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Policy Evaluation: Glucagon-Like Peptide-1 Receptor Agonist and Metformin in the Fee for Service Population

Plain Language Summary

- There are many different kinds, or classes of medicines, to treat type 2 diabetes mellitus to help lower sugar levels for people with type 2 diabetes mellitus.
- This report focuses on a class called glucagon-like-peptide-1 receptor agonists (GLP-1 RA). Some of the medicines in this class are also Food and Drug Administration (FDA) approved to treat heart disease and obesity.
- Providers must tell Medicaid why they are prescribing certain medications before Medicaid Open Card will pay for the prescription. This process is called prior authorization.
- In May 2019 the prior authorization (PA) for the GLP-1 RA class was changed. The preferred medicines were updated and the medicines classified as preferred received an automatic-PA approval when a person was already taking a different medicine called metformin. This update to the PA was done to make it simpler for patients already taking metformin to also get a GLP-1 RA.
- This report looks at GLP-1 RAs use between 2017-2022 to see if the automatic-PA changed use of GLP-1 RAs and metformin.
- Between 2017-2022, use of GLP-1 RA went up. The update to the PA could have impacted this increase by improving access to patients.
- Most patients continued taking metformin regularly after starting a GLP-1 RA.
- This class of medicine has FDA indications for heart disease and weight loss benefits, but there were few patients with heart disease and no change in use in those with type 2 diabetes mellitus and obesity.
- We do not recommend any new changes to the current PA policy for GLP-1 RAs.

Research Questions:

- How have the prescribing patterns and utilization of glucagon-like peptide-1 receptor agonists (GLP-1 RA) changed over time in response to clinical prior authorization changes implemented in May 2019?
- What percentage of patients continue to adhere to metformin after initiation of a GLP-1 RA?
- What are the common patient characteristics and comorbidities (e.g., obesity) associated with those prescribed GLP-1 RA?

Conclusions:

- There was a sustained increase in utilization of GLP-1 RA from 2017-2022, consistent with expanded use in clinical practice. The change to the prior authorization criteria to automatically approve preferred GLP-1 RA medications for patients with prior claims of metformin, may have improved access for patients.
- Of the patients prescribed metformin before initiating a GLP-1 RA, 84.2% vs 87.5% had continued use of metformin after starting second-line treatment, with a percent daily coverage of 83.6% vs. 85.8% between the two groups, which showcased high adherence to the medication.
- GLP-1 RAs have indications for use in cardiovascular disease and weight loss, but there were few patients [on GLP-1 RAs] with atherosclerotic cardiovascular disease (ASCVD) and no change in use was observed in those with concomitant type 2 diabetes mellitus (T2DM) and obesity.

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Recommendations:

- Maintain current prior authorization (PA) policy for GLP-1 RAs.

Background

In the United States (US), 37.3 million people, or 11.3% of the population, have diabetes. Diabetes mellitus can be classified as either type 1 (T1DM) or type 2 (T2DM). Type 1 DM is caused by destruction of the insulin producing beta cells of the pancreas and is classified as an autoimmune disease or insulin-dependent diabetes. In contrast, T2DM is highly influenced by genetic and environmental factors, where blood glucose levels become chronically high due to deficits in insulin function that can lead to insulin resistance.[6] Both forms can result in serious health complications, and T2DM is the seventh leading cause of death in the US.[1] There is no cure for DM but morbidity and mortality can be reduced with lifestyle interventions, medications, and regular monitoring both at home and by health care providers. The leading cause of morbidity and mortality for individuals with T2DM is ASCVD, defined as acute coronary syndrome, stable/unstable angina, coronary revascularization, transient ischemic attack, stroke, peripheral artery disease and myocardial infarction.[2]

Metformin is the preferred first-line oral blood glucose-lowering agent to manage T2DM. This medication has become the most prescribed blood glucose-lowering therapy worldwide due to its favorable benefit in regards to clinical efficacy in controlling T2DM and cost effectiveness.[5] Other oral medication classes used for T2DM include sodium-glucose cotransporter 2 (SGLT2) inhibitors, which are also indicated for chronic heart failure as well as reduction in atherosclerotic cardiovascular disease risk and kidney disease with or without diabetes, dipeptidyl peptidase-4 (DPP-4) inhibitors and sulfonylureas[2]. Insulins are also used for some T2DM patients if they fail to achieve desired glucose goals, or have contraindications with oral therapy. Regarding other options to control T2DM, the use of GLP-1 RAs have continued to increase over the past couple of years due to their ASCVD risk reduction benefit and weight loss[4]. The GLP-1 RAs are FDA-approved for use in patients with T2DM, and two GLP-1 RAs (Saxenda and Wegovy) are FDA-approved for weight loss without concomitant T2DM (**Table 2**). The 2022 American Diabetes Association (ADA) guidelines classified GLP-1 RA as an appropriate initial therapy with or without metformin for individuals with T2DM who have, or are at high risk for, ASCVD, heart failure or chronic kidney disease. A small risk reduction in all-cause mortality with exenatide ER and liraglutide have been found as well as a moderate reduction in risk for CV death/CV events with dulaglutide, liraglutide and injectable semaglutide. Since there is no universally accepted second-line medication, the choice should be based on the degree of glucose lowering necessary to help the patient reach their target HbA1c levels, their unique characteristics and the risks associated with the therapy.[2]

Metformin step therapy is required for Oregon Health Plan (OHP) fee-for-service (FFS) participants before a PA for additional T2DM medications will be approved. Prior authorization requirements and medication status on the Preferred Drug List (PDL) for medications to treat T2DM have changed over time (**Table 1**). For patients with OHP FFS, PA requirements changed in May 2019 to allow automatic approval for preferred GLP-1 RAs for patients currently on metformin (defined as a metformin claim in the previous 40 days). This auto-PA eliminates the need to send manual PA requests for preferred GLP-1 RAs (**Table 2**). Dulaglutide was added as a preferred agent and became eligible for the auto-PA in September 2020. Exenatide and liraglutide were preferred formulary options when the auto-PA was initially implemented, which was determined after evaluation of efficacy and cost.

The purpose of this drug use evaluation is to determine how the PA revisions (**Table 1**) affected utilization of both metformin and GLP-1 RAs among OHP FFS members. Additionally, effects on metformin adherence and prevalent patient comorbidities among this population will be evaluated.

Table 1: Updates to Glucagon Like Peptide-1 Receptor Agonist Prior Authorization Criteria

Implementation Date		
February 1, 2015	**May 1, 2019**	**September 1, 2020**
- Include at least one GLP-1 RA on the PDL as a preferred third-line option for T2DM after metformin and a sulfonylurea - **Preferred GLP-1 RA:** exenatide (BYETTA) - All GLP-1 RAs subject to clinical PA criteria	- Modified clinical PA criteria to allow use of basal insulin when in combination with a GLP-1 RA - Allow auto-PA for preferred GLP-1 RA in patients with claims for metformin in the previous 40 days - **Preferred GLP-1 RA:** liraglutide (VICTOZA and exenatide (BYETTA)]	- Step therapy was removed from the clinical PA criteria for all agents other than metformin - Auto-PA was still only allowed for preferred products. - **Preferred GLP-1 RA:** liraglutide (VICTOZA and exenatide (BYETTA), dulaglutide (TRULICITY)

Abbreviations: DPP-4 = Dipeptidyl Peptidase-4 Inhibitors; GLP-1 RA = Glucagon-like peptide-1 receptor agonist; PA = prior authorization; PDL = Preferred drug list; SGLT-2 = Sodium-glucose Cotransporter-2; T2DM = Type 2 diabetes mellitus

Table 2: GLP-1 RA FDA-Approved Uses and Preferred Status in OHP FFS.

Brand Name	Generic Name	Route	FDA Approved Uses	Preferred Drug List Status
BYDUREON	exenatide, extended-release	subcutaneous	Type 2 Diabetes mellitus	Nonpreferred
BYETTA	exenatide	subcutaneous	Type 2 Diabetes mellitus	Preferred
ADLYXIN	lixisenatide	subcutaneous	Type 2 Diabetes mellitus	Nonpreferred
VICTOZA	liraglutide*	subcutaneous	Type 2 Diabetes mellitus	Preferred
TRULICITY	dulaglutide	subcutaneous	Type 2 Diabetes mellitus	Preferred
OZEMPIC	semaglutide**	subcutaneous	Type 2 Diabetes mellitus	Nonpreferred
RYBELSUS	semaglutide	oral	Type 2 Diabetes mellitus	Nonpreferred
MOUNJARO	tirzepatide	subcutaneous	Type 2 Diabetes mellitus	Nonpreferred

- SAXENDA* and WEGOVY**brands are indicated for weight loss. Weight loss is not currently included in the Oregon Medicaid state plan

Methods:

All paid FFS pharmacy claims for any GLP-1 RA (**Table 2**) from May 2017 to July 2022 was assessed and reported as per-member-per-month (PMPM).

In order to assess utilization of both metformin and GLP-1 RA and evaluate implementation of the auto-PA in May 2019, pre- and post-policy change cohorts were identified of patients who were newly started on a GLP-1 RA. Patients with a new, paid pharmacy claim for any GLP-1 RA from May 1, 2018 through April 30, 2019 were defined as the control group (pre-policy change), and patients with a new claim from May 1, 2019 through April 30, 2020 were defined as the

study group (post-policy change). Patients were assumed to be treatment-experienced if they met the following criteria: 1) had prior claims for GLP-1 RA paid by OHP; 2) the pharmacy indicated that the first paid claim was a refill; or 3) the member did not have any paid medical claims during the two-timeline cohort. Patients with less than 6 months of continuous enrollment prior to the first paid GLP-1 RA claim in FFS Medicaid were excluded. Descriptive statistics and percentages were used to evaluate changes between the cohorts. Patients were categorized by demographics, common comorbidities using ICD-10 codes (**Appendix 1**), and concurrent insulin use (**Appendix 2**). Common comorbidities were collected from OHP members from the last 6 months of medical records before the first GLP-1 RA claim. Insulin utilization was evaluated based on pharmacy claims in the 3 months prior to the first paid GLP-1 RA claim.

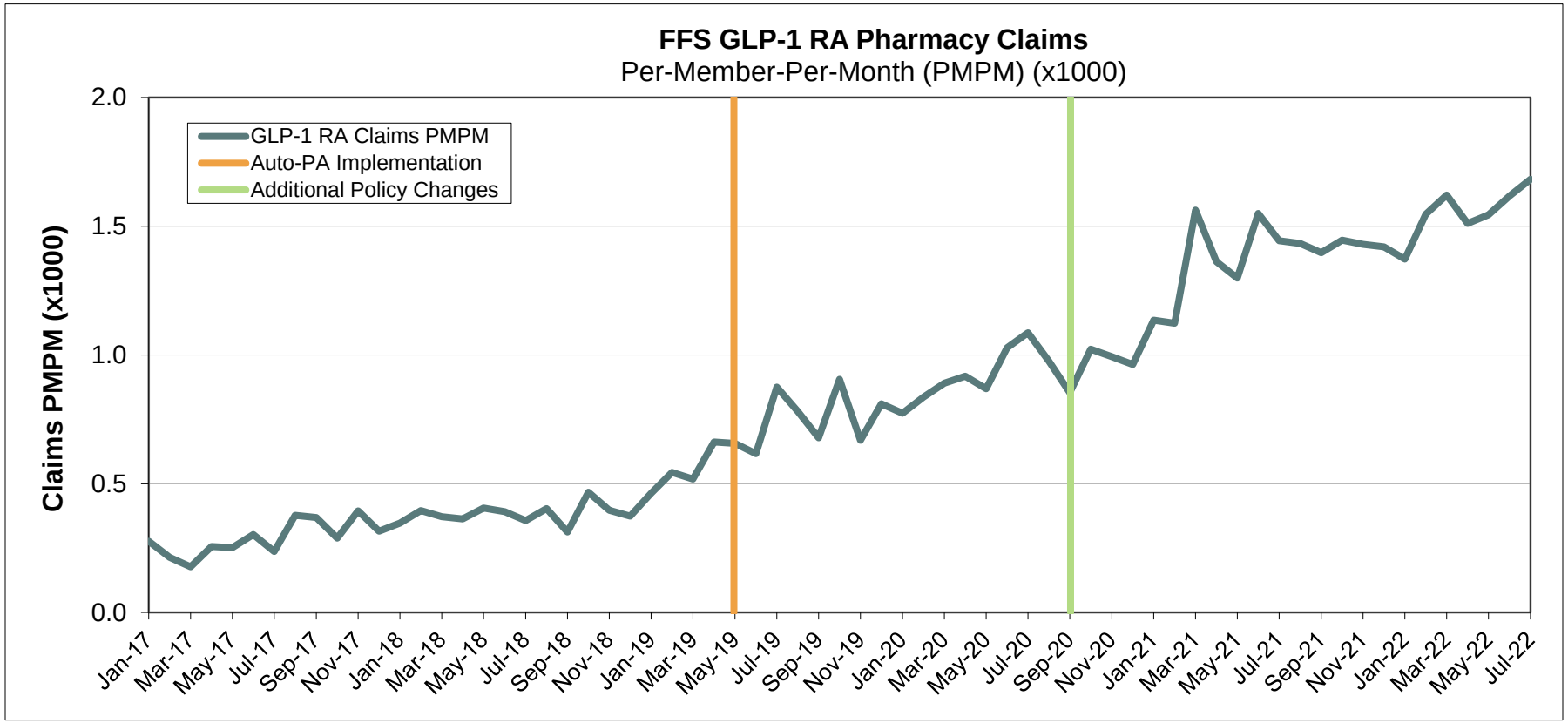
The percentage of patients who continued to adhere to metformin after GLP-1 RA initiation was compared in the pre and post cohorts. Metformin adherence was quantified by looking at actual daily coverage of the medication in the 3 months following the GLP-1 RA new start. Three months was chosen as a base to quantify metformin adherence due to the possibility that some prescriptions having been filled for a 90-day supply as well as to demonstrate adequate trial of the medication. For patients on metformin, the average percent daily coverage (PDC) of metformin was described. Patients with primary insurance or third-party liability (TPL) were excluded from the metformin adherence study objective.

Lastly, differences among PA types (fax, phone, auto-PA, or web/provider portal) before and after the PA change were compared. Patients with new paid pharmacy claims as well as renewed claims for a GLP-1 RA were included. This data included patients with TPL.

Results:

Figure 1 represents the utilization of GLP-1 RA use PMPM (PMPM x1000) from May 1, 2017 to July 30, 2022 for OHP FFS members. GLP-1 RA utilization increased after the implementation of the auto-PA was implemented in May 2019, showcased by the orange line. The green line demonstrates when dulaglutide was added as a preferred GLP-RA option. Among Oregon FFS Medicaid patients, GLP-1 RA utilization increased from 2017 to 2022 with 0.28 PMPM claims in January 2017 to 1.68 PMPM claims in July 2022.

Figure 1. Trend of GLP-1 RA Utilization PMPM from May 2017 to July 2022



Demographics of OHP FFS members in the control and study groups are presented in **Table 3**. There were 85 GLP-1 RA new starts in the control group from May 2018 to April 2019 and 129 in the study group from May 2019 to April 2020. Baseline characteristics appear similar between groups. (**Table 3**). Most patients were adults 35-64 years of age (89.7%), female (66.4%), and White (36%). The most prescribed agents in each group were dulaglutide and liraglutide, with a slight increase in liraglutide utilization in the study group compared to the control (55% vs. 39%). There was also a slight increase in patients with a history of ASCVD in the study group compared to control (12.4% vs. 4.7%) and lower frequencies of hypertension (50% vs. 60%) and obesity (39.5% vs. 43.5%) in the study group vs. control, respectively. Approximately half the patients in the control and study groups were on insulin in the 3 months prior to GLP-1 RA initiation (41.2% vs. 48.8%).

Table 3. Demographics.

Characteristic	Control Group: 5/1/18 – 4/30/19	Study Group: 5/1/19 – 4/30/20
Total New GLP-1 RA Claims	N=85	N=129
Average Age, years (%)	48 years	48 years
18-34	9 (10.6%)	12 (9.3%)
35-64	75 (88.2%)	117 (90.7%)
>65	1 (1.2%)	0 (0%)
Sex		
Male	32 (37.6%)	40 (31.0%)
Female	53 (62.4%)	89 (69.0%)
Race/Ethnicity		
Unknown	19 (22.4%)	40 (31.0%)
White	33 (38.8%)	44 (34.1%)
Hispanic	9 (10.6%)	8 (6.2%)
Other	10 (11.8%)	10 (7.8%)
GLP-1 RA Medication		
Dulaglutide	32 (37.6%)	35 (27.1%)
Exenatide	3 (3.5%)	6 (4.7%)
Exenatide microspheres	13 (15.3%)	10 (7.8%)
Liraglutide	33 (38.8%)	71 (55%)
Semaglutide	4 (4.7%)	7 (5.4%)
Diagnoses 6 Months Prior to New Start		
Any ASCVD History	4 (4.7%)	16 (12.4%)
Chronic Kidney Disease	7 (8.2%)	10 (7.8%)
Heart Failure	3 (3.5%)	6 (4.7%)
Hypertension	51 (60%)	64 (49.6%)
Obesity	37 (43.5%)	51 (39.5%)
Type 2 Diabetes	81 (95.3%)	114 (88.4%)
Insulin Claim 3 Months Prior to GLP-1 RA New Start		
Any insulin	35 (41.2%)	63 (48.8%)
Basal	31 (36.5%)	60 (46.5%)
Bolus	17 (20%)	22 (17.1%)
Basal/Bolus Combo products	0 (0%)	1 (0.8%)
Basal/GLP-1 RA Combo Products	0 (0%)	0 (0%)
Patients With TPL at Time of New GLP-1 RA New Start	29 (34.1%)	30 (23.3%)

In patients who had Medicaid as a primary payer, 67.9% (pre) vs. 64.6% (post) of patients had claims for metformin in the 3 months before initiating a GLP-1 RA at baseline (**Table 4**). Of the patients who had metformin at baseline, most continued metformin (84.2% vs 87.5%) after starting a GLP-1 RA. A small number of patients started metformin after initiation of a GLP-1 RA (5 vs 17%) who were not on it at baseline but 15.8% vs 12.5% discontinued metformin after starting a GLP-1 RA. The average percent-daily-coverage of metformin was similar in each group (83.6% vs. 85.8%).

Table 4: Metformin Utilization with New Start GLP-1 RA Use in OHP FFS Members (Excluding Patients with TPL Insurance)

	Control Group 5/1/18 – 4/30/19	**Study Group** 5/1/19 – 4/30/20
Total New GLP-1 RA Claims Without TPL	N=56	N=99
Metformin Use at Baseline in 3 months Before GLP-1 RA New Start	**38 (67.9%)**	**64 (64.6%)**
Continued Metformin After GLP-1 RA New Start	32 (84.2%)	56 (87.5%)
Discontinued Metformin after GLP-1 RA New Start	6 (15.8%)	8 (12.5%)
No Metformin Use at Baseline in 3 Months Before GLP-RA New Start	**18 (32.1%)**	**35 (35.4%)**
Started Metformin in 3 Months After GLP-1 RA	1 (5.6%)	6 (17.1%)
No Metformin Use After GLP-1 RA New Start	17 (94.4%)	29 (82.9%)
Average Percent Daily Coverage (PDC) of Metformin in Subsequent Three Months	83.6%	85.8%

Table 5 describes the differences between pre- and post-auto-PA implementation among types of PAs requested for a GLP-1 RA. In the year prior to implementation, there were a total of 222 PAs compared to 334 PAs one year after implementation. The proportion of fax and phone PAs decreased in the year after the change (post auto-PA) compared to the previous year (fax 49.7% vs. 64%; phone 24.9% vs. 34.2%), with 24% of the PAs processed as auto-PAs.

Table 5: PA Classification for GLP-1 Medications

	One Year Prior to Auto-PA Implementation 5/1/18 – 4/30/19	**One Year After Auto-PA Implementation** 5/1/19 – 4/30/20
Number of GLP-1 RA PAs	222	334
PA Type (%)		
Fax	142 (64%)	166 (49.7%)
Phone	76 (34.2%)	83 (24.9%)
Auto-PA	0 (0%)	80 (24%)
Web/Provider Portal	4 (1.8%)	5 (1.5%)

Discussion:
This DUE demonstrates trends in GLP-1 RA utilization following implementation of an auto-PA. As of May 2019, all patients with a pharmacy claim for metformin in the previous 40 days received auto-PA approval when a preferred GLP-1 RA was requested. **Figure 1** showcases the consistent increase in utilization of GLP-1 RAs from 2017-2022, with higher overall increase in claims after the auto-PA implementation. GLP-1 RA utilization increased from 2017 to 2022 with 0.28 PMPM claims in January 2017 to 1.68 PMPM claims in July 2022. Virtually, most of the increased utilization occurred with liraglutide, which is consistent with the PA change when it was made a preferred option with the auto-PA update in May 2019.

GLP-1 RA use in OHP FFS members has increased for several reasons, including increased prescriber familiarity with GLP-1 RAs, expanded indications as well as recommendations by guidelines for their use. The changes in clinical PA criteria and increasing the number of preferred products from 1 agent to 3 over time, may have also improved patient access by reducing barriers to prescribing. Data from **Table 5** show an overall increase in GLP-1 PAs but decreased use of both fax and phone PA types. The decrease in manual PAs after implementation of the auto-PA could have reduced barriers to prescribing.

Adherence to metformin was evaluated in this DUE because metformin continues to be recommended as a first-line treatment for T2DM (**Table 4**). Results regarding metformin use at baseline was lower than expected (67.9% (pre) vs. 64.6% (post), since use of metformin at baseline is a requirement for auto-PA approval. Patients who continued metformin after starting GLP-1 RA was appropriate, given the requirements needed. The moderate percentage of patients who discontinued metformin after initiating a GLP-1 RA is likely due to either an intolerance, contraindication to metformin, not following guideline directed therapy or possibly already taking an alternative agent. The high percentages of manual PAs that were submitted by fax or phone corresponds to the significant proportion of patients who were prescribed a non-preferred GLP-1 RA or did not have a recent metformin claim. Most patients who continued metformin, remained adherent in both groups, with PDC of >80%.

Despite indications for use in cardiovascular disease and weight loss, there were relatively few patients with a diagnosis of ASCVD or obesity in medical claims and no change in use in those with these concomitant diagnoses among the control and study groups.

DUE Limitations:
Retrospective claims data have inherent limitations. Causality cannot be determined and results should be interpreted with caution. Medication claims from pharmacies were used as a surrogate for metformin adherence. Using claims data also may have impacted the data collected regarding comorbidities and baseline characteristic since analysis relies on ICD-10 codes. When utilizing claims history data, the assumption is made that the medications of interest are being prescribed for the diagnosis of interest and not for any off-label use. Delays in submission and processing of medical claims may result in incomplete information.

The OHP includes a significant proportion of patients who are only transiently enrolled in FFS. Often patients are quickly enrolled into a CCO upon eligibility for OHP and remain in FFS for only a few months. To accurately capture data from this population in the analysis, patients with less than 6 months of continuous enrollment in OHP FFS were excluded. This limitation did lead to several assumptions when identifying patients who may be treatment-naïve, as only patients newly started on a GLP-1 RA were included in the study. Patients were assumed to be treatment-experienced if they met the following criteria: 1) had prior claims for GLP-1 RA paid by OHP; 2) the pharmacy indicated that the first paid claim was a refill; or 3) the member did not have any paid medical claims during the two timeline cohorts. Patients with a remote history of medication use would not be captured. There are also limitations when using PDC calculations as patients do not necessarily consume all the drugs filled. Additionally, exclusion of patients with incomplete or atypical administrative claims data (e.g.

percentage eligibility, third-party insurance) limits sample size and may not represent utilization across the OHP FFS population or the Oregon Medicaid population.

References:

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Appendix 1: ICD-10 Codes Used for Patient Demographics

Any ASCVD History: I25x	CKD: N18x
Acute Coronary Syndrome: I24x	Obesity: E66x
Stable/Unstable Angina: I20x	Metabolic Syndrome: E88x (counted as Obesity)
Stroke: G45x	Heart failure: I50x
Peripheral Artery Disease: I73x	Type 2 Diabetes: E11x
Myocardial infarction: I21x	Hypertension: I10x

Appendix 2: List of Insulin Products

Bolus Insulin		
Generic	Brand	Route/Form
Insulin regular, human	HUMULIN R U-500	Subcutaneous/vial
Insulin regular, human	AFREZZA	Inhalation/cartridge
Insulin regular, human	HUMULIN U-500 KWIKPEN	Subcutaneous/pen
Insulin lispro	ADMELOG	Subcutaneous/vial
Insulin lispro	HUMALOG	Subcutaneous/vial
Insulin lispro	INSULIN LISPRO	Subcutaneous/vial
Insulin lispro	HUMALOG	Subcutaneous/cartridge
Insulin lispro	ADMELOG SOLOSTAR	Subcutaneous/pen
Insulin lispro	HUMALOG KIWKPEN U-100	Subcutaneous/pen
Insulin lispro	INSULIN LISPRO KWIKPEN U-100	Subcutaneous/pen
Insulin lispro	HUMALOG KWIKPEN U-200	Subcutaneous/pen
Insulin lispro	HUMALOG JUNIOR KWIKPEN	Subcutaneous/Pen HF
Insulin lispro	INSULIN LISPRO JUNIOR KWIKPEN	Subcutaneous/Pen HF
Insulin aspart	INSULIN ASPART PENFILL	Subcutaneous/cartridge
Insulin aspart	NOVOLOG PENFILL	Subcutaneous/cartridge

Basal Insulin		
Generic	Brand	Route/Form
Insulin glargine, hum.rec.analog	Insulin glargine	Subcutaneous/vial
Insulin glargine, hum.rec.analog	LANTUS	Subcutaneous/vial
Insulin glargine, hum.rec.analog	SEMGLEE	Subcutaneous/vial
Insulin glargine, hum.rec.analog	BASAGLAR KWIKPEN U-100	Subcutaneous/pen
Insulin glargine, hum.rec.analog	INSULIN GLARGINE SOLOSTAR	Subcutaneous/pen
Insulin glargine, hum.rec.analog	LANTUS SOLOSTAR	Subcutaneous/pen
Insulin glargine, hum.rec.analog	SEMGLEE PEN	Subcutaneous/pen
Insulin glargine, hum.rec.analog	TOUJEO SOLOSTAR	Subcutaneous/pen
Insulin glargine, hum.rec.analog	TOUJEO MAX SOLOSTAR	Subcutaneous/pen
Insulin detemir	LEVEMIR FLEXTOUCH	Subcutaneous/pen
Insulin detemir	LEVEMIR	Subcutaneous/vial
Insulin glulisine	APIDRA	Subcutaneous/vial
Insulin glulisine	APIDRA SOLOSTAR	Subcutaneous/pen
Insulin degludec	TRESIBA FLEXTOUCH U-100	Subcutaneous/pen
Insulin degludec	TRESIBA FLEXTOUCH U-200	Subcutaneous/pen
Insulin degludec	TRESIBA	Subcutaneous/vial

Insulin aspart	INSULIN ASPART	Subcutaneous/vial
Insulin aspart	NOVOLOG	Subcutaneous/vial
Insulin aspart	INSULIN ASPART FLEXPLEN	Subcutaneous/pen
Insulin aspart	NOVOLOG FLEXPEN	Subcutaneous/pen
Insulin aspart (niacinamide)	FIASP PENFILL	Subcutaneous/cartridge
Insulin aspart (niacinamide)	FIASP FLEXTOUCH	Subcutaneous/pen
Insulin aspart (niacinamide)	FIASP	Subcutaneous/vial
Insulin aspart	LYUMJEV	Subcutaneous/vial
Insulin aspart	LYUMJEV KWIKPEN U-100	Subcutaneous/pen
Insulin aspart	LYUMJEV KWIKPEN U-200	Subcutaneous/pen
Insulin regular, human	HUMULIN R	Subcutaneous/vial
Insulin/ regular, human	NOVOLIN R	Subcutaneous/vial
Insulin regular/ human	NOVOLIN R FLEXPEN	Subcutaneous/pen

Combo Basal/bolus		
Generic	Brand	Route/Form
Insulin NPH hum/reg insulin hm	HUMULIN 70-30	Subcutaneous/vial
Insulin NPH hum/reg insulin hm	NOVOLIN 70-30	Subcutaneous/vial
Insulin NPH hum/reg insulin hm	HUMULIN 70/30 KWIKPEN	Subcutaneous/pen
Insulin NPH hum/reg insulin hm	NOVOLIN 70-30 FLEXPEN	Subcutaneous/pen
Insulin aspart prot/insulin asp	INSULIN ASPART PROT MIX 70-30	Subcutaneous/pen
Insulin aspart prot/insulin asp	NOVOLOG MIX 70-30 FLEXPEN	Subcutaneous/pen
Insulin aspart prot/insulin asp	INSULIN ASPART PROT MIX 70-30	Subcutaneous/vial

Insulin glargine-yfgn	INSULIN GLARGINE-YFGN	Subcutaneous/vial
Insulin glargine-yfgn	SEMGLEE (YFGN)	Subcutaneous/vials
Insulin glargine-yfgn	INSULIN GLARGINE-YFGN	Subcutaneous/pen
Insulin glargine-yfgn	SEMGLEE (YFGN) PEN	Subcutaneous/pen
Insulin NPH human isophane	HUMULIN N	Subcutaneous/vial
Insulin NPH human isophane	NOVOLIN N	Subcutaneous/vial
Insulin NPH human isophane	HUMULIN N KWIKPEN	Subcutaneous/pen
Insulin NPH human isophane	NOVOLIN N FLEXPEN	Subcutaneous/pen
Combo Basal/GLP-1 Subcutaneous pen		
Insulin degludec/liraglutide	XULTOPHY 100-3.6	Subcutaneous/pen
Insulin glargine/lixisenatide	SOLIQUA 100-33	Subcutaneous/pen

Insulin aspart prot/insulin asp	NOVOLOG MIX 70-30	Subcutaneous/vial
Insulin lispro protamine/lispro	HUMALOG MIX 75-25 KWIKPEN	Subcutaneous/pen
Insulin lispro protamine/lispro	INSULIN LISPRO PROTAMINE MIX	Subcutaneous/pen
Insulin lispro protamine/lispro	HUMALOG MIX 50-50 KWIKPEN	Subcutaneous/pen
Insulin lispro protamine/lispro	HUMALOG MIX 75-25	Subcutaneous/vial
Insulin lispro protamine/lispro	HUMALOG MIX 50-50	Subcutaneous/vial

Glucagon-like Peptide-1 (GLP-1) Receptor Agonists and Glucose Dependent Insulinotropic Polypeptide (GIP) Receptor Agonist

Goal(s):

- Promote cost-effective and safe step-therapy for management of type 2 diabetes mellitus (T2DM).

Length of Authorization:

- Up to 12 months

Requires PA:

- All non-preferred GLP-1 receptor agonists and GLP-1 receptor + GIP receptor agonists. Preferred products do not require PA when prescribed as second-line therapy in conjunction with metformin.

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code	
2. Does the patient have a diagnosis of Type 2 diabetes mellitus?	**Yes:** Go to #3	**No:** Pass to RPh. Deny; medical appropriateness.
3. Will the prescriber consider a change to a preferred product? Message: • Preferred products are evidence-based reviewed for comparative effectiveness and safety by the Oregon Pharmacy and Therapeutics (P&T) Committee.	**Yes:** Inform prescriber of covered alternatives in class	**No:** Go to #4

Approval Criteria		
4. Has the patient tried and failed to meet hemoglobin A1C goals with metformin or have contraindications to metformin? (document contraindication, if any)	**Yes:** Approve for up to 12 months	**No:** Pass to RPh. Deny; medical appropriateness. Recommend trial of metformin. See below for metformin titration schedule.

Initiating Metformin

1.	Begin with low-dose metformin (500 mg) taken once or twice per day with meals (breakfast and/or dinner) or 850 mg once per day.
2.	After 5-7 days, if gastrointestinal side effects have not occurred, advance dose to 850 mg, or two 500 mg tablets, twice per day (medication to be taken before breakfast and/or dinner).
3.	If gastrointestinal side effects appear with increasing doses, decrease to previous lower dose and try to advance the dose at a later time.
4.	The maximum effective dose can be up to 1,000 mg twice per day. Modestly greater effectiveness has been observed with doses up to about 2,500 mg/day. Gastrointestinal side effects may limit the dose that can be used.

Nathan, et al. Medical management of hyperglycemia in Type 2 Diabetes: a consensus algorithm for the initiation and adjustment of therapy. *Diabetes Care*. 2008; 31;1-11.

P&T Review: *10/22 (KS), 8/20 (KS), 6/20), 3/19, 7/18, 9/17; 1/17; 11/16; 9/16; 9/15; 1/15; 9/14; 9/13; 4/12; 3/11*
Implementation: *1/1/23; 9/1/20; 5/1/19; 8/15/18; 4/1/17; 2/15; 1/14*