PRIOR AUTHORIZATION POLICY

POLICY: Diabetes – Glucagon-Like Peptide-1 Agonists Prior Authorization Policy
- Adlyxin® (lixisenatide subcutaneous injection – sanofi-aventis)
- Bydureon® (exenatide extended-release subcutaneous injection – AstraZeneca [obsolete 03/10/2021])
- Bydureon BCise® (exenatide extended-release subcutaneous injection – AstraZeneca)
- Byetta® (exenatide subcutaneous injection – AstraZeneca)
- 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: 10/25/2023

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CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

The glucagon-like peptide-1 (GLP-1) receptor agonists 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/Bydureon BCise are additionally indicated for type 2 diabetes in patients ≥ 10 years of age.[2,3,7,8] 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 (2023), first-line therapy for type 2 diabetes depends on comorbidities, patient-centered treatment factors, and management needs and generally includes metformin and

comprehensive lifestyle modification.[9] Among patients with type 2 diabetes with established atherosclerotic CV disease (ASCVD) or indicators of high ASCVD risk, GLP-1 agonists with proven CV disease 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 disease benefit is an alternative to an SGLT-2 inhibitor with primary evidence of reducing chronic kidney disease (CKD) progression if an SGLT-2 inhibitor is not tolerated or contraindicated in patients with chronic kidney disease, regardless of baseline metformin use. GLP-1 agonists are additionally recommended in patients without other cardiorenal risk factors with or without metformin based on glycemic needs. No preference is given for one GLP-1 agonist over the others; it is noted that when choosing an agent, weight loss, glycemic efficacy, administration schedule, and patient preference should be considered.

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, or 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.

POLICY STATEMENT

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

- **Adlyxin, Byetta, 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, 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.

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is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indication

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

CONDITIONS NOT COVERED

- **Adlyxin® (lixisenatide subcutaneous injection – sanofi-aventis)**
- **Bydureon® (exenatide extended-release subcutaneous injection – AstraZeneca [obsolete 03/10/2021])**
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is(are) considered experimental, investigational or unproven for ANY other use(s) 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 contains the same chemical entity as Victoza and is indicated at a higher dose for chronic weight management. Wegovy contains the same chemical entity as Ozempic and is indicated at a higher dose 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 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 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 are not indicated in a patient with elevated blood glucose who does not have type 2 diabetes. The American Diabetes Association Standards of Care (2023) 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 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.

REFERENCES

1. Adlyxin® subcutaneous injection [prescribing information]. Bridgewater, NJ: sanofi-aventis; September 2023.
2. Bydureon® subcutaneous injection [prescribing information]. Wilmington, DE: AstraZeneca; December 2022.
3. Bydureon BCise® subcutaneous injection [prescribing information]. Wilmington, DE: AstraZeneca; December 2022.
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 2023.
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 – 2023. *Diabetes Care*. 2023;46(Suppl 1):S1-S291.
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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	11/16/2022
Selected Revision	**Trulicity:** Automation and criteria were updated to reflect that the age of approval for Trulicity has been lowered from 18 years of age to 10 years of age. In automation, a claim for Trulicity will adjudicate if the patient meets the lookback for one oral medication for diabetes and the patient is ≥ 10 years of age (previously ≥ 18 years of age). In criteria, Trulicity will approve for a diagnosis of type 2 diabetes if the patient is ≥ 10 years of age (previously ≥ 18 years of age).	11/30/2022
Selected Revision	**Automation:** Automation for all products was updated to remove single-entity metformin as an oral medication that has been used for diabetes in the past 130 days. Previously, Rybelsus was the only oral agent not included in this automation.	03/01/2023
Selected Revision	**Conditions Not Covered:** **Metabolic Syndrome** was added to Conditions Not Covered; this applies to patients without a diagnosis of type 2 diabetes.	07/05/2023
Early Annual Revision	No criteria changes.	10/25/2023