Disclaimer

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

Data obtained through 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 Sentinel in the public domain as soon as possible. Any public health actions taken by FDA regarding products involved in 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: cder_mpl1r_wp293

Request ID: cder_mpl1r_wp293

Request Description: In this query, we characterized siponimod use among females in the Sentinel Distributed Database (SDD).

Sentinel Routine Querying Module: Cohort Identification and Descriptive Analysis (CIDA) module, version 14.1.1

Data Source: We distributed this request to six Sentinel Data Partners on January 28, 2025. These six Data Partners are a subset of the SDD. Data from Medicare and fee-for-service Medicaid enrollees are included. The study period included data from April 15, 2019 through July 31, 2024. Please see Appendix A for a list of dates of available data for each Data Partner.

Study Design: We identified all episodes of exposure to siponimod separately among all females and females of childbearing age (15-50 years). This is a Type 1 analysis in the Query Request Package (QRP) documentation.

Exposure of Interest: The exposure of interest was siponimod, captured through National Drug Codes (NDCs). Please refer to Appendix B for a list of generic and brand names used to define siponimod.

Cohort Eligibility Criteria: A total of 4 cohorts were created: siponimod episodes among all females and among females of childbearing age, each repeated with and without health plan enrollment requirements. For the cohorts with enrollment requirements, patients were required to have continuous enrollment in health plans with medical and drug coverage for 183 days prior to the index date, during which gaps in coverage of up to 45 days were allowed. The date of the first siponimod dispensing within each siponimod episode served as the index date.

Baseline Characteristics: Race and Hispanic status were reported for all cohorts. Age on the index date and year of the index date were summarized across all siponimod episodes. For cohorts with a pre-index enrollment requirement, we also assessed combined comorbidity scores[1] and health service utilization metrics in the 183 days prior to the index date.

Please see Appendices C, D, and E for the specifications of parameters used in the analyses and a design diagram of cohort entry requirements for this request.

Limitations: Algorithms used to define exposures and inclusion/exclusion criteria are imperfect; thus, it is possible that there may be misclassification. Data should be interpreted with this limitation in mind.

Notes: Please contact the Sentinel Operations Center (info@sentinelsystem.org) for questions and to provide comments/suggestions for future enhancements to this document. For more information on Sentinel's routine querying modules, please refer to the documentation (https://dev.sentinelsystem.org/projects/SENTINEL/repos/sentinel-routine-querying-tool-documentation/browse).

[1]Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-59.

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Glossary of Terms for Analyses Using
Cohort Identification and Descriptive Analysis (CIDA) Module*

Amount Supplied - number of units (pills, tablets, vials) dispensed. Net amount per NDC per dispensing.
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). For laboratory results, possible care settings include: Emergency Department (E), Home (H), Inpatient (I), Outpatient (O), or Unknown or Missing (U). The Care Setting, along with the Principal Diagnosis Indicator (PDX), forms the Care Setting/PDX parameter.

- **Ambulatory Visit (AV) -** includes visits at outpatient clinics, same-day surgeries, urgent care visits, and other same-day ambulatory hospital encounters, but excludes emergency department encounters.
- **Emergency Department (ED) -** includes ED encounters that become inpatient stays (in which case inpatient stays would be a separate encounter). Excludes urgent care visits.
- **Inpatient Hospital Stay (IP) -** includes all inpatient stays, same-day hospital discharges, hospital transfers, and acute hospital care where the discharge is after the admission date.
- **Non-Acute Institutional Stay (IS) -** includes hospice, skilled nursing facility (SNF), rehab center, nursing home, residential, overnight non-hospital dialysis and other non-hospital stays.
- **Other Ambulatory Visit (OA) -** includes other non overnight AV encounters such as hospice visits, home health visits, skilled nursing facility visits, other non-hospital visits, as well as telemedicine, telephone and email consultations.

Charlson/Elixhauser Combined Comorbidity Score - calculated based on comorbidities observed during a requester-defined window around the exposure episode start date (e.g., in the 183 days prior to index).
Code Days - the minimum number of times the diagnosis must be found during the evaluation period in order to fulfill the algorithm to identify the corresponding patient characteristic.
Cohort Definition (drug/exposure) - indicates how the cohort will be defined: 01: Cohort includes only the first valid treatment episode during the query period; 02: Cohort includes all valid treatment episodes during the query period; 03: Cohort includes all valid treatment episodes during the query period until an event occurs.
Computed Start Marketing Date - represents the first observed dispensing date among all valid users within a GROUP (scenario) within each Data Partner site.
Days Supplied - number of days supplied for all dispensings in qualifying treatment episodes.
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.
Episodes - treatment episodes; length of episode is determined by days supplied in one dispensing or consecutive dispensings bridged by the episode gap.
Episode Gap - number of days allowed between two (or more) consecutive exposures (dispensings/procedures) to be considered the same treatment episode.
Event Deduplication - specifies how events are counted by the Modular Program (MP) algorithm: 0: Counts all occurrences of a health outcome of interest (HOI) during an exposure episode; 1: de-duplicates occurrences of the same HOI code and code type on the same day; 2: de-duplicates occurrences of the same HOI group on the same day (e.g., de-duplicates at the group level).
Exposure Episode Length - number of days after exposure initiation that is considered "exposed time."
Exposure Extension Period - number of days post treatment period in which the outcomes/events are counted for a treatment episode. Extensions are added after any episode gaps have been bridged.
Lookback Period - number of days wherein a member is required to have evidence of pre-existing condition (diagnosis/procedure/drug dispensing).

Maximum Episode Duration - truncates exposure episodes after a requester-specified number of exposed days. Applied after any gaps are bridged and extension days added to the length of the exposure episode.
Member-Years - sum of all days of enrollment with medical and drug coverage in the query period preceded by an exposure washout period all divided by 365.25.
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. Applied after any gaps are bridged and extension days added to the length of the exposure episode.
Monitoring Period - used to define time periods of interest for both sequential analysis and simple cohort characterization requests.
Principal Diagnosis (PDX) - diagnosis or condition established to be chiefly responsible for admission of the patient to the hospital. 'P' = principal diagnosis, 'S' = secondary diagnosis, 'X' = unspecified diagnosis, '.' = blank. Along with the Care Setting values, forms the Caresetting/PDX parameter.
Query Period - period in which the modular program looks for exposures and outcomes of interest.
Switch Evaluation Step Value - value used to differentiate evaluation step. Each switch pattern can support up to 2 evaluation steps (0 = switch pattern evaluation start; 1 = first evaluation; 2 = second evaluation).
Switch Gap Inclusion Indicator - indicator for whether gaps in treatment episodes that are included in a switch episode will be counted as part of the switch episode duration.
Switch Pattern Cohort Inclusion Date - indicates which date to use for inclusion into the switch pattern cohort of interest as well as optionally as the index date of the treatment episode initiating the switch pattern. Valid options are the product approval date, product marketing date, other requester defined date, or computed start marketing date.
Switch Pattern Cohort Inclusion Strategy - indicates how the switch pattern cohort inclusion date will be used: 01: used only as a switch cohort entry date. First treatment episode dispensing date is used as index for computing time to first switch; 02: used as switch cohort entry date and as initial switch step index date for computing time to first switch.
Treatment Episode Truncation Indicator - indicates whether the exposure episode will be truncated at the occurrence of a requester-specified code.
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.
Years at Risk - number of days supplied plus any episode gaps and exposure extension periods all divided by 365.25.

*all terms may not be used in this report

Table 1a. Aggregated Characteristics of Female Users of Siponimod, with Pre-Index Enrollment Requirement, in the Sentinel Distributed Database (SDD) from April 15, 2019 to July 31, 2024

	Female Users of Siponimod	
Patient Characteristics[1]	**Number**	**Percent**
Unique patients	1,766	N/A
Episodes	22,977	100.0%
Demographic Characteristics	**Mean**	**Standard Deviation**
Age (years)	53.2	10.5
Age	**Number**	**Percent**
0-14 years	0	0.0%
15-19 years	0	0.0%
20-29 years	608	2.6%
30-39 years	2,805	12.2%
40-50 years	5,476	23.8%
51-64 years	10,501	45.7%
≥ 65 years	3,587	15.6%
Sex		
Female	1,766	100.0%
Race[2]		
American Indian or Alaska Native	*****	*****
Asian	*****	*****
Black or African American	219	12.4%
Multi-racial	*****	*****
Native Hawaiian or Other Pacific Islander	*****	*****
Unknown	539	30.5%
White	980	55.5%
Hispanic origin		
Yes	*****	*****
No	1,078	61.0%
Unknown	*****	*****

Table 1a. Aggregated Characteristics of Female Users of Siponimod, with Pre-Index Enrollment Requirement, in the Sentinel Distributed Database (SDD) from April 15, 2019 to July 31, 2024

	Female Users of Siponimod	
Demographic Characteristics	**Number**	**Percent**
Year		
2019	707	3.1%
2020	4,931	21.5%
2021	6,587	28.7%
2022	4,789	20.8%
2023	4,656	20.3%
2024	1,307	5.7%
Health Characteristics	**Mean**	**Standard Deviation**
Combined comorbidity score[3]	0.9	1.5
Health Service Utilization Intensity Metrics		
Mean number of ambulatory encounters	11.7	11.1
Mean number of emergency room encounters	0.3	0.8
Mean number of inpatient hospital encounters	0.1	0.4
Mean number of non-acute institutional encounters	0.0	0.2
Mean number of other ambulatory encounters	6.1	16.5
Mean number of filled prescriptions	22.6	21.2
Mean number of generics dispensed	8.1	5.5
Mean number of unique drug classes dispensed	7.7	5.0

[1]All metrics are based on total number of episodes per group, except for sex, race, and Hispanic origin which are based on total number of unique patients.

[2]Race data may not be completely populated at all Data Partners; therefore, data about race may be incomplete.

[3]Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759. Sun JW, Rogers JR, Her Q, Welch EC, Panozzo CA, Toh S, Gagne JJ. Adaptation and validation of the combined comorbidity score for ICD-10-CM. Med Care. 2017;55(12):1046-1051.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

N/A = Not applicable

Table 1b. Aggregated Characteristics of Female Users of Siponimod of Childbearing Age, with Pre-Index Enrollment Requirement, in the Sentinel Distributed Database (SDD) from April 15, 2019 to July 31, 2024

	Female Users of Siponimod of Childbearing Age	
Patient Characteristics[1]	**Number**	**Percent**
Unique patients	772	N/A
Episodes	8,889	100.0%
Demographic Characteristics	**Mean**	**Standard Deviation**
Age (years)	41.4	6.6
Age	**Number**	**Percent**
15-19 years	0	0.0%
20-29 years	608	6.8%
30-39 years	2,805	31.6%
40-50 years	5,476	61.6%
Sex		
Female	772	100.0%
Race[2]		
American Indian or Alaska Native	*****	*****
Asian	*****	*****
Black or African American	117	15.2%
Multi-racial	*****	*****
Native Hawaiian or Other Pacific Islander	*****	*****
Unknown	305	39.5%
White	331	42.9%
Hispanic origin		
Yes	*****	*****
No	408	52.8%
Unknown	*****	*****
Year		
2019	219	2.5%
2020	2,072	23.3%

Table 1b. Aggregated Characteristics of Female Users of Siponimod of Childbearing Age, with Pre-Index Enrollment Requirement, in the Sentinel Distributed Database (SDD) from April 15, 2019 to July 31, 2024

	Female Users of Siponimod of Childbearing Age	
Demographic Characteristics	**Number**	**Percent**
2021	2,902	32.6%
2022	1,685	19.0%
2023	1,514	17.0%
2024	497	5.6%
Health Characteristics	**Mean**	**Standard Deviation**
Combined comorbidity score[3]	0.6	1.2
Health Service Utilization Intensity Metrics		
Mean number of ambulatory encounters	9.8	9.0
Mean number of emergency room encounters	0.3	0.8
Mean number of inpatient hospital encounters	0.1	0.4
Mean number of non-acute institutional encounters	0.0	0.1
Mean number of other ambulatory encounters	5.0	16.1
Mean number of filled prescriptions	18.1	18.7
Mean number of generics dispensed	6.8	5.4
Mean number of unique drug classes dispensed	6.4	4.9

[1]All metrics are based on total number of episodes per group, except for sex, race, and Hispanic origin which are based on total number of unique patients.

[2]Race data may not be completely populated at all Data Partners; therefore, data about race may be incomplete.

[3]Gagne JJ, Glynn RJ, Avorn J, Levin R, Schneeweiss S. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol. 2011;64(7):749-759. Sun JW, Rogers JR, Her Q, Welch EC, Panozzo CA, Toh S, Gagne JJ. Adaptation and validation of the combined comorbidity score for ICD-10-CM. Med Care. 2017;55(12):1046-1051.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

N/A = Not applicable

Table 1c. Aggregated Characteristics of Female Users of Siponimod, without Pre-Index Enrollment Requirement, in the Sentinel Distributed Database (SDD) from April 15, 2019 to July 31, 2024

	Female Users of Siponimod	
Patient Characteristics[1]	**Number**	**Percent**
Unique patients	1,958	N/A
Episodes	24,724	100.0%
Demographic Characteristics	**Mean**	**Standard Deviation**
Age (years)	53.1	10.5
Age	**Number**	**Percent**
0-14 years	0	0.0%
15-19 years	*****	*****
20-29 years	*****	*****
30-39 years	3,042	12.3%
40-50 years	5,965	24.1%
51-64 years	11,279	45.6%
≥ 65 years	3,786	15.3%
Sex		
Female	1,958	100.0%
Race[2]		
American Indian or Alaska Native	*****	*****
Asian	*****	*****
Black or African American	250	12.8%
Multi-racial	15	0.8%
Native Hawaiian or Other Pacific Islander	*****	*****
Unknown	613	31.3%
White	1,065	54.4%
Hispanic origin		
Yes	75	3.8%
No	1,165	59.5%
Unknown	718	36.7%

Table 1c. Aggregated Characteristics of Female Users of Siponimod, without Pre-Index Enrollment Requirement, in the Sentinel Distributed Database (SDD) from April 15, 2019 to July 31, 2024

	Female Users of Siponimod	
Demographic Characteristics	**Number**	**Percent**
Year		
2019	749	3.0%
2020	5,229	21.1%
2021	7,028	28.4%
2022	5,162	20.9%
2023	5,038	20.4%
2024	1,518	6.1%

[1]All metrics are based on total number of episodes per group, except for sex, race, and Hispanic origin which are based on total number of unique patients.

[2]Race data may not be completely populated at all Data Partners; therefore, data about race may be incomplete.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

N/A = Not applicable

Table 1d. Aggregated Characteristics of Female Users of Siponimod of Childbearing Age, without Pre-Index Enrollment Requirement, in the Sentinel Distributed Database (SDD) from April 15, 2019 to July 31, 2024

	Female Users of Siponimod of Childbearing Age	
Patient Characteristics[1]	**Number**	**Percent**
Unique patients	863	N/A
Episodes	9,659	100.0%
Demographic Characteristics	**Mean**	**Standard Deviation**
Age (years)	41.4	6.6
Age	**Number**	**Percent**
15-19 years	*****	*****
20-29 years	*****	*****
30-39 years	3,042	31.5%
40-50 years	5,965	61.8%
Sex		
Female	863	100.0%
Race[2]		
American Indian or Alaska Native	*****	*****
Asian	*****	*****
Black or African American	131	15.2%
Multi-racial	*****	*****
Native Hawaiian or Other Pacific Islander	*****	*****
Unknown	347	40.2%
White	365	42.3%
Hispanic origin		
Yes	53	6.1%
No	445	51.6%
Unknown	365	42.3%

Table 1d. Aggregated Characteristics of Female Users of Siponimod of Childbearing Age, without Pre-Index Enrollment Requirement, in the Sentinel Distributed Database (SDD) from April 15, 2019 to July 31, 2024

	Female Users of Siponimod of Childbearing Age	
Demographic Characteristics	**Number**	**Percent**
Year		
2019	239	2.5%
2020	2,206	22.8%
2021	3,108	32.2%
2022	1,827	18.9%
2023	1,684	17.4%
2024	595	6.2%

[1]All metrics are based on total number of episodes per group, except for sex, race, and Hispanic origin which are based on total number of unique patients.

[2]Race data may not be completely populated at all Data Partners; therefore, data about race may be incomplete.

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

N/A = Not applicable

Table 2. Summary of Use of Mayzent (Siponimod) Among Female Patients in the Sentinel Distributed Database (SDD) from April 15, 2019 to July 31, 2024

	Number of Patients	Number of Index Dates	Number of Eligible Members[1]	Total Eligible Member-Years[1]	Number of Patients per 10,000 Eligible Members[1]	Number of Patients per 10,000 Eligible Member-Years (95% Confidence Interval)[1]
Patients with Pre-Index Enrollment Requirement						
All Female Patients	1,766	22,977	103,603,456	221,241,030.7	0.17	0.08 (0.08, 0.08)
Female Patients of Childbearing Age	772	8,889	47,680,146	80,921,444.0	0.16	0.10 (0.09, 0.10)
Patients without Pre-Index Enrollment Requirement						
All Female Patients	1,958	24,724	116,682,091	251,148,326.9	0.17	0.08 (0.07, 0.08)
Female Patients of Childbearing Age	863	9,659	54,523,832	95,639,583.2	0.16	0.09 (0.08, 0.10)

[1]Eligible Members and Member-Years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period.

Table 3. Summary of Episode-Level[1] Cohort Attrition in the Sentinel Distributed Database (SDD) from April 15, 2019 to July 31, 2024

	Patients with Pre-Index Enrollment Requirement				Patients without Pre-Index Enrollment Requirement			
	All Female Patients		Female Patients of Childbearing Age		All Female Patients		Female Patients of Childbearing Age	
	Remaining	Excluded	Remaining	Excluded	Remaining	Excluded	Remaining	Excluded
Members meeting enrollment and demographic requirements								
Enrolled at any point during the query period	298,870,299	N/A	298,870,299	N/A	298,870,299	N/A	298,870,299	N/A
Had required coverage type (medical and/or drug coverage)	221,515,090	77,355,209	221,515,090	77,355,209	221,515,090	77,355,209	221,515,090	77,355,209
Enrolled during specified age range	221,509,323	5,767	106,934,662	114,580,428	221,509,323	5,767	106,934,662	114,580,428
Had requestable medical charts	221,509,323	0	106,934,662	0	221,509,323	0	106,934,662	0
Met demographic requirements (sex, race, and Hispanic origin)	116,682,504	104,826,819	56,649,092	50,285,570	116,682,504	104,826,819	56,649,092	50,285,570
Members with a valid index event								
Had any cohort-defining claim during the query period	1,958	116,680,546	997	56,648,095	1,958	116,680,546	997	56,648,095
Cohort episodes with a valid index date								
Total number of claims with cohort-identifying codes during the query period	24,734	N/A	11,810	N/A	24,724	N/A	11,806	N/A
Claim recorded during specified age range	24,734	0	9,662	2,148	24,724	0	9,659	2,147
Episode defining index claim recorded during the query period	24,734	0	9,662	0	24,724	0	9,659	0
Cohort episodes with required pre-index history								
Had sufficient pre-index continuous enrollment	22,977	1,757	8,889	773	24,724	0	9,659	0
Met inclusion and exclusion criteria	22,977	0	8,889	0	24,724	0	9,659	0
Had sufficient post-index continuous enrollment	22,977	0	8,889	0	24,724	0	9,659	0
Final cohort								
Number of members	1,766	N/A	772	N/A	1,958	N/A	863	N/A
Number of episodes	22,977	N/A	8,889	N/A	24,724	N/A	9,659	N/A

[1]Cohorts are formed by first evaluating enrollment and demographic requirements as well as index events among members, then evaluating index dates, pre-index history, and post-index follow-up among episodes. Because of this, the number remaining often increases from the member- to episode-level steps.

N/A = Not applicable

Appendix A. Dates of Available Data for Each Data Partner (DP) as of Request Distribution Date (January 28, 2025)

Masked DP ID	DP Start Date	DP End Date[1]
DP01	01/01/2006	07/31/2024
DP02	01/01/2007	06/30/2024
DP03	01/01/2008	04/30/2024
DP04	01/01/2014	12/31/2021
DP05	01/01/2008	05/31/2024
DP06	01/01/2010	12/31/2023

[1]End Date represents the earliest of: (1) query end date, or (2) last day of the most recent month for which all of a Data Partner's data tables (enrollment, dispensing, etc.) have at least 80% of the record count relative to the prior month.

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

Generic Name	Brand Name
Siponimod	
siponimod	Mayzent
siponimod	Mayzent Starter(for 1mg maint)
siponimod	Mayzent Starter(for 2mg maint)

Appendix C. Specifications Defining Parameters Used in this Request

This request executed the Cohort Identification and Descriptive Analysis (CIDA) tool, version 14.1.1, to estimate rates of siponimod use among female patients in the Sentinel Distributed Database (SDD).

Query Period: April 15, 2019 - Most recently available data [July 31, 2024]
Coverage Requirement: Medical & Drug Coverage
Minimum Post-Index Required Days (optional): 0
Sex: Female
Other Demographic Restrictions: N/A
Stratifications: N/A
Censor Output Categorization: N/A
Data Restrictions: N/A
Distribution of Index-Defining Codes: No
Envelope Macro: Reclassify encounters during inpatient stay as inpatient (0)
Freeze data: No
Drop Censor Output Indicator: Yes

		Exposure/Event					
Run	Scenario	Index Exposure	Age Group	Pre-Index Enrollment Requirement	Enrollment Gap	Cohort Definition	Washout Period
1	1	Mayzent (siponimod)	0-14, 15-19, 20-29, 30-39, 40-50, 51-64, 65+ years	183 days	45 days	**02:** Cohort includes all valid index dates per individual during the query period.	0
1	2	Mayzent (siponimod)	15-19, 20-29, 30-39, 40-50 years	183 days	45 days	**02:** Cohort includes all valid index dates per individual during the query period.	0
2	3	Mayzent (siponimod)	0-14, 15-19, 20-29, 30-39, 40-50, 51-64, 65+ years	0 days	0 days	**02:** Cohort includes all valid index dates per individual during the query period.	0
2	4	Mayzent (siponimod)	15-19, 20-29, 30-39, 40-50 years	0 days	0 days	**02:** Cohort includes all valid index dates per individual during the query period.	0

Appendix C. Specifications Defining Parameters Used in this Request

		Exposure/Event					
Run	Scenario	Exclude Evidence of Days Supply if Event Washout Includes Dispensings	Care Setting and Diagnosis Position Requirements	Forced Supply to Attach to Dispensings	Create Baseline Table?	Output Denominator Indicator	End At-Risk Period at Evidence Of
1	1	n/a	n/a	n/a	Yes	Yes	*Death *Data Partner End Date *Query End Date
1	2	n/a	n/a	n/a	Yes	Yes	*Death *Data Partner End Date *Query End Date
2	3	n/a	n/a	n/a	Yes	Yes	*Death *Data Partner End Date *Query End Date
2	4	n/a	n/a	n/a	Yes	Yes	*Death *Data Partner End Date *Query End Date

International Classification of Diseases, Ninth Revision (ICD-9), International Classification of Diseases, Tenth Revision (ICD-10), Healthcare Common Procedure Coding System (HCPCS), and CPT (Current Procedural Terminology) codes are provided by Optum360.

National Drug Codes (NDCs) are checked against FirstDataBank's FDBMedKnowledge®

N/A = Not Applicable

Appendix D. Specifications Defining Risk Score and Utilization Parameters Used in this Request

Risk Score

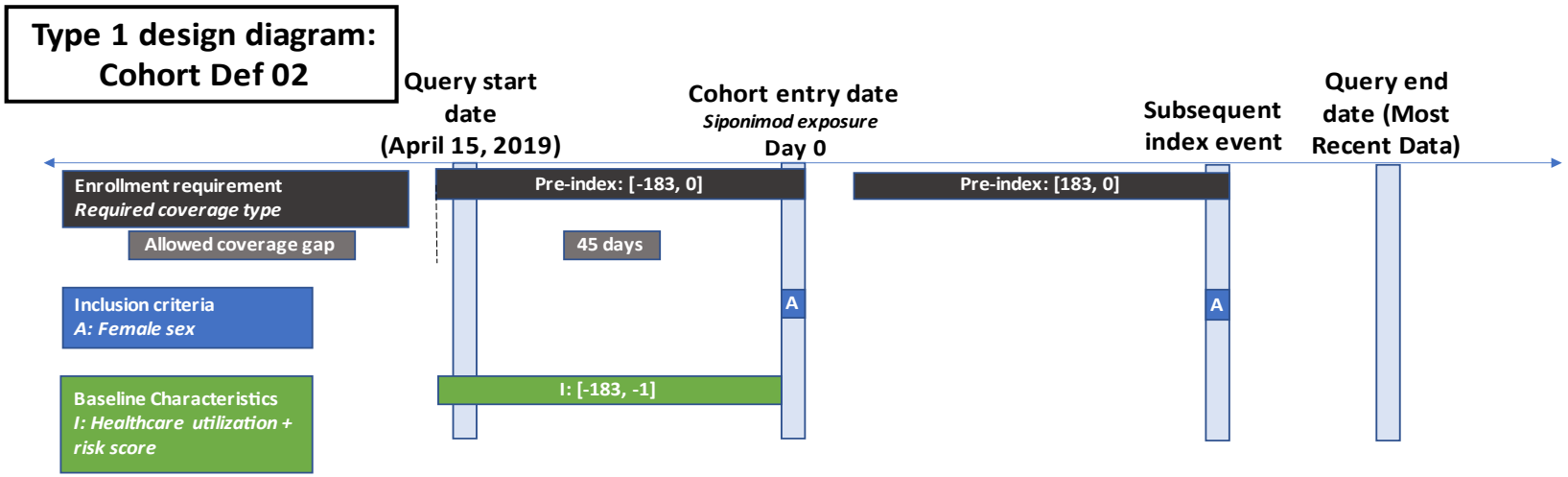
Risk Score	Evaluation Period Start	Evaluation Period End	Risk Score Categories
CCI: Combined comorbidity index	-183	-1	n/a

Utilization

Medical Utilization Evaluation Period Start	Medical Utilization Evaluation Period End	Drug Utilization Evaluation Period Start	Drug Utilization Evaluation Period End
-183	-1	-183	-1

Appendix E. Design Diagrams of Cohort Entry Requirements and Index Exposure

WITH ENROLLMENT REQUIREMENT:



WITHOUT ENROLLMENT REQUIREMENT: