<i>Kidney Stones</i>	<i>Any</i>	183	<i>MULT</i>	730
15	<i>Zonisamide</i>	<i>All AEDs</i>	183	<i>SING</i>	10	10	0	0	NA	NA	NA	NA	NA	<i>Kidney Stones</i>	<i>Any</i>	<i>Kidney Stones</i>	<i>Any</i>	183	<i>MULT</i>	730
16	<i>All AEDs</i>	<i>All AEDs</i>	183	<i>SING</i>	10	10	0	0	NA	NA	NA	NA	NA	<i>Kidney Stones</i>	<i>Any</i>	<i>Kidney Stones</i>	<i>Any</i>	183	<i>MULT</i>	0
17	<i>All AEDs minus topiramate, gabapentin, and zonisamide</i>	<i>All AEDs</i>	183	<i>SING</i>	10	10	0	0	NA	NA	NA	NA	NA	<i>Kidney Stones</i>	<i>Any</i>	<i>Kidney Stones</i>	<i>Any</i>	183	<i>MULT</i>	0
18	<i>Lamotrigine, levetiracetam, carbamazepine, oxcarbazepine, phenytoin, or valproic acid</i>	<i>All AEDs</i>	183	<i>SING</i>	10	10	0	0	NA	NA	NA	NA	NA	<i>Kidney Stones</i>	<i>Any</i>	<i>Kidney Stones</i>	<i>Any</i>	183	<i>MULT</i>	0
19	<i>Lamotrigine, levetiracetam, carbamazepine, oxcarbazepine, phenytoin, or valproic acid</i>	<i>All AEDs</i>	183	<i>SING</i>	10	10	0	0	NA	NA	NA	NA	NA	<i>Kidney Stones</i>	<i>Any</i>	<i>Kidney Stones</i>	<i>Any</i>	183	<i>MULT</i>	90
20	<i>Lamotrigine, levetiracetam, carbamazepine, oxcarbazepine, phenytoin, or valproic acid</i>	<i>All AEDs</i>	183	<i>SING</i>	10	10	0	0	NA	NA	NA	NA	NA	<i>Kidney Stones</i>	<i>Any</i>	<i>Kidney Stones</i>	<i>Any</i>	183	<i>MULT</i>	183
21	<i>Lamotrigine, levetiracetam, carbamazepine, oxcarbazepine, phenytoin, or valproic acid</i>	<i>All AEDs</i>	183	<i>SING</i>	10	10	0	0	NA	NA	NA	NA	NA	<i>Kidney Stones</i>	<i>Any</i>	<i>Kidney Stones</i>	<i>Any</i>	183	<i>MULT</i>	365

Scenario	Drug/Exposure							Pre-Existing Condition					Event/Outcome							
	Incident exposure	Incident w/ respect to:	Wash out (days)	Incidence Type*	Episode Gap	Exposure Extension Period	Min Episode Duration	Min Days Supplied	Pre-Existing Condition	Include or Exclude	Lookback Start	Lookback End	Care Setting	Event/Outcome	Care Setting	Incident w/ respect to:	Incident Only Care Setting	Washout (days)	Incidence Type**	Blackout Period
22	Lamotrigine, levetiracetam, carbamazepine, oxcarbazepine, phenytoin, or valproic acid	All AEDs	183	SING	10	10	0	0	NA	NA	NA	NA	NA	Kidney Stones	Any	Kidney Stones	Any	183	MULT	730
23	Topiramate	All AEDs	183	SING	10	10	0	0	Epilepsy	Include	-183	-1	Any	Kidney Stones	Any	Kidney Stones	Any	183	MULT	0
24	Gabapentin	All AEDs	183	SING	10	10	0	0	Epilepsy	Include	-183	-1	Any	Kidney Stones	Any	Kidney Stones	Any	183	MULT	0
25	Zonisamide	All AEDs	183	SING	10	10	0	0	Epilepsy	Include	-183	-1	Any	Kidney Stones	Any	Kidney Stones	Any	183	MULT	0
26	Topiramate	All AEDs	183	SING	10	10	0	0	Epilepsy	Include	-365	-1	Any	Kidney Stones	Any	Kidney Stones	Any	183	MULT	0
27	Gabapentin	All AEDs	183	SING	10	10	0	0	Epilepsy	Include	-365	-1	Any	Kidney Stones	Any	Kidney Stones	Any	183	MULT	0
28	Zonisamide	All AEDs	183	SING	10	10	0	0	Epilepsy	Include	-365	-1	Any	Kidney Stones	Any	Kidney Stones	Any	183	MULT	0
29	Topiramate	All AEDs	183	SING	10	10	0	0	Any Anti-Diabetic Agent	Exclude	-183	-1	Any	Kidney Stones	Any	Kidney Stones	Any	183	MULT	0
30	Gabapentin	All AEDs	183	SING	10	10	0	0	Any Anti-Diabetic Agent	Exclude	-183	-1	Any	Kidney Stones	Any	Kidney Stones	Any	183	MULT	0
31	Zonisamide	All AEDs	183	SING	10	10	0	0	Any Anti-Diabetic Agent	Exclude	-183	-1	Any	Kidney Stones	Any	Kidney Stones	Any	183	MULT	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

*Single incidence type for the exposure will only consider the first incident episode for each user during the query period that satisfies the Washout Period criteria (183 or 365 days). There can be at most one episode per user.

**Mult incidence type for the event will only consider the first event for each episode that satisfies the Washout Period criteria of 183 days. There can be at most one event per episode and consequently, one event per user.

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 Anti-Epileptic Drug Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by Drug Product, Pre-Existing Condition Criteria, and Lookback Period

	New Users	New Episodes	Total Days Dispensings	Total Days Supplied	Years at Risk	New Events	Eligible Members	Member-Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	Events / 10K Years at Risk
Gabapentin (Pre-Existing Condition of Epilepsy, 183-Day Lookback Period)													
	5,341	5,341	13,889	476,152	1,345	50	369,606	176,817	14.45	89.15	2.60	34.28	371.62
Gabapentin (Pre-Existing Condition of Epilepsy, 365-Day Lookback Period)													
	7,834	7,834	19,714	673,800	1,916	65	400,016	290,338	19.58	86.01	2.52	34.18	339.28
Gabapentin (Exclusion of Individuals with Pre-Existing Anti-Diabetic Agent Use, 183-Day Lookback)													
	1,087,633	1,087,633	2,303,021	79,851,156	237,817	5,781	84,182,372	188,626,047	12.92	73.42	2.12	34.67	243.09
Topiramate (Pre-Existing Condition of Epilepsy, 183-Day Lookback Period)													
	6,769	6,769	21,461	725,929	2,041	49	369,606	176,677	18.31	107.24	3.17	33.83	240.05
Topiramate (Pre-Existing Condition of Epilepsy, 365-Day Lookback Period)													
	8,209	8,209	25,089	854,957	2,410	60	400,016	290,045	20.52	104.15	3.06	34.08	249.00
Topiramate (Exclusion of Individuals with Pre-Existing Anti-Diabetic Agent Use, 183-Day Lookback)													
	332,841	332,841	830,382	28,368,852	83,507	1,999	84,182,383	189,291,296	3.95	85.23	2.49	34.16	239.38
Zonisamide (Pre-Existing Condition of Epilepsy, 183-Day Lookback Period)													
	1,556	1,556	6,128	204,016	563	10	369,606	177,061	4.21	131.12	3.94	33.29	177.53
Zonisamide (Pre-Existing Condition of Epilepsy, 365-Day Lookback Period)													
	1,820	1,820	6,799	227,069	629	11	400,017	291,070	4.55	124.76	3.74	33.40	174.75
Zonisamide (Exclusion of Individuals with Pre-Existing Anti-Diabetic Agent Use, 183-Day Lookback)													
	16,710	16,710	42,825	1,386,937	4,057	118	84,182,422	189,525,628	0.20	83.00	2.56	32.39	290.88

Table 2: Summary of Incident Anti-Epileptic Drug Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by Drug Product, Pre-Existing Condition Criteria, Lookback Period, and Age Group

	New Users	New Episodes	Dispensings	Total Days Supplied	Years at Risk	New Events	Eligible Members	Member-Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	Events / 10K Years at Risk
Gabapentin (Pre-Existing Condition of Epilepsy, 183-Day Lookback Period)													
0 to 9 Years	120	120	598	18,844	53	0	55,388	24,328	2.17	157.03	4.98	31.51	0.00
10 to 16 Years	134	134	399	12,190	32	2	39,359	19,391	3.40	90.97	2.98	30.55	629.96
17 to 64 Years	3,819	3,819	9,005	301,765	861	30	215,881	100,911	17.69	79.02	2.36	33.51	348.27
65+ Years	1,268	1,268	3,887	143,353	400	18	68,744	32,186	18.45	113.05	3.07	36.88	450.34
Gabapentin (Pre-Existing Condition of Epilepsy, 365-Day Lookback Period)													
0 to 9 Years	148	148	653	20,457	58	0	58,944	40,753	2.51	138.22	4.41	31.33	0.00
10 to 16 Years	180	180	486	14,562	39	2	44,105	31,689	4.08	80.90	2.70	29.96	511.77
17 to 64 Years	5,597	5,597	13,018	433,951	1,244	38	237,419	167,221	23.57	77.53	2.33	33.33	305.37
65+ Years	1,909	1,909	5,557	204,830	575	25	73,449	50,675	25.99	107.30	2.91	36.86	434.90
Gabapentin (Exclusion of Individuals with Pre-Existing Anti-Diabetic Agent Use, 183-Day Lookback)													
0 to 9 Years	2,616	2,616	6,869	212,511	632	3	12,525,023	24,497,660	0.21	81.24	2.63	30.94	47.50
10 to 16 Years	10,534	10,534	21,355	662,383	2,030	14	10,527,423	19,945,539	1.00	62.88	2.03	31.02	68.96
17 to 64 Years	797,173	797,173	1,601,977	52,924,380	159,453	3,857	60,813,785	126,467,713	13.11	66.39	2.01	33.04	241.89
65+ Years	277,310	277,310	672,820	26,051,882	75,703	1,907	6,949,176	17,715,136	39.91	93.94	2.43	38.72	251.91
Topiramate (Pre-Existing Condition of Epilepsy, 183-Day Lookback Period)													
0 to 9 Years	685	685	2,863	93,887	260	2	55,388	24,275	12.37	137.06	4.18	32.79	77.04
10 to 16 Years	963	963	3,526	123,000	349	4	39,319	19,324	24.49	127.73	3.66	34.88	114.58
17 to 64 Years	4,877	4,877	14,197	475,342	1,343	39	215,814	100,792	22.60	97.47	2.91	33.48	290.43
65+ Years	244	244	875	33,700	90	4	68,756	32,287	3.55	138.11	3.59	38.51	446.01
Topiramate (Pre-Existing Condition of Epilepsy, 365-Day Lookback Period)													
0 to 9 Years	756	756	3,086	101,100	280	3	58,944	40,657	12.83	133.73	4.08	32.76	106.98
10 to 16 Years	1,115	1,115	4,018	140,191	399	5	44,033	31,549	25.32	125.73	3.60	34.89	125.34
17 to 64 Years	6,042	6,042	16,970	574,627	1,626	48	237,305	166,942	25.46	95.11	2.81	33.86	295.29
65+ Years	296	296	1,015	39,039	105	4	73,471	50,897	4.03	131.89	3.43	38.46	381.97
Topiramate (Exclusion of Individuals with Pre-Existing Anti-Diabetic Agent Use, 183-Day Lookback)													
0 to 9 Years	4,223	4,223	12,625	404,287	1,193	3	12,525,023	24,497,698	0.34	95.73	2.99	32.02	25.15
10 to 16 Years	24,726	24,726	58,274	1,889,065	5,736	42	10,526,699	19,938,262	2.35	76.40	2.36	32.42	73.22
17 to 64 Years	294,390	294,390	736,102	25,149,968	73,934	1,896	60,809,209	126,885,275	4.84	85.43	2.50	34.17	256.44
65+ Years	9,502	9,502	23,381	925,532	2,644	58	6,969,167	17,970,061	1.36	97.40	2.46	39.58	219.37

Table 2: Summary of Incident Anti-Epileptic Drug Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by Drug Product, Pre-Existing Condition Criteria, Lookback Period, and Age Group

	New Users	New Episodes	Dispensings	Total Days Supplied	Years at Risk	New Events	Eligible Members	Member-Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	Events / 10K Years at Risk
Zonisamide (Pre-Existing Condition of Epilepsy, 183-Day Lookback Period)													
0 to 9 Years	240	240	1,212	37,345	99	2	55,388	24,308	4.33	155.60	5.05	30.81	201.55
10 to 16 Years	240	240	1,188	39,569	110	0	39,355	19,379	6.10	164.87	4.95	33.31	0.00
17 to 64 Years	989	989	3,271	109,692	307	6	215,865	101,075	4.58	110.91	3.31	33.53	195.37
65+ Years	87	87	457	17,410	47	2	68,763	32,299	1.27	200.11	5.25	38.10	424.12
Zonisamide (Pre-Existing Condition of Epilepsy, 365-Day Lookback Period)													
0 to 9 Years	268	268	1,298	40,426	108	2	58,944	40,726	4.55	150.84	4.84	31.14	185.24
10 to 16 Years	264	264	1,252	41,585	116	0	44,099	31,683	5.99	157.52	4.74	33.21	0.00
17 to 64 Years	1,185	1,185	3,745	125,888	354	7	237,397	167,727	4.99	106.23	3.16	33.61	197.84
65+ Years	103	103	504	19,170	52	2	73,487	50,933	1.40	186.12	4.89	38.04	383.22
Zonisamide (Exclusion of Individuals with Pre-Existing Anti-Diabetic Agent Use, 183-Day Lookback)													
0 to 9 Years	547	547	2,602	85,905	236	3	12,525,023	24,499,307	0.04	157.05	4.76	33.01	127.31
10 to 16 Years	1,181	1,181	4,120	132,859	386	1	10,528,184	19,952,414	0.11	112.50	3.49	32.25	25.91
17 to 64 Years	14,147	14,147	33,476	1,076,344	3,178	104	60,817,512	127,094,856	0.23	76.08	2.37	32.15	327.29
65+ Years	835	835	2,627	91,829	257	10	6,970,962	17,979,052	0.12	109.97	3.15	34.96	388.56

Table 3: Summary of Incident Anti-Epileptic Drug Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by Drug Product, Pre-Existing Condition Criteria, Lookback Period, and Sex

	New Users	New Episodes	Dispensings	Total Days Supplied	Years at Risk	New Events	Eligible Members	Member-Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	Events / 10K Years at Risk
Gabapentin (Pre-Existing Condition of Epilepsy, 183-Day Lookback Period)													
Female	3,145	3,145	8,270	280,325	797	23	191,374	88,662	16.43	89.13	2.63	33.90	288.46
Male	2,196	2,196	5,619	195,827	548	27	178,217	88,151	12.32	89.17	2.56	34.85	492.59
Unknown	0	0	0	0	0	0	15	4	0.00	---	---	---	---
Gabapentin (Pre-Existing Condition of Epilepsy, 365-Day Lookback Period)													
Female	4,727	4,727	11,968	407,098	1,164	30	208,223	146,980	22.70	86.12	2.53	34.02	257.76
Male	3,107	3,107	7,746	266,702	752	35	191,778	143,350	16.20	85.84	2.49	34.43	465.43
Unknown	0	0	0	0	0	0	15	7	0.00	---	---	---	---
Gabapentin (Exclusion of Individuals with Pre-Existing Anti-Diabetic Agent Use, 183-Day Lookback)													
Female	663,672	663,672	1,398,058	48,645,468	145,004	2,857	42,705,797	96,142,461	15.54	73.30	2.11	34.80	197.03
Male	423,925	423,925	904,898	31,202,607	92,805	2,924	41,472,742	92,477,182	10.22	73.60	2.13	34.48	315.07
Unknown	36	36	65	3,081	9	0	3,833	6,405	9.39	85.58	1.81	47.40	0.00
Topiramate (Pre-Existing Condition of Epilepsy, 183-Day Lookback Period)													
Female	4,824	4,824	14,990	507,470	1,432	31	191,373	88,535	25.21	105.20	3.11	33.85	216.47
Male	1,944	1,944	6,469	218,399	609	18	178,218	88,138	10.91	112.35	3.33	33.76	295.56
Unknown	1	1	2	60	0	0	15	4	66.67	60.00	2.00	30.00	0.00
Topiramate (Pre-Existing Condition of Epilepsy, 365-Day Lookback Period)													
Female	5,908	5,908	17,735	606,486	1,713	39	208,221	146,692	28.37	102.66	3.00	34.20	227.64
Male	2,300	2,300	7,352	248,411	696	21	191,780	143,347	11.99	108.00	3.20	33.79	301.60
Unknown	1	1	2	60	0	0	15	7	66.67	60.00	2.00	30.00	0.00
Topiramate (Exclusion of Individuals with Pre-Existing Anti-Diabetic Agent Use, 183-Day Lookback)													
Female	271,049	271,049	690,350	23,637,783	69,501	1,515	42,705,794	96,505,331	6.35	87.21	2.55	34.24	217.98
Male	61,778	61,778	140,013	4,730,515	14,005	484	41,472,756	92,779,556	1.49	76.57	2.27	33.79	345.60
Unknown	14	14	19	554	2	0	3,833	6,410	3.65	39.57	1.36	29.16	0.00
Zonisamide (Pre-Existing Condition of Epilepsy, 183-Day Lookback Period)													
Female	871	871	3,322	110,430	306	6	191,374	88,818	4.55	126.79	3.81	33.24	195.79
Male	685	685	2,806	93,586	257	4	178,217	88,240	3.84	136.62	4.10	33.35	155.74
Unknown	0	0	0	0	0	0	15	4	0.00	---	---	---	---

Table 3: Summary of Incident Anti-Epileptic Drug Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by Drug Product, Pre-Existing Condition Criteria, Lookback Period, and Sex

	New Users	New Episodes	Dispensings	Total Days Supplied	Years at Risk	New Events	Eligible Members	Member-Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	Events / 10K Years at Risk
Zonisamide (Pre-Existing Condition of Epilepsy, 365-Day Lookback Period)													
Female	1,042	1,042	3,761	126,004	351	6	208,223	147,437	5.00	120.93	3.61	33.50	170.82
Male	778	778	3,038	101,065	278	5	191,779	143,625	4.06	129.90	3.90	33.27	179.70
Unknown	0	0	0	0	0	0	15	7	0.00	---	---	---	---
Zonisamide (Exclusion of Individuals with Pre-Existing Anti-Diabetic Agent Use, 183-Day Lookback)													
Female	12,364	12,364	30,187	978,844	2,884	75	42,705,832	96,692,524	0.29	79.17	2.44	32.43	260.03
Male	4,345	4,345	12,637	408,063	1,172	43	41,472,757	92,826,688	0.10	93.92	2.91	32.29	366.81
Unknown	1	1	1	30	0	0	3,833	6,416	0.26	30.00	1.00	30.00	0.00

Table 4: Summary of Incident Anti-Epileptic Drug Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by Drug Product, Pre-Existing Condition Criteria, Lookback Period, and Year

	New Users	New Episodes	Dispensings	Total Days Supplied	Years at Risk	New Events	Eligible Members	Member-Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	Events / 10K Years at Risk
Gabapentin (Pre-Existing Condition of Epilepsy, 183-Day Lookback Period)													
2004	116	116	498	17,921	51	1	11,737	3,544	9.88	154.49	4.29	35.99	195.29
2005	96	96	241	9,598	28	0	12,461	3,892	7.70	99.98	2.51	39.83	0.00
2006	153	153	472	17,183	49	1	27,363	7,310	5.59	112.31	3.08	36.40	204.44
2007	295	295	986	32,541	90	5	43,421	12,996	6.79	110.31	3.34	33.00	556.19
2008	693	693	1,970	69,485	200	3	83,926	23,950	8.26	100.27	2.84	35.27	150.23
2009	882	882	2,397	82,549	233	5	102,559	31,856	8.60	93.59	2.72	34.44	214.60
2010	964	964	2,639	89,661	255	7	101,773	32,051	9.47	93.01	2.74	33.98	274.89
2011	1,023	1,023	2,539	86,781	248	12	102,631	32,442	9.97	84.83	2.48	34.18	483.10
2012	1,119	1,119	2,147	70,433	192	16	93,599	28,775	11.96	62.94	1.92	32.81	832.83
Gabapentin (Pre-Existing Condition of Epilepsy, 365-Day Lookback Period)													
2004	180	180	631	22,660	65	1	15,448	6,278	11.65	125.89	3.51	35.91	153.12
2005	134	134	333	13,192	38	0	16,305	6,845	8.22	98.45	2.49	39.62	0.00
2006	200	200	649	23,995	67	2	32,003	11,374	6.25	119.98	3.25	36.97	298.19
2007	407	407	1,254	42,099	118	5	52,454	21,079	7.76	103.44	3.08	33.57	424.08
2008	948	948	2,609	90,669	262	3	96,771	37,265	9.80	95.64	2.75	34.75	114.66
2009	1,307	1,307	3,363	115,078	329	6	127,059	52,704	10.29	88.05	2.57	34.22	182.29
2010	1,452	1,452	3,785	127,269	366	12	126,216	53,244	11.50	87.65	2.61	33.62	328.21
2011	1,570	1,570	3,932	135,509	388	15	127,257	53,974	12.34	86.31	2.50	34.46	386.97
2012	1,636	1,636	3,158	103,329	283	21	117,628	47,573	13.91	63.16	1.93	32.72	740.94
Gabapentin (Exclusion of Individuals with Pre-Existing Anti-Diabetic Agent Use, 183-Day Lookback)													
2004	29,389	29,389	78,275	2,827,023	8,291	152	8,003,790	6,343,854	3.67	96.19	2.66	36.12	183.34
2005	26,058	26,058	62,022	2,532,175	7,399	110	8,209,334	6,661,067	3.17	97.17	2.38	40.83	148.67
2006	45,329	45,329	108,233	4,287,203	12,556	202	18,685,842	11,206,108	2.43	94.58	2.39	39.61	160.88
2007	74,555	74,555	175,066	6,483,149	19,162	399	22,099,241	15,878,675	3.37	86.96	2.35	37.03	208.22
2008	134,655	134,655	301,285	10,504,830	31,415	689	42,097,888	25,954,330	3.20	78.01	2.24	34.87	219.32
2009	187,454	187,454	409,816	14,063,881	42,213	983	43,835,105	33,279,869	4.28	75.03	2.19	34.32	232.87
2010	191,989	191,989	420,005	14,222,330	42,702	1,095	41,894,139	31,944,533	4.58	74.08	2.19	33.86	256.43
2011	203,206	203,206	418,505	14,128,514	42,463	1,185	40,575,396	31,205,769	5.01	69.53	2.06	33.76	279.06
2012	194,998	194,998	329,814	10,802,051	31,616	966	37,502,989	26,151,842	5.20	55.40	1.69	32.75	305.54

Table 4: Summary of Incident Anti-Epileptic Drug Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by Drug Product, Pre-Existing Condition Criteria, Lookback Period, and Year

	New Users	New Episodes	Dispensings	Total Days Supplied	Years at Risk	New Events	Eligible Members	Member-Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	Events / 10K Years at Risk
Topiramate (Pre-Existing Condition of Epilepsy, 183-Day Lookback Period)													
2004	181	181	781	25,642	73	3	11,737	3,544	15.42	141.67	4.31	32.83	411.19
2005	144	144	519	21,723	61	0	12,449	3,888	11.57	150.85	3.60	41.86	0.00
2006	346	346	1,316	45,844	127	4	27,349	7,306	12.65	132.50	3.80	34.84	315.16
2007	556	556	2,308	77,917	218	8	43,400	12,990	12.81	140.14	4.15	33.76	367.33
2008	1,030	1,030	3,774	129,182	364	11	83,876	23,939	12.28	125.42	3.66	34.23	301.91
2009	1,292	1,292	4,110	135,514	387	3	102,481	31,832	12.61	104.89	3.18	32.97	77.59
2010	1,137	1,137	3,768	124,497	346	10	101,651	32,019	11.19	109.50	3.31	33.04	289.05
2011	1,095	1,095	3,026	103,071	294	8	102,519	32,410	10.68	94.13	2.76	34.06	272.56
2012	988	988	1,859	62,539	172	2	93,473	28,749	10.57	63.30	1.88	33.64	116.21
Topiramate (Pre-Existing Condition of Epilepsy, 365-Day Lookback Period)													
2004	230	230	945	32,921	94	4	15,448	6,277	14.89	143.13	4.11	34.84	426.88
2005	183	183	664	25,722	70	1	16,290	6,834	11.23	140.56	3.63	38.74	142.75
2006	398	398	1,508	52,678	145	4	31,978	11,362	12.45	132.36	3.79	34.93	275.05
2007	665	665	2,623	90,442	253	10	52,376	21,053	12.70	136.00	3.94	34.48	394.49
2008	1,185	1,185	4,202	143,741	405	14	96,684	37,232	12.26	121.30	3.55	34.21	345.27
2009	1,575	1,575	4,834	161,683	463	3	126,948	52,659	12.41	102.66	3.07	33.45	64.78
2010	1,405	1,405	4,421	149,363	418	12	126,004	53,179	11.15	106.31	3.15	33.78	287.37
2011	1,341	1,341	3,589	120,887	346	9	127,143	53,929	10.55	90.15	2.68	33.68	260.39
2012	1,227	1,227	2,303	77,520	215	3	117,497	47,521	10.44	63.18	1.88	33.66	139.47
Topiramate (Exclusion of Individuals with Pre-Existing Anti-Diabetic Agent Use, 183-Day Lookback)													
2004	8,678	8,678	25,434	923,031	2,678	57	8,003,789	6,344,524	1.08	106.36	2.93	36.29	212.85
2005	7,584	7,584	20,954	796,454	2,304	45	8,221,684	6,668,775	0.92	105.02	2.76	38.01	195.33
2006	16,154	16,154	49,116	1,872,039	5,356	128	18,705,428	11,219,723	0.86	115.89	3.04	38.11	238.97
2007	25,468	25,468	76,664	2,756,509	8,022	192	22,135,318	15,904,667	1.15	108.23	3.01	35.96	239.33
2008	43,901	43,901	116,379	3,983,060	11,778	287	42,162,966	26,002,640	1.04	90.73	2.65	34.22	243.67
2009	61,210	61,210	162,587	5,437,373	16,088	367	43,950,139	33,364,213	1.39	88.83	2.66	33.44	228.13
2010	59,339	59,339	151,096	5,058,627	14,998	362	42,068,851	32,075,217	1.41	85.25	2.55	33.48	241.37
2011	56,291	56,291	130,590	4,365,991	12,978	314	40,804,039	31,379,426	1.38	77.56	2.32	33.43	241.95
2012	54,216	54,216	97,562	3,175,768	9,305	247	37,770,154	26,332,110	1.44	58.58	1.80	32.55	265.45

Table 4: Summary of Incident Anti-Epileptic Drug Use and Kidney Stones in the MSDD between January 1, 2004 and December 31, 2012, by Drug Product, Pre-Existing Condition Criteria, Lookback Period, and Year

	New Users	New Episodes	Dispensings	Total Days Supplied	Years at Risk	New Events	Eligible Members	Member-Years	New Users / 1K Eligible Members	Days Supplied/ User	Dispensings / User	Days Supplied/ Dispensing	Events / 10K Years at Risk
Zonisamide (Pre-Existing Condition of Epilepsy, 183-Day Lookback Period)													
2004	57	57	268	9,111	25	0	11,737	3,544	4.86	159.84	4.70	34.00	0.00
2005	43	43	177	5,974	17	0	12,464	3,893	3.45	138.93	4.12	33.75	0.00
2006	83	83	431	16,036	45	0	27,362	7,310	3.03	193.20	5.19	37.21	0.00
2007	143	143	650	20,910	59	1	43,439	13,004	3.29	146.22	4.55	32.17	169.17
2008	232	232	979	30,521	86	2	83,963	23,967	2.76	131.56	4.22	31.18	232.46
2009	264	264	1,150	39,236	107	1	102,642	31,889	2.57	148.62	4.36	34.12	93.49
2010	274	274	1,169	38,559	106	4	101,897	32,093	2.69	140.73	4.27	32.98	378.51
2011	240	240	816	27,451	75	1	102,783	32,500	2.34	114.38	3.40	33.64	133.04
2012	220	220	488	16,218	44	1	93,800	28,860	2.35	73.72	2.22	33.23	228.21
Zonisamide (Pre-Existing Condition of Epilepsy, 365-Day Lookback Period)													
2004	70	70	296	10,021	28	0	15,448	6,279	4.53	143.16	4.23	33.85	0.00
2005	52	52	195	6,655	19	0	16,329	6,854	3.18	127.98	3.75	34.13	0.00
2006	92	92	452	16,786	47	0	32,036	11,387	2.87	182.46	4.91	37.14	0.00
2007	160	160	690	22,414	63	1	52,500	21,097	3.05	140.09	4.31	32.48	157.93
2008	273	273	1,095	34,291	97	2	96,880	37,314	2.82	125.61	4.01	31.32	206.09
2009	327	327	1,346	45,712	125	2	127,301	52,805	2.57	139.79	4.12	33.96	160.32
2010	301	301	1,248	41,429	114	4	126,554	53,385	2.38	137.64	4.15	33.20	351.30
2011	285	285	917	31,298	87	1	127,737	54,165	2.23	109.82	3.22	34.13	115.31
2012	260	260	560	18,463	50	1	118,123	47,785	2.20	71.01	2.15	32.97	199.44
Zonisamide (Exclusion of Individuals with Pre-Existing Anti-Diabetic Agent Use, 183-Day Lookback)													
2004	917	917	2,894	87,663	256	5	8,003,790	6,344,701	0.11	95.60	3.16	30.29	195.41
2005	582	582	1,358	44,351	131	4	8,225,962	6,671,269	0.07	76.20	2.33	32.66	305.97
2006	943	943	2,953	98,011	284	5	18,713,152	11,224,959	0.05	103.94	3.13	33.19	176.16
2007	1,404	1,404	4,058	133,601	393	9	22,149,926	15,914,305	0.06	95.16	2.89	32.92	229.26
2008	2,340	2,340	6,256	203,015	596	16	42,189,204	26,020,367	0.06	86.76	2.67	32.45	268.57
2009	3,083	3,083	7,741	249,081	732	15	43,994,663	33,394,145	0.07	80.79	2.51	32.18	204.87
2010	2,772	2,772	7,274	235,674	689	27	42,136,377	32,121,482	0.07	85.02	2.62	32.40	391.86
2011	2,493	2,493	6,190	203,232	594	21	40,890,306	31,440,179	0.06	81.52	2.48	32.83	353.51
2012	2,176	2,176	4,101	132,309	383	16	37,865,844	26,394,222	0.06	60.80	1.88	32.26	418.19

Appendix A. List of Codes included in this Request

Epilepsy Code:

International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) Diagnosis Code

345* Epilepsy

Kidney Stone Codes:

International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) Diagnosis Codes

592.0 Calculus of kidney
 592.1 Calculus of ureter
 592.9 Urinary calculus, unspecified
 274.11 Uric acid nephrolithiasis
 594 Calculus of lower urinary tract

International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) Procedure Codes

55.04 Percutaneous Nephrostomy With Fragmentation
 55.92 Percutaneous aspiration of kidney (pelvis)
 56.2 Ureterotomy
 59.8 Ureteral Catheterization
 59.95 Ultrasonic Fragmentation Of Urinary Stones
 98.51 Extracorporeal shockwave lithotripsy of the kidney, ureter and/or bladder
 55.04 Percutaneous Nephrostomy With Fragmentation
 98.51 Extracorporeal shockwave lithotripsy of the kidney, ureter and/or bladder
 59.95 Ultrasonic Fragmentation Of Urinary Stones

Healthcare Common Procedure Coding System (HCPCS)

50060 Removal of Kidney Stone
 50065 Incision of Kidney
 50070 Incision of Kidney
 50075 Removal of Kidney Stone
 50080 Removal of Kidney Stone
 50081 Removal of Kidney Stone
 50130 Removal of Kidney Stone
 50590 Fragmenting of Kidney Stone
 50610 Removal of Ureter Stone
 50620 Removal of Ureter Stone
 50630 Removal of Ureter Stone
 52320 Cystoscopy and Treatment
 52325 Cystoscopy Stone Removal
 52330 Cystoscopy and Treatment
 52336 Cystourethroscopy with Ureteroscopy; with Remove Calculus
 52337 Cystourethroscopy with Ureteroscopy; with Lith
 50945 Laparoscopy Ureterolithotomy
 50561 Kidney Endoscopy and Treatment
 50580 Kidney Endoscopy and Treatment
 51060 Removal of Ureter Stone
 51065 Remove Ureter Calculus
 50080 Removal of Kidney Stone
 50081 Removal of Kidney Stone
 50060 Removal of Kidney Stone
 50070 Incision of Kidney
 50075 Removal of Kidney Stone
 50610 Removal of Ureter Stone
 50620 Removal of Ureter Stone

Healthcare Common Procedure Coding System (HCPCS) - continued

50630	Removal of Ureter Stone
50590	Fragmenting of Kidney Stone
52320	Cystoscopy and Treatment
52325	Cystoscopy Stone Removal
52352	Cystouretero with Stone Remove
52353	Cystouretero with Lithotripsy
