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 to09y05_mpr_wp30_v01
Request ID: to09y05_mpr_wp30_v01   **Request Description:** Analyses were conducted to calculate the prevalence and incidence of fingolimod use in the Mini-Sentinel Distributed Database (MSDD). Results comprise counts of prevalent and incident (new) users, new starts, dispensings, days supplied, amounts supplied, eligible members, member-years, days supplied and dispensings per user, days supplied per dispensing, and prevalent and incident (new) users per 1,000 eligible members.   **Mini-Sentinel Modular Program Tool Used**: Modular Program 9, version 3.0   **Data Source**: Data from January 1, 2010 to May 31, 2013 from 17 Data Partners contributing to the MSDD were included in the analyses. The request was distributed on April 18, 2014; this report contains information from 17 Data Partners. See Appendix A for a list of the dates of available data for each Data Partner.   **Study Design**: This request was designed to identify the prevalence and incidence of fingolimod use. Fingolimod products were identified using National Drug Codes (NDCs).   **Cohort Eligibility Criteria**: Patients were required to be continuously enrolled for at least 90 days, 180 days, or 270 days, during which enrollment gaps of up to 45 days were allowed. The following age groups were included in the cohort: 0-21, 22-44, 45-64, and 65+ years. Incidence was defined as fingolimod use without prior fingolimod use in the 90, 180, or 270 days before the index date.   **Please see *Appendix B* for the specifications of parameters that were used in the analyses for this request.**   **Notes:** Please contact the Sentinel Operations Center (info@sentinelsystem.org) for questions and to provide comments/suggestions for future enhancements to this document. Please refer to the Sentinel Distributed Query Tool Modular Program documentation and Investigator manual on the Sentinel website (https://www.sentinelinitiative.org/sentinel/routine-querying-tools/level-1-modular-program-queries) for more details.

Table of Contents

Glossary of Terms in Modular Program 9*

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

Care Setting - Contains the care settings considered for the individual diagnosis or procedure codes of interest. The following are valid entries:

    IP: inpatient hospital stays

    IS: non-acute institutional stays

    ED: emergency department visits

    AV: ambulatory visits

    OA: other ambulatory visits.

Days Supplied - Number of days supplied for <u>all dispensings</u> encountered by individuals in the prevalent or incident cohort. The number is reported by the pharmacist as the number of days that the medications supports, based on the number of doses. (To be included in the incident-based cohort, a member must have a dispensing that meets the criteria specified for incidence type and washout period. However, if a member has more than one dispensings claim on the index date, all claims identified on that date will be included in the number of dispensings. Claims identified any time after the index date are not included in

Dispensings - Total number of dispensings for members included in the prevalent- or incident-based cohort. To be included in the incident-based cohort, a member must have a dispensing that meets the criteria specified for incidence type and washout period. However, if a member has more than one dispensings claim on the index date, all claims identified on that date will be included in the number of dispensings. Claims identified any time after the index date are not included in dispensings.

Eligible Members (incidence-based cohort) - Number of members eligible for incident diagnosis (defined by the washout period) with drug and/or medical coverage during the query period.

Eligible Members (prevalence-based cohort) - Number of members with at least one day of drug and/or medical coverage during the query period.

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

Exposure - NDC and/or procedure and/or diagnosis code values for the exposure(s) of interest.

Incidence Type (incidence-based cohort) - *Minimum incidence type* will only consider the first claim in the query period as long as it is the first claim in the user's entire available history. *Single incidence type* will consider the first claim in the query period that satisfies the washout period criteria. That is, incidence is defined as the first claim during the query period with no evidence of a prior claim during the previous washout period days. *Multiple incidence type* will use the washout period to establish incidence and consider all qualifying incident claims.

"Incident with Respect to" Codes - NDC and/or procedure and/or diagnosis codes to be used to refine the incident definition for the exposure(s) of interest. For example, if a requester is examining exposure to DRUG A but wants incidence of DRUG A to be defined with respect to DRUG A and DRUG B, the Incident with Respect to Code fields would include both DRUG A and DRUG B codes.

Incident Only Care Setting - Contains the care settings considered for the individual diagnosis or procedure codes included as "Incident with Respect to" codes.

Member-Years (incidence-based cohort) - Sum of all years of enrollment with drug and/or medical coverage in the query period preceded by a washout period.

Member-Years (prevalence-based cohort) - Sum of all years members are enrolled with drug and/or medical coverage during the query period.

New Starts- Number of incident dispensings during the query period. Patient must have no prior dispensings of interest in the washout period. For a single and minimum incidence type, an individual may have no more than one new start. For a multiple incidence type, an individual may have more than one new start.

New Users - Number of members with incident claims during the query period. Member must have no evidence of claims of interest (defined by incidence criteria) in the prior washout period. A patient may only be counted once in a query period.

Query Period - Period in which the modular program looks for diagnoses of interest.

Washout Period (incidence-based cohort) - Number of days a patient is required to have no evidence of prior claim of interest and continuous drug and/or medical coverage.

*all terms may not be used in this report

Table 1a. Prevalent Fingolimod Use in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2010 and May 31, 2013

Users	Dispensings	Days Supplied	Amount Supplied	Eligible Members	Member-Years	Days Supplied per User	Dispensings per User	Days Supplied per Dispensing	Users per 1K Eligible Members
4,382	40,595	1,319,865	1,319,640	75,859,455	135,377,287	301.20	9.26	32.51	0.06

Table 1b. Incident Fingolimod Use in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2010 and May 31, 2013, by Washout Period

Group	New Users	New Starts	Dispensings	Days Supplied	Amount Supplied	Eligible Members	Member-Years	Days Supplied per user	Dispensings per User	Days Supplied per Dispensing	New Users per 1K Eligible Members
90-Day Washout	3,733	3,733	3,733	139,847	139,897	71,938,011	125,439,450	37.46	1.00	37.46	0.05
180-Day Washout	3,375	3,375	3,375	125,784	125,835	65,680,255	116,558,989	37.27	1.00	37.27	0.05
270-Day Washout	3,182	3,182	3,182	118,644	118,695	61,697,600	108,700,938	37.29	1.00	37.29	0.05

Table 2a. Prevalent Fingolimod Use in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2010 and May 31, 2013, by Age Group

Group	Users	Dispensings	Days Supplied	Amount Supplied	Eligible Members	Member-Years	Days Supplied per user	Dispensings per User	Days Supplied per Dispensing	Users per 1K Eligible Members
0 to 21 Years	52	371	11,172	11,118	22,458,775	37,445,257	214.85	7.13	30.11	0.00
22 to 44 Years	2,144	18,469	603,481	603,509	29,323,747	43,944,239	281.47	8.61	32.68	0.07
45 to 64 Years	2,249	21,074	683,069	682,814	21,890,605	39,371,057	303.72	9.37	32.41	0.10
65+ Years	93	681	22,143	22,199	7,128,719	14,616,734	238.10	7.32	32.52	0.01

Table 2b. Incident Fingolimod Use in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2010 and May 31, 2013, by Washout Period and Age Group

Group	New Users	New Starts	Dispensings	Days Supplied	Amount Supplied	Eligible Members	Member-Years	Days Supplied per user	Dispensings per User	Days Supplied per Dispensing	New Users per 1K Eligible Members
90-Day Washout											
0 to 21 Years	42	42	42	1,292	1,288	20,985,582	34,410,977	30.76	1.00	30.76	0.00
22 to 44 Years	1,813	1,813	1,813	68,434	68,455	27,475,923	39,943,872	37.75	1.00	37.75	0.07
45 to 64 Years	1,818	1,818	1,818	67,825	67,858	20,836,388	37,104,210	37.31	1.00	37.31	0.09
65+ Years	60	60	60	2,296	2,296	6,977,407	13,980,391	38.27	1.00	38.27	0.01
180-Day Washout											
0 to 21 Years	40	40	40	1,180	1,176	19,026,206	31,726,609	29.50	1.00	29.50	0.00
22 to 44 Years	1,618	1,618	1,618	60,929	60,919	24,763,165	36,402,203	37.66	1.00	37.66	0.07
45 to 64 Years	1,661	1,661	1,661	61,491	61,556	19,434,395	35,042,311	37.02	1.00	37.02	0.09
65+ Years	56	56	56	2,184	2,184	6,473,744	13,387,866	39.00	1.00	39.00	0.01
270-Day Washout											
0 to 21 Years	38	38	38	1,124	1,120	17,698,980	29,353,128	29.58	1.00	29.58	0.00
22 to 44 Years	1,506	1,506	1,506	56,953	56,943	22,825,510	33,297,622	37.82	1.00	37.82	0.07
45 to 64 Years	1,585	1,585	1,585	58,467	58,532	18,583,437	33,175,441	36.89	1.00	36.89	0.09
65+ Years	53	53	53	2,100	2,100	6,335,157	12,874,747	39.62	1.00	39.62	0.01

Table 3a. Prevalent Fingolimod Use in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2010 and May 31, 2013, by Sex

Group	Users	Dispensings	Days Supplied	Amount Supplied	Eligible Members	Member-Years	Days Supplied per user	Dispensings per User	Days Supplied per Dispensing	Users per 1K Eligible Members
Female	3,307	30,424	985,446	985,084	38,432,990	69,302,450	297.99	9.20	32.39	0.09
Male	1,072	10,161	334,139	334,264	37,394,640	66,039,936	311.70	9.48	32.88	0.03
Unknown	3	10	280	292	31,825	34,901	93.33	3.33	28.00	0.09

Table 3b. Incident Fingolimod Use in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2010 and May 31, 2013, by Washout Period and Sex

Group	New Users	New Starts	Dispensings	Days Supplied	Amount Supplied	Eligible Members	Member-Years	Days Supplied per user	Dispensings per User	Days Supplied per Dispensing	New Users per 1K Eligible Members
90-Day Washout											
Female	2,820	2,820	2,820	104,355	104,387	36,547,958	64,320,199	37.01	1.00	37.01	0.08
Male	910	910	910	35,408	35,426	35,369,092	61,090,828	38.91	1.00	38.91	0.03
Unknown	3	3	3	84	84	20,961	28,423	28.00	1.00	28.00	0.14
180-Day Washout											
Female	2,540	2,540	2,540	93,316	93,349	33,426,617	59,851,928	36.74	1.00	36.74	0.08
Male	832	832	832	32,384	32,402	32,235,733	56,682,710	38.92	1.00	38.92	0.03
Unknown	3	3	3	84	84	17,905	24,351	28.00	1.00	28.00	0.17
270-Day Washout											
Female	2,393	2,393	2,393	87,968	88,001	31,441,500	55,891,284	36.76	1.00	36.76	0.08
Male	786	786	786	30,592	30,610	30,238,949	52,788,805	38.92	1.00	38.92	0.03
Unknown	3	3	3	84	84	17,151	20,849	28.00	1.00	28.00	0.17

Table 4a. Prevalent Fingolimod Use in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2010 and May 31, 2013, by Year

Group	Users	Dispensings	Days Supplied	Amount Supplied	Eligible Members	Member-Years	Days Supplied per user	Dispensings per User	Days Supplied per Dispensing	Users per 1K Eligible Members
2010	187	222	9,398	9,369	50,254,201	41,002,392	50.26	1.19	42.33	0.00
2011	2,252	11,405	382,285	382,404	49,083,903	40,347,801	169.75	5.06	33.52	0.05
2012	2,857	19,713	638,490	638,243	47,815,454	38,834,168	223.48	6.90	32.39	0.06
2013	2,535	9,255	289,692	289,624	39,582,243	15,192,926	114.28	3.65	31.30	0.06

Table 4b. Incident Fingolimod Use in the Mini-Sentinel Distributed Database (MSDD) between January 1, 2010 and May 31, 2013, by Washout Period and Year

Group	New Users	New Starts	Dispensings	Days Supplied	Amount Supplied	Eligible Members	Member-Years	Days Supplied per user	Dispensings per User	Days Supplied per Dispensing	New Users per 1K Eligible Members
90-Day Washout											
2010	183	183	183	8,108	8,079	48,015,287	37,983,104	44.31	1.00	44.31	0.00
2011	1,913	1,913	1,913	72,814	72,878	46,988,233	37,463,758	38.06	1.00	38.06	0.04
2012	1,100	1,100	1,100	40,273	40,288	45,783,286	36,134,183	36.61	1.00	36.61	0.02
2013	537	537	537	18,652	18,652	37,795,292	13,858,405	34.73	1.00	34.73	0.01
180-Day Washout											
2010	173	173	173	7,714	7,687	44,898,795	35,269,703	44.59	1.00	44.59	0.00
2011	1,784	1,784	1,784	67,997	68,030	43,885,815	34,848,531	38.11	1.00	38.11	0.04
2012	962	962	962	34,249	34,294	42,770,806	33,668,353	35.60	1.00	35.60	0.02
2013	456	456	456	15,824	15,824	33,618,117	12,772,402	34.70	1.00	34.70	0.01
270-Day Washout											
2010	168	168	168	7,518	7,491	42,034,148	32,813,287	44.75	1.00	44.75	0.00
2011	1,686	1,686	1,686	64,301	64,334	41,110,933	32,450,730	38.14	1.00	38.14	0.04
2012	902	902	902	32,177	32,222	40,081,156	31,415,330	35.67	1.00	35.67	0.02
2013	426	426	426	14,648	14,648	31,844,052	12,021,591	34.38	1.00	34.38	0.01

Appendix A. Dates of Available Data for Each Data Partner as of Request Send Date (April 18, 2014)

Data Partner ID	Start Date	End Date
DP001	1/1/2010	5/31/2013
DP002	1/1/2010	5/31/2013
DP003	1/1/2010	5/31/2013
DP004	1/1/2010	5/31/2013
DP005	1/1/2010	12/31/2012
DP006	1/1/2010	5/31/2013
DP007	1/1/2010	5/31/2013
DP008	1/1/2010	12/31/2012
DP009	1/1/2010	12/31/2013
DP010	1/1/2010	5/31/2013
DP011	1/1/2010	5/31/2013
DP012	1/1/2010	6/30/2012
DP013	1/1/2010	6/30/2012
DP014	1/1/2010	5/31/2013
DP015	1/1/2010	5/31/2013
DP016	1/1/2010	5/31/2013
DP017	1/1/2010	5/31/2013

Appendix B. Specifications with List of Parameters used in this Request

Modular Program #9 was used to analyze prevalent and incident use of fingolimod in the Mini-Sentinel Distributed Database (MSDD). In total, three scenarios were examined in this request with differing enrollment and washout criteria. See below for a description of each of these scenarios.

Coverage Requirement	Drug and Medical Coverage
Query Period	January 1, 2010 to May 31, 2013
Enrollment Gap	45 Days
Age Stratifications	0-21,22-44,45-64,65+ years

Scenario	Drug/Exposure				
	Incident exposure	Incident w/ respect to:	Enrollment Days	Washout (days)	Incidence Type*
1	Fingolimod	Fingolimod	90	90	SING
2	Fingolimod	Fingolimod	180	180	SING
3	Fingolimod	Fingolimod	270	270	SING

*Single incidence type for the exposure will only consider the first incident dispensing for each user during the query period that satisfies the Washout Period criteria.
National Drug Codes (NDCs) checked against First Data Bank's "National Drug Data File (NDDF®) Plus"