PRIOR AUTHORIZATION POLICY

POLICY: Diabetes – Glucagon-Like Peptide-1 Agonists Prior Authorization Policy

- Adlyxin® (lixisenatide subcutaneous injection – sanofi-aventis [obsolete 01/01/2023])
- Bydureon BCise® (exenatide extended-release subcutaneous injection – AstraZeneca)
- Byetta® (exenatide subcutaneous injection – AstraZeneca)
- 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)

REVIEW DATE: 06/05/2024

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] Victoza, Trulicity, and Bydureon BCise are additionally indicated for type 2 diabetes in patients ≥ 10 years of age.[3,7,8] Victoza, 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 (Ozempic, Trulicity, or Victoza) 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 (Ozempic, Victoza) and SGLT-2 inhibitors to reduce the risk of major adverse CV events in adults with type 2 diabetes and peripheral arterial disease.[14]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of the GLP-1 agonists and GLP-1/GIP agonist targeted in this policy. Of note, Saxenda® (liraglutide subcutaneous injection), Wegovy® (semaglutide subcutaneous injection), and Zepbound® (tirzepatide subcutaneous injection) are not indicated for the treatment of diabetes and are not targeted in this policy. All approvals are provided for the duration noted below.

Automation: The following automation is applied in this policy:

- **Adlyxin, Byetta, Mounjaro, Ozempic, Rybelsus:** If criteria for previous use of an oral medication for diabetes (not including Rybelsus or single-entity metformin) in the past 130 days are not met at the point of service, OR if the patient is < 18 years of age, coverage will be determined by Prior Authorization criteria.
- **Bydureon BCise, Trulicity, Victoza:** If criteria for previous use of an oral medication for diabetes (not including Rybelsus or single-entity metformin) in the past 130 days are not met at the point of service, OR if the patient is < 10 years of age, coverage will be determined by Prior Authorization criteria.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Type 2 Diabetes Mellitus.** Approve for 1 year if the patient meets ONE of the following (A or B):
   - **A)** If the request is for Adlyxin, Byetta, Mounjaro, Ozempic, Rybelsus: Approve if the patient is ≥ 18 years of age; OR
   - **B)** If the request is for Bydureon BCise, Trulicity, Victoza: Approve if the patient is ≥ 10 years of age.

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Coverage is not recommended in the following situations:

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 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).

6. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. 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].