Drug Coverage Policy

Effective Date.....4/1/2025
Coverage Policy Number.....IP0702
Policy Title.....Diabetes - Glucagon-Like Peptide-1 Agonists for Individual and Family Plans

Diabetes – Glucagon-Like Peptide-1 Agonists for Individual and Family Plans

- Bydureon BCise® (exenatide extended-release subcutaneous injection – AstraZeneca)
- Byetta® (exenatide subcutaneous injection – AstraZeneca)
- Liraglutide subcutaneous injection (generic for Victoza)
- Mounjaro® (tirzepatide subcutaneous injection – Eli Lilly)
- Ozempic® (semaglutide subcutaneous injection – Novo Nordisk)
- Rybelsus® (semaglutide tablets – Novo Nordisk)
- Trulicity® (dulaglutide subcutaneous injection – Eli Lilly)
- Victoza® (liraglutide subcutaneous injection – Novo Nordisk)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview
The glucagon-like peptide-1 (GLP-1) receptor agonists and the GLP-1/glucose-dependent insulinotropic polypeptide-1 (GIP) agonist addressed in this policy are indicated as adjuncts to diet and exercise to improve glycemic control in adults with **type 2 diabetes**.[1-8] Liraglutide, Trulicity, and Bydureon BCise are additionally indicated for type 2 diabetes in patients ≥ 10 years of age.[3,7,8] Liraglutide, Ozempic, and Trulicity also have labeled indications related to cardiovascular (CV) risk reduction in adults with type 2 diabetes.[5,7,8]

Guidelines
According to the American Diabetes Association Standards of Care (2024), pharmacologic therapy should be guided by person-centric treatment factors including comorbid conditions, as well as treatment goals, and preferences.[9] Pharmacotherapy should be initiated at the time type 2 diabetes is diagnosed unless there are contraindications. Therapies, such as metformin or other agents, including combination therapy, that provide adequate efficacy to achieve and maintain treatment goals should be considered.

In adults with type 2 diabetes and established atherosclerotic cardiovascular disease (ASCVD), heart failure (HF), and/or chronic kidney disease (CKD), treatment should include agents that reduce CV or kidney disease risk.[9] Among patients with type 2 diabetes with established ASCVD or indicators of high ASCVD risk, GLP-1 agonists with proven CV benefit (i.e., label indication of reducing CV disease events) or a sodium glucose co-transporter-2 (SGLT-2) inhibitor are preferred regardless of baseline metformin use. A GLP-1 agonist with proven CV benefit is an alternative to an SGLT-2 inhibitor if an SGLT-2 inhibitor is not tolerated or contraindicated in patients with CKD, regardless of baseline metformin use.

In patients without cardiorenal risk factors described above, the GLP-1 agonists are additionally recommended in patients based on glycemic needs.[9] In general, higher efficacy approaches have a greater likelihood of achieving glycemic goals. The GLP-1 agonists, Ozempic and Trulicity (high dose) and the GLP-1/GIP agonist, Mounjaro (tirzepatide subcutaneous injection), are among the agents considered to have "very high" efficacy for glucose lowering; the other GLP-1 agonists are considered to have "high" efficacy for glucose lowering.

Weight management is also a treatment goal in individuals with type 2 diabetes due to multiple benefits including improved glycemic control, reduction in hepatic steatosis, and improvement in CV risk factors.[9] The choice of therapy for glycemic control should support weight management goals; Mounjaro and Ozempic are noted to have the highest weight loss efficacy among the agents approved for glycemic management. Additional weight management approaches, alone or in combination, should be used if needed to achieve an individual's weight loss goals (i.e., intensive behavioral therapy, weight loss pharmacotherapy, or metabolic surgery).

American Association of Clinical Endocrinologists statement on the comprehensive care for type 2 diabetes (2023) provides principles for the management of type 2 diabetes.[12] In patients with type 2 diabetes and established ASCVD or at high risk for ASCVD, GLP-1 agonists and SGLT-2 inhibitors are recommended. In a patient with type 2 diabetes and established ASCVD or are at high risk, a GLP-1 agonist with proven CV benefit (liraglutide, Ozempic, Trulicity) should be initiated as a first-line therapy independent of the glycemic goal or other antihyperglycemic treatments, including metformin; SGLT-2 inhibitors are an alternative. In patients with type 2 diabetes and ASCVD or at high risk of ASCVD, use of a GLP-1 agonist is also recommended to reduce the risk of stroke. To reduce the risk of progression of diabetic kidney disease and CV disease in patients with type 2 diabetes, SGLT-2 inhibitors are recommended; GLP-1 agonists are

also an option to reduce progression of albuminuria, renal function decline, and ASCVD risk in individuals with type 2 diabetes and diabetic kidney disease (Ozempic and Trulicity are cited). For patients with type 2 diabetes but without established or high risk for ASCVD, heart failure, stroke, or CKD, metformin should be the initial therapy unless contraindicated. In patients who are overweight or obese, the following therapies are recommended and listed in order of preference: Mounjaro, GLP-1 agonists, and SGLT-2 inhibitors. In patients with a history of hypoglycemia, at high risk of hypoglycemia, or at risk of severe complications from hypoglycemia, recommended therapies (in order of preference) are: GLP-1 agonists, SGLT-2 inhibitors, Mounjaro, thiazolidinediones, and dipeptidyl peptidase-4 inhibitors.

Kidney Diseases Improving Global Outcomes 2024 guidelines for the clinical evaluation and management of CKD recommend a long-acting GLP-1 agonist (prioritizing agents with documented CV benefits) in adults with type 2 diabetes and CKD who have not achieved individualized glycemic targets despite use of metformin and an SGLT-2 inhibitors, or who are unable to take those medications.[13]

A report of the American College of Cardiology and American Heart Association (2024) recommends GLP-1 agonists (liraglutide, Ozempic) and SGLT-2 inhibitors to reduce the risk of major adverse CV events in adults with type 2 diabetes and peripheral arterial disease.[14]

Documentation: Documentation is required for use of GLP1 Products as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory results, claims records, and/or other information.

Medical Necessity Criteria

I. Bydureon BCise, Byetta, Liraglutide subcutaneous injection, Mounjaro, Ozempic, and Trulicity are considered medically necessary when the following is met:

FDA-Approved Indication

1. **Type 2 Diabetes Mellitus.** Approve for 1 year if the patient meets the following:
   A) Diagnosis of Type 2 diabetes mellitus **[Documentation Required]**

II. Rybelsus is considered medically necessary when the following is met:

FDA-Approved Indication

1. **Type 2 Diabetes Mellitus.** Approve for 1 year if the patient meets **BOTH** of the following the following (A and B):
   A) Patient is 18 years of age or older
   B) Diagnosis of Type 2 diabetes mellitus **[Documentation Required]**

III. Victoza is considered medically necessary when the following is met:

FDA-Approved Indication

1. **Type 2 Diabetes Mellitus.** Approve for 1 year if the patient meets **BOTH** of the following (A and B):
   A) Diagnosis of Type 2 diabetes mellitus **[Documentation Required]**
   B) Preferred product criteria is met for the product(s) as listed in the below table(s)

Individual and Family Plans:

Product	Criteria
Victoza (liraglutide subcutaneous injection)	The patient has tried **liraglutide subcutaneous injection** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) [for example, difference in dyes, fillers, preservatives] between the brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Weight Loss Treatment**. Saxenda (liraglutide subcutaneous injection) contains the same chemical entity as Victoza and is indicated at a higher dose for chronic weight management. Wegovy (semaglutide subcutaneous injection) contains the same chemical entity as Ozempic and is indicated at a higher dose for chronic weight management. Zepbound (tirzepatide subcutaneous injection) contains the same chemical entity as Mounjaro and is indicated at the same doses for chronic weight management. Endocrine Society guidelines for pharmacological management of obesity (2015) advise against off-label prescribing of medications such as GLP-1 receptor agonists for the sole purpose of producing weight loss.[10] The American Gastroenterology Association guidelines for pharmacological interventions for adults with obesity only provide recommendations for the GLP-1 agonists approved for weight loss (i.e., Saxenda and Wegovy).[11] The GLP-1 agonists and GLP-1/glucose-dependent insulinotropic polypeptide-1 agonist in this policy are not FDA-approved for weight loss in a patient who is overweight (body mass index [BMI] ≥ 27 kg/m^2) or obese (BMI ≥ 30 kg/m^2) without type 2 diabetes. Note: If the patient has type 2 diabetes, refer to FDA-Approved Indication.

2. **Type 1 Diabetes Mellitus.** None of the GLP-1 agonists or GLP-1/ glucose-dependent insulinotropic polypeptide-1 agonist are indicated for patients with type 1 diabetes.[1-8] Addition of GLP-1 receptor agonists to insulin therapy resulted in small (0.2%) reductions in hemoglobin A_{1c} among patients with type 1 diabetes compared with insulin alone.[9]

3. **Prediabetes/Diabetes Prevention.** GLP-1 agonists and the GLP-1/ glucose-dependent insulinotropic polypeptide-1 agonist are not indicated in a patient with elevated blood glucose who does not have type 2 diabetes. The American Diabetes Association Standards of Care (2024) state that metformin therapy should be considered in adults at high-risk of diabetes.[9] Further, the standards note that metformin has the longest history of safety data as a pharmacologic therapy for diabetes prevention. Note: If the patient has type 2 diabetes, refer to FDA-Approved Indication.

4. **Metabolic Syndrome.** The GLP-1 agonists and the GLP-1/glucose-dependent insulinotropic polypeptide-1 agonist are not indicated in a patient with metabolic syndrome

who does not have type 2 diabetes. Note: If the patient has type 2 diabetes, refer to FDA-Approved Indication.

5. **Concomitant Use with Glucagon-Like Peptide-1 (GLP-1) Agonists or GLP-1/ Glucose-Dependent Insulinotropic Polypeptide (GIP) Agonist.** The GLP-1 agonists and the GLP-1/GIP agonist should not be combined with each other or with any other GLP-1 agonists or GLP-1/GIP agonist. There are other GLP-1 and GLP-1/GIP products not included in this policy that are FDA-approved for weight loss and are not indicated for type 2 diabetes. Note: Examples of other GLP-1 agonists not included in this policy include but are not limited to Saxenda (liraglutide subcutaneous injection) and Wegovy (semaglutide subcutaneous injection). An example of a GLP-1/GIP agonist not included in this policy is Zepbound (tirzepatide subcutaneous injection).

References

1. Adlyxin® subcutaneous injection [prescribing information]. Bridgewater, NJ: sanofi-aventis; September 2023. Adlyxin® subcutaneous injection [prescribing information]. Bridgewater, NJ: sanofi-aventis; September 2023.
2. Mounjaro® subcutaneous injection [prescribing information]. Indianapolis, IN: Lilly; July 2023.
3. Bydureon BCise® subcutaneous injection [prescribing information]. Wilmington, DE: AstraZeneca; May 2023.
4. Byetta® subcutaneous injection [prescribing information]. Wilmington, DE: AstraZeneca; December 2022.
5. Ozempic® subcutaneous injection [prescribing information]. Plainsboro, NJ: Novo Nordisk; September 2023.
6. Rybelsus® tablets [prescribing information]. Plainsboro, NJ: Novo Nordisk; January 2024.
7. Trulicity® subcutaneous injection [prescribing information]. Indianapolis, IN: Lilly; November 2022.
8. Victoza® subcutaneous injection [prescribing information]. Plainsboro, NJ: Novo Nordisk; July 2023.
9. American Diabetes Association. Standards of medical care in diabetes – 2024. *Diabetes Care*. 2024;47(Suppl 1):S1-S321.
10. Apovian CM, Aronne LJ, Bessesen DH, et al. Pharmacological management of obesity: An endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2015;100(2):342-362.
11. Grunvald E, Shah R, Hernaez R, et al. AGA clinical practice guideline on pharmacological interventions for adults with obesity. *Gastroenterol.* 2022;163:1198-1225.
12. Samson SL, Vellanki P, Blonde L, et al. American Association of Clinical Endocrinology consensus statement: comprehensive type 2 diabetes management algorithm – 2023 update. *Endocr Pract.* 2023;29:305-340.
13. Kidney Diseases Improving Global Outcomes (KDIGO). KDIGO 2024 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int.* 2024;105(4S):S117-S314.
14. Gornik HL, Aronow HD, Goodney PP, et al. 2024 ACC/AHA/AACVPR/APMA/ABC/SCAI/SVN/SVS/SIR/VESS guideline for the management of lower extremity peripheral arterial disease: a report of the American College of Cardiology/American Heart Association Joint Committee on clinical practice guidelines. *Circulation.* 2024. [Epub ahead of Print 2024 May 14].

Revision Details

Type of Revision	Summary of Changes	Date
New	New policy	12/01/2024
Selected Revision	**Removed** the metformin requirement from all products. **Removed** preferred product requirements from Liraglutide, Mounjaro, Ozempic and Rybelsus. **Updated** the Victoza preferred product requirement to a Multi-Source Brand approach.	04/01/2025

The policy effective date is in force until updated or retired.