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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_wp099, Report 1

Request ID: cder_mpl1r_wp099_nsdp_v01

Request Description: The goal of this request was to estimate the length of follow-up time for patients diagnosed with Type 2 Diabetes and for patients dispensed non-insulin antidiabetic drugs available in the Sentinel Distributed Database (SDD). This is report 1 of 2. Report 2 summarizes utilization of non-insulin antidiabetic drugs available in the SDD.

Sentinel Modular Program Tool Used: Cohort Identification and Descriptive Analysis (CIDA) tool, version 5.4.3

Data Source: Data from January 1, 2008 to January 31, 2018 from 17 Data Partners contributing to the SDD were included in this report. This request was distributed to Data Partners on June 28, 2018. Please see Appendix A for a list of dates of available data for each Data Partner.

Study Design: This request used a retrospective cohort design. The purpose of this request was to estimate follow-up time for patients diagnosed with Type 2 Diabetes and for patients dispensed with antidiabetic drugs from select classes. The number of patients with diagnoses and exposures was stratified by age group, sex, year, and categories of follow-up time.

Events/Exposures of Interest: There were two analyses in this request, based on the events or exposures of interest:

Analysis 1: The events of interest were diagnoses of Type 2 Diabetes, which was defined three ways: 1) the first diagnosis in the inpatient setting; 2) the second of two outpatient diagnoses within a 90-day period; or 3) the first diagnosis in the inpatient setting or the second of two outpatient diagnoses within a 90-day period. Each event definition was evaluated using a 0-day washout period and a 365-day washout period. Type 2 Diabetes was defined using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis codes. Please refer to Appendix B for specific codes used to define Type 2 Diabetes in this request.

Analysis 2: The exposures of interest were eight classes of non-insulin antidiabetic drugs: alpha-glucosidase inhibitors, biguanides, dipeptidyl peptidase-4 inhibitors, glucagon-like peptide-1 receptor agonists, meglitinides, second generation sulfonylureas, sodium glucose cotransporter-2 inhibitors, and thiazolidinediones. The exposures were defined using National Drug Codes (NDCs). Please refer to Appendix C for generic and brand drug names used to define antidiabetic drug exposures in this request.

Cohort Eligibility Criteria: For both analyses, the first valid exposure or event per patient was included; no cohort re-entry was allowed. The following age groups were included in the cohorts: 18-44, 45-54, 55-64, 65-74, and 75+ years.

Analysis 1: Patients included in the cohorts with a 0-day washout period were required to be enrolled in plans with at least medical coverage on the date of their event. Patients included in the cohorts with a 365-day washout period were required to be enrolled in plans with medical coverage for the 365 days before their event, during which gaps in coverage of up to 45 days were allowed. Patients included in the cohorts with the 365-day washout period were also required to have had 365 days without the same event definition prior to their event of interest.

Analysis 2: Patients included in the cohort were required to be enrolled in plans with at least drug coverage on the date of their exposure of interest.

Follow-Up Time: Follow-up time was grouped into the following categories: <6 months, 6-<12 months, 12-<24 months, 34-<36 months, 36-<48 months, and 48+ months. Follow-up began on the day of the first exposure or event of interest and continued until either 1) disenrollment; 2) death; or 3) the end of Data Partners' data.

Please refer to Appendices D and E for detailed specifications of parameters used in this request.

Limitations: Algorithms used to define events and outcomes may not have been validated; thus, it is possible that cohort members may be misclassified. Therefore, data should be interpreted with this limitation in mind.

Notes: Please contact the Sentinel Operations Center Query Fulfillment Team (qf@sentinelsystem.org) for questions and to provide comments/suggestions for future enhancements to this document.

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

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, forms the Care Setting/PDX parameter.

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

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.

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 MP algorithm: 0: Counts all occurrences of an 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 days 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.

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 1. Summary of Follow-Up Time Since the First Observed Valid Diagnosis of Type 2 Diabetes in the Sentinel Distributed Database (SDD) from January 1, 2008 to January 31, 2018, by Washout Period and Type 2 Diabetes Diagnosis Definition

			Number of Patients by Follow-Up Time													
	TOTAL		< 6 months		6 to < 12 months		12 to < 24 months		24 to < 36 months		36 to < 48 months		48 months or longer		Mean Follow-Up Time	Median Follow-Up Time
0-Day Washout	**Number**	**Percent**	**Number**	**Percent**	**Number**	**Percent**	**Number**	**Percent**	**Number**	**Percent**	**Number**	**Percent**	**Number**	**Percent**	**Months**	**Months**
Type 2 Diabetes, First Inpatient or Second Outpatient Diagnosis	26,512,514	100%	3,450,438	13.0%	3,096,471	11.7%	4,389,706	16.6%	3,404,949	12.8%	2,853,473	10.8%	9,317,477	35.1%	37.3	32.3
Type 2 Diabetes, First Inpatient Diagnosis	11,243,657	100%	2,270,130	20.2%	1,382,893	12.3%	2,050,251	18.2%	1,601,251	14.2%	1,324,623	11.8%	2,614,509	23.3%	29.2	23.4
Type 2 Diabetes, Second Outpatient Diagnosis	25,387,264	100%	3,123,653	12.3%	2,956,995	11.6%	4,205,100	16.6%	3,277,388	12.9%	2,752,705	10.8%	9,071,423	35.7%	37.8	32.9
365-Day Washout																
Type 2 Diabetes, First Inpatient or Second Outpatient Diagnosis	13,225,754	100%	1,937,140	14.6%	1,611,283	12.2%	2,593,872	19.6%	2,165,003	16.4%	1,876,560	14.2%	3,041,896	23.0%	31.4	26.5
Type 2 Diabetes, First Inpatient Diagnosis	8,660,915	100%	1,800,307	20.8%	1,109,373	12.8%	1,713,748	19.8%	1,382,006	16.0%	1,164,279	13.4%	1,491,202	17.2%	26.6	21.7
Type 2 Diabetes, Second Outpatient Diagnosis	12,552,619	100%	1,720,128	13.7%	1,529,012	12.2%	2,476,961	19.7%	2,080,103	16.6%	1,807,917	14.4%	2,938,498	23.4%	31.9	27.0

Table 2. Summary of Follow-Up Time Since the First Observed Valid Diagnosis of Type 2 Diabetes in the Sentinel Distributed Database (SDD) from January 1, 2008 to January 31, 2018, by Washout Period, Type 2 Diabetes Diagnosis Definition, and Age Group

	Number of Patients by Follow-Up Time					
Age Group (Years)	**< 6 months**	**6 to < 12 months**	**12 to < 24 months**	**24 to < 36 months**	**36 to < 48 months**	**48 months or longer**
0-Day Washout						
Type 2 Diabetes, First Inpatient or Second Outpatient Diagnosis						
18-44	390,730	327,404	428,887	285,362	208,368	562,134
45-54	534,498	484,457	658,115	461,452	355,344	1,082,234
55-64	771,756	722,175	994,631	710,646	556,067	1,557,702
65-74	945,968	920,055	1,344,601	1,136,579	1,019,726	3,615,895
75+	807,486	642,380	963,472	810,910	713,968	2,499,512
Type 2 Diabetes, First Inpatient Diagnosis						
18-44	106,226	78,748	109,268	76,872	58,814	129,788
45-54	171,858	131,475	190,465	138,955	110,663	257,796
55-64	342,148	250,143	362,023	263,263	206,078	431,866
65-74	627,997	420,589	642,332	529,736	462,409	947,488
75+	1,021,901	501,938	746,163	592,425	486,659	847,571
Type 2 Diabetes, Second Outpatient Diagnosis						
18-44	363,279	308,708	405,169	270,717	197,856	536,792
45-54	508,290	467,317	635,460	447,190	344,390	1,051,585
55-64	726,432	696,865	960,751	688,739	539,989	1,516,325
65-74	874,649	889,001	1,302,432	1,105,304	992,521	3,541,693
75+	651,003	595,104	901,288	765,438	677,949	2,425,028

Table 2. Summary of Follow-Up Time Since the First Observed Valid Diagnosis of Type 2 Diabetes in the Sentinel Distributed Database (SDD) from January 1, 2008 to January 31, 2018, by Washout Period, Type 2 Diabetes Diagnosis Definition, and Age Group

	Number of Patients by Follow-Up Time					
Age Group (Years)	**< 6 months**	**6 to < 12 months**	**12 to < 24 months**	**24 to < 36 months**	**36 to < 48 months**	**48 months or longer**
365-Day Washout						
Type 2 Diabetes, First Inpatient or Second Outpatient Diagnosis						
18-44	182,185	158,275	229,678	167,138	128,548	268,922
45-54	260,829	232,369	352,409	269,767	217,663	490,015
55-64	385,606	339,290	522,372	399,659	318,368	630,062
65-74	521,293	465,455	787,605	706,819	653,510	951,184
75+	587,227	415,894	701,808	621,620	558,471	701,713
Type 2 Diabetes, First Inpatient Diagnosis						
18-44	61,821	49,288	73,752	55,449	44,262	75,111
45-54	110,963	89,262	137,320	106,721	88,081	151,066
55-64	239,058	181,342	275,613	208,678	167,420	259,287
65-74	493,012	340,224	539,719	456,214	403,901	510,927
75+	895,453	449,257	687,344	554,944	460,615	494,811
Type 2 Diabetes, Second Outpatient Diagnosis						
18-44	169,742	149,272	216,777	158,392	122,099	256,256
45-54	248,549	224,849	340,815	261,852	211,439	476,668
55-64	362,659	327,850	505,223	388,055	309,695	613,632
65-74	475,629	446,643	759,910	685,938	634,863	924,446
75+	463,549	380,398	654,236	585,866	529,821	667,496

Table 3. Summary of Follow-Up Time Since the First Observed Valid Diagnosis of Type 2 Diabetes in the Sentinel Distributed Database (SDD) from January 1, 2008 to January 31, 2018, by Washout Period, Type 2 Diabetes Diagnosis Definition, and Sex

	Number of Patients by Follow-Up Time					
Sex	**< 6 months**	**6 to < 12 months**	**12 to < 24 months**	**24 to < 36 months**	**36 to < 48 months**	**48 months or longer**
0-Day Washout						
Type 2 Diabetes, First Inpatient or Second Outpatient Diagnosis						
Female	1,675,621	1,508,514	2,158,253	1,697,619	1,436,874	4,852,026
Male	1,774,817	1,587,957	2,231,453	1,707,330	1,416,599	4,465,451
Type 2 Diabetes, First Inpatient Diagnosis						
Female	1,113,286	683,502	1,033,441	822,285	694,884	1,405,924
Male	1,156,844	699,391	1,016,810	778,966	629,739	1,208,585
Type 2 Diabetes, Second Outpatient Diagnosis						
Female	1,510,499	1,437,360	2,062,807	1,630,326	1,383,594	4,721,574
Male	1,613,154	1,519,635	2,142,293	1,647,062	1,369,111	4,349,849
365-Day Washout						
Type 2 Diabetes, First Inpatient or Second Outpatient Diagnosis						
Female	942,168	782,093	1,277,329	1,078,380	943,953	1,510,711
Male	994,972	829,190	1,316,543	1,086,623	932,607	1,531,185
Type 2 Diabetes, First Inpatient Diagnosis						
Female	888,679	552,387	871,159	717,301	619,139	792,821
Male	911,628	556,986	842,589	664,705	545,140	698,381
Type 2 Diabetes, Second Outpatient Diagnosis						
Female	830,115	739,035	1,215,929	1,032,663	907,654	1,455,001
Male	890,013	789,977	1,261,032	1,047,440	900,263	1,483,497

Table 4. Summary of Follow-Up Time Since the First Observed Valid Diagnosis of Type 2 Diabetes in the Sentinel Distributed Database (SDD) from January 1, 2008 to January 31, 2018, by Washout Period, Type 2 Diabetes Diagnosis Definition, and Year

	Number of Patients by Follow-Up Time					
Year	< 6 months	6 to < 12 months	12 to < 24 months	24 to < 36 months	36 to < 48 months	48 months or longer
0-Day Washout						
Type 2 Diabetes, First Inpatient or Second Outpatient Diagnosis						
2008	307,473	317,063	502,176	330,673	257,376	1,446,100
2009	155,701	151,673	192,262	135,919	101,720	542,110
2010	545,256	495,667	787,337	705,303	651,382	5,008,630
2011	278,796	215,739	321,590	268,590	227,468	1,561,909
2012	257,316	197,787	294,312	229,393	1,048,670	449,510
2013	238,423	185,934	265,467	1,041,466	165,225	308,266
2014	262,930	209,658	1,137,627	201,478	400,423	952
2015	731,526	681,425	281,082	490,387	1,209	-
2016	159,970	275,367	605,937	1,740	-	-
2017	511,591	366,158	1,916	-	-	-
2018	1,456	-	-	-	-	-
Type 2 Diabetes, First Inpatient Diagnosis						
2008	105,230	65,492	103,690	64,911	49,260	225,989
2009	83,363	54,608	68,958	49,456	38,121	183,537
2010	341,793	183,235	277,657	231,148	197,963	1,081,376
2011	290,369	141,164	217,808	181,217	156,021	851,554
2012	244,172	118,935	183,572	150,796	680,167	159,640
2013	215,659	108,268	161,623	674,482	69,942	111,888
2014	210,421	103,528	716,068	83,536	132,586	525
2015	510,994	404,660	108,116	164,983	563	-
2016	75,704	97,941	212,022	722	-	-
2017	192,134	105,062	737	-	-	-
2018	291	-	-	-	-	-

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Table 4. Summary of Follow-Up Time Since the First Observed Valid Diagnosis of Type 2 Diabetes in the Sentinel Distributed Database (SDD) from January 1, 2008 to January 31, 2018, by Washout Period, Type 2 Diabetes Diagnosis Definition, and Year

	Number of Patients by Follow-Up Time					
Year	< 6 months	6 to < 12 months	12 to < 24 months	24 to < 36 months	36 to < 48 months	48 months or longer
Type 2 Diabetes, Second Outpatient Diagnosis						
2008	275,735	300,117	478,366	315,958	246,294	1,396,372
2009	140,801	144,607	184,023	130,576	98,066	526,431
2010	492,510	475,780	759,786	683,980	633,352	4,904,105
2011	236,057	202,524	304,142	255,778	216,976	1,509,147
2012	220,352	186,017	278,839	218,402	1,009,056	434,740
2013	205,726	175,734	251,949	1,001,647	158,401	299,753
2014	231,521	199,100	1,091,196	192,949	389,418	875
2015	680,152	652,492	268,866	476,482	1,142	-
2016	148,336	264,649	586,133	1,616	-	-
2017	491,014	355,975	1,800	-	-	-
2018	1,449	-	-	-	-	-
365-Day Washout						
Type 2 Diabetes, First Inpatient or Second Outpatient Diagnosis						
2008	45,577	35,851	59,098	42,699	39,103	263,326
2009	107,737	90,313	125,781	99,081	77,836	470,664
2010	89,247	73,969	115,241	87,037	80,119	384,702
2011	206,812	148,118	247,604	225,238	192,449	1,412,517
2012	190,324	136,126	237,755	198,072	1,110,267	291,691
2013	175,325	132,081	209,569	1,044,263	122,987	218,169
2014	164,819	114,497	1,014,166	145,283	252,873	827
2015	564,466	532,980	183,066	322,365	926	-
2016	80,661	164,862	400,356	965	-	-
2017	311,438	182,486	1,236	-	-	-
2018	734	-	-	-	-	-

Table 4. Summary of Follow-Up Time Since the First Observed Valid Diagnosis of Type 2 Diabetes in the Sentinel Distributed Database (SDD) from January 1, 2008 to January 31, 2018, by Washout Period, Type 2 Diabetes Diagnosis Definition, and Year

	Number of Patients by Follow-Up Time					
Year	< 6 months	6 to < 12 months	12 to < 24 months	24 to < 36 months	36 to < 48 months	48 months or longer
Type 2 Diabetes, First Inpatient Diagnosis						
2008	34,473	19,310	30,349	21,497	18,288	98,941
2009	70,136	43,715	56,741	42,919	33,829	168,144
2010	58,030	35,955	52,330	40,077	34,284	151,812
2011	281,377	134,069	213,440	180,707	156,491	839,229
2012	252,648	120,924	194,119	163,242	747,276	134,398
2013	215,524	106,299	165,457	719,317	60,529	98,190
2014	194,148	92,682	729,520	72,397	113,059	488
2015	484,008	394,091	90,106	141,253	523	-
2016	56,636	79,255	181,049	597	-	-
2017	153,067	83,073	637	-	-	-
2018	260	-	-	-	-	-
Type 2 Diabetes, Second Outpatient Diagnosis						
2008	38,402	33,324	55,445	40,337	37,065	252,851
2009	96,823	86,033	120,571	95,134	75,049	457,204
2010	80,117	70,238	110,135	83,183	77,131	371,481
2011	170,144	137,966	233,440	214,252	183,213	1,364,458
2012	157,575	127,344	225,439	188,705	1,072,006	280,317
2013	146,413	124,664	199,074	1,007,030	117,783	211,397
2014	138,328	107,205	971,878	138,924	244,783	790
2015	521,173	508,258	173,988	311,647	887	-
2016	73,023	157,657	385,805	891	-	-
2017	297,405	176,323	1,186	-	-	-
2018	725	-	-	-	-	-

Table 5. Summary of Follow-Up Time Since the First Observed Valid Dispensings of Antidiabetic Drugs in the Sentinel Distributed Database (SDD) from January 1, 2008 to January 31, 2018, by Drug Class

	TOTAL		Number of Patients by Follow-Up Time												Mean Follow-Up Time	Median Follow-Up Time
			< 6 months		6 to < 12 months		12 to < 24 months		24 to < 36 months		36 to < 48 months		48 months or longer			
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Months	Months
Alpha-Glucosidase Inhibitors	135,624	100%	18,825	13.9%	17,197	12.7%	24,901	18.4%	20,749	15.3%	15,666	11.6%	38,286	28.2%	34.0	28.2
Biguanides	14,798,290	100%	2,221,303	15.0%	2,166,807	14.6%	2,727,378	18.4%	2,140,726	14.5%	1,497,053	10.1%	4,045,023	27.3%	33.4	25.8
Dipeptidyl Peptidase-4 Inhibitors	3,506,542	100%	550,003	15.7%	504,855	14.4%	697,479	19.9%	577,494	16.5%	416,096	11.9%	760,615	21.7%	29.6	23.9
Glucagon-Like Peptide-1 Receptor Agonists	1,158,706	100%	220,070	19.0%	199,074	17.2%	251,872	21.7%	179,662	15.5%	113,308	9.8%	194,720	16.8%	26.3	19.7
Meglitinides	403,039	100%	55,335	13.7%	53,023	13.2%	72,701	18.0%	62,041	15.4%	45,205	11.2%	114,734	28.5%	34.0	28.5
Second Generation Sulfonylureas	8,069,775	100%	1,108,140	13.7%	1,104,863	13.7%	1,402,420	17.4%	1,165,507	14.4%	839,100	10.4%	2,449,745	30.4%	35.4	29.2
Sodium Glucose Cotransporter-2 Inhibitors	701,159	100%	192,565	27.5%	178,167	25.4%	197,113	28.1%	97,045	13.8%	32,006	4.6%	4,263	0.6%	14.2	11.3
Thiazolidinediones	2,578,288	100%	295,208	11.4%	327,097	12.7%	408,103	15.8%	321,185	12.5%	232,899	9.0%	993,796	38.5%	40.4	34.6

Table 6. Summary of Follow-Up Time Since the First Observed Valid Dispensings of Antidiabetic Drugs in the Sentinel Distributed Database (SDD) from January 1, 2008 to January 31, 2018, by Drug Class and Age Group

	Number of Patients by Follow-Up Time					
Age Group (Years)	< 6 months	6 to < 12 months	12 to < 24 months	24 to < 36 months	36 to < 48 months	48 months or longer
Alpha-Glucosidase Inhibitors						
18-44	1,707	1,364	1,913	1,224	913	2,078
45-54	2,288	2,088	2,738	2,010	1,548	4,066
55-64	3,808	3,506	4,748	3,423	2,720	6,304
65-74	6,427	5,922	8,768	7,956	6,058	15,196
75+	4,595	4,317	6,734	6,136	4,427	10,642
Biguanides						
18-44	390,825	324,091	391,552	237,171	161,347	364,212
45-54	408,628	363,518	452,524	296,864	215,339	564,102
55-64	533,946	504,216	626,488	431,800	311,645	733,409
65-74	629,464	690,330	884,741	810,842	562,192	1,626,314
75+	258,440	284,652	372,073	364,049	246,530	756,986
Dipeptidyl Peptidase-4 Inhibitors						
18-44	46,583	38,725	50,860	32,845	23,752	45,947
45-54	85,277	74,490	99,171	67,504	50,253	101,215
55-64	128,863	114,490	153,577	108,352	79,872	137,537
65-74	175,287	172,025	241,196	225,870	164,147	303,479
75+	113,993	105,125	152,675	142,923	98,072	172,437
Glucagon-Like Peptide-1 Receptor Agonists						
18-44	36,705	28,962	35,824	20,869	13,531	24,367
45-54	53,519	44,579	56,268	34,574	22,782	43,913
55-64	63,787	56,238	70,734	45,918	29,729	48,825
65-74	53,144	56,330	72,171	63,335	38,809	64,002
75+	12,915	12,965	16,875	14,966	8,457	13,613

Table 6. Summary of Follow-Up Time Since the First Observed Valid Dispensings of Antidiabetic Drugs in the Sentinel Distributed Database (SDD) from January 1, 2008 to January 31, 2018, by Drug Class and Age Group

	Number of Patients by Follow-Up Time					
Age Group (Years)	**< 6 months**	**6 to < 12 months**	**12 to < 24 months**	**24 to < 36 months**	**36 to < 48 months**	**48 months or longer**
Meglitinides						
18-44	2,255	2,045	2,655	1,818	1,382	3,667
45-54	4,964	4,509	6,192	4,444	3,386	9,597
55-64	9,569	8,868	12,132	8,664	6,579	15,902
65-74	17,727	17,886	24,381	22,679	16,769	45,014
75+	20,820	19,715	27,341	24,436	17,089	40,554
Second Generation Sulfonylureas						
18-44	116,993	97,110	117,297	75,630	54,060	135,761
45-54	171,677	153,993	191,995	130,418	98,474	275,436
55-64	255,726	242,753	304,630	217,464	161,548	409,050
65-74	341,807	372,398	475,382	441,927	317,803	994,952
75+	221,937	238,609	313,116	300,068	207,215	634,546
Sodium Glucose Cotransporter-2 Inhibitors						
18-44	23,693	18,954	22,036	12,157	4,184	528
45-54	42,990	36,271	43,264	25,035	9,407	1,283
55-64	57,205	49,548	56,611	31,597	11,427	1,567
65-74	53,668	57,799	58,781	22,306	5,646	714
75+	15,009	15,595	16,421	5,950	1,342	171
Thiazolidinediones						
18-44	29,857	27,808	33,638	21,407	15,220	56,368
45-54	51,520	52,672	66,664	44,124	32,405	128,524
55-64	73,734	79,328	100,727	69,555	51,015	181,316
65-74	92,351	109,576	133,295	117,500	84,495	410,016
75+	47,746	57,713	73,779	68,599	49,764	217,572

Table 7. Summary of Follow-Up Time Since the First Observed Valid Dispensings of Antidiabetic Drugs in the Sentinel Distributed Database (SDD) from January 1, 2008 to January 31, 2018, by Drug Class and Sex

	Number of Patients by Follow-Up Time					
Sex	**< 6 months**	**6 to < 12 months**	**12 to < 24 months**	**24 to < 36 months**	**36 to < 48 months**	**48 months or longer**
Alpha-Glucosidase Inhibitors						
Female	10,063	8,815	13,154	10,797	8,469	20,934
Male	8,762	8,382	11,747	9,952	7,197	17,352
Biguanides						
Female	1,179,468	1,114,256	1,411,401	1,108,637	790,217	2,223,656
Male	1,041,835	1,052,551	1,315,977	1,032,089	706,836	1,821,367
Dipeptidyl Peptidase-4 Inhibitors						
Female	277,742	245,282	345,750	290,316	215,325	405,670
Male	272,261	259,573	351,729	287,178	200,771	354,945
Glucagon-Like Peptide-1 Receptor Agonists						
Female	121,968	108,305	137,700	98,769	62,950	111,920
Male	98,102	90,769	114,172	80,893	50,358	82,800
Meglitinides						
Female	29,198	27,342	37,895	32,919	24,468	64,166
Male	26,137	25,681	34,806	29,122	20,737	50,568
Second Generation Sulfonylureas						
Female	544,444	525,680	673,972	566,844	420,239	1,292,842
Male	563,696	579,183	728,448	598,663	418,861	1,156,903
Sodium Glucose Cotransporter-2 Inhibitors						
Female	88,677	81,625	91,314	44,625	14,684	1,903
Male	103,888	96,542	105,799	52,420	17,322	2,360
Thiazolidinediones						
Female	137,655	146,351	181,893	143,940	108,105	501,955
Male	157,553	180,746	226,210	177,245	124,794	491,841

Sentinel

Table 8. Summary of Follow-Up Time Since the First Observed Valid Dispensings of Antidiabetic Drugs in the Sentinel Distributed Database (SDD) from January 1, 2008 to January 31, 2018, by Drug Class and Year

	Number of Patients by Follow-Up Time					
Year	< 6 months	6 to < 12 months	12 to < 24 months	24 to < 36 months	36 to < 48 months	48 months or longer
Alpha-Glucosidase Inhibitors						
2008	1,349	1,998	2,236	1,346	1,000	5,474
2009	607	560	789	526	361	2,083
2010	1,999	1,760	2,896	2,687	2,382	17,997
2011	1,393	1,095	1,670	1,408	1,348	8,054
2012	1,286	1,091	1,775	1,564	7,163	2,483
2013	1,468	1,334	1,965	9,259	941	2,188
2014	1,612	1,243	8,838	1,134	2,461	7
2015	5,247	4,867	1,492	2,816	10	-
2016	985	1,405	3,217	9	-	-
2017	2,859	1,844	23	-	-	-
2018	20	-	-	-	-	-
Biguanides						
2008	195,614	289,682	318,196	205,123	142,339	747,286
2009	76,992	81,169	99,979	65,543	42,233	201,750
2010	218,522	191,473	287,871	247,219	220,801	1,891,888
2011	139,740	122,238	159,928	124,891	104,848	686,847
2012	138,727	116,142	162,479	126,112	534,410	263,275
2013	151,617	142,719	187,924	796,405	110,583	252,935
2014	183,474	163,109	756,739	150,179	340,564	1,042
2015	484,101	498,939	225,081	422,911	1,275	-
2016	169,308	245,504	527,112	2,343	-	-
2017	460,450	315,832	2,069	-	-	-
2018	2,758	-	-	-	-	-

Table 8. Summary of Follow-Up Time Since the First Observed Valid Dispensings of Antidiabetic Drugs in the Sentinel Distributed Database (SDD) from January 1, 2008 to January 31, 2018, by Drug Class and Year

	Number of Patients by Follow-Up Time					
Year	< 6 months	6 to < 12 months	12 to < 24 months	24 to < 36 months	36 to < 48 months	48 months or longer
Dipeptidyl Peptidase-4 Inhibitors						
2008	23,038	27,220	37,027	23,188	16,536	64,228
2009	13,389	14,104	17,523	12,114	7,657	32,245
2010	38,020	32,363	52,296	45,354	40,605	301,889
2011	38,565	32,996	48,912	41,356	36,084	226,300
2012	41,661	35,374	55,287	46,504	211,084	71,095
2013	43,903	42,929	60,595	278,981	30,174	64,755
2014	48,900	43,040	255,593	35,543	73,854	103
2015	162,151	159,505	50,753	94,329	102	-
2016	37,287	50,823	119,383	125	-	-
2017	103,026	66,501	110	-	-	-
2018	63	-	-	-	-	-
Glucagon-Like Peptide-1 Receptor Agonists						
2008	11,436	15,786	19,852	12,585	8,858	34,740
2009	4,259	4,762	5,990	4,037	2,505	10,345
2010	8,239	7,673	11,968	8,935	8,414	61,489
2011	8,078	8,090	11,114	9,318	7,258	46,527
2012	9,244	8,891	14,410	10,723	47,916	19,357
2013	11,503	12,682	17,375	77,761	11,902	22,212
2014	13,032	13,583	77,341	15,134	26,405	50
2015	58,552	54,834	28,647	41,058	50	-
2016	19,906	34,519	65,066	111	-	-
2017	75,673	38,254	109	-	-	-
2018	148	-	-	-	-	-

Table 8. Summary of Follow-Up Time Since the First Observed Valid Dispensings of Antidiabetic Drugs in the Sentinel Distributed Database (SDD) from January 1, 2008 to January 31, 2018, by Drug Class and Year

	Number of Patients by Follow-Up Time					
Year	< 6 months	6 to < 12 months	12 to < 24 months	24 to < 36 months	36 to < 48 months	48 months or longer
Meglitinides						
2008	5,945	9,268	9,847	6,038	4,087	18,887
2009	2,186	2,160	2,612	1,686	1,217	5,279
2010	8,391	7,095	11,789	10,445	9,029	59,081
2011	4,644	3,524	5,104	4,320	3,919	21,625
2012	4,150	3,197	5,010	4,448	20,002	5,211
2013	4,034	3,802	5,505	27,066	2,117	4,643
2014	4,003	3,376	23,024	2,236	4,829	8
2015	13,944	13,580	2,820	5,798	5	-
2016	2,103	2,723	6,985	4	-	-
2017	5,934	4,298	5	-	-	-
2018	1	-	-	-	-	-
Second Generation Sulfonylureas						
2008	115,519	185,254	192,356	124,896	87,256	472,610
2009	38,609	40,857	48,693	31,578	21,354	106,297
2010	158,657	138,524	213,138	188,376	166,346	1,236,151
2011	82,404	69,259	92,560	72,969	63,375	384,953
2012	78,138	63,238	88,849	72,062	299,159	132,037
2013	80,464	74,846	99,703	429,863	49,280	117,210
2014	88,110	76,796	365,914	62,087	151,737	487
2015	224,576	234,551	87,524	182,727	593	-
2016	66,083	90,222	212,869	949	-	-
2017	174,603	131,316	814	-	-	-
2018	977	-	-	-	-	-

Table 8. Summary of Follow-Up Time Since the First Observed Valid Dispensings of Antidiabetic Drugs in the Sentinel Distributed Database (SDD) from January 1, 2008 to January 31, 2018, by Drug Class and Year

	Number of Patients by Follow-Up Time					
Year	< 6 months	6 to < 12 months	12 to < 24 months	24 to < 36 months	36 to < 48 months	48 months or longer
Sodium Glucose Cotransporter-2 Inhibitors						
2008	-	-	-	-	-	-
2009	-	-	-	-	-	-
2010	-	-	-	-	-	-
2011	-	-	-	-	-	-
2012	-	-	-	-	-	-
2013	3,911	2,382	4,197	13,934	4,683	4,251
2014	15,251	11,389	74,900	22,493	27,258	12
2015	73,897	80,627	38,886	60,493	65	-
2016	21,569	39,280	78,979	125	-	-
2017	77,663	44,489	151	-	-	-
2018	274	-	-	-	-	-
Thiazolidinediones						
2008	61,851	100,502	108,276	68,732	46,613	229,278
2009	19,589	22,181	27,203	17,705	11,626	55,065
2010	57,012	51,443	78,854	70,484	63,348	543,742
2011	22,626	21,023	26,135	20,518	19,083	120,855
2012	12,258	10,384	14,392	12,017	55,628	22,164
2013	11,944	12,743	16,921	85,011	9,317	22,654
2014	13,370	13,053	73,336	11,396	27,234	38
2015	46,717	49,858	17,297	35,220	50	-
2016	11,809	18,889	45,610	102	-	-
2017	37,903	27,021	79	-	-	-
2018	129	-	-	-	-	-

Appendix A. Dates of Available Data for Each Data Partner (DP) as of Request Distribution Date (June 28, 2018)

Data Partner ID	Start Date[1]	End Date[1]
DP01	1/1/2008	11/30/2017
DP02	1/1/2012	6/30/2017
DP03	1/1/2010	12/31/2015
DP04	1/1/2006	10/31/2017
DP05	1/1/2004	1/31/2018
DP06	1/1/2000	6/30/2017
DP07	1/1/2000	1/31/2017
DP08	1/1/2000	3/31/2016
DP09	1/1/2000	5/31/2015
DP10	6/1/2007	10/31/2017
DP11	1/1/2000	10/31/2017
DP12	1/1/2000	7/31/2017
DP13	1/1/2005	12/17/2017
DP14	1/1/2000	12/31/2017
DP15	1/1/2000	8/31/2017
DP16	1/1/2008	6/30/2017
DP17	1/1/2000	12/31/2016

[1]The start and end dates are based on the minimum and maximum dates within each DP. The month with the maximum date must have at least 80% of the number of records in the previous month.

Appendix B. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Diagnosis Codes Used to Define Type 2 Diabetes Events in this Request

Code	Description	Code Type
	Type 2 Diabetes	
250.00	Diabetes mellitus without mention of complication, type II or unspecified type, not stated as uncontrolled	ICD-9-CM
250.10	Diabetes with ketoacidosis, type II or unspecified type, not stated as uncontrolled	ICD-9-CM
250.20	Diabetes with hyperosmolarity, type II or unspecified type, not stated as uncontrolled	ICD-9-CM
250.30	Diabetes with other coma, type II or unspecified type, not stated as uncontrolled	ICD-9-CM
250.40	Diabetes with renal manifestations, type II or unspecified type, not stated as uncontrolled	ICD-9-CM
250.50	Diabetes with ophthalmic manifestations, type II or unspecified type, not stated as uncontrolled	ICD-9-CM
250.60	Diabetes with neurological manifestations, type II or unspecified type, not stated as uncontrolled	ICD-9-CM
250.70	Diabetes with peripheral circulatory disorders, type II or unspecified type, not stated as uncontrolled	ICD-9-CM
250.80	Diabetes with other specified manifestations, type II or unspecified type, not stated as uncontrolled	ICD-9-CM
250.90	Diabetes with unspecified complication, type II or unspecified type, not stated as uncontrolled	ICD-9-CM
250.02	Diabetes mellitus without mention of complication, type II or unspecified type, uncontrolled	ICD-9-CM
250.12	Diabetes with ketoacidosis, type II or unspecified type, uncontrolled	ICD-9-CM
250.22	Diabetes with hyperosmolarity, type II or unspecified type, uncontrolled	ICD-9-CM
250.32	Diabetes with other coma, type II or unspecified type, uncontrolled	ICD-9-CM
250.42	Diabetes with renal manifestations, type II or unspecified type, uncontrolled	ICD-9-CM
250.52	Diabetes with ophthalmic manifestations, type II or unspecified type, uncontrolled	ICD-9-CM
250.62	Diabetes with neurological manifestations, type II or unspecified type, uncontrolled	ICD-9-CM
250.72	Diabetes with peripheral circulatory disorders, type II or unspecified type, uncontrolled	ICD-9-CM
250.82	Diabetes with other specified manifestations, type II or unspecified type, uncontrolled	ICD-9-CM
250.92	Diabetes with unspecified complication, type II or unspecified type, uncontrolled	ICD-9-CM
E11.00	Type 2 diabetes mellitus with hyperosmolarity without nonketotic hyperglycemic-hyperosmolar coma (NKHHC)	ICD-10-CM
E11.01	Type 2 diabetes mellitus with hyperosmolarity with coma	ICD-10-CM
E11.10	Type 2 diabetes mellitus with ketoacidosis without coma	ICD-10-CM
E11.11	Type 2 diabetes mellitus with ketoacidosis with coma	ICD-10-CM
E11.21	Type 2 diabetes mellitus with diabetic nephropathy	ICD-10-CM
E11.22	Type 2 diabetes mellitus with diabetic chronic kidney disease	ICD-10-CM
E11.29	Type 2 diabetes mellitus with other diabetic kidney complication	ICD-10-CM
E11.311	Type 2 diabetes mellitus with unspecified diabetic retinopathy with macular edema	ICD-10-CM
E11.319	Type 2 diabetes mellitus with unspecified diabetic retinopathy without macular edema	ICD-10-CM
E11.3211	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, right eye	ICD-10-CM
E11.3212	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, left eye	ICD-10-CM

Appendix B. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Diagnosis Codes Used to Define Type 2 Diabetes Events in this Request

Code	Description	Code Type
E11.3213	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, bilateral	ICD-10-CM
E11.3219	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, unspecified eye	ICD-10-CM
E11.3291	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, right eye	ICD-10-CM
E11.3292	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, left eye	ICD-10-CM
E11.3293	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, bilateral	ICD-10-CM
E11.3299	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, unspecified eye	ICD-10-CM
E11.3311	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, right eye	ICD-10-CM
E11.3312	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, left eye	ICD-10-CM
E11.3313	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, bilateral	ICD-10-CM
E11.3319	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, unspecified eye	ICD-10-CM
E11.3391	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, right eye	ICD-10-CM
E11.3392	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, left eye	ICD-10-CM
E11.3393	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, bilateral	ICD-10-CM
E11.3399	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, unspecified eye	ICD-10-CM
E11.3411	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, right eye	ICD-10-CM
E11.3412	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, left eye	ICD-10-CM
E11.3413	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, bilateral	ICD-10-CM
E11.3419	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, unspecified eye	ICD-10-CM
E11.3491	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, right eye	ICD-10-CM
E11.3492	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, left eye	ICD-10-CM
E11.3493	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, bilateral	ICD-10-CM

Appendix B. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Diagnosis Codes Used to Define Type 2 Diabetes Events in this Request

Code	Description	Code Type
E11.3499	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, unspecified eye	ICD-10-CM
E11.3511	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, right eye	ICD-10-CM
E11.3512	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, left eye	ICD-10-CM
E11.3513	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, bilateral	ICD-10-CM
E11.3519	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, unspecified eye	ICD-10-CM
E11.3521	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, right eye	ICD-10-CM
E11.3522	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, left eye	ICD-10-CM
E11.3523	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, bilateral	ICD-10-CM
E11.3529	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment in	ICD-10-CM
E11.3531	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment n	ICD-10-CM
E11.3532	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment n	ICD-10-CM
E11.3533	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment n	ICD-10-CM
E11.3539	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, unspecified eye	ICD-10-CM
E11.3541	Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, right eye	ICD-10-CM
E11.3542	Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, left eye	ICD-10-CM
E11.3543	Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, bilateral	ICD-10-CM
E11.3549	Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, unspecified eye	ICD-10-CM
E11.3551	Type 2 diabetes mellitus with stable proliferative diabetic retinopathy, right eye	ICD-10-CM
E11.3552	Type 2 diabetes mellitus with stable proliferative diabetic retinopathy, left eye	ICD-10-CM
E11.3553	Type 2 diabetes mellitus with stable proliferative diabetic retinopathy, bilateral	ICD-10-CM
E11.3559	Type 2 diabetes mellitus with stable proliferative diabetic retinopathy, unspecified eye	ICD-10-CM
E11.3591	Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema, right eye	ICD-10-CM
E11.3592	Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema, left eye	ICD-10-CM
E11.3593	Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema, bilateral	ICD-10-CM
E11.3599	Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema, unspecified eye	ICD-10-CM

Appendix B. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Diagnosis Codes Used to Define Type 2 Diabetes Events in this Request

Code	Description	Code Type
E11.36	Type 2 diabetes mellitus with diabetic cataract	ICD-10-CM
E11.37X1	Type 2 diabetes mellitus with diabetic macular edema, resolved following treatment, right eye	ICD-10-CM
E11.37X2	Type 2 diabetes mellitus with diabetic macular edema, resolved following treatment, left eye	ICD-10-CM
E11.37X3	Type 2 diabetes mellitus with diabetic macular edema, resolved following treatment, bilateral	ICD-10-CM
E11.37X9	Type 2 diabetes mellitus with diabetic macular edema, resolved following treatment, unspecified eye	ICD-10-CM
E11.39	Type 2 diabetes mellitus with other diabetic ophthalmic complication	ICD-10-CM
E11.40	Type 2 diabetes mellitus with diabetic neuropathy, unspecified	ICD-10-CM
E11.41	Type 2 diabetes mellitus with diabetic mononeuropathy	ICD-10-CM
E11.42	Type 2 diabetes mellitus with diabetic polyneuropathy	ICD-10-CM
E11.43	Type 2 diabetes mellitus with diabetic autonomic (poly)neuropathy	ICD-10-CM
E11.44	Type 2 diabetes mellitus with diabetic amyotrophy	ICD-10-CM
E11.49	Type 2 diabetes mellitus with other diabetic neurological complication	ICD-10-CM
E11.51	Type 2 diabetes mellitus with diabetic peripheral angiopathy without gangrene	ICD-10-CM
E11.52	Type 2 diabetes mellitus with diabetic peripheral angiopathy with gangrene	ICD-10-CM
E11.59	Type 2 diabetes mellitus with other circulatory complications	ICD-10-CM
E11.610	Type 2 diabetes mellitus with diabetic neuropathic arthropathy	ICD-10-CM
E11.618	Type 2 diabetes mellitus with other diabetic arthropathy	ICD-10-CM
E11.620	Type 2 diabetes mellitus with diabetic dermatitis	ICD-10-CM
E11.621	Type 2 diabetes mellitus with foot ulcer	ICD-10-CM
E11.622	Type 2 diabetes mellitus with other skin ulcer	ICD-10-CM
E11.628	Type 2 diabetes mellitus with other skin complications	ICD-10-CM
E11.630	Type 2 diabetes mellitus with periodontal disease	ICD-10-CM
E11.638	Type 2 diabetes mellitus with other oral complications	ICD-10-CM
E11.641	Type 2 diabetes mellitus with hypoglycemia with coma	ICD-10-CM
E11.649	Type 2 diabetes mellitus with hypoglycemia without coma	ICD-10-CM
E11.65	Type 2 diabetes mellitus with hyperglycemia	ICD-10-CM
E11.69	Type 2 diabetes mellitus with other specified complication	ICD-10-CM
E11.8	Type 2 diabetes mellitus with unspecified complications	ICD-10-CM
E11.9	Type 2 diabetes mellitus without complications	ICD-10-CM

Appendix C. List of Generic and Brand Drug Names Used to Define Antidiabetic Exposures in this Request

Generic Name	Brand Name
Alpha-Glucosidase Inhibitors	
ACARBOSE	Acarbose
ACARBOSE	Precose
MIGLITOL	Glyset
MIGLITOL	Miglitol
Biguanides	
METFORMIN HCL	Metformin
METFORMIN HCL	Glucophage
METFORMIN HCL	Glucophage Xr
METFORMIN HCL	Riomet
METFORMIN HCL	Fortamet
METFORMIN HCL	Glumetza
CANAGLIFLOZIN/METFORMIN HCL	Invokamet
CANAGLIFLOZIN/METFORMIN HCL	Invokamet Xr
DAPAGLIFLOZIN PROPANEDIOL/METFORMIN HCL	Xigduo Xr
EMPAGLIFLOZIN/METFORMIN HCL	Synjardy
EMPAGLIFLOZIN/METFORMIN HCL	Synjardy Xr
ALOGLIPTIN BENZOATE/METFORMIN HCL	Kazano
ALOGLIPTIN BENZOATE/METFORMIN HCL	Alogliptin-Metformin
LINAGLIPTIN/METFORMIN HCL	Jentadueto
LINAGLIPTIN/METFORMIN HCL	Jentadueto Xr
SAXAGLIPTIN HCL/METFORMIN HCL	Kombiglyze Xr
SITAGLIPTIN PHOSPHATE/METFORMIN HCL	Janumet
SITAGLIPTIN PHOSPHATE/METFORMIN HCL	Janumet Xr
REPAGLINIDE/METFORMIN HCL	Prandimet
REPAGLINIDE/METFORMIN HCL	Repaglinide-Metformin
GLIPIZIDE/METFORMIN HCL	Glipizide-Metformin
GLIPIZIDE/METFORMIN HCL	Metaglip
GLYBURIDE/METFORMIN HCL	Glucovance
GLYBURIDE/METFORMIN HCL	Glyburide-Metformin
PIOGLITAZONE HCL/METFORMIN HCL	Actoplus Met
PIOGLITAZONE HCL/METFORMIN HCL	Pioglitazone-Metformin
PIOGLITAZONE HCL/METFORMIN HCL	Actoplus Met Xr
METFORMIN HCL/BLOOD SUGAR DIAGNOSTIC	Dm2
ROSIGLITAZONE MALEATE/METFORMIN HCL	Avandamet
Dipeptidyl Peptidase-4 Inhibitors	
ALOGLIPTIN BENZOATE	Nesina
ALOGLIPTIN BENZOATE	Alogliptin
LINAGLIPTIN	Tradjenta
SAXAGLIPTIN HCL	Onglyza
SITAGLIPTIN PHOSPHATE	Januvia
ALOGLIPTIN BENZOATE/METFORMIN HCL	Kazano
ALOGLIPTIN BENZOATE/METFORMIN HCL	Alogliptin-Metformin
LINAGLIPTIN/METFORMIN HCL	Jentadueto

Appendix C. List of Generic and Brand Drug Names Used to Define Antidiabetic Exposures in this Request

Generic Name	Brand Name
LINAGLIPTIN/METFORMIN HCL	Jentadueto Xr
SAXAGLIPTIN HCL/METFORMIN HCL	Kombiglyze Xr
SITAGLIPTIN PHOSPHATE/METFORMIN HCL	Janumet
SITAGLIPTIN PHOSPHATE/METFORMIN HCL	Janumet Xr
ALOGLIPTIN BENZOATE/PIOGLITAZONE HCL	Oseni
ALOGLIPTIN BENZOATE/PIOGLITAZONE HCL	Alogliptin-Pioglitazone
DAPAGLIFLOZIN PROPANEDIOL/SAXAGLIPTIN HCL	Qtern
EMPAGLIFLOZIN/LINAGLIPTIN	Glyxambi
Glucagon-Like Peptide-1 Receptor Agonists	
ALBIGLUTIDE	Tanzeum
EXENATIDE	Byetta
EXENATIDE MICROSPHERES	Bydureon Bcise
EXENATIDE MICROSPHERES	Bydureon
LIRAGLUTIDE	Victoza 3-Pak
LIRAGLUTIDE	Victoza 2-Pak
DULAGLUTIDE	Trulicity
INSULIN DEGLUDEC/LIRAGLUTIDE	Xultophy 100/3.6
LIXISENATIDE	Adlyxin
SEMAGLUTIDE	Ozempic
Meglitinides	
NATEGLINIDE	Nateglinide
NATEGLINIDE	Starlix
REPAGLINIDE	Prandin
REPAGLINIDE	Repaglinide
REPAGLINIDE/METFORMIN HCL	Prandimet
REPAGLINIDE/METFORMIN HCL	Repaglinide-Metformin
Second Generation Sulfonylureas	
GLIMEPIRIDE	Glimepiride
GLIMEPIRIDE	Amaryl
GLIPIZIDE	Glipizide
GLIPIZIDE	Glucotrol Xl
GLIPIZIDE	Glucotrol
GLYBURIDE	Glyburide
GLYBURIDE	Micronase
GLYBURIDE	Diabeta
GLYBURIDE,MICRONIZED	Glyburide Micronized
GLYBURIDE,MICRONIZED	Glynase
GLYBURIDE,MICRONIZED	Glycron
GLIPIZIDE/METFORMIN HCL	Glipizide-Metformin
GLIPIZIDE/METFORMIN HCL	Metaglip
GLYBURIDE/METFORMIN HCL	Glucovance
GLYBURIDE/METFORMIN HCL	Glyburide-Metformin
PIOGLITAZONE HCL/GLIMEPIRIDE	Pioglitazone-Glimepiride
PIOGLITAZONE HCL/GLIMEPIRIDE	Duetact

Appendix C. List of Generic and Brand Drug Names Used to Define Antidiabetic Exposures in this Request

Generic Name	Brand Name
ROSIGLITAZONE MALEATE/GLIMEPIRIDE	Avandaryl
Sodium Glucose Cotransporter-2 Inhibitors	
CANAGLIFLOZIN	Invokana
CANAGLIFLOZIN/METFORMIN HCL	Invokamet
CANAGLIFLOZIN/METFORMIN HCL	Invokamet Xr
DAPAGLIFLOZIN PROPANEDIOL	Farxiga
DAPAGLIFLOZIN PROPANEDIOL/METFORMIN HCL	Xigduo Xr
DAPAGLIFLOZIN PROPANEDIOL/SAXAGLIPTIN HCL	Qtern
EMPAGLIFLOZIN	Jardiance
EMPAGLIFLOZIN/LINAGLIPTIN	Glyxambi
EMPAGLIFLOZIN/METFORMIN HCL	Synjardy
EMPAGLIFLOZIN/METFORMIN HCL	Synjardy Xr
Thiazolidinediones	
PIOGLITAZONE HCL	Actos
PIOGLITAZONE HCL	Pioglitazone
PIOGLITAZONE HCL/METFORMIN HCL	Actoplus Met
PIOGLITAZONE HCL/METFORMIN HCL	Pioglitazone-Metformin
PIOGLITAZONE HCL/METFORMIN HCL	Actoplus Met Xr
PIOGLITAZONE HCL/GLIMEPIRIDE	Pioglitazone-Glimepiride
PIOGLITAZONE HCL/GLIMEPIRIDE	Duetact
ALOGLIPTIN BENZOATE/PIOGLITAZONE HCL	Oseni
ALOGLIPTIN BENZOATE/PIOGLITAZONE HCL	Alogliptin-Pioglitazone
ROSIGLITAZONE MALEATE	Avandia
ROSIGLITAZONE MALEATE/METFORMIN HCL	Avandamet
ROSIGLITAZONE MALEATE/GLIMEPIRIDE	Avandaryl

Appendix D. Specifications for Parameters for this Request, Analysis 1

This request used the Cohort Identification and Descriptive Analysis (CIDA) tool, version 5.4.3, to estimate available follow-up time for patients diagnosed with Type 2 diabetes in the Sentinel Distributed Database (SDD).

Query Period: January 1, 2008 - January 31, 2018
Coverage Requirement: At least medical coverage
Enrollment Requirement: Varies by scenario; see below
Enrollment Gap: 45 days
Age Groups: 18-44, 45-54, 55-64, 65-74, 75+ years
Sex: Male and Female

	Event											Follow-up			
Scenario	Event	Code Days	Minimum Code Distance (days)	Maximum Code Distance (days)	Code Date	Event Care Setting	Washout (days)	Incidence with Respect to	Washout Care Setting	Cohort Definition	Enrollment Requirement (days)	Follow-up Start	Follow-up End	Censor due to Evidence of Death	Categories of Follow-up Time
1	Type 2 diabetes	1	n/a	n/a	n/a	IP*	0	n/a	n/a	Include the first valid event	0	First Event	Censoring	Yes	<6m, 6-11m, 12-23m, 24-35m, 36-47m, 48m+
		2	1	90	Max	AV*, OA*									
2	Type 2 diabetes	1	n/a	n/a	n/a	IP*	0	n/a	n/a	Include the first valid event	0	First Event	Censoring	Yes	<6m, 6-11m, 12-23m, 24-35m, 36-47m, 48m+
3	Type 2 diabetes	2	1	90	Max	AV*, OA*	0	n/a	n/a	Include the first valid event	0	First Event	Censoring	Yes	<6m, 6-11m, 12-23m, 24-35m, 36-47m, 48m+

	Event										Follow-up			
Scenario	Event	Code Days	Minimum Code Distance (days)	Maximum Code Distance (days)	Code Date	Event Care Setting	Washout (days)	Incidence with Respect to	Washout Care Setting	Cohort Definition	Enrollment Requirement (days)	Follow-up Start	Follow-up End	Censor due to Evidence of Death	Categories of Follow-up Time
4	Type 2 diabetes	1	n/a	n/a	n/a	IP*	365	Type 2 diabetes diagnosis	IP*, AV*, OA*	Include the first valid event	365	First Event	Censoring	Yes	<6m, 6-11m, 12-23m, 24-35m, 36-47m, 48m+
		2	1	90	Max	AV*, OA*									
5	Type 2 diabetes	1	n/a	n/a	n/a	IP*	365	Type 2 diabetes diagnosis	IP*	Include the first valid event	365	First Event	Censoring	Yes	<6m, 6-11m, 12-23m, 24-35m, 36-47m, 48m+
6	Type 2 diabetes	2	1	90	Max	AV*, OA*	365	Type 2 diabetes diagnosis	AV*, OA*	Include the first valid event	365	First Event	Censoring	Yes	<6m, 6-11m, 12-23m, 24-35m, 36-47m, 48m+

Code days: minimum number of separate day code occurrences required to meet criteria
Code date: the date of a code occurrence included in code days that defines the index date
Care setting options: potential care settings are inpatient hospital stay (IP), ambulatory visit (AV) or other ambulatory visit (OA), in any diagnosis position.
International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis codes are provided by Optum360

Appendix E. Specifications for Parameters for this Request, Analysis 2

This request used the Cohort Identification and Descriptive Analysis (CIDA) tool, version 5.4.3, to estimate available follow-up time for patients treated with non-insulin antidiabetic drugs in the Sentinel Distributed Database (SDD).

Query Period: January 1, 2008 - January 31, 2018
Coverage Requirement: At least drug coverage
Enrollment Requirement: 0 days
Enrollment Gap: 45 days
Age Groups: 18-44, 45-54, 55-64, 65-74, 75+ years
Sex: Male and Female

	Drug/Exposure					Follow-up			
Scenario	Exposure	Incidence with respect to	Care Setting	Washout (days)	Cohort Definition	Follow-up Start	Follow-up End	Censor due to Evidence of Death	Categories of Follow-up Time
1	Biguanides	n/a	Any	0	Include only the first valid exposure	First exposure	Censoring	Yes	<6m, 6-11m, 12-23m, 24-35m, 36-47m, 48m+
2	Second generation sulfonylureas	n/a	Any	0	Include only the first valid exposure	First exposure	Censoring	Yes	<6m, 6-11m, 12-23m, 24-35m, 36-47m, 48m+
3	Thiazolidinediones	n/a	Any	0	Include only the first valid exposure	First exposure	Censoring	Yes	<6m, 6-11m, 12-23m, 24-35m, 36-47m, 48m+
4	Glucagon-like peptide-1 receptor agonists	n/a	Any	0	Include only the first valid exposure	First exposure	Censoring	Yes	<6m, 6-11m, 12-23m, 24-35m, 36-47m, 48m+
5	Sodium glucose cotransporter-2 inhibitors	n/a	Any	0	Include only the first valid exposure	First exposure	Censoring	Yes	<6m, 6-11m, 12-23m, 24-35m, 36-47m, 48m+
6	Dipeptidyl peptidase-4 inhibitors	n/a	Any	0	Include only the first valid exposure	First exposure	Censoring	Yes	<6m, 6-11m, 12-23m, 24-35m, 36-47m, 48m+
7	Alpha-glucosidase inhibitors	n/a	Any	0	Include only the first valid exposure	First exposure	Censoring	Yes	<6m, 6-11m, 12-23m, 24-35m, 36-47m, 48m+
8	Meglitinides	n/a	Any	0	Include only the first valid exposure	First exposure	Censoring	Yes	<6m, 6-11m, 12-23m, 24-35m, 36-47m, 48m+

National Drug Codes (NDCs) were checked against First Data Bank's "National Drug Data File (NDDF®) Plus"