

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 MSY2_MP3t2

Request ID: MSY2_MP3t2

Request Description: This report investigates acute myocardial infarction (AMI) and stroke among carbidopa/levodopa, entacapone, and combination product carbidopa, levodopa, and entacapone (Stalevo) users with Parkinson's Disease (PD).

Modular Program Tool Used: Modular Program #3 (MP3), version 1.0

Data Source: Data from January 1, 2000 to December 31, 2010 from 15 Data Partners contributing to the Mini-Sentinel Distributed Database (MSDD) were included in this request. The package was distributed to Data Partners on February 24, 2011. (See Appendix A for a list of dates of available data for each Data Partner).

Study Design: The request was designed to count new users, dispensings, total days dispensed, days at risk, and new events of AMI and stroke among carbidopa/levodopa, entacapone, and combination product carbidopa, levodopa, and entacapone (Stalevo) users with PD.

Cohort Eligibility Criteria: The following age groups were included in the cohort: 18-44, 45-64, and 65+ years. For drug and exposure, the episode gap was set to 7 days, and both minimum episode duration and minimum days supplied were set to 0 days. The washout period was set at 183 and 365 days. In total, 12 different scenarios were examined in this report with differing exposures of interest, incidence criteria, washout periods, and events/outcomes. See Appendix B for specifications used in this request.

Limitations: Algorithms used to define exposures and outcomes are imperfect; thus, it is possible that there may be misclassification.

Notes: Please contact the Sentinel Operations Center Query Fulfillment Team (qf@sentinelssystem.org) for questions and to provide comments/suggestions for future enhancements to this document. If you are using a web page screen reader and are unable to access this document, please contact the Sentinel Operations Center for assistance at info@sentinelssystem.org.

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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.

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 Carbidopa/Levodopa, Entacapone, and Combination Product Carbidopa, Levodopa, and Entacapone (Stalevo) Use in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2010, by Drug Product, Washout, and Event

	New Users	Dispensings	Total Days Supplied	Days at Risk	New Events	Dispensings/ User	Days Supplied/ User	Days Supplied/ Dispensing	New Events/100k Days at Risk
Carbidopa/Levodopa									
<i>183-Day Washout</i>									
Stroke	29,986	158,163	8,029,817	7,272,847	314	5.3	267.8	50.8	4.3
AMI	29,986	158,163	8,029,817	7,288,335	185	5.3	267.8	50.8	2.5
<i>365-Day Washout</i>									
Stroke	26,447	140,451	7,317,492	6,610,734	289	5.3	276.7	52.1	4.4
AMI	26,447	140,451	7,317,492	6,623,924	175	5.3	276.7	52.1	2.6
Entacapone									
<i>183-Day Washout</i>									
Stroke	5,928	23,055	1,139,458	1,100,400	40	3.9	192.2	49.4	3.6
AMI	5,928	23,055	1,139,458	1,101,445	25	3.9	192.2	49.4	2.3
<i>365-Day Washout</i>									
Stroke	5,332	20,757	1,054,253	1,014,683	37	3.9	197.7	50.8	3.6
AMI	5,332	20,757	1,054,253	1,015,623	24	3.9	197.7	50.8	2.4
Combination Product*									
<i>183-Day Washout</i>									
Stroke	3,234	14,132	497,868	493,479	7	4.4	153.9	35.2	1.4
AMI	3,234	14,132	497,868	493,694	11	4.4	153.9	35.2	2.2
<i>365-Day Washout</i>									
Stroke	2,548	11,250	400,409	394,526	7	4.4	157.1	35.6	1.8
AMI	2,548	11,250	400,409	394,741	11	4.4	157.1	35.6	2.8

*Combination product comprised of carbidopa, levodopa, and entacapone (Stalevo)

Acute Myocardial Infarction (AMI)

Table 2. Summary of Carbidopa/Levodopa, Entacapone, and Combination Product Carbidopa, Levodopa, and Entacapone (Stalevo) Use in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2010, by Drug Product, Washout, Event, and Age Group

	New Users	Dispensings	Total Days Supplied	Dispensings/ User	Days Supplied/ User	Days Supplied/ Dispensing
Carbidopa/Levodopa						
183-Day Washout						
Stroke						
18 to 44 years	247	1,295	52,931	5.2	214.3	40.9
45 to 64 years	5,255	31,165	1,592,523	5.9	303.0	51.1
65+ years	24,484	125,703	6,384,363	5.1	260.8	50.8
AMI						
18 to 44 years	247	1,295	52,931	5.2	214.3	40.9
45 to 64 years	5,255	31,165	1,592,523	5.9	303.0	51.1
65+ years	24,484	125,703	6,384,363	5.1	260.8	50.8
365-Day Washout						
Stroke						
18 to 44 years	202	1,093	45,649	5.4	226.0	41.8
45 to 64 years	4,510	27,516	1,434,833	6.1	318.1	52.1
65+ years	21,735	111,842	5,837,010	5.1	268.6	52.2
AMI						
18 to 44 years	202	1,093	45,649	5.4	226.0	41.8
45 to 64 years	4,510	27,516	1,434,833	6.1	318.1	52.1
65+ years	21,735	111,842	5,837,010	5.1	268.6	52.2
Entacapone						
183-Day Washout						
Stroke						
18 to 44 years	75	264	11,982	3.5	159.8	45.4
45 to 64 years	1,453	6,351	319,187	4.4	219.7	50.3
65+ years	4,400	16,440	808,289	3.7	183.7	49.2
AMI						
18 to 44 years	75	264	11,982	3.5	159.8	45.4
45 to 64 years	1,453	6,351	319,187	4.4	219.7	50.3
65+ years	4,400	16,440	808,289	3.7	183.7	49.2

Table 2. Summary of Carbidopa/Levodopa, Entacapone, and Combination Product Carbidopa, Levodopa, and Entacapone (Stalevo) Use in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2010, by Drug Product, Washout, Event, and Age Group

	New Users	Dispensings	Total Days Supplied	Dispensings/ User	Days Supplied/ User	Days Supplied/ Dispensing
365-Day Washout						
Stroke						
18 to 44 years	66	223	10,848	3.4	164.4	48.6
45 to 64 years	1,290	5,627	291,123	4.4	225.7	51.7
65+ years	3,976	14,907	752,282	3.7	189.2	50.5
AMI						
18 to 44 years	66	223	10,848	3.4	164.4	48.6
45 to 64 years	1,290	5,627	291,123	4.4	225.7	51.7
65+ years	3,976	14,907	752,282	3.7	189.2	50.5
Combination Product*						
183-Day Washout						
Stroke						
18 to 44 years	47	259	8,759	5.5	186.4	33.8
45 to 64 years	960	5,068	180,507	5.3	188.0	35.6
65+ years	2,227	8,805	308,602	4.0	138.6	35.0
AMI						
18 to 44 years	47	259	8,759	5.5	186.4	33.8
45 to 64 years	960	5,068	180,507	5.3	188.0	35.6
65+ years	2,227	8,805	308,602	4.0	138.6	35.0
365-Day Washout						
Stroke						
18 to 44 years	34	168	6,020	4.9	177.1	35.8
45 to 64 years	757	4,143	147,407	5.5	194.7	35.6
65+ years	1,757	6,939	246,982	3.9	140.6	35.6
AMI						
18 to 44 years	34	168	6,020	4.9	177.1	35.8
45 to 64 years	757	4,143	147,407	5.5	194.7	35.6
65+ years	1,757	6,939	246,982	3.9	140.6	35.6

*Combination product comprised of carbidopa, levodopa, and entacapone (Stalevo)

Acute Myocardial Infarction (AMI)

Table 3. Summary of Carbidopa/Levodopa, Entacapone, and Combination Product Carbidopa, Levodopa, and Entacapone (Stalevo) Use in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2010, by Drug Product, Washout, Event, and Sex

	New Users	Dispensings	Total Days Supplied	Dispensings/ User	Days Supplied/ User	Days Supplied/ Dispensing
Carbidopa/Levodopa						
183-Day Washout						
Stroke						
Female	12,103	64,032	3,134,170	5.3	259.0	48.9
Male	17,877	94,089	4,893,926	5.3	273.8	52.0
Unknown	5	14	579	2.8	115.8	41.4
AMI						
Female	12,103	64,032	3,134,170	5.3	259.0	48.9
Male	17,877	94,089	4,893,926	5.3	273.8	52.0
Unknown	5	14	579	2.8	115.8	41.4
365-Day Washout						
Stroke						
Female	10,705	56,824	2,849,512	5.3	266.2	50.1
Male	15,737	83,593	4,466,648	5.3	283.8	53.4
Unknown	4	6	190	1.5	47.5	31.7
AMI						
Female	10,705	56,824	2,849,512	5.3	266.2	50.1
Male	15,737	83,593	4,466,648	5.3	283.8	53.4
Unknown	4	6	190	1.5	47.5	31.7
Entacapone						
183-Day Washout						
Stroke						
Female	2,138	8,012	394,053	3.7	184.3	49.2
Male	3,788	15,039	745,275	4.0	196.7	49.6
Unknown	1	1	30	1.0	30.0	30.0
AMI						
Female	2,138	8,012	394,053	3.7	184.3	49.2
Male	3,788	15,039	745,275	4.0	196.7	49.6
Unknown	1	1	30	1.0	30.0	30.0

Table 3. Summary of Carbidopa/Levodopa, Entacapone, and Combination Product Carbidopa, Levodopa, and Entacapone (Stalevo) Use in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2010, by Drug Product, Washout, Event, and Sex

	New Users	Dispensings	Total Days Supplied	Dispensings/ User	Days Supplied/ User	Days Supplied/ Dispensing
365-Day Washout						
Stroke						
Female	1,907	7,177	361,359	3.8	189.5	50.3
Male	3,423	13,576	692,764	4.0	202.4	51.0
Unknown	1	1	30	1.0	30.0	30.0
AMI						
Female	1,907	7,177	361,359	3.8	189.5	50.3
Male	3,423	13,576	692,764	4.0	202.4	51.0
Unknown	1	1	30	1.0	30.0	30.0
Combination Product*						
183-Day Washout						
Stroke						
Female	1,220	5,471	190,612	4.5	156.2	34.8
Male	2,014	8,661	307,256	4.3	152.6	35.5
Unknown	0	0	0	0.0	0.0	0.0
AMI						
Female	1,220	5,471	190,612	4.5	156.2	34.8
Male	2,014	8,661	307,256	4.3	152.6	35.5
Unknown	0	0	0	0.0	0.0	0.0
365-Day Washout						
Stroke						
Female	963	4,369	154,849	4.5	160.8	35.4
Male	1,585	6,881	245,560	4.3	154.9	35.7
Unknown	0	0	0	0.0	0.0	0.0
AMI						
Female	963	4,369	154,849	4.5	160.8	35.4
Male	1,585	6,881	245,560	4.3	154.9	35.7
Unknown	0	0	0	0.0	0.0	0.0

*Combination product comprised of carbidopa, levodopa, and entacapone (Stalevo)

Acute Myocardial Infarction (AMI)

A missing value for sex was in the dataset and accounts for the patient numbers in the stratified table

Table 4. Summary of Carbidopa/Levodopa, Entacapone, and Combination Product Carbidopa, Levodopa, and Entacapone (Stalevo) Use in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2010, by Drug Product, Washout, Event, and Year

	New Users	Dispensings	Total Days Supplied		New Events	Dispensings/ User	Days Supplied/ User	Days Supplied/ Dispensing	New Events/100k Days at Risk
			Supplied	Days at Risk					
Carbidopa/Levodopa									
<i>183-Day Washout</i>									
Stroke									
2000	1,697	14,803	792,517	695,993	27	8.7	467.0	53.5	3.9
2001	1,507	10,793	641,883	564,455	42	7.2	425.9	59.5	7.4
2002	1,560	10,084	619,500	542,425	30	6.5	397.1	61.4	5.5
2003	1,577	11,058	670,433	586,505	21	7.0	425.1	60.6	3.6
2004	2,330	13,902	761,547	696,508	23	6.0	326.8	54.8	3.3
2005	2,958	17,925	950,565	867,520	34	6.1	321.4	53.0	3.9
2006	2,948	17,621	856,565	792,209	35	6.0	290.6	48.6	4.4
2007	3,100	16,609	809,472	751,126	28	5.4	261.1	48.7	3.7
2008	4,664	20,731	899,541	853,209	40	4.4	192.9	43.4	4.7
2009	4,848	17,831	755,481	690,803	26	3.7	155.8	42.4	3.8
2010	2,797	6,806	272,313	232,094	8	2.4	97.4	40.0	3.4
AMI									
2000	1,697	14,803	792,517	694,001	19	8.7	467.0	53.5	2.7
2001	1,507	10,793	641,883	566,404	27	7.2	425.9	59.5	4.8
2002	1,560	10,084	619,500	549,034	19	6.5	397.1	61.4	3.5
2003	1,577	11,058	670,433	589,860	18	7.0	425.1	60.6	3.1
2004	2,330	13,902	761,547	693,334	18	6.0	326.8	54.8	2.6
2005	2,958	17,925	950,565	864,401	19	6.1	321.4	53.0	2.2
2006	2,948	17,621	856,565	798,337	9	6.0	290.6	48.6	1.1
2007	3,100	16,609	809,472	755,965	8	5.4	261.1	48.7	1.1
2008	4,664	20,731	899,541	853,444	25	4.4	192.9	43.4	2.9
2009	4,848	17,831	755,481	691,267	20	3.7	155.8	42.4	2.9
2010	2,797	6,806	272,313	232,288	3	2.4	97.4	40.0	1.3

Table 4. Summary of Carbidopa/Levodopa, Entacapone, and Combination Product Carbidopa, Levodopa, and Entacapone (Stalevo) Use in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2010, by Drug Product, Washout, Event, and Year

	New Users	Dispensings	Total Days Supplied	Days at Risk	New Events	Dispensings/ User	Days Supplied/ User	Days Supplied/ Dispensing	New Events/100k Days at Risk
365-Day Washout									
Stroke									
2000	1,422	13,011	694,580	610,489	22	9.1	488.5	53.4	3.6
2001	1,455	10,345	618,780	544,767	41	7.1	425.3	59.8	7.5
2002	1,476	9,521	588,640	515,444	27	6.5	398.8	61.8	5.2
2003	1,528	10,699	646,648	566,871	21	7.0	423.2	60.4	3.7
2004	1,557	9,377	596,730	538,992	18	6.0	383.3	63.6	3.3
2005	2,816	17,172	913,787	836,900	34	6.1	324.5	53.2	4.1
2006	2,697	16,095	801,956	742,681	35	6.0	297.4	49.8	4.7
2007	2,748	14,812	743,665	686,164	25	5.4	270.6	50.2	3.6
2008	3,681	16,521	752,383	707,064	34	4.5	204.4	45.5	4.8
2009	4,440	16,411	700,692	640,066	24	3.7	157.8	42.7	3.7
2010	2,627	6,487	259,631	221,296	8	2.5	98.8	40.0	3.6
AMI									
2000	1,422	13,011	694,580	608,313	18	9.1	488.5	53.4	3.0
2001	1,455	10,345	618,780	546,784	26	7.1	425.3	59.8	4.8
2002	1,476	9,521	588,640	521,385	19	6.5	398.8	61.8	3.6
2003	1,528	10,699	646,648	570,226	18	7.0	423.2	60.4	3.2
2004	1,557	9,377	596,730	534,315	17	6.0	383.3	63.6	3.2
2005	2,816	17,172	913,787	833,781	19	6.1	324.5	53.2	2.3
2006	2,697	16,095	801,956	748,826	8	6.0	297.4	49.8	1.1
2007	2,748	14,812	743,665	690,743	8	5.4	270.6	50.2	1.2
2008	3,681	16,521	752,383	707,662	19	4.5	204.4	45.5	2.7
2009	4,440	16,411	700,692	640,399	20	3.7	157.8	42.7	3.1
2010	2,627	6,487	259,631	221,490	3	2.5	98.8	40.0	1.4

Table 4. Summary of Carbidopa/Levodopa, Entacapone, and Combination Product Carbidopa, Levodopa, and Entacapone (Stalevo) Use in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2010, by Drug Product, Washout, Event, and Year

	New Users	Dispensings	Total Days Supplied	Days at Risk	New Events	Dispensings/ User	Days Supplied/ User	Days Supplied/ Dispensing	New Events/100k Days at Risk
Entacapone									
<i>183-Day Washout</i>									
Stroke									
2000	478	2,644	118,338	116,253	5	5.5	247.6	44.8	4.3
2001	503	2,002	118,330	108,914	5	4.0	235.2	59.1	4.6
2002	359	1,597	92,923	88,853	6	4.4	258.8	58.2	6.8
2003	467	1,787	99,485	96,363	2	3.8	213.0	55.7	2.1
2004	482	2,424	112,994	109,132	3	5.0	234.4	46.6	2.7
2005	561	2,284	107,136	105,819	2	4.1	191.0	46.9	1.9
2006	678	2,962	151,420	146,689	6	4.4	223.3	51.1	4.1
2007	591	2,066	104,313	103,005	2	3.5	176.5	50.5	1.9
2008	688	2,444	108,297	107,354	7	3.6	157.4	44.3	6.5
2009	703	1,932	85,681	83,357	1	2.7	121.9	44.3	1.2
2010	418	913	40,541	34,661	1	2.2	97.0	44.4	2.9
AMI									
2000	478	2,644	118,338	117,260	6	5.5	247.6	44.8	5.1
2001	503	2,002	118,330	108,756	2	4.0	235.2	59.1	1.8
2002	359	1,597	92,923	88,962	3	4.4	258.8	58.2	3.4
2003	467	1,787	99,485	94,923	3	3.8	213.0	55.7	3.2
2004	482	2,424	112,994	109,750	3	5.0	234.4	46.6	2.7
2005	561	2,284	107,136	105,227	1	4.1	191.0	46.9	1.0
2006	678	2,962	151,420	147,194	1	4.4	223.3	51.1	0.7
2007	591	2,066	104,313	103,013	1	3.5	176.5	50.5	1.0
2008	688	2,444	108,297	108,392	2	3.6	157.4	44.3	1.8
2009	703	1,932	85,681	83,289	3	2.7	121.9	44.3	3.6
2010	418	913	40,541	34,679	0	2.2	97.0	44.4	0.0

Table 4. Summary of Carbidopa/Levodopa, Entacapone, and Combination Product Carbidopa, Levodopa, and Entacapone (Stalevo) Use in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2010, by Drug Product, Washout, Event, and Year

	New Users	Dispensings	Total Days Supplied	Days at Risk	New Events	Dispensings/ User	Days Supplied/ User	Days Supplied/ Dispensing	New Events/100k Days at Risk
365-Day Washout									
Stroke									
2000	443	2,424	110,283	108,127	5	5.5	248.9	45.5	4.6
2001	481	1,934	114,725	105,184	5	4.0	238.5	59.3	4.8
2002	338	1,503	86,322	83,337	5	4.4	255.4	57.4	6.0
2003	459	1,764	97,842	94,679	2	3.8	213.2	55.5	2.1
2004	328	1,701	89,756	85,441	3	5.2	273.6	52.8	3.5
2005	522	2,178	103,100	101,518	2	4.2	197.5	47.3	2.0
2006	613	2,692	141,436	136,357	6	4.4	230.7	52.5	4.4
2007	541	1,905	98,622	97,205	1	3.5	182.3	51.8	1.0
2008	567	2,020	94,269	92,954	6	3.6	166.3	46.7	6.5
2009	649	1,776	79,533	77,125	1	2.7	122.5	44.8	1.3
2010	391	860	38,365	32,756	1	2.2	98.1	44.6	3.1
AMI									
2000	443	2,424	110,283	109,134	6	5.5	248.9	45.5	5.5
2001	481	1,934	114,725	105,026	2	4.0	238.5	59.3	1.9
2002	338	1,503	86,322	83,425	2	4.4	255.4	57.4	2.4
2003	459	1,764	97,842	93,239	3	3.8	213.2	55.5	3.2
2004	328	1,701	89,756	86,059	3	5.2	273.6	52.8	3.5
2005	522	2,178	103,100	100,926	1	4.2	197.5	47.3	1.0
2006	613	2,692	141,436	136,862	1	4.4	230.7	52.5	0.7
2007	541	1,905	98,622	97,154	1	3.5	182.3	51.8	1.0
2008	567	2,020	94,269	93,967	2	3.6	166.3	46.7	2.1
2009	649	1,776	79,533	77,057	3	2.7	122.5	44.8	3.9
2010	391	860	38,365	32,774	0	2.2	98.1	44.6	0.0

Table 4. Summary of Carbidopa/Levodopa, Entacapone, and Combination Product Carbidopa, Levodopa, and Entacapone (Stalevo) Use in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2010, by Drug Product, Washout, Event, and Year

	New Users	Dispensings	Total Days Supplied		New Events	Dispensings/ User	Days Supplied/ User	Days Supplied/ Dispensing	New Events/100k Days at Risk
			Supplied	Days at Risk					
Combination Product*									
<i>183-Day Washout</i>									
Stroke									
2000	0	0	0	0	0	0.0	0.0	0.0	0.0
2001	0	0	0	0	0	0.0	0.0	0.0	0.0
2002	0	0	0	0	0	0.0	0.0	0.0	0.0
2003	23	191	6,142	5,532	0	8.3	267.0	32.2	0.0
2004	284	1,454	47,693	48,984	1	5.1	167.9	32.8	2.0
2005	393	2,103	71,245	72,024	1	5.4	181.3	33.9	1.4
2006	434	2,369	85,082	84,782	1	5.5	196.0	35.9	1.2
2007	368	1,686	59,914	59,691	2	4.6	162.8	35.5	3.4
2008	715	2,961	106,511	108,015	2	4.1	149.0	36.0	1.9
2009	643	2,415	85,206	83,044	0	3.8	132.5	35.3	0.0
2010	374	953	36,075	31,407	0	2.5	96.5	37.9	0.0
AMI									
2000	0	0	0	0	0	0.0	0.0	0.0	0.0
2001	0	0	0	0	0	0.0	0.0	0.0	0.0
2002	0	0	0	0	0	0.0	0.0	0.0	0.0
2003	23	191	6,142	5,532	0	8.3	267.0	32.2	0.0
2004	284	1,454	47,693	49,013	0	5.1	167.9	32.8	0.0
2005	393	2,103	71,245	72,024	0	5.4	181.3	33.9	0.0
2006	434	2,369	85,082	85,470	2	5.5	196.0	35.9	2.3
2007	368	1,686	59,914	59,747	0	4.6	162.8	35.5	0.0
2008	715	2,961	106,511	108,030	3	4.1	149.0	36.0	2.8
2009	643	2,415	85,206	82,490	5	3.8	132.5	35.3	6.1
2010	374	953	36,075	31,388	1	2.5	96.5	37.9	3.2

Table 4. Summary of Carbidopa/Levodopa, Entacapone, and Combination Product Carbidopa, Levodopa, and Entacapone (Stalevo) Use in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2000 and December 31, 2010, by Drug Product, Washout, Event, and Year

	New Users	Dispensings	Total Days Supplied		New Events	Dispensings/ User	Days Supplied/ User	Days Supplied/ Dispensing	New Events/100k Days at Risk
365-Day Washout									
Stroke									
2000	0	0	0	0	0	0.0	0.0	0.0	0.0
2001	0	0	0	0	0	0.0	0.0	0.0	0.0
2002	0	0	0	0	0	0.0	0.0	0.0	0.0
2003	19	186	5,991	5,353	0	9.8	315.3	32.2	0.0
2004	43	286	11,230	11,071	1	6.7	261.2	39.3	9.0
2005	356	1,916	65,478	66,161	1	5.4	183.9	34.2	1.5
2006	384	2,153	76,146	75,466	1	5.6	198.3	35.4	1.3
2007	308	1,397	49,608	49,100	2	4.5	161.1	35.5	4.1
2008	533	2,228	81,961	82,875	2	4.2	153.8	36.8	2.4
2009	568	2,214	78,383	76,013	0	3.9	138.0	35.4	0.0
2010	337	870	31,612	28,487	0	2.6	93.8	36.3	0.0
AMI									
2000	0	0	0	0	0	0.0	0.0	0.0	0.0
2001	0	0	0	0	0	0.0	0.0	0.0	0.0
2002	0	0	0	0	0	0.0	0.0	0.0	0.0
2003	19	186	5,991	5,353	0	9.8	315.3	32.2	0.0
2004	43	286	11,230	11,100	0	6.7	261.2	39.3	0.0
2005	356	1,916	65,478	66,161	0	5.4	183.9	34.2	0.0
2006	384	2,153	76,146	76,154	2	5.6	198.3	35.4	2.6
2007	308	1,397	49,608	49,156	0	4.5	161.1	35.5	0.0
2008	533	2,228	81,961	82,890	3	4.2	153.8	36.8	3.6
2009	568	2,214	78,383	75,459	5	3.9	138.0	35.4	6.6
2010	337	870	31,612	28,468	1	2.6	93.8	36.3	3.5

*Combination product comprised of carbidopa, levodopa, and entacapone (Stalevo)

Acute Myocardial Infarction (AMI)

Appendix A. Available Data in the Mini-Sentinel Distributed Database (MSDD) for Each Data Partner as of Request Send Date (February 24, 2011)

DP ID	Start Date	End Date
DP001	1/1/2000	12/31/2010
DP002	1/1/2000	12/31/2010
DP003	1/1/2000	12/31/2010
DP004	1/1/2000	12/31/2010
DP005	1/1/2000	12/31/2010
DP006	1/1/2000	12/31/2010
DP007	1/1/2000	12/31/2010
DP008	1/1/2000	12/31/2010
DP009	1/1/2000	12/31/2010
DP010	1/1/2000	12/31/2010
DP011	1/1/2000	12/31/2010
DP012	1/1/2000	12/31/2010
DP013	1/1/2000	12/31/2010
DP014	1/1/2000	12/31/2010
DP015	1/1/2000	12/31/2010

Appendix B. Specifications for Request MSY2_MP3t2

FDA requested use Modular Program #3 (MP3) (version 1.0) to investigate acute myocardial infarction (AMI) and stroke among entacapone users with Parkinson's Disease (PD). The query was run against the Mini-Sentinel Distributed Database (MSDD) for the time period January 1, 2000 to December 31, 2010. For drug and exposure the episode gap was set to seven days and both minimum episode duration and minimum days supplied were set to 0 days. Age groups were split as follows: 18-44, 45-64, and 65+ years. In total, 12 different scenarios were examined in this report with differing exposures of interest, incidence criteria, washout period, and event/outcome. See below for a description of each of these scenarios.

Scenario	Drug/Exposure				Pre-Existing Condition			Event/Outcome				
	Incident exposure	Incident w/ respect to (incidence criteria):	Washout (days)	Episode Extension Period	Pre-Existing Condition	Lookback Period	Lookback Type	Event/Outcome	Washout (days)	Care Setting	Principal Diagnosis	Blackout Period
1	Carbidopa/Levodopa	Carbidopa/Levodopa	183	Yes	Paralysis Agitans	183	Fixed	Stroke	0	ED, IP	Yes	1
2	Carbidopa/Levodopa	Carbidopa/Levodopa	365	Yes	Paralysis Agitans	183	Fixed	Stroke	0	ED, IP	Yes	1
3	Carbidopa/Levodopa	Carbidopa/Levodopa	183	Yes	Paralysis Agitans	183	Fixed	AMI	0	ED, IP	Yes	1
4	Carbidopa/Levodopa	Carbidopa/Levodopa	365	Yes	Paralysis Agitans	183	Fixed	AMI	0	ED, IP	Yes	1
5	Entacapone	Entacapone	183	Yes	Paralysis Agitans	183	Fixed	Stroke	0	ED, IP	Yes	1
6	Entacapone	Entacapone	365	Yes	Paralysis Agitans	183	Fixed	Stroke	0	ED, IP	Yes	1
7	Entacapone	Entacapone	183	Yes	Paralysis Agitans	183	Fixed	AMI	0	ED, IP	Yes	1
8	Entacapone	Entacapone	365	Yes	Paralysis Agitans	183	Fixed	AMI	0	ED, IP	Yes	1
9	Combination Product*	Combination Product*	183	Yes	Paralysis Agitans	183	Fixed	Stroke	0	ED, IP	Yes	1
10	Combination Product*	Combination Product*	365	Yes	Paralysis Agitans	183	Fixed	Stroke	0	ED, IP	Yes	1
11	Combination Product*	Combination Product*	183	Yes	Paralysis Agitans	183	Fixed	AMI	0	ED, IP	Yes	1
12	Combination Product*	Combination Product*	365	Yes	Paralysis Agitans	183	Fixed	AMI	0	ED, IP	Yes	1

*Combination product comprised of carbidopa, levodopa, and entacapone (Stalevo)