MEDICAL MUTUAL®

Drug Policy

Policy: **Impacted Drugs:**	**Glucose-Dependent Insulinotropic Polypeptide (GIP) and Glucagon-Like Peptide-1 (GLP-1) Agonists** • 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, authorized generic)	**Annual Review Date:** **05/16/2024** **Last Revised Date:** **11/21/2024**

OVERVIEW

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

POLICY STATEMENT

This policy involves the use of glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) agonists. Prior authorization is recommended for pharmacy benefit coverage of glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) agonists. Approval is recommended for those who meet the conditions of coverage in the Criteria and Initial/Extended Approval for the diagnosis provided. Conditions Not Recommended for Approval are listed following the recommended authorization criteria. All approvals are provided for the approval duration noted below. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Automation:

- When available, ICD-10 codes starting with E11.* AND history of metformin use, alone or in combination, within the previous 130 days OR claims history for oral antidiabetic medications (excluding brand or generic single agent metformin products) within the last 365 days AND history of metformin use, alone or in combination, within the previous 130 days will be used for automation to allow approval of the requested medication AND

- For Adlyxin, Byetta, Mounjaro, Ozempic, Rybelsus: Patient is ≥ 18 years of age; OR
- For Bydureon BCise, Trulicity, Victoza, liraglutide recombinant authorized generic: Patient is ≥ 10 years of age.

- When non-preferred medications are requested the above automation applies AND a history of one Preferred medication within the 130-day look-back period, OR if within 365 days there were claims for both nonpreferred and preferred products AND
  - For Adlyxin, Byetta, Mounjaro, Ozempic, Rybelsus: Patient is ≥ 18 years of age; OR
  - For Bydureon BCise, Trulicity, Victoza, liraglutide recombinant authorized generic: Patient is ≥ 10 years of age.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) agonists is recommended in those who meet the following criteria:

1. **Type 2 Diabetes Mellitus**

   Criteria: *Approve for 6 months if the patient meets the following criteria (A and B):*

   A. Patient has a diagnosis of type 2 diabetes confirmed by the history of ONE of the following (a, b, or c):
   - a. Hemoglobin A1c (HbA1c) ≥ 6.5%˜; OR
   - b. Fasting plasma glucose (FPG) ≥ 126 mg/dL˜; OR
   - c. 2-hour plasma glucose (2-h PG) ≥ 200 mg/dL˜.

   B. Patient meets ONE of the following (a or b):
   - a. If the request is for Adlyxin, Byetta, Mounjaro, Ozempic, Rybelsus: Patient is ≥ 18 years of age; OR
   - b. If the request is for Bydureon BCise, Trulicity, Victoza: Patient is ≥ 10 years of age.

Initial Approval/ Extended Approval.

A) *Initial Approval:* 180 days
B) *Extended Approval:* 180 days

PREFERRED SPECIALTY MANAGEMENT

POLICY STATEMENT

A preferred step therapy program has been developed to encourage the use of a preferred product prior to the use of a non-preferred product. If the preferred step therapy rule is not met for a non-preferred agent at the point of service, coverage will be determined by the preferred step therapy criteria below. All approvals are provided for 12 months in duration.

Automation: A patient with a history of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Preferred Medications

- Bydureon (exenatide extended-release)
- Bydureon BCise (exenatide extended-release)

- Byetta (exenatide)
- Mounjaro (tirzepatide)
- Ozempic (semaglutide inection)
- Rybelsus (semaglutide oral tablet)
- Trulicity (dulaglutide)

Non-Preferred Medication

- Victoza (liraglutide [rDNA origin])
- Liraglutide recombinant authorized generic
- Adlyxin (lixisenatide)

PREFERRED STEP THERAPY CRITERIA (FOR APPLICABLE REVIEWS)

1. If the patient has tried a preferred medication, then authorization for a non-preferred medication may be given

2. No other exceptions are recommended.

Approval Duration: 180 days

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) agonists have not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Type 1 Diabetes Mellitus.** None of the glucagon-like peptide-1 (GLP-1) agonists or the GLP-1/ glucose-dependent insulinotropic polypeptide agonist are indicated in a patient with type 1 diabetes.1-7 Addition of GLP-1 receptor agonists to insulin therapy resulted in small (0.2%) reductions in hemoglobin A1c among patients with type 1 diabetes compared with insulin alone.[8]

2. **Weight Loss Treatment**. Saxenda (liraglutide subcutaneous injection) contains the same chemical entity as liraglutide (Victoza, authorized generic) 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 glucagon-like peptide-1 (GLP-1) receptor agonists for the sole purpose of producing weight loss.9 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 agonist in this policy are not FDA-approved for weight loss in a patient who is overweight (body mass index [BMI] ≥ 27 kg/m2) or obese (BMI ≥ 30 kg/m2) without type 2 diabetes. Note: If the patient has type 2 diabetes, refer to FDA-Approved Indication.

3. **Prediabetes/Diabetes Prevention.** The glucagon-like peptide-1 (GLP-1) agonists and the GLP-1/glucose-dependent insulinotropic polypeptide agonist are indicated in patients with type 2 diabetes; they 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.8 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. **Polycystic Ovarian Syndrome (PCOS).** The glucagon-like peptide-1 (GLP-1) agonists and the GLP-1/glucose-dependent insulinotropic polypeptide agonist are not indicated in a patient with polycystic ovarian syndrome who does not have type 2 diabetes. Note: If the patient has type 2 diabetes, refer to FDA-Approved Indication.

5. **Metabolic Syndrome**. The glucagon-like peptide-1 (GLP-1) agonists and the GLP-1/glucose-dependent insulinotropic polypeptide 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.

6. **Concomitant use with other glucagon-like peptide-1 (GLP-1) agonists or GLP-1/glucose-dependent insulinotropic polypeptide (GIP) receptor agonists.** 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).

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

˜Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Adlyxin® subcutaneous injection [prescribing information]. Bridgewater, NJ: sanofi-aventis; September 2023.

2. Bydureon BCise® subcutaneous injection [prescribing information]. Wilmington, DE: AstraZeneca; December 2022.
3. Byetta® subcutaneous injection [prescribing information]. Wilmington, DE: AstraZeneca; December 2022.
4. Ozempic® subcutaneous injection [prescribing information]. Plainsboro, NJ: Novo Nordisk; September 2023.
5. Rybelsus® tablets [prescribing information]. Plainsboro, NJ: Novo Nordisk; January 2024.
6. Trulicity® subcutaneous injection [prescribing information]. Indianapolis, IN: Lilly; November 2022.
7. Victoza® subcutaneous injection [prescribing information]. Plainsboro, NJ: Novo Nordisk; July 2023.
8. American Diabetes Association. Standards of medical care in diabetes – 2024. *Diabetes Care*. 2024;47(Suppl 1):S1-S321.
9. 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.
10. Grunvald E, Shah R, Hernaez R, et al. AGA clinical practice guideline on pharmacological interventions for adults with obesity. *Gastroenterol.* 2022;163:1198-1225.
11. 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.
12. 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.
13. Mounjaro® subcutaneous injection [prescribing information]. Indianapolis, IN: Lilly; July 2023.
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].