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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Modular Program Report

Overview

Request Description

The Applied Surveillance Core and FDA have requested execution of the Cohort Identification and Descriptive Analysis (CIDA) tool along with the Propensity Score Matching (PSM) tool to investigate severe hypoglycemia events following new use of glyburide versus glipizide in the Sentinel Distributed Database. This package was distributed to 15 Data Partners on February 24, 2015. ***This report includes results from the 5 Data Partners for which the high-dimensional propensity score (hdPS) analysis ran successfully and converged.*** The query period for this request was January 1, 2008 to September 30, 2014. Please see Appendices A - C for a list of all codes used to define exposures, outcomes, and covariates in this request.

This is one of four reports for this request. **This report displays the results for severe hypoglycemia events in any diagnosis position for emergency department encounters or first-listed diagnosis for inpatient encounters**. Another report displays the results for severe hypoglycemia events in any diagnosis position for emergency department encounters only for the 5 Data Partners for which the hdPS analysis ran successfully. Two additional reports display results for 13 Data Partners.

Request ID	to16_cap_mpl2r_wp001_nsdp_v01 (Report 1 of 4)
Requester	Sentinel Applied Surveillance Core
Glossary	List of Terms found in this Report and their Definitions
Table 1	Table displaying Cohort of New Initiators of Glyburide and Glipizide (Unmatched)
Table 2	Table displaying Cohort of New Initiators of Glyburide and Glipizide (Matched 1:1 Predefined PS, Caliper = 0.025)
Table 3	Table displaying Cohort of New Initiators of Glyburide and Glipizide (Matched 1:1 HDPS+ Predefined PS, Caliper = 0.025)
Table 4	Table displaying Cohort of New Initiators of Glyburide and Glipizide (Matched 1:1 HDPS only, Caliper= 0.025)
Table 5	Table displaying Sequential Estimates for Severe Hypoglycemia Events by Analysis Type and Drug Pair (Glyburide vs. Glipizide)
Appendix A	Table of Generic Names used to Define Exposures in this Request
Appendix B	Table of Diagnosis Codes and Algorithm used to Define Severe Hypoglycemia in this Request
Appendix C	Table of Codes and Generic Names used to Define Covariates in this Request
Specifications	Program parameter inputs and scenarios

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

Glossary of Terms for Analyses Using Cohort Idendification and Descriptive Analyis (CIDA) Tool*

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

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

Cohort Definition (drug/exposure)- Indicates how the cohort will be defined: (1) 01: Cohort includes only the first valid incident treatment episode during the query period; (2) 02: Cohort includes all valid incident treatment episodes during the query period; (3) 03: Cohort includes all valid incident treatment episodes during the query period until an event occurs

Days Supplied - number of days supplied for all dispensings in qualifying treatment episodes

Episodes - treatment episodes; length of episode is determined by days supplied in one dispensing (or consecutive dispensings bridged by the

Enrollment Gap - number of days allowed between two consecutive enrollment periods without breaking a “continuously enrolled” sequence

Episode Gap - number of days allowed between two (or more) consecutive exposures (dispensings/procedures) to be considered the same

Event Deduplication - specifies how events are counted by the MP algorithm: (0): 0: Counts all occurrences of and HOI during an exposure episode; (1) 1: de-duplicates occurrences of the same HOI code and code type on the same day; (3) 3: de-duplicates occurrences of the same HOI group on the same day (eg. de-duplicates at the group level)

Exposure Extension Period - number of days post treatment period in which the outcomes/events are counted for a treatment episode

Exposure Episode Length - number of days after exposure initiation that is considered "exposed time"

Induction 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

Lookback Period (pre-existing condition) - number of days wherein a member is required to have evidence of pre-existing condition (diagnosis/procedure/drug dispensing)

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

Query Period - period in which the modular program looks for exposures and outcomes of interest

Treatment Episode Truncation Indicator - indicates whether observation of the incident query code during follow-up requires truncation of valid treatment episodes. A value of Y indicates that the treatment episodes should be truncated at the first occurrence of an incident query code. A value of N indicates that the treatment episodes should not be truncated at the occurrence of the incident query code

Users - number of members with exposure during the query period. Member must have no evidence of exposure (s) of interest (defined by incidence criteria) in the prior washout period. A user may only be counted once in a query period.

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

**incident treatment episodes must be incident to both the exposure and the event

Glossary of Terms for Analyses Using Propensity Score Match (PSM) Tool*

Bias Ranking - method for ranking/prioritizing covariates for inclusion in the hdPS model. This method yields a variable list in which variables are selected as ranked by the Bross bias formula.

Covariate Evaluation Window - number of days before the index date to evaluate the occurrence of covariates of interest.Note: members are required to have continuous enrollment during the covariate evaluation window, regardless of the value included in the "Continuous

Covariate Grouping Indicator - a requester-defined name used to indicate how codes should be grouped to identify a single covariate.

Exposure association ranking- default method for ranking/prioritizing covariates for inclusion in the hdPS model. This method yields a variable list in which the variables are selected as ranked by the strength of the relationship between confounder and exposure. This is most suitable for cases where there are fewer than 150 exposed outcomes.

High dimensional Propensity Score (hdPS) - allows for selection of empirically identified covariates in addition to and/or without predefined covariates based on the potential for confounding the exposure/outcome association under investigation.

Mahalanobis Distance- provides a measure of balance across all variables while accounting for their correlation.

Matching Caliper- maximum allowed difference in propensity scores between treatment and control patients. Options are 0.01, 0.025, and

Matching Ratio - patients in exposed and comparators are nearest neighbor matched by a 1:1 or 1:100 (up to 100) matching ratio.

Monitoring Period - used to define time periods of interest for both sequential analysis and simple cohort characterization requests.

Number of covariates from pool of considered covariates to keep in hdPS model - The total number of covariates to keep in the hdPS model. Default value is the fewest of 1) 200; or 2) the number of initiators of the exposure of interest.

Number of covariates to consider for each claim type for inclusion in hdPS model - The number of covariates that are considered for inclusion in the hdPS model for each claim type (NDC, ICD9 diagnosis, ICD9 procedure, HCPCS, and CPT). If a value of 100 is specified in this field, then 500 covariates will be considered for inclusion (100 for each of the 5 claim types), Default value is 100.

Outcome Association Ranking- method for ranking/prioritizing covariates for inclusion in the hdPS model. This method yields a variable list in which the variables are selected as ranked by the strength of the relationship between confounder and the outcome. This is most suitable for

Predefined Propensity Score Matched Analysis - performed by default using the Propensity Score Match Tool. Requester-defined covariates are included along with 12 other covariates: 1. Age (continuous) 2. Sex 3. Time (monitoring period) 4. Year of Exposure 5. Comorbidity Score (calculated during requester-defined lookback) 6. Medical Utilization- number of inpatient stays (during requester-defined lookback) 7. Medical Utilization- number of institutional stays (during requester-defined lookback) 8. Medical utilization- number of emergency department visits (during requester-defined lookback) 9. Medical utilization- number of outpatient visits (during requester-defined lookback) 10. Health care utilization- number of other ambulatory encounters (e.g telemedicine, email consults during requester-defined lookback) 11. Drug utilization- number of dispensings (during requester-defined lookback) 12. Drug utilization- number of unique generics dispensed (during requester-defined lookback).

Propensity Score Match Tool - performs effect estimation by comparing exposure propensity-score matched parallel new user cohorts. The Propensity Score Match Tool generates tables of patient characteristics, stratified by exposure group, for the unmatched cohort and for the 1:1 matched cohort. Tables include measures of covariate balance and the Mahalanobis distance. The program also generates histograms depicting the propensity score distributions for each exposure group, separately for each Data Partner and each monitoring period, before and after matching. Figures include c-statistics. This program provides hazard ratios and 95% confidence intervals, Mantel-Haenszel rate differences, the number needed to treat/harm, the attributable risk, and the population attributable risk.

Query Level - Sentinel routine data queries are grouped into three distinct "levels," indicative of the level of complexity, extent of analytic adjustment, and need for repeated execution and alerting tools (i.e., prospective surveillance).

Zero Cell Correction - An indicator for whether to screen variables with a zero correction added to each cell in the confounder/outcome 2x2 table. Recommended when the number of exposed outcomes is fewer than 150.

*all terms may not be used in this report

Table 1. Cohort of New Initiators of Glyburide and Glipizide at Risk for Severe Hypoglycemia[1] in the Emergency Department or first-listed diagnosis in the Inpatient setting (Unmatched)

	Primary Analysis				Covariate Balance	
Characteristic	**Glyburide**		**Glipizide**			
Patients (N)	139,116	100.0%	181,912	100.0%		
Median person-days at risk*	74		99			
	N	**%/Std Dev[2]**	**N**	**%/Std Dev[2]**	**Absolute Difference**	**Standardized Difference**
Patient Characteristics						
Gender (F)	69,491	50.0%	75,873	41.7%	8.3	0.165
Mean age (std dev)	52.8	14.1	57	12.5	-4.1	-0.311
Recorded History of[3]:						
Chronic Kidney Disease	4,704	3.4%	11,470	6.3%	-2.9	-0.136
Hypoglycemia	2,555	1.8%	4,367	2.4%	-0.6	-0.039
Insulin	8,552	6.1%	14,669	8.1%	-2.0	-0.075
Metformin	44,603	32.1%	79,171	43.5%	-11.4	-0.236
Other ADAs	22,311	16.0%	39,383	21.6%	-5.6	-0.144
Combined Comorbidity Score	0.3	1.5	0.4	1.8	-0.2	-0.103
Health Service Utilization Intensity:	Mean	Std Dev	Mean	Std Dev		
Number of generic drugs	4.9	4.1	5.7	4.5	-0.8	-0.194
Number of filled prescriptions	11.8	12.6	14.5	14.1	-2.7	-0.201
Number of inpatient hospital encounters (IP)	0.1	0.5	0.2	0.5	-0.1	-0.125
Number of non-acute institutional encounters (IS)	0.1	1.0	0.1	1.2	-0.1	-0.055
Number of emergency room encounters (ED)	0.3	0.7	0.3	0.9	0.0	0.000
Number of ambulatory encounters (AV)	6.6	7.6	6.5	8.4	0.1	0.014
Number of other ambulatory encounters (OA)	1.5	3.2	1.4	3.4	0.1	0.036

[1]See Appendix B for the list of codes used to define events

[2]Value represents standard deviation where no % follows the value

[3]See Appendix C for list of codes used to define these covariates

*Median person-days are risk was calculated after several patients were removed due to Data Partner compliance reasons.

Table 2. Cohort of New Initiators of Glyburide and Glipizide at Risk for Severe Hypoglycemia[1] in the Emergency Department or first-listed diagnosis in the Inpatient setting (Matched 1:1 Predefined PS, Caliper = .025)

	Primary Analysis				Covariate Balance	
Characteristic	**Glyburide**		**Glipizide**			
Patients (N)	120,336	86.5%	120,336	66.2%		
Median person-days at risk*	77		86			
	N	**%/Std Dev[2]**	**N**	**%/Std Dev[2]**	**Absolute Difference**	**Standardized Difference**
Patient Characteristics						
Gender (F)	52,058	43.3%	53,888	44.8%	-1.5	-0.031
Mean age (std dev)	55.5	12.9	55.2	12.4	0.3	0.021
Recorded History of[3]:						
Chronic Kidney Disease	4,648	3.9%	5,483	4.6%	-0.7	-0.035
Hypoglycemia	2,465	2.0%	2,547	2.1%	-0.1	-0.005
Insulin	8,272	6.9%	8,427	7.0%	-0.1	-0.005
Metformin	43,977	36.5%	45,167	37.5%	-1.0	-0.020
Other ADAs	22,137	18.4%	22,791	18.9%	-0.5	-0.014
Combined Comorbidity Score	0.3	1.5	0.4	1.6	-0.1	-0.040
Health Service Utilization Intensity:	Mean	Std Dev	Mean	Std Dev		
Number of generic drugs	5.1	4.3	5.3	4.3	-0.1	-0.031
Number of filled prescriptions	12.6	13.0	13	13.3	-0.4	-0.030
Number of inpatient hospital encounters (IP)	0.1	0.5	0.1	0.5	0.0	0.000
Number of non-acute institutional encounters (IS)	0.1	1.0	0.1	1.0	0.0	0.000
Number of emergency room encounters (ED)	0.3	0.8	0.3	0.8	0.0	0.000
Number of ambulatory encounters (AV)	6.1	7.3	6.4	8.8	-0.3	-0.037
Number of other ambulatory encounters (OA)	1.2	2.9	1.3	3.4	-0.1	-0.032

[1]See Appendix B for the list of codes used to define events

[2]Value represents standard deviation where no % follows the value

[3]See Appendix C for list of codes used to define these covariates

*Median person-days are risk was calculated after several patients were removed due to Data Partner compliance reasons.

Table 3. Cohort of New Initiators of Glyburide and Glipizide at Risk for Severe Hypoglycemia[1] in the Emergency Department or first-listed diagnosis in the Inpatient setting (Matched 1:1 hdPS+Predefined PS, Caliper = .025)

	Primary Analysis				Covariate Balance	
Characteristic	**Glyburide**		**Glipizide**			
Patients (N)	116,641	83.8%	116,641	64.1%		
Median person-days at risk*	79		99			
	N	**%/Std Dev[2]**	**N**	**%/Std Dev[2]**	**Absolute Difference**	**Standardized Difference**
Patient Characteristics						
Gender (F)	47,931	41.1%	47,733	40.9%	0.2	0.003
Mean age (std dev)	56.2	12.4	56.2	12.4	0.0	0.003
Recorded History of[3]:						
Chronic Kidney Disease	4,605	3.9%	4,677	4.0%	-0.1	-0.003
Hypoglycemia	2,438	2.1%	2,456	2.1%	0.0	-0.001
Insulin	8,107	7.0%	7,964	6.8%	0.2	0.005
Metformin	42,794	36.7%	42,656	36.6%	0.1	0.002
Other ADAs	22,121	19.0%	22,171	19.0%	0.0	-0.001
Combined Comorbidity Score	0.3	1.6	0.3	1.6	0.0	0.000
Health Service Utilization Intensity:	Mean	Std Dev	Mean	Std Dev		
Number of generic drugs	5.1	4.3	5.1	4.2	0.0	0.000
Number of filled prescriptions	12.7	13.1	12.7	13.0	0.0	0.001
Number of inpatient hospital encounters (IP)	0.1	0.5	0.1	0.5	0.0	0.000
Number of non-acute institutional encounters (IS)	0.1	1.1	0.1	1.1	0.0	-0.001
Number of emergency room encounters (ED)	0.3	0.7	0.3	0.7	0.0	0.000
Number of ambulatory encounters (AV)	5.9	7.5	5.9	7.6	0.0	0.000
Number of other ambulatory encounters (OA)	1.2	2.9	1.2	3.0	0.0	0.000

[1]See Appendix B for the list of codes used to define events

[2]Value represents standard deviation where no % follows the value

[3]See Appendix C for list of codes used to define these covariates

*Median person-days are risk was calculated after several patients were removed due to Data Partner compliance reasons.

Table 4. Cohort of New Initiators of Glyburide and Glipizide at Risk for Severe Hypoglycemia[1] in the Emergency Department or first-listed diagnosis in the Inpatient setting (Matched 1:1 hdPS Only, Caliper = .025)

	Primary Analysis				Covariate Balance	
Characteristic	**Glyburide**		**Glipizide**			
Patients (N)	116,932	84.1%	116,932	64.3%		
Median person-days at risk*	79		103			
	N	**%/Std Dev[2]**	**N**	**%/Std Dev[2]**	**Absolute Difference**	**Standardized Difference**
Patient Characteristics						
Gender (F)	48,028	41.1%	47,968	41.0%	0.1	0.001
Mean age (std dev)	56.2	12.4	56.2	12.4	0.0	0.000
Recorded History of[3]:						
Chronic Kidney Disease	4,604	3.9%	5,402	4.6%	-0.7	-0.034
Hypoglycemia	2,446	2.1%	2,470	2.1%	0.0	-0.001
Insulin	8,095	6.9%	8,736	7.5%	-0.6	-0.021
Metformin	42,705	36.5%	49,924	42.7%	-6.2	-0.126
Other ADAs	22,098	18.9%	24,727	21.1%	-2.2	-0.056
Combined Comorbidity Score	0.3	1.6	0.3	1.6	0.0	0.002
Health Service Utilization Intensity:	Mean	Std Dev	Mean	Std Dev		
Number of generic drugs	5.1	4.3	5.4	4.2	-0.3	-0.060
Number of filled prescriptions	12.7	13.1	13.3	13.0	-0.6	-0.045
Number of inpatient hospital encounters (IP)	0.1	0.5	0.1	0.5	0.0	0.000
Number of non-acute institutional encounters (IS)	0.1	1.1	0.1	1.1	0.0	0.001
Number of emergency room encounters (ED)	0.3	0.7	0.3	0.8	0.0	0.000
Number of ambulatory encounters (AV)	5.9	7.5	6	7.6	-0.1	-0.016
Number of other ambulatory encounters (OA)	1.2	3.0	1.2	3.0	0.0	0.004

[1]See Appendix B for the list of codes used to define events

[2]Value represents standard deviation where no % follows the value

[3]See Appendix C for list of codes used to define these covariates

*Median person-days are risk was calculated after several patients were removed due to Data Partner compliance reasons.

Table 5. Estimates for Severe Hypoglycemia[1] in the Emergency Department or first-listed diagnosis in the Inpatient setting by Analysis Type and

Exposure Definition	New Users[2]	Person Years at Risk	Average Person Years at Risk	Number of Events	Incidence Rate per 1000 Person Years	Risk per 1000 New Users	Incidence Rate Difference per 1000 Person Years	Risk Difference per 1000 New Users	Hazard Ratio (95% CI)	Wald P-Value
Unmatched Analysis (Site-adjusted only)										
Glyburide	139,113	58,075	0.42	905	15.58	6.51	4.22	0.57	1.26 (1.16, 1.38)	<.0001
Glipizide	181,911	94,941	0.52	1,079	11.36	5.93				
1:1 Matched Predefined PS Analysis; Caliper=0.025 (Cox Model Stratified by Matched Pair)										
Glyburide	120,334	24,707	0.21	568	22.99	4.72	6.84	1.40	1.42 (1.25, 1.62)	<.0001
Glipizide	120,335	24,707	0.21	399	16.15	3.32				
1:1 Matched Predefined PS Analysis; Caliper=0.025 (Cox Model NOT Stratified by Matched Pair)										
Glyburide	120,334	53,366	0.44	859	16.10	7.14	5.28	1.60	1.41 (1.27, 1.56)	<.0001
Glipizide	120,335	61,552	0.51	666	10.82	5.53				
1:1 Matched hdPS+Predefined PS Analysis; Caliper=0.025 (Cox Model Stratified by Matched Pair)										
Glyburide	116,639	24,332	0.21	575	23.632	4.93	7.93	1.65	1.51 (1.32, 1.71)	<.0001
Glipizide	116,641	24,332	0.21	382	15.700	3.28				
1:1 Matched hdPS+Predefined PS Analysis; Caliper=0.025 (Cox Model NOT Stratified by Matched Pair)										
Glyburide	116,639	52,713	0.45	868	16.466	7.44	6.04	1.92	1.49 (1.34, 1.65)	<.0001
Glipizide	116,641	61,778	0.53	644	10.425	5.52				
1:1 Matched hdPS Only Analysis; Caliper=0.025 (Cox Model Stratified by Matched Pair)										
Glyburide	116,930	24,494	0.21	581	23.720	4.97	7.84	1.64	1.49 (1.31, 1.70)	<.0001
Glipizide	116,931	24,494	0.21	389	15.881	3.33				
1:1 Matched hdPS Only Analysis; Caliper=0.025 (Cox Model NOT Stratified by Matched Pair)										
Glyburide	116,930	52,816	0.45	870	16.472	7.44	6.17	1.93	1.50 (1.36, 1.66)	<.0001
Glipizide	116,931	62,526	0.53	644	10.300	5.51				

[1]See Appendix B for the list of codes used to define events

[2]Several patients were removed from the matched analysis due to Data Partner compliance reasons

Appendix A. Generic Names Used to Define Exposures in this Request

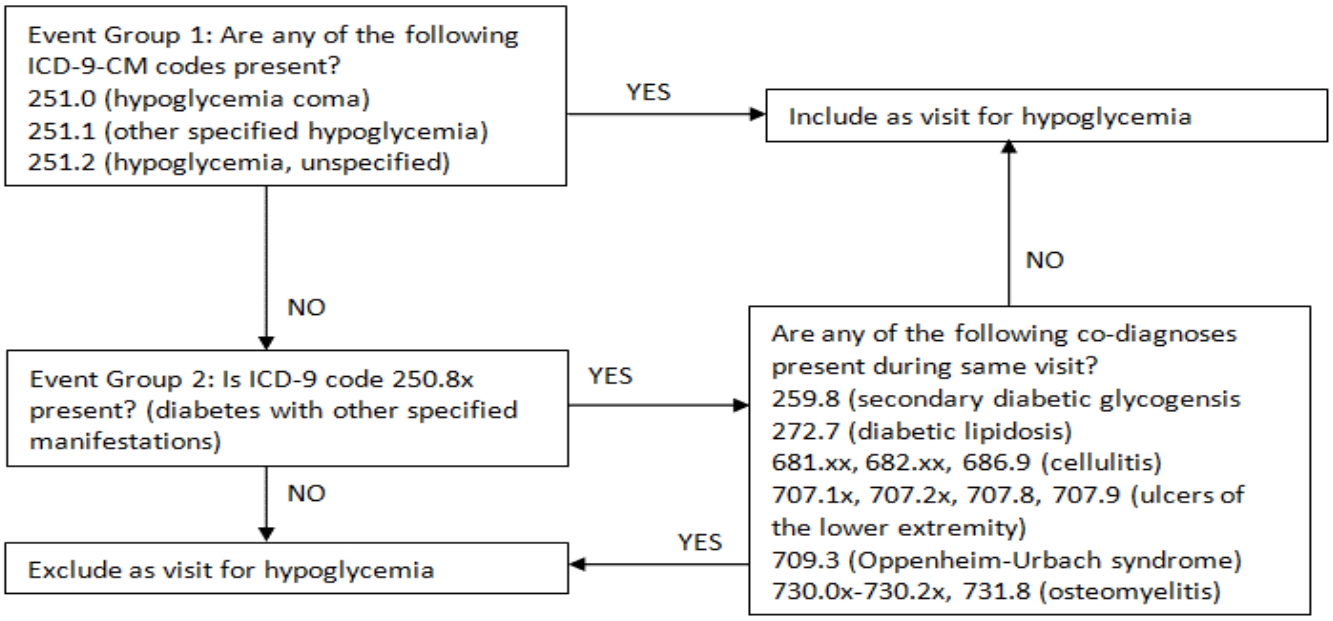
Generic Name
Glyburide
GLYBURIDE
GLYBURIDE,MICRONIZED
GLYBURIDE/METFORMIN HCL
Glipizide
GLIPIZIDE
GLIPIZIDE/METFORMIN HCL
Other Secretagogues
CHLORPROPAMIDE
TOLBUTAMIDE
TOLAZAMIDE
ROSIGLITAZONE MALEATE/GLIMEPIRIDE
GLIMEPIRIDE
PIOGLITAZONE HCL/GLIMEPIRIDE
NATEGLINIDE
REPAGLINIDE
REPAGLINIDE/METFORMIN HCL
ACETOHEXAMIDE

Appendix B. Codes and Algorithm Used to Define Severe Hypoglycemia in this Request

HYPOGLYCEMIA EVENT ALGORITHM

Figure 1 below depicts the algorithm to identify a hypoglycemia event. All outcomes of this algorithm must be identified during the one incident treatment episode identified by the CIDA tool.

Figure 1. Event algorithm



Note 1: Event care setting and diagnosis position is restricted for both Event Groups 1 and 2:

- Primary Outcome of Interest: Any diagnosis position for ED Encounter Type (ED*) or first-listed diagnosis for IP Encounter Type (IPP)
- Secondary Outcome of Interest: Any diagnosis position for ED Encounter Type (ED*)

Note 2: Exact code matches are to be used unless followed by an "x." Use "starts with" when an "x" is used to include all subcodes.

Appendix C. Codes Used to Define Covariates in this Request

Code	Code Type	Description/Generic Name
Chronic Kidney Disease		
582	ICD9-CM Diagnosis	CHRONIC GLOMERULONEPHRITIS
582.*	ICD9-CM Diagnosis	CHRONIC GLOMERULONEPHRITIS
582.**	ICD9-CM Diagnosis	CHRONIC GLOMERULONEPHRITIS
583	ICD9-CM Diagnosis	NEPHRITIS&NEPHRPATH NOT ACUT/CHRN
583.0	ICD9-CM Diagnosis	NEPHRITIS&NEPHROPATHY W/LES PROLIF
583.1	ICD9-CM Diagnosis	NEPHRIT&NEPHROPATH-LES MEMB GLN
583.2	ICD9-CM Diagnosis	NEPHRIT&NEPHROP-LES MEMBRNPROLF GLN
583.4	ICD9-CM Diagnosis	NEPHRIT&NEPHROP-LES RAPID PROG GLN
583.6	ICD9-CM Diagnosis	NEPHRIT&NEPHROP W/LES CRTICL NECROS
583.7	ICD9-CM Diagnosis	NEPHRIT&NEPHROP W/LES MEDULRY NCROS
585	ICD9-CM Diagnosis	CHRONIC KIDNEY DISEASE
585.*	ICD9-CM Diagnosis	CHRONIC KIDNEY DISEASE
586	ICD9-CM Diagnosis	RENAL FAILURE, UNSPECIFIED
586.*	ICD9-CM Diagnosis	RENAL FAILURE, UNSPECIFIED
588	ICD9-CM Diagnosis	DISORDERS RESULTING FROM IMPAIRED RENAL FUNCTION
588.*	ICD9-CM Diagnosis	DISORDERS RESULTING FROM IMPAIRED RENAL FUNCTION
Hypoglycemia		
251.0	ICD9-CM Diagnosis	hypoglycemia coma
251.1	ICD9-CM Diagnosis	other specified hypoglycemia
251.2	ICD9-CM Diagnosis	hypoglycemia, unspecified
250.8	ICD9-CM Diagnosis	diabetes with other specified manifestations
250.8*	ICD9-CM Diagnosis	diabetes with other specified manifestations
Other ADAs		
	NDC	ACARBOSE
	NDC	ALBIGLUTIDE
	NDC	ALOGLIPTIN BENZOATE/PIOGLITAZONE HCL
	NDC	ALOGLIPTIN BENZOATE
	NDC	ALOGLIPTIN BENZOATE/METFORMIN HCL
	NDC	CANAGLIFLOZIN
	NDC	CANAGLIFLOZIN/METFORMIN HCL
	NDC	DAPAGLIFLOZIN PROPANEDIOL
	NDC	DAPAGLIFLOZIN PROPANEDIOL/METFORMIN HCL
	NDC	EMPAGLIFLOZIN
	NDC	EXENATIDE MICROSPHERES
	NDC	EXENATIDE
	NDC	LINAGLIPTIN
	NDC	LINAGLIPTIN/METFORMIN HCL
	NDC	LIRAGLUTIDE
	NDC	MIGLITOL
	NDC	PIOGLITAZONE HCL
	NDC	PIOGLITAZONE HCL/METFORMIN HCL
	NDC	PIOGLITAZONE HCL/GLIMEPIRIDE
	NDC	PRAMLINTIDE ACETATE
	NDC	ROSIGLITAZONE MALEATE/GLIMEPIRIDE
	NDC	ROSIGLITAZONE MALEATE/METFORMIN HCL
	NDC	ROSIGLITAZONE MALEATE
	NDC	SAXAGLIPTIN HCL
	NDC	SAXAGLIPTIN HCL/METFORMIN HCL
	NDC	SITAGLIPTIN PHOSPHATE/METFORMIN HCL
	NDC	SITAGLIPTIN PHOSPHATE

Appendix C. Codes Used to Define Covariates in this Request

Code	Code Type	Description/Generic Name
	NDC	SITAGLIPTIN PHOSPHATE/SIMVASTATIN
	NDC	TROGLITAZONE
Insulin		
	NDC	INSULIN LISPRO
	NDC	INSULIN LISPRO PROTAMINE & INSULIN LISPRO
	NDC	INSULIN REGULAR,BEEF-PORK
	NDC	INSULIN,PORK PURIFIED
	NDC	INSULIN REGULAR, HUMAN
	NDC	INSULIN ISOPHANE NPH,BF-PK
	NDC	INSULIN ISOPHANE,PORK PURE
	NDC	NPH, HUMAN INSULIN ISOPHANE
	NDC	INSULIN ZINC,BEEF-PORK
	NDC	INSULIN ZINC,PORK PURIFIED
	NDC	INSULIN ZINC HUMAN REC
	NDC	INSULIN ZINC EXTEND HUMAN REC
	NDC	NPH, HUMAN INSULIN ISOPHANE/INSULIN REGULAR, HUMAN
	NDC	INSULIN ADMIN. SUPPLIES
	NDC	INSULIN GLARGINE, HUMAN RECOMBINANT ANALOG
	NDC	INSULIN GLULISINE
	NDC	INSULIN REGULAR,HUMAN BUFFERED
	NDC	INSULIN ASPART
	NDC	INSULIN ASPART PROTAMINE HUMAN/INSULIN ASPART
	NDC	INSULIN DETEMIR
	NDC	SYRINGE W-O NEEDL,INSULIN,1 ML
	NDC	INSULIN ZINC BEEF
	NDC	INSULIN ISOPHANE,BEEF
	NDC	INSULIN,PORK
Metformin		
	NDC	SAXAGLIPTIN HCL/METFORMIN HCL
	NDC	SITAGLIPTIN PHOSPHATE/METFORMIN HCL
	NDC	ROSIGLITAZONE MALEATE/METFORMIN HCL
	NDC	METFORMIN HCL
	NDC	PIOGLITAZONE HCL/METFORMIN HCL
	NDC	REPAGLINIDE/METFORMIN HCL
	NDC	DAPAGLIFLOZIN PROPANEDIOL/METFORMIN HCL
	NDC	LINAGLIPTIN/METFORMIN HCL
	NDC	CANAGLIFLOZIN/METFORMIN HCL
	NDC	ALOGLIPTIN BENZOATE/METFORMIN HCL
	NDC	METFORMIN/CAFFEINE/AMINO ACIDS#7/HERBAL COMB#125/CHOLINE BIT
	NDC	METFORMIN/AMINO ACIDS COMB. #7/HERBAL COMB.#125/CHOLINE

Modular Program Report

Specifications for to16_cap_mpl2r_wp001_nsdp_v01

FDA requested use of the Cohort Identification and Descriptive Analysis (CIDA) Tool with Propensity Score Matching (PSM) to investigate severe hypoglycemia events following new use of glyburide versus glipizide. This report displays the results for severe hypoglycemia events in any diagnosis position for emergency department encounters or first-listed diagnosis for inpatient encounters (Run 1, below).

Enrollment Gap: 45 days
Age Groups: 18+
Query Period: 1/1/2008 to 09/30/14
Coverage Requirement: Medical and Drug Coverage
Enrollment Requirement: 183 days

		Run 1		Run 2	
		Exposure of Interest	**Comparator of Interest**	**Exposure of Interest**	**Comparator of Interest**
		Glyburide	Glipizide	Glyburide	Glipizide
Drug/ Exposure:	Incident w/ respect to:	Glyburide, glipizide and other secretagogues including chlorpropamide, tolbutamide, tolazamide, glimepiride, nateglinide, repaglinide, acetohexamide	Glipizide, glyburide and other secretagogues including chlorpropamide, tolbutamide, tolazamide, glimepiride, nateglinide, repaglinide, acetohexamide	Glyburide, glipizide and other secretagogues including chlorpropamide, tolbutamide, tolazamide, glimepiride, nateglinide, repaglinide, acetohexamide	Glipizide, glyburide and other secretagogues including chlorpropamide, tolbutamide, tolazamide, glimepiride, nateglinide, repaglinide, acetohexamide
	Washout (days)	183	183	183	183
	Cohort Definition	01	01	01	01
	Episode Gap	14	14	14	14
	Exposure Extension Period	14	14	14	14
	Minimum Episode Duration	0	0	0	0
	Minimum Days Supplied	0	0	0	0
	Induction Period	0	0	0	0
	Truncation by Death	Yes	Yes	Yes	Yes
	Episode Truncation by Incident Exposure	Yes	Yes	Yes	Yes
Event/ Outcome:	Event/ Outcome	Hypoglycemia (See event algorithm)	Hypoglycemia (See event algorithm)	Hypoglycemia (See event algorithm)	Hypoglycemia (See event algorithm)
	Care Setting/PDX	ED* or IPP	ED* or IPP	ED*	ED*
	Incident w/ respect to:	Hypoglycemia (See event algorithm)	Hypoglycemia (See event algorithm)	Hypoglycemia (See event algorithm)	Hypoglycemia (See event algorithm)
	Washout (days)	30	30	30	30
Propensity Score Match (PSM) Analysis:	PSM Ratio	1:1		1:1	
	PSM Caliper	0.025		0.025	
	Covariate evaluation window (days)	183		183	
	Perform hdPS Analysis	Yes		Yes	
	Number of covariates considered for each claim type	100		100	
	Number of covariates kept from pool of considered covariates	200		200	
	Covariate selection method	Exposure association-based selection		Exposure association-based selection	
	Zero Cell Correction	Yes		Yes	

National Drug Codes (NDCs) checked against First Data Bank's "National Drug Data File (NDDF®) Plus"
ICD-9-CM diagnosis and procedure codes checked against "Ingenix 2012 ICD-9-CM Data File" provided by OptumInsight
HCPCS codes checked against "Optum 2012 HCPCS Level II Data File" provided by OptumInsight
CPT codes checked against "Optum 2012 Current Procedure Codes & Relative Values Data File" provided by OptumInsight