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_wp220

Request ID: cder_mpl1r_wp220_v02

Request Description: In this report we identified new users of alosetron and eluxadoline in the Sentinel Distributed Database (SDD), and examined ischemic colitis events among those individuals using different definitions of the outcome as sensitivity analyses.

Sentinel Routine Querying Module: Cohort Identification and Descriptive Analysis (CIDA) module, version 11.2.4.

Data Source: We distributed this request to six Sentinel Data Partners on February 8, 2022. These six Data Partners are a subset of the SDD. Data from Medicare patients having both fee-for-service medical coverage and Part D drug coverage are included. The study period included data from January 1, 2016 through July 1, 2020. Please see Appendix A for a list of dates of available data for each Data Partner.

Study Design: We identified individuals with incident use of alosetron or eluxadoline and evaluated the occurrence of ischemic colitis within 183 days after exposure, among a cohort who were between zero and 65+ years of age, and did not have a same day dispensing for the incident or comparator drug, respectively. This is a Type 2 analysis in the Query Request Package (QRP) documentation.

Exposure of Interest: We defined the exposure and comparator of interest (alosetron and eluxadoline, respectively) using outpatient dispensing data and National Drug Codes (NDCs). Each qualifying dispensing of alosetron or eluxadoline (index) was identified; cohort re-entry was not allowed. Please see Appendix B for a list of generic and brand names of medical products used to define exposures in this request.

Outcome of Interest: We defined the outcome of interest, ischemic colitis, using 1) International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis codes only and 2) a modification of a validated algorithm.

For new alosetron users, we defined the outcome in five ways: A) presence of a diagnosis code in i) any care setting, and ii) the inpatient or institutional setting; B) the presence of a principal discharge diagnosis code in the inpatient or institutional care setting; C) capture by the modified algorithm in i) any care setting, and ii) the inpatient or institutional setting. Among eluxadoline users, we only defined the outcome as (C)(i) and (C)(ii) above.

The original algorithm was defined by Sands and colleagues,[1] and includes cascading logic with ICD-10-CM diagnosis codes, NDCs, and procedure codes from the following terminologies: Current Procedural Terminology, Second and Fourth Edition (CPT-2 and CPT-4), International Classification of Diseases, Tenth Revision, Procedure Coding System (ICD-10-PCS), and Healthcare Common Procedure Coding System (HCPCS). Please see Appendix C for specific ICD-10-CM diagnosis codes, Appendix D for specific CPT-2, CPT-4, ICD-10-PCS, and HCPCS procedure codes and Appendix E for a list of specific generic names of medical products used to define ischemic colitis in this report.

Cohort Eligibility Criteria: We required members to be enrolled in health plans with medical and drug coverage in the 91 days prior to their index date to be included in the cohort; a gap in coverage of up to 45 days was allowed and treated as continuous enrollment. The following age groups were included in the cohort: <18, 18-44, 45-64, and 65+ years. We also required no evidence of a dispensing for the comparator in the 91 days prior to the index alosetron dispensing (and no evidence of a dispensing of alosetron in the 91 days prior to the index eluxadoline dispensing).

Follow-up Time: We created "point" exposure episodes of 183 days. Follow-up began *the day after* the index dispensing and continued until the first occurrence of: 1) the outcome; 2) a dispensing for eluxadoline among alosetron users or alosetron among eluxadoline users; 3) 183-days; 4) health plan disenrollment; 5) death; 6) the end of the data provided by the Data Partner; or 7) the end of the query period.

Overview for Request: cder_mpl1r_wp220

Characteristics: We assessed the following characteristics in the 91 days prior to and including the index dispensing date: irritable bowel syndrome (IBS) and intestinal ischemia (II). During the entire exposure episode, we also assessed the occurrence of a colonoscopy or colectomy followed by a diagnosis of noninfectious gastroenteritis (NGE) within three months.

We defined IBS as the presence of an ICD-10-CM diagnosis code in any care setting, II as the presence of an ICD-10-CM diagnosis code or CPT-4 procedure code in any care setting, and colonoscopy or colectomy as the presence of a CPT-2, CPT-4, HCPCS, or ICD-10-PCS procedure code in any care setting followed by an NGE ICD-10-CM diagnosis code in any care setting. Please see Appendices F and G for a list of codes used to define characteristics in this request.

Please see Appendices H, I, J, and K for the specifications of parameters used in this request and design diagrams.

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

Note: Please contact the Sentinel Operations Center (info@sentinelsystem.org) for questions and to provide comments/suggestions for future enhancements to this document. 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]Sands, Bruce E., Mei-Sheng Duh, Clorinda Cali, et. al. "Algorithms to Identify Colonic Ischemia, Complications of Constipation and Irritable Bowel Syndrome in Medical Claims Data: Development and Validation." *Pharmacoepidemiology and Drug Safety* 15, no. 1 (2006): 47–56.

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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

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
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 Alosetron New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020

Alosetron New Users		
Patient Characteristics	**Number**	
Unique Patients	4,660	N/A
Demographic Characteristics	**Mean**	**Standard Deviation**
Age (years)	60.6	13.4
Age	**Number**	**Percent**
0-17 years	12	0.3%
18-44 years	829	17.8%
45-64 years	1,538	33.0%
≥ 65 years	2,281	48.9%
Sex		
Female	4,257	91.4%
Male	403	8.6%
Race[1]		
American Indian or Alaska Native	14	0.3%
Asian	*****	*****
Black or African American	139	3.0%
Native Hawaiian or Other Pacific Islander	*****	*****
Unknown	1,622	34.8%
White	2,872	61.6%
Hispanic origin		
Yes	52	1.1%
No	2,816	60.4%
Unknown	1,792	38.5%
Year		
2016	1,387	29.8%
2017	1,194	25.6%
2018	875	18.8%
2019	871	18.7%
2020	333	7.1%
Health Characteristics		
Irritable bowel syndrome [-91,0]	2,639	56.6%
Intestinal ischemia [-91,0]	40	0.9%
Colonscopy or colectomy with noninfectious gastroenteritis within 3 months [0, 183]	0	0.0%

[1]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.

Table 1b. Aggregated Characteristics of Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020

Eluxadoline New Users		
Patient Characteristics	**Number**	
Unique Patients	37,258	N/A
Demographic Characteristics	**Mean**	**Standard Deviation**
Age (years)	56.3	14.7
Age	**Number**	**Percent**
0-17 years	135	0.4%
18-44 years	10,505	28.2%
45-64 years	12,523	33.6%
≥ 65 years	14,095	37.8%
Sex		
Female	25,588	68.7%
Male	11,670	31.3%
Race[1]		
American Indian or Alaska Native	77	0.2%
Asian	415	1.1%
Black or African American	1,177	3.2%
Native Hawaiian or Other Pacific Islander	20	0.1%
Unknown	17,944	48.2%
White	17,625	47.3%
Hispanic origin		
Yes	465	1.2%
No	17,097	45.9%
Unknown	19,696	52.9%
Year		
2016	11,352	30.5%
2017	11,516	30.9%
2018	7,366	19.8%
2019	5,124	13.8%
2020	1,900	5.1%
Health Characteristics		
Irritable bowel syndrome [-91,0]	21,111	56.7%
Intestinal ischemia [-91,0]	143	0.4%
Colonscopy or colectomy with noninfectious gastroenteritis within 3 months [0, 183]	0	0.0%

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

Table 2. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database from January 1, 2016 to July 1, 2020

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Ischemic Colitis Among Alosetron New Users					
Defined by a diagnosis in any care setting	4,660	2,133.1	21	0.005 (0.003, 0.006)	9.845 (6.419, 15.100)
Defined by a diagnosis in the inpatient care setting	4,660	*****	*****	*****	3.743 (1.872, 7.485)
Defined by a diagnosis in the principal position in the inpatient care setting	4,660	2,138.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Defined by a modified validated algorithm in any care setting	4,660	*****	*****	*****	1.872 (0.703, 4.988)
Defined by a modified validated algorithm in the inpatient care setting	4,660	2,138.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Ischemic Colitis Among Eluxadoline New Users					
Defined by a modified validated algorithm in any care setting	37,258	17,010.5	27	0.001 (0.000, 0.001)	1.587 (1.089, 2.315)
Defined by a modified validated algorithm in the inpatient care setting	37,258	*****	*****	*****	0.411 (0.196, 0.863)

*****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.

Table 3. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Age Group

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Ischemic Colitis Among Alosetron New Users					
Defined by a diagnosis in any care setting					
0-17 years	12	5.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years	829	*****	*****	*****	2.663 (0.375, 18.904)
45-64 years	1,538	*****	*****	*****	7.180 (2.989, 17.251)
≥ 65 years	2,281	*****	*****	*****	14.213 (8.568, 23.576)
Defined by a diagnosis in the inpatient care setting					
0-17 years	12	5.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years	829	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years	1,538	*****	*****	*****	4.305 (1.388, 13.347)
≥ 65 years	2,281	*****	*****	*****	4.723 (1.966, 11.348)
Defined by a diagnosis in the principal position in the inpatient care setting					
0-17 years	12	5.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years	829	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years	1,538	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
≥ 65 years	2,281	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Defined by a modified validated algorithm in any care setting					
0-17 years	12	5.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years	829	*****	*****	*****	2.663 (0.375, 18.908)
45-64 years	1,538	*****	*****	*****	1.434 (0.202, 10.183)
≥ 65 years	2,281	*****	*****	*****	1.890 (0.473, 7.557)
Defined by a modified validated algorithm in the inpatient care setting					
0-17 years	12	5.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years	829	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years	1,538	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
≥ 65 years	2,281	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Ischemic Colitis Among Eluxadoline New Users					
Defined by a modified validated algorithm in any care setting					
0-17 years	135	63.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years	10,505	*****	*****	*****	0.645 (0.208, 2.001)
45-64 years	12,523	*****	*****	*****	1.579 (0.822, 3.035)
≥ 65 years	14,095	*****	15	0.001 (0.001, 0.002)	2.273 (1.370, 3.770)
Defined by a modified validated algorithm in the inpatient care setting					
0-17 years	135	63.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years	10,505	4,648.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years	12,523	*****	*****	*****	0.351 (0.088, 1.402)
≥ 65 years	14,095	*****	*****	*****	0.757 (0.315, 1.819)

*****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.

Table 4. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Sex

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Ischemic Colitis Among Alosetron New Users					
Defined by a diagnosis in any care setting					
Female	4,257	*****	*****	*****	9.735 (6.210, 15.263)
Male	403	*****	*****	*****	11.022 (2.757, 44.074)
Defined by a diagnosis in the inpatient care setting					
Female	4,257	*****	*****	*****	4.093 (2.047, 8.184)
Male	403	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Defined by a diagnosis in the principal position in the inpatient care setting					
Female	4,257	1,955.7	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male	403	182.4	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Defined by a modified validated algorithm in any care setting					
Female	4,257	*****	*****	*****	1.535 (0.495, 4.759)
Male	403	*****	*****	*****	5.496 (0.774, 39.021)
Defined by a modified validated algorithm in the inpatient care setting					
Female	4,257	1,955.7	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male	403	182.4	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Ischemic Colitis Among Eluxadoline New Users					
Defined by a modified validated algorithm in any care setting					
Female	25,588	*****	*****	*****	1.877 (1.236, 2.851)
Male	11,670	*****	*****	*****	0.945 (0.393, 2.270)
Defined by a modified validated algorithm in the inpatient care setting					
Female	25,588	*****	*****	*****	0.597 (0.285, 1.252)
Male	11,670	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)

*****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.

Table 5. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Sex and Age Group

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Ischemic Colitis Among Alosetron New Users					
Defined by a diagnosis in any care setting					
Female					
0-17 years	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years	*****	*****	*****	*****	2.989 (0.421, 21.220)
45-64 years	1,417	*****	*****	*****	7.767 (3.233, 18.660)
≥ 65 years	2,096	*****	*****	*****	13.409 (7.786, 23.093)
Male					
0-17 years	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years	121	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
≥ 65 years	185	*****	*****	*****	23.284 (5.823, 93.103)
Defined by a diagnosis in the inpatient care setting					
Female					
0-17 years	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years	1,417	*****	*****	*****	4.656 (1.502, 14.436)
≥ 65 years	2,096	*****	*****	*****	5.145 (2.142, 12.362)
Male					
0-17 years	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years	121	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
≥ 65 years	185	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Defined by a diagnosis in the principal position in the inpatient care setting					
Female					
0-17 years	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years	1,417	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
≥ 65 years	2,096	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male					
0-17 years	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years	121	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
≥ 65 years	185	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)

Table 5. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Sex and Age Group

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Defined by a modified validated algorithm in any care setting					
Female					
0-17 years	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years	*****	*****	*****	0.001 (-0.001, 0.004)	2.990 (0.421, 21.224)
45-64 years	1,417	*****	*****	*****	1.551 (0.219, 11.013)
≥ 65 years	2,096	*****	*****	*****	1.029 (0.145, 7.305)
Male					
0-17 years	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years	121	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
≥ 65 years	185	*****	*****	*****	11.576 (1.631, 82.185)
Defined by a modified validated algorithm in the inpatient care setting					
Female					
0-17 years	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years	1,417	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
≥ 65 years	2,096	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male					
0-17 years	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years	121	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
≥ 65 years	185	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Ischemic Colitis Among Eluxadoline New Users					
Defined by a modified validated algorithm in any care setting					
Female					
0-17 years	72	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years	6,246	*****	*****	*****	0.723 (0.181, 2.891)
45-64 years	8,694	*****	*****	*****	1.516 (0.681, 3.375)
≥ 65 years	10,576	*****	*****	*****	2.822 (1.671, 4.764)
Male					
0-17 years	63	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years	4,259	*****	*****	*****	0.531 (0.075, 3.773)
45-64 years	3,829	*****	*****	*****	1.721 (0.555, 5.336)
≥ 65 years	3,519	*****	*****	*****	0.610 (0.086, 4.334)

Table 5. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Sex and Age Group

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Defined by a modified validated algorithm in the inpatient care setting					
Female					
0-17 years	72	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years	6,246	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years	8,694	*****	*****	*****	0.505 (0.126, 2.020)
≥ 65 years	10,576	*****	*****	*****	1.007 (0.419, 2.419)
Male					
0-17 years	63	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years	4,259	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years	3,829	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
≥ 65 years	3,519	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)

*****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.

Table 6. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Age Group and Year

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Ischemic Colitis Among Alosetron New Users					
Defined by a diagnosis in any care setting					
0-17 years					
2016	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2018	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years					
2016	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2018	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	*****	*****	*****	0.006 (-0.006, 0.018)	13.654 (1.923, 96.936)
2020	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years					
2016	465	*****	*****	*****	18.084 (6.787, 48.185)
2017	424	*****	*****	*****	0.000 (0.000, 0.000)
2018	288	*****	*****	*****	7.473 (1.053, 53.053)
2019	262	*****	*****	*****	0.000 (0.000, 0.000)
2020	99	*****	*****	*****	0.000 (0.000, 0.000)
≥ 65 years					
2016	679	*****	*****	*****	18.463 (8.295, 41.097)
2017	563	*****	*****	*****	14.680 (5.509, 39.113)
2018	410	*****	*****	*****	15.297 (4.934, 47.432)
2019	440	*****	*****	*****	9.367 (2.343, 37.453)
2020	189	*****	*****	*****	0.000 (0.000, 0.000)
Defined by a diagnosis in the inpatient care setting					
0-17 years					
2016	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2018	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years					
2016	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2018	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)

Table 6. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Age Group and Year

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
45-64 years					
2016	465	*****	*****	*****	13.540 (4.367, 41.981)
2017	424	*****	*****	*****	0.000 (0.000, 0.000)
2018	288	*****	*****	*****	0.000 (0.000, 0.000)
2019	262	*****	*****	*****	0.000 (0.000, 0.000)
2020	99	*****	*****	*****	0.000 (0.000, 0.000)
≥ 65 years					
2016	679	*****	*****	*****	6.128 (1.532, 24.501)
2017	563	*****	*****	*****	7.327 (1.833, 29.299)
2018	410	*****	*****	*****	0.000 (0.000, 0.000)
2019	440	*****	*****	*****	4.676 (0.659, 33.194)
2020	189	*****	*****	*****	0.000 (0.000, 0.000)
Defined by a diagnosis in the principal position in the inpatient care setting					
0-17 years					
2016	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2018	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years					
2016	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2018	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years					
2016	465	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	424	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2018	288	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	262	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	99	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
≥ 65 years					
2016	679	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	563	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2018	410	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	440	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	189	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)

Table 6. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Age Group and Year

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Defined by a modified validated algorithm in any care setting					
0-17 years					
2016	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2018	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years					
2016	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2018	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	*****	*****	*****	0.006 (-0.006, 0.018)	13.667 (1.925, 97.030)
2020	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years					
2016	465	*****	*****	*****	0.000 (0.000, 0.000)
2017	424	*****	*****	*****	0.000 (0.000, 0.000)
2018	288	*****	*****	*****	0.000 (0.000, 0.000)
2019	262	*****	*****	*****	8.274 (1.165, 58.742)
2020	99	*****	*****	*****	0.000 (0.000, 0.000)
≥ 65 years					
2016	679	*****	*****	*****	3.066 (0.432, 21.764)
2017	563	*****	*****	*****	0.000 (0.000, 0.000)
2018	410	*****	*****	*****	5.086 (0.716, 36.108)
2019	440	*****	*****	*****	0.000 (0.000, 0.000)
2020	189	*****	*****	*****	0.000 (0.000, 0.000)
Defined by a modified validated algorithm in the inpatient care setting					
0-17 years					
2016	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2018	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years					
2016	*****	*****	*****	*****	0.000 (0.000, 0.000)
2017	*****	*****	*****	*****	0.000 (0.000, 0.000)
2018	*****	*****	*****	*****	0.000 (0.000, 0.000)
2019	*****	*****	*****	*****	0.000 (0.000, 0.000)
2020	*****	*****	*****	*****	0.000 (0.000, 0.000)

Table 6. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Age Group and Year

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
45-64 years					
2016	465	222.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	424	199.6	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2018	288	134.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	262	121.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	99	20.7	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
≥ 65 years					
2016	679	326.6	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	563	273.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2018	410	197.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	440	214.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	189	48.3	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Ischemic Colitis Among Eluxadoline New Users					
Defined by a modified validated algorithm in any care setting					
0-17 years					
2016	40	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2018	30	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	31	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years					
2016	2,907	*****	*****	*****	0.753 (0.106, 5.343)
2017	*****	*****	*****	*****	1.405 (0.351, 5.619)
2018	2,228	1,009.3	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	1,652	748.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years					
2016	3,967	*****	*****	*****	1.629 (0.525, 5.049)
2017	3,788	*****	*****	*****	2.842 (1.183, 6.828)
2018	2,463	*****	*****	*****	0.866 (0.122, 6.150)
2019	1,712	798.4	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	593	145.7	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
≥ 65 years					
2016	4,438	*****	*****	*****	2.838 (1.275, 6.317)
2017	4,593	*****	*****	*****	2.261 (0.941, 5.433)
2018	2,645	*****	*****	*****	3.174 (1.191, 8.458)
2019	1,729	833.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	690	181.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)

Table 6. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Age Group and Year

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Defined by a modified validated algorithm in the inpatient care setting					
0-17 years					
2016	40	19.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2018	30	14.6	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	31	14.7	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years					
2016	2,907	1,328.7	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2018	2,228	1,009.3	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	1,652	748.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years					
2016	3,967	*****	*****	*****	0.543 (0.076, 3.852)
2017	3,788	*****	*****	*****	0.568 (0.080, 4.032)
2018	2,463	1,154.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	1,712	798.4	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	593	145.7	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
≥ 65 years					
2016	4,438	*****	*****	*****	1.418 (0.457, 4.397)
2017	4,593	*****	*****	*****	0.452 (0.064, 3.208)
2018	2,645	*****	*****	*****	0.793 (0.112, 5.629)
2019	1,729	833.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	690	181.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)

*****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.

Table 7. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Sex and Year

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Ischemic Colitis Among Alosetron New Users					
Defined by a diagnosis in any care setting					
Female					
2016	1,266	*****	*****	*****	16.538 (8.898, 30.738)
2017	1,105	*****	*****	*****	7.592 (2.849, 20.228)
2018	796	*****	*****	*****	5.306 (1.327, 21.215)
2019	787	*****	*****	*****	8.088 (2.608, 25.078)
2020	303	72.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male					
2016	121	57.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	89	41.7	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2018	79	*****	*****	*****	56.990 (14.253, 227.877)
2019	84	38.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	30	8.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Defined by a diagnosis in the inpatient care setting					
Female					
2016	1,266	*****	*****	*****	8.245 (3.432, 19.808)
2017	1,105	*****	*****	*****	3.793 (0.949, 15.165)
2018	796	377.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	787	*****	*****	*****	2.691 (0.379, 19.108)
2020	303	72.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male					
2016	121	57.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	89	41.7	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2018	79	36.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	84	38.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	30	8.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Defined by a diagnosis in the principal position in the inpatient care setting					
Female					
2016	1,266	607.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	1,105	527.5	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2018	796	377.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	787	371.7	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	303	72.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)

Table 7. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Sex and Year

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Male					
2016	121	57.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	89	41.7	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2018	79	36.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	84	38.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	30	8.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Defined by a modified validated algorithm in any care setting					
Female					
2016	1,266	*****	*****	*****	1.648 (0.232, 11.702)
2017	1,105	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2018	796	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	787	*****	*****	*****	5.388 (1.347, 21.543)
2020	303	72.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male					
2016	121	57.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	89	*****	*****	*****	0.000 (0.000, 0.000)
2018	79	*****	*****	*****	28.105 (3.959, 199.525)
2019	84	38.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	30	8.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Defined by a modified validated algorithm in the inpatient care setting					
Female					
2016	1,266	607.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	1,105	527.5	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2018	796	377.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	787	371.7	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	303	72.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male					
2016	121	57.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	89	41.7	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2018	79	36.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	84	38.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	30	8.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)

Table 7. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Sex and Year

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Ischemic Colitis Among Eluxadoline New Users					
Defined by a modified validated algorithm in any care setting					
Female					
2016	8,218	*****	*****	*****	2.599 (1.398, 4.830)
2017	7,981	*****	*****	*****	2.130 (1.065, 4.260)
2018	4,814	*****	*****	*****	1.776 (0.667, 4.733)
2019	3,339	1,560.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	1,236	302.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male					
2016	3,134	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	3,535	*****	*****	*****	2.423 (0.909, 6.456)
2018	2,552	*****	*****	*****	0.843 (0.119, 5.982)
2019	1,785	834.3	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	664	164.4	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Defined by a modified validated algorithm in the inpatient care setting					
Female					
2016	8,218	*****	*****	*****	1.039 (0.390, 2.768)
2017	7,981	*****	*****	*****	0.532 (0.133, 2.128)
2018	4,814	*****	*****	*****	0.444 (0.063, 3.151)
2019	3,339	1,560.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	1,236	302.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male					
2016	3,134	1,456.3	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2017	3,535	1,651.9	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2018	2,552	1,187.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2019	1,785	834.3	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
2020	664	164.4	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)

*****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.

Table 8. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Age Group and Irritable Bowel Syndrome

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Ischemic Colitis Among Alosetron New Users					
Defined by a diagnosis in any care setting					
0-17 years					
Evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years					
Evidence of Irritable bowel syndrome	486	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	343	*****	*****	*****	6.426 (0.905, 45.624)
45-64 years					
Evidence of Irritable bowel syndrome	887	*****	*****	*****	2.494 (0.351, 17.705)
No evidence of Irritable bowel syndrome	651	*****	*****	*****	13.542 (5.082, 36.082)
≥ 65 years					
Evidence of Irritable bowel syndrome	1,259	*****	*****	*****	6.847 (2.570, 18.242)
No evidence of Irritable bowel syndrome	1,022	*****	*****	*****	23.347 (12.930, 42.159)
Defined by a diagnosis in the inpatient care setting					
0-17 years					
Evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years					
Evidence of Irritable bowel syndrome	486	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	343	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years					
Evidence of Irritable bowel syndrome	887	*****	*****	*****	2.494 (0.351, 17.705)
No evidence of Irritable bowel syndrome	651	*****	*****	*****	6.758 (1.690, 27.022)
≥ 65 years					
Evidence of Irritable bowel syndrome	1,259	*****	*****	*****	3.421 (0.855, 13.677)
No evidence of Irritable bowel syndrome	1,022	*****	*****	*****	6.331 (2.042, 19.629)
Defined by a diagnosis in the principal position in the inpatient care setting					
0-17 years					
Evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years					
Evidence of Irritable bowel syndrome	486	219.9	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	343	155.9	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years					
Evidence of Irritable bowel syndrome	887	401.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	651	296.3	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)

Table 8. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Age Group and Irritable Bowel Syndrome

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
≥ 65 years					
Evidence of Irritable bowel syndrome	1,259	584.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	1,022	474.3	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Defined by a modified validated algorithm in any care setting					
0-17 years					
Evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years					
Evidence of Irritable bowel syndrome	486	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	343	*****	*****	*****	6.429 (0.906, 45.645)
45-64 years					
Evidence of Irritable bowel syndrome	887	*****	*****	*****	2.495 (0.351, 17.709)
No evidence of Irritable bowel syndrome	651	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
≥ 65 years					
Evidence of Irritable bowel syndrome	1,259	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	1,022	*****	*****	*****	4.225 (1.057, 16.892)
Defined by a modified validated algorithm in the inpatient care setting					
0-17 years					
Evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years					
Evidence of Irritable bowel syndrome	486	219.9	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	343	155.9	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years					
Evidence of Irritable bowel syndrome	887	401.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	651	296.3	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
≥ 65 years					
Evidence of Irritable bowel syndrome	1,259	584.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	1,022	474.3	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Ischemic Colitis Among Eluxadoline New Users					
Defined by a modified validated algorithm in any care setting					
0-17 years					
Evidence of Irritable bowel syndrome	91	42.5	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	44	20.7	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years					
Evidence of Irritable bowel syndrome	6,468	*****	*****	*****	1.050 (0.339, 3.256)
No evidence of Irritable bowel syndrome	4,037	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)

Table 8. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Age Group and Irritable Bowel Syndrome

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
45-64 years					
Evidence of Irritable bowel syndrome	7,078	*****	*****	*****	1.236 (0.464, 3.293)
No evidence of Irritable bowel syndrome	5,445	*****	*****	*****	2.029 (0.845, 4.875)
≥ 65 years					
Evidence of Irritable bowel syndrome	7,474	*****	*****	*****	3.128 (1.732, 5.648)
No evidence of Irritable bowel syndrome	6,621	*****	*****	*****	1.297 (0.487, 3.457)
Defined by a modified validated algorithm in the inpatient care setting					
0-17 years					
Evidence of Irritable bowel syndrome	91	42.5	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	44	20.7	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years					
Evidence of Irritable bowel syndrome	6,468	2,857.4	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	4,037	1,790.7	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years					
Evidence of Irritable bowel syndrome	7,078	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	5,445	*****	*****	*****	0.811 (0.203, 3.244)
≥ 65 years					
Evidence of Irritable bowel syndrome	7,474	*****	*****	*****	0.284 (0.040, 2.016)
No evidence of Irritable bowel syndrome	6,621	*****	*****	*****	1.297 (0.487, 3.457)

*****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.

Table 9. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Sex and Irritable Bowel Syndrome

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Ischemic Colitis Among Alosetron New Users					
Defined by a diagnosis in any care setting					
Female					
Evidence of Irritable bowel syndrome	2,474	*****	*****	*****	4.415 (1.837, 10.606)
No evidence of Irritable bowel syndrome	1,783	*****	*****	*****	17.094 (10.124, 28.863)
Male					
Evidence of Irritable bowel syndrome	165	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	238	*****	*****	*****	18.958 (4.741, 75.805)
Defined by a diagnosis in the inpatient care setting					
Female					
Evidence of Irritable bowel syndrome	2,474	*****	*****	*****	2.648 (0.854, 8.209)
No evidence of Irritable bowel syndrome	1,783	*****	*****	*****	6.085 (2.533, 14.621)
Male					
Evidence of Irritable bowel syndrome	165	76.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	238	106.4	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Defined by a diagnosis in the principal position in the inpatient care setting					
Female					
Evidence of Irritable bowel syndrome	2,474	1,133.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	1,783	822.4	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male					
Evidence of Irritable bowel syndrome	165	76.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	238	106.4	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Defined by a modified validated algorithm in any care setting					
Female					
Evidence of Irritable bowel syndrome	2,474	*****	*****	*****	0.883 (0.124, 6.265)
No evidence of Irritable bowel syndrome	1,783	*****	*****	*****	2.434 (0.609, 9.733)
Male					
Evidence of Irritable bowel syndrome	165	*****	*****	*****	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	238	*****	*****	*****	9.436 (1.329, 66.986)
Defined by a modified validated algorithm in the inpatient care setting					
Female					
Evidence of Irritable bowel syndrome	2,474	1,133.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	1,783	822.4	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male					
Evidence of Irritable bowel syndrome	165	76.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	238	106.4	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)

Table 9. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Sex and Irritable Bowel Syndrome

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Ischemic Colitis Among Eluxadoline New Users					
Defined by a modified validated algorithm in any care setting					
Female					
Evidence of Irritable bowel syndrome	14,825	*****	*****	*****	2.206 (1.330, 3.659)
No evidence of Irritable bowel syndrome	10,763	*****	*****	*****	1.423 (0.678, 2.985)
Male					
Evidence of Irritable bowel syndrome	6,286	*****	*****	*****	1.052 (0.339, 3.260)
No evidence of Irritable bowel syndrome	5,384	*****	*****	*****	0.820 (0.205, 3.278)
Defined by a modified validated algorithm in the inpatient care setting					
Female					
Evidence of Irritable bowel syndrome	14,825	*****	*****	*****	0.147 (0.021, 1.043)
No evidence of Irritable bowel syndrome	10,763	*****	*****	*****	1.220 (0.548, 2.715)
Male					
Evidence of Irritable bowel syndrome	6,286	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	5,384	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)

*****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.

Table 10. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Sex, Age Group, and Irritable Bowel Syndrome

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Ischemic Colitis Among Alosetron New Users					
Defined by a diagnosis in any care setting					
Female, 0-17 years					
Evidence of Irritable bowel syndrome	*****	*****	*****	*****	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	*****	*****	*****	*****	0.000 (0.000, 0.000)
Male, 0-17 years					
Evidence of Irritable bowel syndrome	*****	*****	*****	*****	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	*****	*****	*****	*****	0.000 (0.000, 0.000)
Female, 18-44 years					
Evidence of Irritable bowel syndrome	444	200.9	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	292	*****	*****	*****	7.484 (1.054, 53.130)
Male, 18-44 years					
Evidence of Irritable bowel syndrome	42	19.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	51	22.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, 45-64 years					
Evidence of Irritable bowel syndrome	843	*****	*****	*****	2.620 (0.369, 18.597)
No evidence of Irritable bowel syndrome	574	*****	*****	*****	15.266 (5.729, 40.675)
Male, 45-64 years					
Evidence of Irritable bowel syndrome	44	19.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	77	33.3	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, ≥ 65 years					
Evidence of Irritable bowel syndrome	1,182	*****	*****	*****	7.306 (2.742, 19.466)
No evidence of Irritable bowel syndrome	914	*****	*****	*****	21.328 (11.097, 40.991)
Male, ≥ 65 years					
Evidence of Irritable bowel syndrome	77	36.7	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	108	*****	*****	*****	40.681 (10.174, 162.663)
Defined by a diagnosis in the inpatient care setting					
Female, 0-17 years					
Evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male, 0-17 years					
Evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, 18-44 years					
Evidence of Irritable bowel syndrome	444	200.9	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	292	133.9	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)

Table 10. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Sex, Age Group, and Irritable Bowel Syndrome

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Male, 18-44 years					
Evidence of Irritable bowel syndrome	42	19.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	51	22.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, 45-64 years					
Evidence of Irritable bowel syndrome	843	*****	*****	*****	2.620 (0.369, 18.597)
No evidence of Irritable bowel syndrome	574	*****	*****	*****	7.616 (1.905, 30.453)
Male, 45-64 years					
Evidence of Irritable bowel syndrome	44	19.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	77	33.3	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, ≥ 65 years					
Evidence of Irritable bowel syndrome	1,182	*****	*****	*****	3.650 (0.913, 14.594)
No evidence of Irritable bowel syndrome	914	*****	*****	*****	7.079 (2.283, 21.950)
Male, ≥ 65 years					
Evidence of Irritable bowel syndrome	77	36.7	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	108	50.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Defined by a diagnosis in the principal position in the inpatient care setting					
Female, 0-17 years					
Evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male, 0-17 years					
Evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, 18-44 years					
Evidence of Irritable bowel syndrome	444	200.9	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	292	133.9	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male, 18-44 years					
Evidence of Irritable bowel syndrome	42	19.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	51	22.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, 45-64 years					
Evidence of Irritable bowel syndrome	843	381.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	574	263.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male, 45-64 years					
Evidence of Irritable bowel syndrome	44	19.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	77	33.3	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, ≥ 65 years					
Evidence of Irritable bowel syndrome	1,182	548.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	914	424.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)

Table 10. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Sex, Age Group, and Irritable Bowel Syndrome

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Male, ≥ 65 years					
Evidence of Irritable bowel syndrome	77	36.7	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	108	50.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Defined by a modified validated algorithm in any care setting					
Female, 0-17 years					
Evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male, 0-17 years					
Evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, 18-44 years					
Evidence of Irritable bowel syndrome	444	*****	*****	*****	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	292	*****	*****	*****	7.488 (1.055, 53.159)
Male, 18-44 years					
Evidence of Irritable bowel syndrome	42	*****	*****	*****	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	51	*****	*****	*****	0.000 (0.000, 0.000)
Female, 45-64 years					
Evidence of Irritable bowel syndrome	843	*****	*****	*****	2.620 (0.369, 18.602)
No evidence of Irritable bowel syndrome	574	*****	*****	*****	0.000 (0.000, 0.000)
Male, 45-64 years					
Evidence of Irritable bowel syndrome	44	19.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	77	33.3	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, ≥ 65 years					
Evidence of Irritable bowel syndrome	1,182	*****	*****	*****	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	914	*****	*****	*****	2.360 (0.332, 16.753)
Male, ≥ 65 years					
Evidence of Irritable bowel syndrome	77	*****	*****	*****	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	108	*****	*****	*****	20.141 (2.837, 142.985)
Defined by a modified validated algorithm in the inpatient care setting					
Female, 0-17 years					
Evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male, 0-17 years					
Evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, 18-44 years					
Evidence of Irritable bowel syndrome	444	*****	*****	*****	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	292	*****	*****	*****	0.000 (0.000, 0.000)

Table 10. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Sex, Age Group, and Irritable Bowel Syndrome

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Male, 18-44 years					
Evidence of Irritable bowel syndrome	42	*****	*****	*****	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	51	*****	*****	*****	0.000 (0.000, 0.000)
Female, 45-64 years					
Evidence of Irritable bowel syndrome	843	381.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	574	263.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male, 45-64 years					
Evidence of Irritable bowel syndrome	44	19.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	77	33.3	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, ≥ 65 years					
Evidence of Irritable bowel syndrome	1,182	548.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	914	424.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male, ≥ 65 years					
Evidence of Irritable bowel syndrome	77	36.7	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	108	50.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Ischemic Colitis Among Eluxadoline New Users					
Defined by a modified validated algorithm in any care setting					
Female, 0-17 years					
Evidence of Irritable bowel syndrome	44	20.4	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	28	13.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male, 0-17 years					
Evidence of Irritable bowel syndrome	47	22.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	16	7.4	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, 18-44 years					
Evidence of Irritable bowel syndrome	3,890	*****	*****	*****	1.162 (0.291, 4.648)
No evidence of Irritable bowel syndrome	2,356	*****	*****	*****	0.000 (0.000, 0.000)
Male, 18-44 years					
Evidence of Irritable bowel syndrome	2,578	*****	*****	*****	0.880 (0.124, 6.247)
No evidence of Irritable bowel syndrome	1,681	*****	*****	*****	0.000 (0.000, 0.000)
Female, 45-64 years					
Evidence of Irritable bowel syndrome	5,043	*****	*****	*****	1.301 (0.419, 4.033)
No evidence of Irritable bowel syndrome	3,651	*****	*****	*****	1.818 (0.586, 5.637)
Male, 45-64 years					
Evidence of Irritable bowel syndrome	2,035	*****	*****	*****	1.076 (0.152, 7.638)
No evidence of Irritable bowel syndrome	1,794	*****	*****	*****	2.458 (0.615, 9.827)
Female, ≥ 65 years					
Evidence of Irritable bowel syndrome	5,848	*****	*****	*****	3.634 (1.955, 6.754)
No evidence of Irritable bowel syndrome	4,728	*****	*****	*****	1.810 (0.679, 4.823)

Table 10. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Sex, Age Group, and Irritable Bowel Syndrome

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Male, ≥ 65 years					
Evidence of Irritable bowel syndrome	1,626	*****	*****	*****	1.307 (0.184, 9.280)
No evidence of Irritable bowel syndrome	1,893	*****	*****	*****	0.000 (0.000, 0.000)
Defined by a modified validated algorithm in the inpatient care setting					
Female, 0-17 years					
Evidence of Irritable bowel syndrome	44	20.4	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	28	13.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male, 0-17 years					
Evidence of Irritable bowel syndrome	47	22.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	16	7.4	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, 18-44 years					
Evidence of Irritable bowel syndrome	3,890	1,720.6	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	2,356	1,045.5	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male, 18-44 years					
Evidence of Irritable bowel syndrome	2,578	1,136.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	1,681	745.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, 45-64 years					
Evidence of Irritable bowel syndrome	5,043	*****	*****	*****	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	3,651	*****	*****	*****	1.212 (0.303, 4.845)
Male, 45-64 years					
Evidence of Irritable bowel syndrome	2,035	929.6	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	1,794	814.4	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, ≥ 65 years					
Evidence of Irritable bowel syndrome	5,848	*****	*****	*****	0.363 (0.051, 2.577)
No evidence of Irritable bowel syndrome	4,728	*****	*****	*****	1.810 (0.679, 4.823)
Male, ≥ 65 years					
Evidence of Irritable bowel syndrome	1,626	765.4	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of Irritable bowel syndrome	1,893	873.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)

*****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.

Table 11. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Age Group and Intestinal Ischemia

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Ischemic Colitis Among Alosetron New Users					
Defined by a diagnosis in any care setting					
0-17 years					
Evidence of intestinal ischemia	0	0.0	0	NaN	NaN
No evidence of intestinal ischemia	12	5.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years					
Evidence of intestinal ischemia	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	*****	0.001 (-0.001, 0.004)	2.677 (0.377, 19.003)
45-64 years					
Evidence of intestinal ischemia	*****	*****	*****	*****	414.586 (103.684, 1,657.737)
No evidence of intestinal ischemia	*****	*****	*****	*****	4.338 (1.399, 13.451)
≥ 65 years					
Evidence of intestinal ischemia	23	*****	*****	*****	618.230 (257.320, 1,485.339)
No evidence of intestinal ischemia	2,258	*****	*****	*****	9.548 (5.138, 17.746)
Defined by a diagnosis in the inpatient care setting					
0-17 years					
Evidence of intestinal ischemia	0	0.0	0	NaN	NaN
No evidence of intestinal ischemia	12	5.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years					
Evidence of intestinal ischemia	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years					
Evidence of intestinal ischemia	*****	*****	*****	*****	199.481 (28.099, 1,416.182)
No evidence of intestinal ischemia	*****	*****	*****	*****	2.891 (0.723, 11.558)
≥ 65 years					
Evidence of intestinal ischemia	23	*****	*****	*****	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	2,258	*****	*****	*****	4.769 (1.985, 11.458)
Defined by a diagnosis in the principal position in the inpatient care setting					
0-17 years					
Evidence of intestinal ischemia	0	0.0	0	NaN	NaN
No evidence of intestinal ischemia	12	5.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years					
Evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years					
Evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)

Table 11. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Age Group and Intestinal Ischemia

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
≥ 65 years					
Evidence of intestinal ischemia	23	10.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	2,258	1,048.9	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Defined by a modified validated algorithm in any care setting					
0-17 years					
Evidence of intestinal ischemia	0	0.0	0	NaN	NaN
No evidence of intestinal ischemia	12	5.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years					
Evidence of intestinal ischemia	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	*****	0.001 (-0.001, 0.004)	2.677 (0.377, 19.007)
45-64 years					
Evidence of intestinal ischemia	*****	*****	*****	*****	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	*****	*****	1.445 (0.204, 10.258)
≥ 65 years					
Evidence of intestinal ischemia	23	*****	*****	*****	102.829 (14.484, 730.019)
No evidence of intestinal ischemia	2,258	*****	*****	*****	0.954 (0.134, 6.771)
Defined by a modified validated algorithm in the inpatient care setting					
0-17 years					
Evidence of intestinal ischemia	0	0.0	0	NaN	NaN
No evidence of intestinal ischemia	12	5.8	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years					
Evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
45-64 years					
Evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
≥ 65 years					
Evidence of intestinal ischemia	23	10.2	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	2,258	1,048.9	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Ischemic Colitis Among Eluxadoline New Users					
Defined by a modified validated algorithm in any care setting					
0-17 years					
Evidence of intestinal ischemia	0	0.0	0	NaN	NaN
No evidence of intestinal ischemia	135	63.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years					
Evidence of intestinal ischemia	12	*****	*****	*****	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	10,493	*****	*****	*****	0.646 (0.208, 2.004)

Table 11. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Age Group and Intestinal Ischemia

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
45-64 years					
Evidence of intestinal ischemia	53	*****	*****	*****	83.744 (20.944, 334.854)
No evidence of intestinal ischemia	12,470	*****	*****	*****	1.233 (0.588, 2.587)
≥ 65 years					
Evidence of intestinal ischemia	78	*****	*****	*****	150.210 (62.520, 360.889)
No evidence of intestinal ischemia	14,017	*****	*****	*****	1.523 (0.819, 2.830)
Defined by a modified validated algorithm in the inpatient care setting					
0-17 years					
Evidence of intestinal ischemia	0	0.0	0	NaN	NaN
No evidence of intestinal ischemia	135	63.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
18-44 years					
Evidence of intestinal ischemia	12	*****	*****	*****	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	10,493	*****	*****	*****	0.000 (0.000, 0.000)
45-64 years					
Evidence of intestinal ischemia	53	*****	*****	*****	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	12,470	*****	*****	*****	0.352 (0.088, 1.409)
≥ 65 years					
Evidence of intestinal ischemia	78	*****	*****	*****	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	14,017	*****	*****	*****	0.761 (0.317, 1.829)

*****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.

Table 12. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Sex and Intestinal Ischemia

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Ischemic Colitis Among Alosetron New Users					
Defined by a diagnosis in any care setting					
Female					
Evidence of intestinal ischemia	*****	*****	*****	0.158 (0.042, 0.274)	418.225 (187.889, 930.932)
No evidence of intestinal ischemia	*****	*****	*****	0.003 (0.001, 0.005)	6.710 (3.896, 11.557)
Male					
Evidence of intestinal ischemia	*****	*****	*****	0.500 (-0.193, 1.193)	1,932.540 (272.214, 13,719.731)
No evidence of intestinal ischemia	*****	*****	*****	0.002 (-0.002, 0.007)	5.527 (0.779, 39.238)
Defined by a diagnosis in the inpatient care setting					
Female					
Evidence of intestinal ischemia	*****	*****	*****	0.026 (-0.025, 0.077)	61.896 (8.719, 439.422)
No evidence of intestinal ischemia	*****	*****	*****	0.002 (0.000, 0.003)	3.611 (1.721, 7.574)
Male					
Evidence of intestinal ischemia	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Defined by a diagnosis in the principal position in the inpatient care setting					
Female					
Evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male					
Evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Defined by a modified validated algorithm in any care setting					
Female					
Evidence of intestinal ischemia	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	*****	0.001 (-0.000, 0.002)	1.548 (0.499, 4.799)
Male					
Evidence of intestinal ischemia	*****	*****	*****	0.500 (-0.193, 1.193)	1,873.077 (263.839, 13,297.586)
No evidence of intestinal ischemia	*****	*****	*****	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Defined by a modified validated algorithm in the inpatient care setting					
Female					
Evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male					
Evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)

Table 12. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Sex and Intestinal Ischemia

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Ischemic Colitis Among Eluxadoline New Users					
Defined by a modified validated algorithm in any care setting					
Female					
Evidence of intestinal ischemia	110	*****	*****	*****	148.089 (70.598, 310.636)
No evidence of intestinal ischemia	25,478	*****	*****	*****	1.285 (0.775, 2.132)
Male					
Evidence of intestinal ischemia	33	*****	*****	*****	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	11,637	*****	*****	*****	0.948 (0.394, 2.276)
Defined by a modified validated algorithm in the inpatient care setting					
Female					
Evidence of intestinal ischemia	110	*****	*****	*****	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	25,478	*****	*****	*****	0.600 (0.286, 1.258)
Male					
Evidence of intestinal ischemia	33	*****	*****	*****	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	11,637	*****	*****	*****	0.000 (0.000, 0.000)

*****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.

Table 13. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Sex, Age Group, and Intestinal Ischemia

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Ischemic Colitis Among Alosetron New Users					
Defined by a diagnosis in any care setting					
Female, 0-17 years					
Evidence of intestinal ischemia	*****	*****	0	*****	*****
No evidence of intestinal ischemia	*****	*****	0	*****	*****
Male, 0-17 years					
Evidence of intestinal ischemia	*****	*****	0	*****	*****
No evidence of intestinal ischemia	*****	*****	0	*****	*****
Female, 18-44 years					
Evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	*****	0.001 (-0.001, 0.004)	3.007 (0.423, 21.344)
Male, 18-44 years					
Evidence of intestinal ischemia	0	0.0	0	NaN	NaN
No evidence of intestinal ischemia	93	41.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, 45-64 years					
Evidence of intestinal ischemia	12	*****	*****	*****	414.586 (103.684, 1,657.737)
No evidence of intestinal ischemia	1,405	*****	*****	*****	4.695 (1.514, 14.558)
Male, 45-64 years					
Evidence of intestinal ischemia	0	0.0	0	NaN	NaN
No evidence of intestinal ischemia	121	52.6	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, ≥ 65 years					
Evidence of intestinal ischemia	*****	*****	*****	*****	528.391 (198.311, 1,407.874)
No evidence of intestinal ischemia	*****	*****	*****	*****	9.356 (4.868, 17.982)
Male, ≥ 65 years					
Evidence of intestinal ischemia	*****	*****	*****	*****	1,932.540 (272.214, 13,719.731
No evidence of intestinal ischemia	*****	*****	*****	*****	11.713 (1.650, 83.153)
Defined by a diagnosis in the inpatient care setting					
Female, 0-17 years					
Evidence of intestinal ischemia	*****	*****	0	*****	*****
No evidence of intestinal ischemia	*****	*****	0	*****	*****
Male, 0-17 years					
Evidence of intestinal ischemia	*****	*****	0	*****	*****
No evidence of intestinal ischemia	*****	*****	0	*****	*****
Female, 18-44 years					
Evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)

Table 13. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Sex, Age Group, and Intestinal Ischemia

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Male, 18-44 years					
Evidence of intestinal ischemia	0	0.0	0	NaN	NaN
No evidence of intestinal ischemia	93	41.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, 45-64 years					
Evidence of intestinal ischemia	12	*****	*****	*****	199.481 (28.099, 1,416.182)
No evidence of intestinal ischemia	1,405	*****	*****	*****	3.128 (0.782, 12.509)
Male, 45-64 years					
Evidence of intestinal ischemia	0	0.0	0	NaN	NaN
No evidence of intestinal ischemia	121	52.6	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, ≥ 65 years					
Evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	*****	*****	5.195 (2.162, 12.480)
Male, ≥ 65 years					
Evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Defined by a diagnosis in the principal position in the inpatient care setting					
Female, 0-17 years					
Evidence of intestinal ischemia	*****	*****	0	*****	*****
No evidence of intestinal ischemia	*****	*****	0	*****	*****
Male, 0-17 years					
Evidence of intestinal ischemia	*****	*****	0	*****	*****
No evidence of intestinal ischemia	*****	*****	0	*****	*****
Female, 18-44 years					
Evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male, 18-44 years					
Evidence of intestinal ischemia	0	0.0	0	NaN	NaN
No evidence of intestinal ischemia	93	41.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, 45-64 years					
Evidence of intestinal ischemia	12	5.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	1,405	639.6	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male, 45-64 years					
Evidence of intestinal ischemia	0	0.0	0	NaN	NaN
No evidence of intestinal ischemia	121	52.6	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, ≥ 65 years					
Evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)

Table 13. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Sex, Age Group, and Intestinal Ischemia

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Male, ≥ 65 years					
Evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Defined by a modified validated algorithm in any care setting					
Female, 0-17 years					
Evidence of intestinal ischemia	*****	*****	0	NaN	NaN
No evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male, 0-17 years					
Evidence of intestinal ischemia	*****	*****	0	NaN	NaN
No evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, 18-44 years					
Evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	*****	0.001 (-0.001, 0.004)	3.007 (0.424, 21.349)
Male, 18-44 years					
Evidence of intestinal ischemia	0	0.0	0	NaN	NaN
No evidence of intestinal ischemia	93	41.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, 45-64 years					
Evidence of intestinal ischemia	12	*****	*****	*****	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	1,405	*****	*****	*****	1.564 (0.220, 11.102)
Male, 45-64 years					
Evidence of intestinal ischemia	0	0.0	0	NaN	NaN
No evidence of intestinal ischemia	121	52.6	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, ≥ 65 years					
Evidence of intestinal ischemia	*****	*****	*****	*****	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	*****	*****	1.039 (0.146, 7.375)
Male, ≥ 65 years					
Evidence of intestinal ischemia	*****	*****	*****	*****	1,873.077 (263.839, 13,297.586
No evidence of intestinal ischemia	*****	*****	*****	*****	0.000 (0.000, 0.000)
Defined by a modified validated algorithm in the inpatient care setting					
Female, 0-17 years					
Evidence of intestinal ischemia	*****	*****	0	NaN	NaN
No evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male, 0-17 years					
Evidence of intestinal ischemia	*****	*****	0	NaN	NaN
No evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, 18-44 years					
Evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)

Table 13. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Sex, Age Group, and Intestinal Ischemia

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Male, 18-44 years					
Evidence of intestinal ischemia	0	0.0	0	NaN	NaN
No evidence of intestinal ischemia	93	41.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, 45-64 years					
Evidence of intestinal ischemia	12	5.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	1,405	639.6	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male, 45-64 years					
Evidence of intestinal ischemia	0	0.0	0	NaN	NaN
No evidence of intestinal ischemia	121	52.6	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, ≥ 65 years					
Evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male, ≥ 65 years					
Evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Ischemic Colitis Among Eluxadoline New Users					
Defined by a modified validated algorithm in any care setting					
Female, 0-17 years					
Evidence of intestinal ischemia	0	0.0	0	NaN	NaN
No evidence of intestinal ischemia	72	33.6	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male, 0-17 years					
Evidence of intestinal ischemia	0	0.0	0	NaN	NaN
No evidence of intestinal ischemia	63	29.5	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, 18-44 years					
Evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	*****	0.000 (-0.000, 0.001)	0.724 (0.181, 2.895)
Male, 18-44 years					
Evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	*****	0.000 (-0.000, 0.001)	0.532 (0.075, 3.778)
Female, 45-64 years					
Evidence of intestinal ischemia	40	*****	*****	*****	112.126 (28.042, 448.340)
No evidence of intestinal ischemia	8,654	*****	*****	*****	1.016 (0.381, 2.706)
Male, 45-64 years					
Evidence of intestinal ischemia	13	*****	0	*****	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	3,816	*****	*****	*****	1.727 (0.557, 5.355)
Female, ≥ 65 years					
Evidence of intestinal ischemia	63	*****	*****	*****	191.230 (79.594, 459.444)
No evidence of intestinal ischemia	10,513	*****	*****	*****	1.824 (0.949, 3.505)

Table 13. Summary of Ischemic Colitis Among Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020, by Sex, Age Group, and Intestinal Ischemia

	New Users	Years at Risk	New Episodes with an Event	Proportion of Episodes with an Event (95% Confidence Interval)	Event Rate per 1,000 Person-Years (95% Confidence Interval)
Male, ≥ 65 years					
Evidence of intestinal ischemia	15	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	3,504	*****	*****	*****	0.613 (0.086, 4.352)
Defined by a modified validated algorithm in the inpatient care setting					
Female, 0-17 years					
Evidence of intestinal ischemia	0	0.0	0	NaN	NaN
No evidence of intestinal ischemia	72	33.6	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male, 0-17 years					
Evidence of intestinal ischemia	0	0.0	0	NaN	NaN
No evidence of intestinal ischemia	63	29.5	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, 18-44 years					
Evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Male, 18-44 years					
Evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	*****	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, 45-64 years					
Evidence of intestinal ischemia	40	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	8,654	*****	*****	*****	0.508 (0.127, 2.030)
Male, 45-64 years					
Evidence of intestinal ischemia	13	6.0	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	3,816	1,737.9	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
Female, ≥ 65 years					
Evidence of intestinal ischemia	63	*****	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	10,513	*****	*****	*****	1.013 (0.422, 2.433)
Male, ≥ 65 years					
Evidence of intestinal ischemia	15	7.1	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)
No evidence of intestinal ischemia	3,504	1,631.4	0	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)

*****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.

Table 14. Summary of Patient Level Cohort Attrition in the Sentinel Distributed Database from January 1, 2016 to July 1, 2020

	Alosetron New Users		Eluxadoline New Users	
	Remaining	Excluded	Remaining	Excluded
Members meeting enrollment and demographic requirements				
Enrolled at any point during the query period	202,167,459	N/A	202,167,459	N/A
Had required coverage type (medical and/or drug coverage)	126,519,935	75,647,524	126,519,935	75,647,524
Enrolled during specified age range	126,516,278	3,657	126,516,278	3,657
Had requestable medical charts	126,516,278	0	126,516,278	0
Met demographic requirements (sex, race, and Hispanic origin)	126,509,315	6,963	126,509,315	6,963
Members with a valid index event				
Had any cohort-defining claim during the query period	6,764	126,502,551	42,730	126,466,585
Claim recorded during specified age range	6,764	0	42,730	0
Episode defining index claim recorded during the query period	5,873	891	42,710	20
Met exposure incidence criteria	5,873	0	42,710	0
Members with required pre-index history				
Had sufficient pre-index continuous enrollment	5,004	869	37,534	5,176
Met inclusion and exclusion criteria[1]	4,660	344	37,258	276
Evidence of comparator	N/A	344	N/A	276
Met event incidence criteria	4,660	0	37,258	0
Members with required post-index follow-up				
Had sufficient post-index continuous enrollment	4,660	0	37,258	0
Had minimum days' supply on index date	4,660	0	37,258	0
Had index episode of at least required length	4,660	0	37,258	0
Had index episode longer than blackout period	4,660	0	37,258	0
Did not have an event during blackout period	4,660	0	37,258	0
Final cohort				
Number of members	4,660	N/A	37,258	N/A

[1]Patients can meet multiple inclusion and/or exclusion criteria; therefore, the total number of patients excluded overall may not equal the sum of all patients in each criterion.

Table 15. Summary of Reasons for End of At-Risk Period for Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020[1]

		End of Exposure Episode[2]		Censoring Reason Occurence of Event[3]		Evidence of Death[4]	
	Total Number of Patients	Number of Patients	Percent of Total Patients	Number of Patients	Percent of Total Patients	Number of Patients	Percent of Total Patients
Ischemic Colitis Among Alosetron New Users							
Defined by a diagnosis in any care setting	4,660	3,910	83.9%	21	0.5%	48	1.0%
Defined by a diagnosis in the inpatient care setting	4,660	3,923	84.2%	*****	0.2%	48	1.0%
Defined by a diagnosis in the principal position in the inpatient care setting	4,660	3,931	84.4%	0	0.0%	48	1.0%
Defined by a modified validated algorithm in any care setting	4,660	3,927	84.3%	*****	0.1%	48	1.0%
Defined by a modified validated algorithm in the inpatient care setting	4,660	3,931	84.4%	0	0.0%	48	1.0%
Ischemic Colitis Among Eluxadoline New Users							
Defined by a modified validated algorithm in any care setting	37,258	31,190	83.7%	27	0.1%	425	1.1%
Defined by a modified validated algorithm in the inpatient care setting	37,258	31,209	83.8%	*****	0.0%	425	1.1%

[1]An episode may be censored due to more than one reason if they occur on the same date. Therefore, the sum of the reasons for censoring may be greater than the total number of Patients.

[2]Represents Patients censored due to end of the exposure episode. In point exposure analyses, exposure Patients end when a pre-determined maximum episode duration is met.

[3]Represents Patients censored due to occurrence of request-defined event.

[4]Represents Patients censored due to evidence of death. Death data source and completeness varies by Data Partner.

*****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.

Table 15. Summary of Reasons for End of At-Risk Period for Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020[1]

	Censoring Reason					
	Disenrollment[2]		End of data partner data[3]		End of query period[4]	
	Number of Patients	Percent of Total Patients	Number of Patients	Percent of Total Patients	Number of Patients	Percent of Total Patients
Ischemic Colitis Among Alosetron New Users						
Defined by a diagnosis in any care setting	358	7.7%	12	0.3%	324	7.0%
Defined by a diagnosis in the inpatient care setting	358	7.7%	12	0.3%	324	7.0%
Defined by a diagnosis in the principal position in the inpatient care setting	358	7.7%	12	0.3%	324	7.0%
Defined by a modified validated algorithm in any care setting	358	7.7%	12	0.3%	324	7.0%
Defined by a modified validated algorithm in the inpatient care setting	358	7.7%	12	0.3%	324	7.0%
Ischemic Colitis Among Eluxadoline New Users						
Defined by a modified validated algorithm in any care setting	3,836	10.3%	46	0.1%	1,816	4.9%
Defined by a modified validated algorithm in the inpatient care setting	3,837	10.3%	46	0.1%	1,816	4.9%

[1]An episode may be censored due to more than one reason if they occur on the same date. Therefore, the sum of the reasons for censoring may be greater than the total number of Patients.

[2]Represents Patients censored due to disenrollment from health plan. Data Partners often artificially assign a "disenrollment" date equal to data end date for members still enrolled on that date. Therefore, a patient may have dual reasons for censoring as "disenrollment" and "end of data" on the same day - this can be interpreted as right-censoring in most cases.

[3]Represents Patients censored due to Data Partner data end date. This end date represents the last day of the most recent year-month in which all of a Data Partner's data tables in the Sentinel Common Data Model have at least 80% of the record count relative to the prior month.

[4]Represents Patients censored due to user-specified study end date.

*****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.

Table 16. Summary of Time to End of At-Risk Period for Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020

		Number of Episodes by Episode Length							
		0-7 days		8-14 days		15-30 days		31-60 days	
	Total Number of Episodes	Number of Episodes	Percent of Episodes	Number of Episodes	Percent of Episodes	Number of Episodes	Percent of Episodes	Number of Episodes	Percent of Episodes
Ischemic Colitis Among Alosetron New Users									
Defined by a diagnosis in any care setting	4,660	43	0.9%	29	0.6%	64	1.4%	116	2.5%
Defined by a diagnosis in the inpatient care setting	4,660	42	0.9%	26	0.6%	63	1.4%	114	2.4%
Defined by a diagnosis in the principal position in the inpatient care setting	4,660	42	0.9%	26	0.6%	63	1.4%	114	2.4%
Defined by a modified validated algorithm in any care setting	4,660	42	0.9%	27	0.6%	64	1.4%	115	2.5%
Defined by a modified validated algorithm in the inpatient care setting	4,660	42	0.9%	26	0.6%	63	1.4%	114	2.4%
Ischemic Colitis Among Eluxadoline New Users									
Defined by a modified validated algorithm in any care setting	37,258	283	0.8%	255	0.7%	561	1.5%	1,020	2.7%
Defined by a modified validated algorithm in the inpatient care setting	37,258	281	0.8%	252	0.7%	556	1.5%	1,017	2.7%

Table 16. Summary of Time to End of At-Risk Period for Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020

	Number of Episodes by Episode Length							
	61-90 days		91-120 days		121-150 days		151-183 days	
	Number of Episodes	Percent of Episodes	Number of Episodes	Percent of Episodes	Number of Episodes	Percent of Episodes	Number of Episodes	Percent of Episodes
Ischemic Colitis Among Alosetron New Users								
Defined by a diagnosis in any care setting	121	2.6%	125	2.7%	119	2.6%	4,043	86.8%
Defined by a diagnosis in the inpatient care setting	119	2.6%	123	2.6%	119	2.6%	4,054	87.0%
Defined by a diagnosis in the principal position in the inpatient care setting	119	2.6%	121	2.6%	116	2.5%	4,059	87.1%
Defined by a modified validated algorithm in any care setting	119	2.6%	121	2.6%	117	2.5%	4,055	87.0%
Defined by a modified validated algorithm in the inpatient care setting	119	2.6%	121	2.6%	116	2.5%	4,059	87.1%
Ischemic Colitis Among Eluxadoline New Users								
Defined by a modified validated algorithm in any care setting	987	2.6%	978	2.6%	1,042	2.8%	32,132	86.2%
Defined by a modified validated algorithm in the inpatient care setting	985	2.6%	977	2.6%	1,041	2.8%	32,149	86.3%

Table 16. Summary of Time to End of At-Risk Period for Alosetron and Eluxadoline New Users in the Sentinel Distributed Database (SDD) from January 1, 2016 to July 1, 2020

	Distribution of At-Risk Time[1] in Days, by Episode						
	Minimum	**Q1**	**Median**	**Q3**	**Maximum**	**Mean**	**Standard Deviation**
Ischemic Colitis Among Alosetron New Users							
Defined by a diagnosis in any care setting	0	182	182	182	182	167.2	40.0
Defined by a diagnosis in the inpatient care setting	0	182	182	182	182	167.5	39.5
Defined by a diagnosis in the principal position in the inpatient care setting	0	182	182	182	182	167.6	39.5
Defined by a modified validated algorithm in any care setting	0	182	182	182	182	167.5	39.6
Defined by a modified validated algorithm in the inpatient care setting	0	182	182	182	182	167.6	39.5
Ischemic Colitis Among Eluxadoline New Users							
Defined by a modified validated algorithm in any care setting	0	182	182	182	182	166.8	40.5
Defined by a modified validated algorithm in the inpatient care setting	0	182	182	182	182	166.8	40.4

[1] Day 0 is the first day of follow-up

Appendix A. Dates of Available Data for Each Data Partner (DP) as of Request Distribution Date (February 8, 2022)

Masked DP ID	DP Start Date	DP End Date[1]
DP01	01/01/2007	07/01/2020
DP02	01/01/2008	07/01/2020
DP03	01/01/2000	12/31/2019
DP04	01/01/2010	07/01/2020
DP05	01/01/2008	07/01/2020
DP06	01/01/2006	07/01/2020

[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 Exposure, Exclusion Criteria, and Incidence Criteria in this Request

Generic Name	Brand Name
Alosetron	
alosetron HCl	Alosetron
alosetron HCl	Lotronex
Eluxadoline	
eluxadoline	Viberzi

Appendix C. List of International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Codes Used to Define Outcomes in this Request

Code	Description	Code Category	Code Type
	Ischemic Colitis		
K55.0	Acute vascular disorders of intestine	Diagnosis	ICD-10-CM
K55.03	Acute (reversible) ischemia of large intestine	Diagnosis	ICD-10-CM
K55.031	Focal (segmental) acute (reversible) ischemia of large intestine	Diagnosis	ICD-10-CM
K55.032	Diffuse acute (reversible) ischemia of large intestine	Diagnosis	ICD-10-CM
K55.039	Acute (reversible) ischemia of large intestine, extent unspecified	Diagnosis	ICD-10-CM
K55.04	Acute infarction of large intestine	Diagnosis	ICD-10-CM
K55.041	Focal (segmental) acute infarction of large intestine	Diagnosis	ICD-10-CM
K55.042	Diffuse acute infarction of large intestine	Diagnosis	ICD-10-CM
K55.049	Acute infarction of large intestine, extent unspecified	Diagnosis	ICD-10-CM
K55.05	Acute (reversible) ischemia of intestine, part unspecified	Diagnosis	ICD-10-CM
K55.051	Focal (segmental) acute (reversible) ischemia of intestine, part unspecified	Diagnosis	ICD-10-CM
K55.052	Diffuse acute (reversible) ischemia of intestine, part unspecified	Diagnosis	ICD-10-CM
K55.059	Acute (reversible) ischemia of intestine, part and extent unspecified	Diagnosis	ICD-10-CM
K55.06	Acute infarction of intestine, part unspecified	Diagnosis	ICD-10-CM
K55.061	Focal (segmental) acute infarction of intestine, part unspecified	Diagnosis	ICD-10-CM
K55.062	Diffuse acute infarction of intestine, part unspecified	Diagnosis	ICD-10-CM
K55.069	Acute infarction of intestine, part and extent unspecified	Diagnosis	ICD-10-CM
K55.9	Vascular disorder of intestine, unspecified	Diagnosis	ICD-10-CM
	Crohn's Disease		
K50	Crohn's disease [regional enteritis]	Diagnosis	ICD-10-CM
K50.0	Crohn's disease of small intestine	Diagnosis	ICD-10-CM
K50.00	Crohn's disease of small intestine without complications	Diagnosis	ICD-10-CM
K50.01	Crohn's disease of small intestine with complications	Diagnosis	ICD-10-CM
K50.011	Crohn's disease of small intestine with rectal bleeding	Diagnosis	ICD-10-CM
K50.012	Crohn's disease of small intestine with intestinal obstruction	Diagnosis	ICD-10-CM
K50.013	Crohn's disease of small intestine with fistula	Diagnosis	ICD-10-CM
K50.014	Crohn's disease of small intestine with abscess	Diagnosis	ICD-10-CM
K50.018	Crohn's disease of small intestine with other complication	Diagnosis	ICD-10-CM
K50.019	Crohn's disease of small intestine with unspecified complications	Diagnosis	ICD-10-CM
K50.1	Crohn's disease of large intestine	Diagnosis	ICD-10-CM
K50.10	Crohn's disease of large intestine without complications	Diagnosis	ICD-10-CM
K50.11	Crohn's disease of large intestine with complications	Diagnosis	ICD-10-CM
K50.111	Crohn's disease of large intestine with rectal bleeding	Diagnosis	ICD-10-CM
K50.112	Crohn's disease of large intestine with intestinal obstruction	Diagnosis	ICD-10-CM
K50.113	Crohn's disease of large intestine with fistula	Diagnosis	ICD-10-CM
K50.114	Crohn's disease of large intestine with abscess	Diagnosis	ICD-10-CM
K50.118	Crohn's disease of large intestine with other complication	Diagnosis	ICD-10-CM
K50.119	Crohn's disease of large intestine with unspecified complications	Diagnosis	ICD-10-CM
K50.8	Crohn's disease of both small and large intestine	Diagnosis	ICD-10-CM

Appendix C. List of International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Codes Used to Define Outcomes in this Request

Code	Description	Code Category	Code Type
K50.80	Crohn's disease of both small and large intestine without complications	Diagnosis	ICD-10-CM
K50.81	Crohn's disease of both small and large intestine with complications	Diagnosis	ICD-10-CM
K50.811	Crohn's disease of both small and large intestine with rectal bleeding	Diagnosis	ICD-10-CM
K50.812	Crohn's disease of both small and large intestine with intestinal obstruction	Diagnosis	ICD-10-CM
K50.813	Crohn's disease of both small and large intestine with fistula	Diagnosis	ICD-10-CM
K50.814	Crohn's disease of both small and large intestine with abscess	Diagnosis	ICD-10-CM
K50.818	Crohn's disease of both small and large intestine with other complication	Diagnosis	ICD-10-CM
K50.819	Crohn's disease of both small and large intestine with unspecified complications	Diagnosis	ICD-10-CM
K50.9	Crohn's disease, unspecified	Diagnosis	ICD-10-CM
K50.90	Crohn's disease, unspecified, without complications	Diagnosis	ICD-10-CM
K50.91	Crohn's disease, unspecified, with complications	Diagnosis	ICD-10-CM
K50.911	Crohn's disease, unspecified, with rectal bleeding	Diagnosis	ICD-10-CM
K50.912	Crohn's disease, unspecified, with intestinal obstruction	Diagnosis	ICD-10-CM
K50.913	Crohn's disease, unspecified, with fistula	Diagnosis	ICD-10-CM
K50.914	Crohn's disease, unspecified, with abscess	Diagnosis	ICD-10-CM
K50.918	Crohn's disease, unspecified, with other complication	Diagnosis	ICD-10-CM
K50.919	Crohn's disease, unspecified, with unspecified complications	Diagnosis	ICD-10-CM
	Ulcerative Colitis		
K51	Ulcerative colitis	Diagnosis	ICD-10-CM
K51.0	Ulcerative (chronic) pancolitis	Diagnosis	ICD-10-CM
K51.00	Ulcerative (chronic) pancolitis without complications	Diagnosis	ICD-10-CM
K51.01	Ulcerative (chronic) pancolitis with complications	Diagnosis	ICD-10-CM
K51.011	Ulcerative (chronic) pancolitis with rectal bleeding	Diagnosis	ICD-10-CM
K51.012	Ulcerative (chronic) pancolitis with intestinal obstruction	Diagnosis	ICD-10-CM
K51.013	Ulcerative (chronic) pancolitis with fistula	Diagnosis	ICD-10-CM
K51.014	Ulcerative (chronic) pancolitis with abscess	Diagnosis	ICD-10-CM
K51.018	Ulcerative (chronic) pancolitis with other complication	Diagnosis	ICD-10-CM
K51.019	Ulcerative (chronic) pancolitis with unspecified complications	Diagnosis	ICD-10-CM
K51.2	Ulcerative (chronic) proctitis	Diagnosis	ICD-10-CM
K51.20	Ulcerative (chronic) proctitis without complications	Diagnosis	ICD-10-CM
K51.21	Ulcerative (chronic) proctitis with complications	Diagnosis	ICD-10-CM
K51.211	Ulcerative (chronic) proctitis with rectal bleeding	Diagnosis	ICD-10-CM
K51.212	Ulcerative (chronic) proctitis with intestinal obstruction	Diagnosis	ICD-10-CM
K51.213	Ulcerative (chronic) proctitis with fistula	Diagnosis	ICD-10-CM
K51.214	Ulcerative (chronic) proctitis with abscess	Diagnosis	ICD-10-CM
K51.218	Ulcerative (chronic) proctitis with other complication	Diagnosis	ICD-10-CM
K51.219	Ulcerative (chronic) proctitis with unspecified complications	Diagnosis	ICD-10-CM
K51.3	Ulcerative (chronic) rectosigmoiditis	Diagnosis	ICD-10-CM
K51.30	Ulcerative (chronic) rectosigmoiditis without complications	Diagnosis	ICD-10-CM
K51.31	Ulcerative (chronic) rectosigmoiditis with complications	Diagnosis	ICD-10-CM

Appendix C. List of International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Codes Used to Define Outcomes in this Request

Code	Description	Code Category	Code Type
K51.311	Ulcerative (chronic) rectosigmoiditis with rectal bleeding	Diagnosis	ICD-10-CM
K51.312	Ulcerative (chronic) rectosigmoiditis with intestinal obstruction	Diagnosis	ICD-10-CM
K51.313	Ulcerative (chronic) rectosigmoiditis with fistula	Diagnosis	ICD-10-CM
K51.314	Ulcerative (chronic) rectosigmoiditis with abscess	Diagnosis	ICD-10-CM
K51.318	Ulcerative (chronic) rectosigmoiditis with other complication	Diagnosis	ICD-10-CM
K51.319	Ulcerative (chronic) rectosigmoiditis with unspecified complications	Diagnosis	ICD-10-CM
K51.4	Inflammatory polyps of colon	Diagnosis	ICD-10-CM
K51.40	Inflammatory polyps of colon without complications	Diagnosis	ICD-10-CM
K51.41	Inflammatory polyps of colon with complications	Diagnosis	ICD-10-CM
K51.411	Inflammatory polyps of colon with rectal bleeding	Diagnosis	ICD-10-CM
K51.412	Inflammatory polyps of colon with intestinal obstruction	Diagnosis	ICD-10-CM
K51.413	Inflammatory polyps of colon with fistula	Diagnosis	ICD-10-CM
K51.414	Inflammatory polyps of colon with abscess	Diagnosis	ICD-10-CM
K51.418	Inflammatory polyps of colon with other complication	Diagnosis	ICD-10-CM
K51.419	Inflammatory polyps of colon with unspecified complications	Diagnosis	ICD-10-CM
K51.5	Left sided colitis	Diagnosis	ICD-10-CM
K51.50	Left sided colitis without complications	Diagnosis	ICD-10-CM
K51.51	Left sided colitis with complications	Diagnosis	ICD-10-CM
K51.511	Left sided colitis with rectal bleeding	Diagnosis	ICD-10-CM
K51.512	Left sided colitis with intestinal obstruction	Diagnosis	ICD-10-CM
K51.513	Left sided colitis with fistula	Diagnosis	ICD-10-CM
K51.514	Left sided colitis with abscess	Diagnosis	ICD-10-CM
K51.518	Left sided colitis with other complication	Diagnosis	ICD-10-CM
K51.519	Left sided colitis with unspecified complications	Diagnosis	ICD-10-CM
K51.8	Other ulcerative colitis	Diagnosis	ICD-10-CM
K51.80	Other ulcerative colitis without complications	Diagnosis	ICD-10-CM
K51.81	Other ulcerative colitis with complications	Diagnosis	ICD-10-CM
K51.811	Other ulcerative colitis with rectal bleeding	Diagnosis	ICD-10-CM
K51.812	Other ulcerative colitis with intestinal obstruction	Diagnosis	ICD-10-CM
K51.813	Other ulcerative colitis with fistula	Diagnosis	ICD-10-CM
K51.814	Other ulcerative colitis with abscess	Diagnosis	ICD-10-CM
K51.818	Other ulcerative colitis with other complication	Diagnosis	ICD-10-CM
K51.819	Other ulcerative colitis with unspecified complications	Diagnosis	ICD-10-CM
K51.9	Ulcerative colitis, unspecified	Diagnosis	ICD-10-CM
K51.90	Ulcerative colitis, unspecified, without complications	Diagnosis	ICD-10-CM
K51.91	Ulcerative colitis, unspecified, with complications	Diagnosis	ICD-10-CM
K51.911	Ulcerative colitis, unspecified with rectal bleeding	Diagnosis	ICD-10-CM
K51.912	Ulcerative colitis, unspecified with intestinal obstruction	Diagnosis	ICD-10-CM
K51.913	Ulcerative colitis, unspecified with fistula	Diagnosis	ICD-10-CM
K51.914	Ulcerative colitis, unspecified with abscess	Diagnosis	ICD-10-CM

Appendix C. List of International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Codes Used to Define Outcomes in this Request

Code	Description	Code Category	Code Type
K51.918	Ulcerative colitis, unspecified with other complication	Diagnosis	ICD-10-CM
K51.919	Ulcerative colitis, unspecified with unspecified complications	Diagnosis	ICD-10-CM
	Clostridium difficile		
A04.7	Enterocolitis due to Clostridium difficile	Diagnosis	ICD-10-CM
A04.71	Enterocolitis due to Clostridium difficile, recurrent	Diagnosis	ICD-10-CM
A04.72	Enterocolitis due to Clostridium difficile, not specified as recurrent	Diagnosis	ICD-10-CM
	Abdominal Pain		
R10	Abdominal and pelvic pain	Diagnosis	ICD-10-CM
R10.0	Acute abdomen	Diagnosis	ICD-10-CM
R10.1	Pain localized to upper abdomen	Diagnosis	ICD-10-CM
R10.10	Upper abdominal pain, unspecified	Diagnosis	ICD-10-CM
R10.11	Right upper quadrant pain	Diagnosis	ICD-10-CM
R10.12	Left upper quadrant pain	Diagnosis	ICD-10-CM
R10.13	Epigastric pain	Diagnosis	ICD-10-CM
R10.3	Pain localized to other parts of lower abdomen	Diagnosis	ICD-10-CM
R10.30	Lower abdominal pain, unspecified	Diagnosis	ICD-10-CM
R10.31	Right lower quadrant pain	Diagnosis	ICD-10-CM
R10.32	Left lower quadrant pain	Diagnosis	ICD-10-CM
R10.33	Periumbilical pain	Diagnosis	ICD-10-CM
R10.8	Other abdominal pain	Diagnosis	ICD-10-CM
R10.81	Abdominal tenderness	Diagnosis	ICD-10-CM
R10.811	Right upper quadrant abdominal tenderness	Diagnosis	ICD-10-CM
R10.812	Left upper quadrant abdominal tenderness	Diagnosis	ICD-10-CM
R10.813	Right lower quadrant abdominal tenderness	Diagnosis	ICD-10-CM
R10.814	Left lower quadrant abdominal tenderness	Diagnosis	ICD-10-CM
R10.815	Periumbilic abdominal tenderness	Diagnosis	ICD-10-CM
R10.816	Epigastric abdominal tenderness	Diagnosis	ICD-10-CM
R10.817	Generalized abdominal tenderness	Diagnosis	ICD-10-CM
R10.819	Abdominal tenderness, unspecified site	Diagnosis	ICD-10-CM
R10.82	Rebound abdominal tenderness	Diagnosis	ICD-10-CM
R10.821	Right upper quadrant rebound abdominal tenderness	Diagnosis	ICD-10-CM
R10.822	Left upper quadrant rebound abdominal tenderness	Diagnosis	ICD-10-CM
R10.823	Right lower quadrant rebound abdominal tenderness	Diagnosis	ICD-10-CM
R10.824	Left lower quadrant rebound abdominal tenderness	Diagnosis	ICD-10-CM
R10.825	Periumbilic rebound abdominal tenderness	Diagnosis	ICD-10-CM
R10.826	Epigastric rebound abdominal tenderness	Diagnosis	ICD-10-CM
R10.827	Generalized rebound abdominal tenderness	Diagnosis	ICD-10-CM
R10.829	Rebound abdominal tenderness, unspecified site	Diagnosis	ICD-10-CM
R10.83	Colic	Diagnosis	ICD-10-CM
R10.84	Generalized abdominal pain	Diagnosis	ICD-10-CM

Appendix C. List of International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Codes Used to Define Outcomes in this Request

Code	Description	Code Category	Code Type
R10.9	Unspecified abdominal pain	Diagnosis	ICD-10-CM
	Acute Pancreatitis		
K85	Acute pancreatitis	Diagnosis	ICD-10-CM
K85.0	Idiopathic acute pancreatitis	Diagnosis	ICD-10-CM
K85.00	Idiopathic acute pancreatitis without necrosis or infection	Diagnosis	ICD-10-CM
K85.01	Idiopathic acute pancreatitis with uninfected necrosis	Diagnosis	ICD-10-CM
K85.02	Idiopathic acute pancreatitis with infected necrosis	Diagnosis	ICD-10-CM
K85.1	Biliary acute pancreatitis	Diagnosis	ICD-10-CM
K85.10	Biliary acute pancreatitis without necrosis or infection	Diagnosis	ICD-10-CM
K85.11	Biliary acute pancreatitis with uninfected necrosis	Diagnosis	ICD-10-CM
K85.12	Biliary acute pancreatitis with infected necrosis	Diagnosis	ICD-10-CM
K85.2	Alcohol induced acute pancreatitis	Diagnosis	ICD-10-CM
K85.20	Alcohol induced acute pancreatitis without necrosis or infection	Diagnosis	ICD-10-CM
K85.21	Alcohol induced acute pancreatitis with uninfected necrosis	Diagnosis	ICD-10-CM
K85.22	Alcohol induced acute pancreatitis with infected necrosis	Diagnosis	ICD-10-CM
K85.3	Drug induced acute pancreatitis	Diagnosis	ICD-10-CM
K85.30	Drug induced acute pancreatitis without necrosis or infection	Diagnosis	ICD-10-CM
K85.31	Drug induced acute pancreatitis with uninfected necrosis	Diagnosis	ICD-10-CM
K85.32	Drug induced acute pancreatitis with infected necrosis	Diagnosis	ICD-10-CM
K85.8	Other acute pancreatitis	Diagnosis	ICD-10-CM
K85.80	Other acute pancreatitis without necrosis or infection	Diagnosis	ICD-10-CM
K85.81	Other acute pancreatitis with uninfected necrosis	Diagnosis	ICD-10-CM
K85.82	Other acute pancreatitis with infected necrosis	Diagnosis	ICD-10-CM
K85.9	Acute pancreatitis, unspecified	Diagnosis	ICD-10-CM
K85.90	Acute pancreatitis without necrosis or infection, unspecified	Diagnosis	ICD-10-CM
K85.91	Acute pancreatitis with uninfected necrosis, unspecified	Diagnosis	ICD-10-CM
K85.92	Acute pancreatitis with infected necrosis, unspecified	Diagnosis	ICD-10-CM

Appendix D. List of Current Procedural Terminology, Fourth Edition (CPT-4), Current Procedural Terminology, Second Edition (CPT-2), Healthcare Common Procedure Coding System, Level II (HCPCS), and International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS) Codes Used to Define Outcomes in this Request

Code	Description	Code Category	Code Type
	Colonoscopy and Colectomy		
00812	Anesthesia for lower intestinal endoscopic procedures, endoscope introduced distal to duodenum; screening colonoscopy	Procedure	CPT-4
0DJD8ZZ	Inspection of Lower Intestinal Tract, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
0DTE0ZZ	Resection of Large Intestine, Open Approach	Procedure	ICD-10-PCS
0DTE4ZZ	Resection of Large Intestine, Percutaneous Endoscopic Approach	Procedure	ICD-10-PCS
0DTE7ZZ	Resection of Large Intestine, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
0DTE8ZZ	Resection of Large Intestine, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
0DTF0ZZ	Resection of Right Large Intestine, Open Approach	Procedure	ICD-10-PCS
0DTF4ZZ	Resection of Right Large Intestine, Percutaneous Endoscopic Approach	Procedure	ICD-10-PCS
0DTF7ZZ	Resection of Right Large Intestine, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
0DTF8ZZ	Resection of Right Large Intestine, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
0DTG0ZZ	Resection of Left Large Intestine, Open Approach	Procedure	ICD-10-PCS
0DTG4ZZ	Resection of Left Large Intestine, Percutaneous Endoscopic Approach	Procedure	ICD-10-PCS
0DTG7ZZ	Resection of Left Large Intestine, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
0DTG8ZZ	Resection of Left Large Intestine, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
0DTGFZZ	Resection of Left Large Intestine, Via Natural or Artificial Opening With Percutaneous Endoscopic Assistance	Procedure	ICD-10-PCS
0DTK0ZZ	Resection of Ascending Colon, Open Approach	Procedure	ICD-10-PCS
3018F	Pre-procedure risk assessment and depth of insertion and quality of the bowel prep and complete description of polyp(s) found, including location of each polyp, size, number and gross morphology and recommendations for follow-up in final colonoscopy report documented (End/Polyp)	Procedure	CPT-2
3775F	Adenoma(s) or other neoplasm detected during screening colonoscopy (SCADR)	Procedure	CPT-2
44139	Mobilization (take-down) of splenic flexure performed in conjunction with partial colectomy (List separately in addition to primary procedure)	Procedure	CPT-4
44140	Colectomy, partial; with anastomosis	Procedure	CPT-4
44141	Colectomy, partial; with skin level cecostomy or colostomy	Procedure	CPT-4
44143	Colectomy, partial; with end colostomy and closure of distal segment (Hartmann type procedure)	Procedure	CPT-4
44144	Colectomy, partial; with resection, with colostomy or ileostomy and creation of mucofistula	Procedure	CPT-4
44145	Colectomy, partial; with coloproctostomy (low pelvic anastomosis)	Procedure	CPT-4
44146	Colectomy, partial; with coloproctostomy (low pelvic anastomosis), with colostomy	Procedure	CPT-4
44147	Colectomy, partial; abdominal and transanal approach	Procedure	CPT-4
44150	Colectomy, total, abdominal, without proctectomy; with ileostomy or ileoproctostomy	Procedure	CPT-4
44151	Colectomy, total, abdominal, without proctectomy; with continent ileostomy	Procedure	CPT-4
44155	Colectomy, total, abdominal, with proctectomy; with ileostomy	Procedure	CPT-4
44156	Colectomy, total, abdominal, with proctectomy; with continent ileostomy	Procedure	CPT-4
44157	Colectomy, total, abdominal, with proctectomy; with ileoanal anastomosis, includes loop ileostomy, and rectal mucosectomy, when performed	Procedure	CPT-4
44158	Colectomy, total, abdominal, with proctectomy; with ileoanal anastomosis, creation of ileal reservoir (S or J), includes loop ileostomy, and rectal mucosectomy, when performed	Procedure	CPT-4
44160	Colectomy, partial, with removal of terminal ileum with ileocolostomy	Procedure	CPT-4

Appendix D. List of Current Procedural Terminology, Fourth Edition (CPT-4), Current Procedural Terminology, Second Edition (CPT-2), Healthcare Common Procedure Coding System, Level II (HCPCS), and International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS) Codes Used to Define Outcomes in this Request

Code	Description	Code Category	Code Type
44204	Laparoscopy, surgical; colectomy, partial, with anastomosis	Procedure	CPT-4
44205	Laparoscopy, surgical; colectomy, partial, with removal of terminal ileum with ileocolostomy	Procedure	CPT-4
44206	Laparoscopy, surgical; colectomy, partial, with end colostomy and closure of distal segment (Hartmann type procedure)	Procedure	CPT-4
44207	Laparoscopy, surgical; colectomy, partial, with anastomosis, with coloproctostomy (low pelvic anastomosis)	Procedure	CPT-4
44208	Laparoscopy, surgical; colectomy, partial, with anastomosis, with coloproctostomy (low pelvic anastomosis) with colostomy	Procedure	CPT-4
44210	Laparoscopy, surgical; colectomy, total, abdominal, without proctectomy, with ileostomy or ileoproctostomy	Procedure	CPT-4
44211	Laparoscopy, surgical; colectomy, total, abdominal, with proctectomy, with ileoanal anastomosis, creation of ileal reservoir (S or J), with loop ileostomy, includes rectal mucosectomy, when performed	Procedure	CPT-4
44212	Laparoscopy, surgical; colectomy, total, abdominal, with proctectomy, with ileostomy	Procedure	CPT-4
44213	Laparoscopy, surgical, mobilization (take-down) of splenic flexure performed in conjunction with partial colectomy (List separately in addition to primary procedure)	Procedure	CPT-4
44388	Colonoscopy through stoma; diagnostic, including collection of specimen(s) by brushing or washing, when performed (separate procedure)	Procedure	CPT-4
44389	Colonoscopy through stoma; with biopsy, single or multiple	Procedure	CPT-4
44390	Colonoscopy through stoma; with removal of foreign body(s)	Procedure	CPT-4
44391	Colonoscopy through stoma; with control of bleeding, any method	Procedure	CPT-4
44392	Colonoscopy through stoma; with removal of tumor(s), polyp(s), or other lesion(s) by hot biopsy forceps	Procedure	CPT-4
44393	Colonoscopy through stoma; with ablation of tumor(s), polyp(s), or other lesion(s) not amenable to removal by hot biopsy forceps, bipolar cautery or snare technique	Procedure	CPT-4
44394	Colonoscopy through stoma; with removal of tumor(s), polyp(s), or other lesion(s) by snare technique	Procedure	CPT-4
44397	Colonoscopy through stoma; with transendoscopic stent placement (includes predilation)	Procedure	CPT-4
44401	Colonoscopy through stoma; with ablation of tumor(s), polyp(s), or other lesion(s) (includes pre-and post-dilation and guide wire passage, when performed)	Procedure	CPT-4
44402	Colonoscopy through stoma; with endoscopic stent placement (including pre- and post-dilation and guide wire passage, when performed)	Procedure	CPT-4
44403	Colonoscopy through stoma; with endoscopic mucosal resection	Procedure	CPT-4
44404	Colonoscopy through stoma; with directed submucosal injection(s), any substance	Procedure	CPT-4
44405	Colonoscopy through stoma; with transendoscopic balloon dilation	Procedure	CPT-4
44406	Colonoscopy through stoma; with endoscopic ultrasound examination, limited to the sigmoid, descending, transverse, or ascending colon and cecum and adjacent	Procedure	CPT-4
44407	Colonoscopy through stoma; with transendoscopic ultrasound guided intramural or transmural fine needle aspiration/biopsy(s), includes endoscopic ultrasound examination limited to the sigmoid, descending, transverse, or ascending colon and cecum and adjacent structures	Procedure	CPT-4
44408	Colonoscopy through stoma; with decompression (for pathologic distention) (eg, volvulus, megacolon), including placement of decompression tube, when performed	Procedure	CPT-4

Appendix D. List of Current Procedural Terminology, Fourth Edition (CPT-4), Current Procedural Terminology, Second Edition (CPT-2), Healthcare Common Procedure Coding System, Level II (HCPCS), and International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS) Codes Used to Define Outcomes in this Request

Code	Description	Code Category	Code Type
45121	Proctectomy, complete (for congenital megacolon), abdominal and perineal approach; with subtotal or total colectomy, with multiple biopsies	Procedure	CPT-4
45355	Colonoscopy, rigid or flexible, transabdominal via colotomy, single or multiple	Procedure	CPT-4
45378	Colonoscopy, flexible; diagnostic, including collection of specimen(s) by brushing or washing, when performed (separate procedure)	Procedure	CPT-4
45379	Colonoscopy, flexible; with removal of foreign body(s)	Procedure	CPT-4
45380	Colonoscopy, flexible; with biopsy, single or multiple	Procedure	CPT-4
45381	Colonoscopy, flexible; with directed submucosal injection(s), any substance	Procedure	CPT-4
45382	Colonoscopy, flexible; with control of bleeding, any method	Procedure	CPT-4
45383	Colonoscopy, flexible, proximal to splenic flexure; with ablation of tumor(s), polyp(s), or other lesion(s) not amenable to removal by hot biopsy forceps, bipolar cautery or snare technique	Procedure	CPT-4
45384	Colonoscopy, flexible; with removal of tumor(s), polyp(s), or other lesion(s) by hot biopsy forceps	Procedure	CPT-4
45385	Colonoscopy, flexible; with removal of tumor(s), polyp(s), or other lesion(s) by snare technique	Procedure	CPT-4
45386	Colonoscopy, flexible; with transendoscopic balloon dilation	Procedure	CPT-4
45387	Colonoscopy, flexible, proximal to splenic flexure; with transendoscopic stent placement (includes predilation)	Procedure	CPT-4
45388	Colonoscopy, flexible; with ablation of tumor(s), polyp(s), or other lesion(s) (includes pre- and post-dilation and guide wire passage, when performed)	Procedure	CPT-4
45389	Colonoscopy, flexible; with endoscopic stent placement (includes pre- and post-dilation and guide wire passage, when performed)	Procedure	CPT-4
45390	Colonoscopy, flexible; with endoscopic mucosal resection	Procedure	CPT-4
45391	Colonoscopy, flexible; with endoscopic ultrasound examination limited to the rectum, sigmoid, descending, transverse, or ascending colon and cecum, and adjacent	Procedure	CPT-4
45392	Colonoscopy, flexible; with transendoscopic ultrasound guided intramural or transmural fine needle aspiration/biopsy(s), includes endoscopic ultrasound examination limited to the rectum, sigmoid, descending, transverse, or ascending colon and cecum, and adjacent structures	Procedure	CPT-4
45393	Colonoscopy, flexible; with decompression (for pathologic distention) (eg, volvulus, megacolon), including placement of decompression tube, when performed	Procedure	CPT-4
45398	Colonoscopy, flexible; with band ligation(s) (eg, hemorrhoids)	Procedure	CPT-4
G0105	Colorectal cancer screening; colonoscopy on individual at high risk	Procedure	HCPCS
G0120	Colorectal cancer screening; alternative to G0105, screening colonoscopy, barium enema	Procedure	HCPCS
G0121	Colorectal cancer screening; colonoscopy on individual not meeting criteria for high	Procedure	HCPCS
G6019	Colonoscopy through stoma; with ablation of tumor(s), polyp(s), or other lesion(s) not amenable to removal by hot biopsy forceps, bipolar cautery or snare technique	Procedure	HCPCS
G6020	Colonoscopy through stoma; with transendoscopic stent placement (includes predilation)	Procedure	HCPCS
G6024	Colonoscopy, flexible; proximal to splenic flexure; with ablation of tumor(s), polyp(s), or other lesion(s) not amenable to removal by hot biopsy forceps, bipolar cautery or snare tehnique	Procedure	HCPCS

Appendix D. List of Current Procedural Terminology, Fourth Edition (CPT-4), Current Procedural Terminology, Second Edition (CPT-2), Healthcare Common Procedure Coding System, Level II (HCPCS), and International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS) Codes Used to Define Outcomes in this Request

Code	Description	Code Category	Code Type
G6025	Colonoscopy, flexible, proximal to splenic flexure; with transendoscopic stent placement (includes predilation)	Procedure	HCPCS
G9659	Patients greater than or equal to 86 years of age who underwent a screening colonoscopy and did not have a history of colorectal cancer or other valid medical reason for the colonoscopy, including: iron deficiency anemia, lower gastrointestinal bleeding, Crohn's disease (i.e., regional enteritis), familial adenomatous polyposis, Lynch syndrome (i.e., hereditary nonpolyposis colorectal cancer), inflammatory bowel disease, ulcerative colitis, abnormal finding of gastrointestinal tract, or changes in	Procedure	HCPCS
G9660	Documentation of medical reason(s) for a colonoscopy performed on a patient greater than or equal to 86 years of age (e.g., iron deficiency anemia, lower gastrointestinal bleeding, Crohn's disease (i.e., regional enteritis), familial history of adenomatous polyposis, Lynch syndrome (i.e., hereditary nonpolyposis colorectal cancer), inflammatory bowel disease, ulcerative colitis, abnormal finding of gastrointestinal tract, or changes in bowel habits)	Procedure	HCPCS
G9661	Patients greater than or equal to 86 years of age who received a colonoscopy for an assessment of signs/symptoms of GI tract illness, and/or because the patient meets high risk criteria, and/or to follow-up on previously diagnosed advanced lesions	Procedure	HCPCS
G9933	Adenoma(s) or colorectal cancer detected during screening colonoscopy	Procedure	HCPCS
G9935	Adenoma(s) or colorectal cancer not detected during screening colonoscopy	Procedure	HCPCS
G9936	Surveillance colonoscopy - personal history of colonic polyps, colon cancer, or other malignant neoplasm of rectum, rectosigmoid junction, and anus	Procedure	HCPCS
G9937	Diagnostic colonoscopy	Procedure	HCPCS
	Enterectomy		
44120	Enterectomy, resection of small intestine; single resection and anastomosis	Procedure	CPT-4
44121	Enterectomy, resection of small intestine; each additional resection and anastomosis (List separately in addition to code for primary procedure)	Procedure	CPT-4
44125	Enterectomy, resection of small intestine; with enterostomy	Procedure	CPT-4
44126	Enterectomy, resection of small intestine for congenital atresia, single resection and anastomosis of proximal segment of intestine; without tapering	Procedure	CPT-4
44127	Enterectomy, resection of small intestine for congenital atresia, single resection and anastomosis of proximal segment of intestine; with tapering	Procedure	CPT-4
44128	Enterectomy, resection of small intestine for congenital atresia, single resection and anastomosis of proximal segment of intestine; each additional resection and anastomosis (List separately in addition to code for primary procedure)	Procedure	CPT-4
44202	Laparoscopy, surgical; enterectomy, resection of small intestine, single resection and anastomosis	Procedure	CPT-4

Appendix E. List of Generic Names of Medical Products Used to Define Outcomes in this Request

Generic Name	Brand Name
5-Aminosalicylic acid	
balsalazide disodium	Balsalazide
balsalazide disodium	Colazal
balsalazide disodium	Giazo
mesalamine	Delzicol
mesalamine	Asacol HD
mesalamine	sfRowasa
mesalamine	Rowasa
mesalamine	Mesalamine
mesalamine	Apriso
mesalamine	Pentasa
mesalamine	Lialda
mesalamine	Canasa
mesalamine with cleansing wipes	Mesalamine with cleansing wipe
mesalamine with cleansing wipes	Rowasa
olsalazine sodium	Dipentum
sulfasalazine	Azulfidine
sulfasalazine	Azulfidine EN-tabs
sulfasalazine	Sulfasalazine
sulfasalazine	Sulfazine

Appendix F. List of International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Codes Used to Define Characteristics in this Request

Code	Description	Code Category	Code Type
	Intestinal Ischemia		
K55.0	Acute vascular disorders of intestine	Diagnosis	ICD-10-CM
K55.01	Acute (reversible) ischemia of small intestine	Diagnosis	ICD-10-CM
K55.011	Focal (segmental) acute (reversible) ischemia of small intestine	Diagnosis	ICD-10-CM
K55.012	Diffuse acute (reversible) ischemia of small intestine	Diagnosis	ICD-10-CM
K55.019	Acute (reversible) ischemia of small intestine, extent unspecified	Diagnosis	ICD-10-CM
K55.02	Acute infarction of small intestine	Diagnosis	ICD-10-CM
K55.021	Focal (segmental) acute infarction of small intestine	Diagnosis	ICD-10-CM
K55.022	Diffuse acute infarction of small intestine	Diagnosis	ICD-10-CM
K55.029	Acute infarction of small intestine, extent unspecified	Diagnosis	ICD-10-CM
K55.03	Acute (reversible) ischemia of large intestine	Diagnosis	ICD-10-CM
K55.031	Focal (segmental) acute (reversible) ischemia of large intestine	Diagnosis	ICD-10-CM
K55.032	Diffuse acute (reversible) ischemia of large intestine	Diagnosis	ICD-10-CM
K55.039	Acute (reversible) ischemia of large intestine, extent unspecified	Diagnosis	ICD-10-CM
K55.04	Acute infarction of large intestine	Diagnosis	ICD-10-CM
K55.041	Focal (segmental) acute infarction of large intestine	Diagnosis	ICD-10-CM
K55.042	Diffuse acute infarction of large intestine	Diagnosis	ICD-10-CM
K55.049	Acute infarction of large intestine, extent unspecified	Diagnosis	ICD-10-CM
K55.05	Acute (reversible) ischemia of intestine, part unspecified	Diagnosis	ICD-10-CM
K55.051	Focal (segmental) acute (reversible) ischemia of intestine, part unspecified	Diagnosis	ICD-10-CM
K55.052	Diffuse acute (reversible) ischemia of intestine, part unspecified	Diagnosis	ICD-10-CM
K55.059	Acute (reversible) ischemia of intestine, part and extent unspecified	Diagnosis	ICD-10-CM
K55.06	Acute infarction of intestine, part unspecified	Diagnosis	ICD-10-CM
K55.061	Focal (segmental) acute infarction of intestine, part unspecified	Diagnosis	ICD-10-CM
K55.062	Diffuse acute infarction of intestine, part unspecified	Diagnosis	ICD-10-CM
K55.069	Acute infarction of intestine, part and extent unspecified	Diagnosis	ICD-10-CM
K55.1	Chronic vascular disorders of intestine	Diagnosis	ICD-10-CM
K55.2	Angiodysplasia of colon	Diagnosis	ICD-10-CM
K55.20	Angiodysplasia of colon without hemorrhage	Diagnosis	ICD-10-CM
K55.21	Angiodysplasia of colon with hemorrhage	Diagnosis	ICD-10-CM
K55.3	Necrotizing enterocolitis	Diagnosis	ICD-10-CM
K55.30	Necrotizing enterocolitis, unspecified	Diagnosis	ICD-10-CM
K55.31	Stage 1 necrotizing enterocolitis	Diagnosis	ICD-10-CM
K55.32	Stage 2 necrotizing enterocolitis	Diagnosis	ICD-10-CM
K55.33	Stage 3 necrotizing enterocolitis	Diagnosis	ICD-10-CM
K55.8	Other vascular disorders of intestine	Diagnosis	ICD-10-CM
K55.9	Vascular disorder of intestine, unspecified	Diagnosis	ICD-10-CM
	Irritable Bowel Syndrome		
K58	Irritable bowel syndrome	Diagnosis	ICD-10-CM
K58.0	Irritable bowel syndrome with diarrhea	Diagnosis	ICD-10-CM
K58.1	Irritable bowel syndrome with constipation	Diagnosis	ICD-10-CM
K58.2	Mixed irritable bowel syndrome	Diagnosis	ICD-10-CM
K58.8	Other irritable bowel syndrome	Diagnosis	ICD-10-CM
K58.9	Irritable bowel syndrome without diarrhea	Diagnosis	ICD-10-CM
	Noninfective Gastroenteritis and Colitis		
K52	Other and unspecified noninfective gastroenteritis and colitis	Diagnosis	ICD-10-CM

Appendix F. List of International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Codes Used to Define Characteristics in this Request

Code	Description	Code Category	Code Type
K52.0	Gastroenteritis and colitis due to radiation	Diagnosis	ICD-10-CM
K52.1	Toxic gastroenteritis and colitis	Diagnosis	ICD-10-CM
K52.2	Allergic and dietetic gastroenteritis and colitis	Diagnosis	ICD-10-CM
K52.21	Food protein-induced enterocolitis syndrome	Diagnosis	ICD-10-CM
K52.22	Food protein-induced enteropathy	Diagnosis	ICD-10-CM
K52.29	Other allergic and dietetic gastroenteritis and colitis	Diagnosis	ICD-10-CM
K52.3	Indeterminate colitis	Diagnosis	ICD-10-CM
K52.8	Other specified noninfective gastroenteritis and colitis	Diagnosis	ICD-10-CM
K52.81	Eosinophilic gastritis or gastroenteritis	Diagnosis	ICD-10-CM
K52.82	Eosinophilic colitis	Diagnosis	ICD-10-CM
K52.83	Microscopic colitis	Diagnosis	ICD-10-CM
K52.831	Collagenous colitis	Diagnosis	ICD-10-CM
K52.832	Lymphocytic colitis	Diagnosis	ICD-10-CM
K52.838	Other microscopic colitis	Diagnosis	ICD-10-CM
K52.839	Microscopic colitis, unspecified	Diagnosis	ICD-10-CM
K52.89	Other specified noninfective gastroenteritis and colitis	Diagnosis	ICD-10-CM
K52.9	Noninfective gastroenteritis and colitis, unspecified	Diagnosis	ICD-10-CM

Appendix G. List of Current Procedural Terminology, Fourth Edition (CPT-4), Current Procedural Terminology, Second Edition (CPT-2), Healthcare Common Procedure Coding System, Level II (HCPCS), and International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS) Codes Used to Define Characteristics in this Request

Code	Description	Code Category	Code Type
	Intestinal Ischemia		
37243	Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; for tumors, organ ischemia, or infarction	Procedure	CPT-4
	Colonoscopy and Colectomy		
00812	Anesthesia for lower intestinal endoscopic procedures, endoscope introduced distal to duodenum; screening colonoscopy	Procedure	CPT-4
0DJD8ZZ	Inspection of Lower Intestinal Tract, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
0DTE0ZZ	Resection of Large Intestine, Open Approach	Procedure	ICD-10-PCS
0DTE4ZZ	Resection of Large Intestine, Percutaneous Endoscopic Approach	Procedure	ICD-10-PCS
0DTE7ZZ	Resection of Large Intestine, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
0DTE8ZZ	Resection of Large Intestine, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
0DTF0ZZ	Resection of Right Large Intestine, Open Approach	Procedure	ICD-10-PCS
0DTF4ZZ	Resection of Right Large Intestine, Percutaneous Endoscopic Approach	Procedure	ICD-10-PCS
0DTF7ZZ	Resection of Right Large Intestine, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
0DTF8ZZ	Resection of Right Large Intestine, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
0DTG0ZZ	Resection of Left Large Intestine, Open Approach	Procedure	ICD-10-PCS
0DTG4ZZ	Resection of Left Large Intestine, Percutaneous Endoscopic Approach	Procedure	ICD-10-PCS
0DTG7ZZ	Resection of Left Large Intestine, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
0DTG8ZZ	Resection of Left Large Intestine, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
0DTGFZZ	Resection of Left Large Intestine, Via Natural or Artificial Opening With Percutaneous Endoscopic Assistance	Procedure	ICD-10-PCS
0DTK0ZZ	Resection of Ascending Colon, Open Approach	Procedure	ICD-10-PCS
3018F	Pre-procedure risk assessment and depth of insertion and quality of the bowel prep and complete description of polyp(s) found, including location of each polyp, size, number and gross morphology and recommendations for follow-up in final colonoscopy report documented (End/Polyp)	Procedure	CPT-2
3775F	Adenoma(s) or other neoplasm detected during screening colonoscopy (SCADR)	Procedure	CPT-2
44139	Mobilization (take-down) of splenic flexure performed in conjunction with partial colectomy (List separately in addition to primary procedure)	Procedure	CPT-4
44140	Colectomy, partial; with anastomosis	Procedure	CPT-4
44141	Colectomy, partial; with skin level cecostomy or colostomy	Procedure	CPT-4
44143	Colectomy, partial; with end colostomy and closure of distal segment (Hartmann type procedure)	Procedure	CPT-4
44144	Colectomy, partial; with resection, with colostomy or ileostomy and creation of mucofistula	Procedure	CPT-4
44145	Colectomy, partial; with coloproctostomy (low pelvic anastomosis)	Procedure	CPT-4
44146	Colectomy, partial; with coloproctostomy (low pelvic anastomosis), with colostomy	Procedure	CPT-4
44147	Colectomy, partial; abdominal and transanal approach	Procedure	CPT-4
44150	Colectomy, total, abdominal, without proctectomy; with ileostomy or ileoproctostomy	Procedure	CPT-4
44151	Colectomy, total, abdominal, without proctectomy; with continent ileostomy	Procedure	CPT-4
44155	Colectomy, total, abdominal, with proctectomy; with ileostomy	Procedure	CPT-4
44156	Colectomy, total, abdominal, with proctectomy; with continent ileostomy	Procedure	CPT-4
44157	Colectomy, total, abdominal, with proctectomy; with ileoanal anastomosis, includes loop ileostomy, and rectal mucosectomy, when performed	Procedure	CPT-4

Appendix G. List of Current Procedural Terminology, Fourth Edition (CPT-4), Current Procedural Terminology, Second Edition (CPT-2), Healthcare Common Procedure Coding System, Level II (HCPCS), and International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS) Codes Used to Define Characteristics in this Request

Code	Description	Code Category	Code Type
44158	Colectomy, total, abdominal, with proctectomy; with ileoanal anastomosis, creation of ileal reservoir (S or J), includes loop ileostomy, and rectal mucosectomy, when performed	Procedure	CPT-4
44160	Colectomy, partial, with removal of terminal ileum with ileocolostomy	Procedure	CPT-4
44204	Laparoscopy, surgical; colectomy, partial, with anastomosis	Procedure	CPT-4
44205	Laparoscopy, surgical; colectomy, partial, with removal of terminal ileum with ileocolostomy	Procedure	CPT-4
44206	Laparoscopy, surgical; colectomy, partial, with end colostomy and closure of distal segment (Hartmann type procedure)	Procedure	CPT-4
44207	Laparoscopy, surgical; colectomy, partial, with anastomosis, with coloproctostomy (low pelvic anastomosis)	Procedure	CPT-4
44208	Laparoscopy, surgical; colectomy, partial, with anastomosis, with coloproctostomy (low pelvic anastomosis) with colostomy	Procedure	CPT-4
44210	Laparoscopy, surgical; colectomy, total, abdominal, without proctectomy, with ileostomy or ileoproctostomy	Procedure	CPT-4
44211	Laparoscopy, surgical; colectomy, total, abdominal, with proctectomy, with ileoanal anastomosis, creation of ileal reservoir (S or J), with loop ileostomy, includes rectal mucosectomy, when performed	Procedure	CPT-4
44212	Laparoscopy, surgical; colectomy, total, abdominal, with proctectomy, with ileostomy	Procedure	CPT-4
44213	Laparoscopy, surgical, mobilization (take-down) of splenic flexure performed in conjunction with partial colectomy (List separately in addition to primary procedure)	Procedure	CPT-4
44388	Colonoscopy through stoma; diagnostic, including collection of specimen(s) by brushing or washing, when performed (separate procedure)	Procedure	CPT-4
44389	Colonoscopy through stoma; with biopsy, single or multiple	Procedure	CPT-4
44390	Colonoscopy through stoma; with removal of foreign body(s)	Procedure	CPT-4
44391	Colonoscopy through stoma; with control of bleeding, any method	Procedure	CPT-4
44392	Colonoscopy through stoma; with removal of tumor(s), polyp(s), or other lesion(s) by hot biopsy forceps	Procedure	CPT-4
44393	Colonoscopy through stoma; with ablation of tumor(s), polyp(s), or other lesion(s) not amenable to removal by hot biopsy forceps, bipolar cautery or snare technique	Procedure	CPT-4
44394	Colonoscopy through stoma; with removal of tumor(s), polyp(s), or other lesion(s) by snare technique	Procedure	CPT-4
44397	Colonoscopy through stoma; with transendoscopic stent placement (includes predilation)	Procedure	CPT-4
44401	Colonoscopy through stoma; with ablation of tumor(s), polyp(s), or other lesion(s) (includes pre-and post-dilation and guide wire passage, when performed)	Procedure	CPT-4
44402	Colonoscopy through stoma; with endoscopic stent placement (including pre- and post-dilation and guide wire passage, when performed)	Procedure	CPT-4
44403	Colonoscopy through stoma; with endoscopic mucosal resection	Procedure	CPT-4
44404	Colonoscopy through stoma; with directed submucosal injection(s), any substance	Procedure	CPT-4
44405	Colonoscopy through stoma; with transendoscopic balloon dilation	Procedure	CPT-4
44406	Colonoscopy through stoma; with endoscopic ultrasound examination, limited to the sigmoid, descending, transverse, or ascending colon and cecum and adjacent	Procedure	CPT-4

Appendix G. List of Current Procedural Terminology, Fourth Edition (CPT-4), Current Procedural Terminology, Second Edition (CPT-2), Healthcare Common Procedure Coding System, Level II (HCPCS), and International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS) Codes Used to Define Characteristics in this Request

Code	Description	Code Category	Code Type
44407	Colonoscopy through stoma; with transendoscopic ultrasound guided intramural or transmural fine needle aspiration/biopsy(s), includes endoscopic ultrasound examination limited to the sigmoid, descending, transverse, or ascending colon and cecum and adjacent structures	Procedure	CPT-4
44408	Colonoscopy through stoma; with decompression (for pathologic distention) (eg, volvulus, megacolon), including placement of decompression tube, when performed	Procedure	CPT-4
45121	Proctectomy, complete (for congenital megacolon), abdominal and perineal approach; with subtotal or total colectomy, with multiple biopsies	Procedure	CPT-4
45355	Colonoscopy, rigid or flexible, transabdominal via colotomy, single or multiple	Procedure	CPT-4
45378	Colonoscopy, flexible; diagnostic, including collection of specimen(s) by brushing or washing, when performed (separate procedure)	Procedure	CPT-4
45379	Colonoscopy, flexible; with removal of foreign body(s)	Procedure	CPT-4
45380	Colonoscopy, flexible; with biopsy, single or multiple	Procedure	CPT-4
45381	Colonoscopy, flexible; with directed submucosal injection(s), any substance	Procedure	CPT-4
45382	Colonoscopy, flexible; with control of bleeding, any method	Procedure	CPT-4
45383	Colonoscopy, flexible, proximal to splenic flexure; with ablation of tumor(s), polyp(s), or other lesion(s) not amenable to removal by hot biopsy forceps, bipolar cautery or snare technique	Procedure	CPT-4
45384	Colonoscopy, flexible; with removal of tumor(s), polyp(s), or other lesion(s) by hot biopsy forceps	Procedure	CPT-4
45385	Colonoscopy, flexible; with removal of tumor(s), polyp(s), or other lesion(s) by snare technique	Procedure	CPT-4
45386	Colonoscopy, flexible; with transendoscopic balloon dilation	Procedure	CPT-4
45387	Colonoscopy, flexible, proximal to splenic flexure; with transendoscopic stent placement (includes predilation)	Procedure	CPT-4
45388	Colonoscopy, flexible; with ablation of tumor(s), polyp(s), or other lesion(s) (includes pre- and post-dilation and guide wire passage, when performed)	Procedure	CPT-4
45389	Colonoscopy, flexible; with endoscopic stent placement (includes pre- and post-dilation and guide wire passage, when performed)	Procedure	CPT-4
45390	Colonoscopy, flexible; with endoscopic mucosal resection	Procedure	CPT-4
45391	Colonoscopy, flexible; with endoscopic ultrasound examination limited to the rectum, sigmoid, descending, transverse, or ascending colon and cecum, and adjacent	Procedure	CPT-4
45392	Colonoscopy, flexible; with transendoscopic ultrasound guided intramural or transmural fine needle aspiration/biopsy(s), includes endoscopic ultrasound examination limited to the rectum, sigmoid, descending, transverse, or ascending colon and cecum, and adjacent structures	Procedure	CPT-4
45393	Colonoscopy, flexible; with decompression (for pathologic distention) (eg, volvulus, megacolon), including placement of decompression tube, when performed	Procedure	CPT-4
45398	Colonoscopy, flexible; with band ligation(s) (eg, hemorrhoids)	Procedure	CPT-4
G0105	Colorectal cancer screening; colonoscopy on individual at high risk	Procedure	HCPCS
G0120	Colorectal cancer screening; alternative to G0105, screening colonoscopy, barium enema	Procedure	HCPCS
G0121	Colorectal cancer screening; colonoscopy on individual not meeting criteria for high	Procedure	HCPCS
G6019	Colonoscopy through stoma; with ablation of tumor(s), polyp(s), or other lesion(s) not amenable to removal by hot biopsy forceps, bipolar cautery or snare technique	Procedure	HCPCS

Appendix G. List of Current Procedural Terminology, Fourth Edition (CPT-4), Current Procedural Terminology, Second Edition (CPT-2), Healthcare Common Procedure Coding System, Level II (HCPCS), and International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS) Codes Used to Define Characteristics in this Request

Code	Description	Code Category	Code Type
G6020	Colonoscopy through stoma; with transendoscopic stent placement (includes predilation)	Procedure	HCPCS
G6024	Colonoscopy, flexible; proximal to splenic flexure; with ablation of tumor(s), polyp(s), or other lesion(s) not amenable to removal by hot biopsy forceps, bipolar cautery or snare tehnique	Procedure	HCPCS
G6025	Colonoscopy, flexible, proximal to splenic flexure; with transendoscopic stent placement (includes predilation)	Procedure	HCPCS
G9659	Patients greater than or equal to 86 years of age who underwent a screening colonoscopy and did not have a history of colorectal cancer or other valid medical reason for the colonoscopy, including: iron deficiency anemia, lower gastrointestinal bleeding, Crohn's disease (i.e., regional enteritis), familial adenomatous polyposis, Lynch syndrome (i.e., hereditary nonpolyposis colorectal cancer), inflammatory bowel disease, ulcerative colitis, abnormal finding of gastrointestinal tract, or changes in	Procedure	HCPCS
G9660	Documentation of medical reason(s) for a colonoscopy performed on a patient greater than or equal to 86 years of age (e.g., iron deficiency anemia, lower gastrointestinal bleeding, Crohn's disease (i.e., regional enteritis), familial history of adenomatous polyposis, Lynch syndrome (i.e., hereditary nonpolyposis colorectal cancer), inflammatory bowel disease, ulcerative colitis, abnormal finding of gastrointestinal tract, or changes in bowel habits)	Procedure	HCPCS
G9661	Patients greater than or equal to 86 years of age who received a colonoscopy for an assessment of signs/symptoms of GI tract illness, and/or because the patient meets high risk criteria, and/or to follow-up on previously diagnosed advanced lesions	Procedure	HCPCS
G9933	Adenoma(s) or colorectal cancer detected during screening colonoscopy	Procedure	HCPCS
G9935	Adenoma(s) or colorectal cancer not detected during screening colonoscopy	Procedure	HCPCS
G9936	Surveillance colonoscopy - personal history of colonic polyps, colon cancer, or other malignant neoplasm of rectum, rectosigmoid junction, and anus	Procedure	HCPCS
G9937	Diagnostic colonoscopy	Procedure	HCPCS

Appendix H. Specifications Defining Parameters for this Request

This request executed the Cohort Identification and Descriptive Analysis (CIDA) tool version 11.2.4 to estimate rates of of ischemic colitis in patient populations exposed to alosetron or eluxadoline in the treatment of irritable bowel syndrome (IBS) in the Sentinel Distributed Database (SDD).

Query period: 01/01/2016-07/01/2020
Coverage requirement: Medical & Drug Coverage
Pre-index enrollment requirement: 91 days
Post-index enrollment requirement: 0 days
Enrollment gap: 45 days
Age groups: <18 years, 18-44, 45-64, 65+ years
Stratifications: Age group, Sex, Calendar year, IBS, Intestinal colitis, Sex*Age group, Sex*Calendar year, Agegroup*Calendar year, Sex*Age*IBS, Sex*Age*Intestinal colitis
Censor output categorization: ≤7, 8-14, 15-30, 31-60, 61-90, 91-120, 121-150, 151-183 days
Restrictions: M/F
Envelope macro: Reclassify encounters during inpatient stay as inpatient
Distribution of index-defining codes: N
Never-exposed cohort: N
Freeze data: Y

		Exposure								
Scenario	Index Exposure	Cohort definition	Incident exposure washout period	Incident with respect to:	Exclude evidence of days supply if exposure washout includes dispensings	Build Episodes on Point Exposure?	Maximum exposure episode duration	Care setting	Create Baseline Table?	Censor treatment episode at evidence of:
1	Alosetron	First valid exposure episodes during query period	91 days	Alosetron	Washout lookback period should search for only evidence of a dispensing date	Yes	183 days	Any care setting	Yes	(1) dispensing for eluxadoline, (2) date of death, (3) health plan disenrollment date, (4) Data Partner end date
2	Alosetron	First valid exposure episodes during query period	91 days	Alosetron	Washout lookback period should search for only evidence of a dispensing date	Yes	183 days	Any care setting	No	(1) dispensing for eluxadoline, (2) date of death, (3) health plan disenrollment date, (4) Data Partner end date

Appendix H. Specifications Defining Parameters for this Request

	Exposure									
Scenario	Index Exposure	Cohort definition	Incident exposure washout period	Incident with respect to:	Exclude evidence of days supply if exposure washout includes dispensings	Build Episodes on Point Exposure?	Maximum exposure episode duration	Care setting	Create Baseline Table?	Censor treatment episode at evidence of:
3	Alosetron	First valid exposure episodes during query period	91 days	Alosetron	Washout lookback period should search for only evidence of a dispensing date	Yes	183 days	Any care setting	No	(1) dispensing for eluxadoline, (2) date of death, (3) health plan disenrollment date, (4) Data Partner end date
4	Alosetron	First valid exposure episodes during query period	91 days	Alosetron	Washout lookback period should search for only evidence of a dispensing date	Yes	183 days	Any care setting	No	(1) dispensing for eluxadoline, (2) date of death, (3) health plan disenrollment date, (4) Data Partner end date
5	Alosetron	First valid exposure episodes during query period	91 days	Alosetron	Washout lookback period should search for only evidence of a dispensing date	Yes	183 days	Any care setting	No	(1) dispensing for eluxadoline, (2) date of death, (3) health plan disenrollment date, (4) Data Partner end date
6	Eluxadoline	First valid exposure episodes during query period	91 days	Eluxadoline	Washout lookback period should search for only evidence of a dispensing date	Yes	183 days	Any care setting	Yes	(1) dispensing for alosetron, (2) date of death, (3) health plan disenrollment date, (4) Data Partner end date
7	Eluxadoline	First valid exposure episodes during query period	91 days	Eluxadoline	Washout lookback period should search for only evidence of a dispensing date	Yes	183 days	Any care setting	No	(1) dispensing for alosetron, (2) date of death, (3) health plan disenrollment date, (4) Data Partner end date

International Classification of Diseases, Ninth and Tenth Revisions, (ICD-9 and ICD-10), Healthcare Common Procedure Coding System (HCPCS), and Current Procedural Terminology, Fourth Edition (CPT-4) codes are provided by Optum 360.

National Drug Codes (NDCs) are checked against First Data Bank's FDB MedKnowledge®.

Appendix H. Specifications Defining Parameters for this Request

	Inclusion/Exclusion Criteria						
Scenario	Inclusion/ Exclusion group	Criteria	Care setting	Evaluation period start (days)	Evaluation period end (days)	Exclude evidence of days supply if inclusion/exclusion evaluation period includes dispensings	Number of instances the criteria should be found in evaluation period
1	Eluxadoline	Exclusion	Any care setting	-91	0	Evaluation period should search for evidence of a date only	1
2	Eluxadoline	Exclusion	Any care setting	-91	0	Evaluation period should search for evidence of a date only	1
3	Eluxadoline	Exclusion	Any care setting	-91	0	Evaluation period should search for evidence of a date only	1
4	Eluxadoline	Exclusion	Any care setting	-91	0	Evaluation period should search for evidence of a date only	1
5	Eluxadoline	Exclusion	Any care setting	-91	0	Evaluation period should search for evidence of a date only	1
6	Alosetron	Exclusion	Any care setting	-91	0	Evaluation period should search for evidence of a date only	1
7	Alosetron	Exclusion	Any care setting	-91	0	Evaluation period should search for evidence of a date only	1

International Classification of Diseases, Ninth and Tenth Revisions, (ICD-9 and ICD-10), Healthcare Common Procedure Coding System (HCPCS), and Current Procedural Terminology, Fourth Edition (CPT-4) codes are provided by Optum 360.
National Drug Codes (NDCs) are checked against First Data Bank's FDB MedKnowledge®.

Appendix H. Specifications Defining Parameters for this Request

	Event Outcome						
Scenario	Event	Incident event washout period (days)	Incident with respect to:	Care setting	Principal diagnosis position	Event de-duplication	Risk Window Interval Start (days)
1	Ischemic Colitis Diagnosis	0	N/A	Any	N/A	De-duplicates occurrences of the same event group on the same day	1
2	Ischemic Colitis Diagnosis	0	N/A	IP/IS	Any	De-duplicates occurrences of the same event group on the same day	1
3	Ischemic Colitis Diagnosis	0	N/A	IP/IS	Principal	De-duplicates occurrences of the same event group on the same day	1
4	"Ischemic Colitis in Any Care Setting Defined by a Modified Validated Algorithm" = Earlier of: Outpatient or Inpatient Ischemic Colitis Combo	90	N/A	Any	Any	De-duplicates occurrences of the same event group on the same day	1
5	"Ischemic Colitis in the Inpatient Setting Defined by a Modified Validated Algorithm" = Inpatient Ischemic Colitis Combo	90	N/A	IP/IS	N/A	De-duplicates occurrences of the same event group on the same day	1

Appendix H. Specifications Defining Parameters for this Request

	Event Outcome						
Scenario	**Event**	**Incident event washout period (days)**	**Incident with respect to:**	**Care setting**	**Principal diagnosis position**	**Event de-duplication**	**Risk Window Interval Start (days)**
6	"Ischemic Colitis in Any Care Setting Defined by a Modified Validated Algorithm" = Earlier of: Outpatient or Inpatient Ischemic Colitis Combo	90	N/A	Any	Any	De-duplicates occurrences of the same event group on the same day	1
7	"Ischemic Colitis in the Inpatient Setting Defined by a Modified Validated Algorithm" = Inpatient Ischemic Colitis Combo	90	N/A	IP/IS	N/A	De-duplicates occurrences of the same event group on the same day	1

International Classification of Diseases, Ninth and Tenth Revisions, (ICD-9 and ICD-10), Healthcare Common Procedure Coding System (HCPCS), and Current Procedural Terminology, Fourth Edition (CPT-4) codes are provided by Optum 360.

National Drug Codes (NDCs) are checked against First Data Bank's FDB MedKnowledge®.

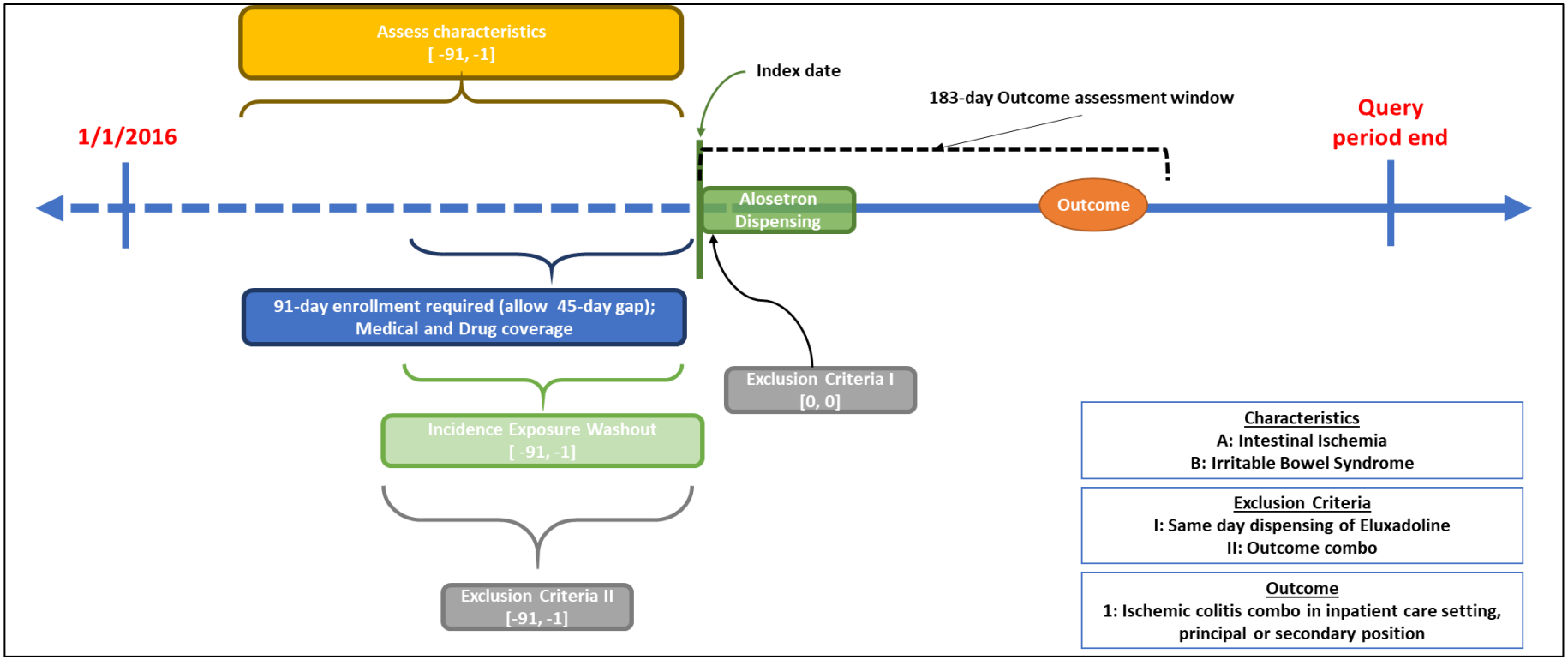
Appendix I. Specifications Defining Parameters for Baseline Characteristics in this Request

Covariate	Care setting	Principal diagnosis position	Code Category	Evaluation period start (days)	Evaluation period end (days)	Number of instances the covariate should be found in evaluation period
Irritable Bowel Syndrome	Any	Any	Diagnosis Code	-91	0	1
Intestinal Ischemia	Any	Any	Diagnosis Code	-91	0	1
Colonoscopy or colectomy with noninfectious gastroenteritis within 3 months (combo)	Any	Any	Combo	0	183	1

Appendix J. Specifications Defining Parameters for Combination Definition in this Request

Combination Name	Condition	Care setting	Diagnosis Position	Inclusion/Exclusion	Observation Window	Combined to Date
Colonscopy/colectomy and noninfectious gastroenteritis and colitis covariate	Colonscopy/colectomy	Any	Any	-----	-----	-----
	Noninfectious gastroenteritis and colitis	Any	Any	Inclusion	(0,91)	AdateB
Outpatient Care Setting Ischemic colitis combo	Vascular insufficiency of intestine	AV/OA/ED	N/A	Inclusion	-----	-----
	Crohn's Disease, Ulcerative Colitis, Clostridium difficile enteritis, Enterectomy, or Dispensing of a 5-aminosalicylate drug	Any	N/A	Exclusion	(-14, 14)	AdateB
	Colonscopy/colectomy	Any	N/A	Inclusion	(-91, 0)	
	Colonscopy/colectomy, acute pancreatitis, abdominal pain	Any	N/A	Inclusion	(-91,0)	AdateC (earliest occurance)
Inpatient Care Setting Ischemic colitis combo	Vascular insufficiency of intestine	IP/IS	Any	Inclusion	-----	-----
	Crohn's Disease, Ulcerative Colitis, Clostridium difficile enteritis, Enterectomy, or Dispensing of a 5-aminosalicylate drug	Any	N/A	Exclusion	(-14, 14)	AdateB
	Colonscopy/colectomy	Any	N/A	Inclusion	(0, 0)	

Appendix K. Diagrams Detailing the Design of this Request



Appendix K. Diagrams Detailing the Design of this Request