Pharmacy Medical Necessity Guidelines: Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists

Effective: February 1, 2021

Prior Authorization Required	√	Type of Review – Care Management	
Not Covered		Type of Review – Clinical Review	√
Pharmacy (RX) or Medical (MED) Benefit	RX	Department to Review	RXUM

These pharmacy medical necessity guidelines apply to the following:

Commercial Products

☐ Tufts Health Plan Commercial products – large group plans
☐ Tufts Health Plan Commercial products – small group and individual plans
☐ Tufts Health Freedom Plan products – large group plans
☐ Tufts Health Freedom Plan products – small group plans
- CareLink℠ – Refer to CareLink Procedures, Services and Items Requiring Prior Authorization

Tufts Health Public Plans Products

☐ Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product)
☐ Tufts Health Together – MassHealth MCO Plan and Accountable Care Partnership Plans
☒ Tufts Health RITogether – A Rhode Island Medicaid Plan

Fax Numbers:
RXUM: 617.673.0988

Note: This guideline does not apply to Medicare Members (includes dual eligible Members).

OVERVIEW

FOOD AND DRUG ADMINISTRATION-APPROVED INDICATIONS

Adlyxin (lixisentide) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 tiabetes. It is administered once daily within one hour before the first meal of the day. Adlyxin should be initiated at 10 mcg once daily for 14 days. On day 15, the dose should be increased to 20 mcg once daily.

Byetta (exenatide) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. It is injected subcutaneously within 60 minutes prior to morning and evening meals (or before the two main meals of the day, approximately six hours or more apart). Byetta is initiated as 5 mcg per dose twice daily and then increased to 10 mcg twice daily after one month, based on clinical response.

Bydureon (exenatide) is an extended release formulation of exenatide and should not be co-administered with Byetta. Like Byetta, Bydureon is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Bydureon 2 mg is administered by subcutaneous injection once every seven days, at any time of day, with or without meals.

Ozempic (semaglutide) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Ozempic is also indicated to reduce the major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease. Ozempic is administered once weekly at any time of day, with or without meals. The dose should be initiated at 0.25 mg once weekly. After four weeks, the dose should be increased to 0.5 mg once weekly. If, after at least four weeks, additional glycemic control is needed, the dose should be increased to 1 mg once weekly.

Rybelsus (semaglutide) is the first oral GLP1 agonist approved as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes. It should be administered at least 30 minutes before the first food, beverage, or other oral medications of the day with no more than 4 ounces of plain water only. Waiting less than 30 minutes, or take with food, beverages (other than plain water), or other oral medications will lessen the effect of Rybelsus. Waiting more than 30 minutes to eat may increase the absorption of Rybelsus. The starting dose of Rybelsus is 3 mg once daily for 30 days. After 30 days on the 3 mg/day dose, increase the dose to 7 mg once daily. The dose may be increased to 14 mg once daily if additional glycemic control is needed after at least 30 days on the 7 mg dose.

Victoza (liraglutide) is indicated as an adjunct to diet and exercise to improve glycemic control in patients 10 years of age and older with type 2 diabetes mellitus. Victoza is also indicated to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease. Victoza is injected

subcutaneously once daily at any time of day, regardless of meals. The dose should be initiated at 0.6 mg per day for one week and then increased to 1.2 mg. The dose can be increased to 1.8 mg for additional glycemic control.

Tanzeum (albiglutide) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Tanzeum is administered once weekly at any time of the day, without regards to meals. The dose is initiated at 30 mg once weekly and then increased to 50 mg once weekly if the patient requires additional glycemic control.

Trulicity (dulaglutide) is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus. Trulicity is also indicated to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus who have established cardiovascular disease or multiple cardiovascular risk factors. Trulicity is administered subcutaneously once weekly at any time of day. The dose should be initiated at 0.75 mg once weekly. If additional glycemic control is needed, the dose can be increased to 3 mg once weekly after at least four weeks on the 1.5 mg dose. The maximum dose is 4.5 mg once weekly; a patient should be on the 3 mg dose for at least four weeks before the dose increased to 4.5 mg/week for glycemic control.

All of the GLP-1 agonists except Adlyxin and Byetta have a Black Box Warning for thyroid C-cell tumors, including medullary thyroid carcinoma (MTC) in humans. Victoza was the first GLP-1 agonist to have this Black Box Warning; cases were seen in both genders of rats and mice during clinical trials. It is not known whether the GLP-1 agonists cause thyroid C-cell tumors, including MTC, in humans, as the human relevance of GLP-1-induced rodent thyroid C-cell tumors has not been determined. Patients should be counseled on the potential risk of MTC and the symptoms of thyroid tumors.

COVERAGE GUIDELINES

The plan may authorize coverage of a GLP-1 agonist for Members when **all** of the following criteria are met:

1. Member has a diagnosis of type 2 diabetes mellitus

AND

2. Member has had an inadequate response, intolerance, or contraindication to metformin at the highest tolerated dose

AND

3. The Member meets ONE of the following:

    a. There is a clinical rationale why the Member cannot take (e.g., clinical inappropriateness of therapy with or an inadequate response, intolerance, or contraindication to) at least one additional generic oral antidiabetic agent besides metformin. Examples include sulfonylureas (glimepiride, glipizide, glyburide), thiazolidinedione (pioglitazone), meglitinide analogues (nateglinide, replaglinide), and DPP-4 inhibitor (alogliptin).

    OR

    b. The Member has established cardiovascular disease (CVD) (e.g., ASCVD[†], heart failure) and the request is for Ozempic, Trulicity, or Victoza

    OR

    c. The Member has two or more cardiovascular risk factors* and the request is for Trulicity

AND

4. **Rybelsus only:** Member has had an inadequate response, intolerance, or contraindication to an injectable GLP-1 agonist or the provider submits documentation that the member cannot administer an injectable GLP-1 agonist

[†]ASCVD defined as:

- Coronary heart disease (CHD) (myocardial infarction, angina, coronary artery disease)
- Cerebrovascular disease (e.g., transient ischemic attack, ischemic stroke)
- Peripheral artery disease
- Aortic atherosclerotic disease

*Cardiovascular risk factors include (but not limited to):

- Dyslipidemia
- Hypertension
- Current tobacco use
- Obesity/overweight
- Family history of premature ASCVD
- Chronic kidney disease

- Metabolic syndrome
- Presence of albuminuria

LIMITATIONS

1. Documentation of a Member having needle phobia does not qualify as a medically acceptable contraindication or clinical inappropriateness for an injectable GLP-1 agonist.
2. Rybelsus will be limited to 30 tablets per 30 days.

CODES

None

REFERENCES

1. Adlyxin (lixisenatide) [prescribing information]. Bridgewater, NJ: Sanofi-Aventis; January 2019.
2. Byetta (exentaide) [prescribing information]. Wilmington, DE: AstraZeneca; February 2020.
3. Bydureon (exenatide) [prescribing information]. Wilmington, DE: AstraZeneca; February 2020.
4. Victoza (liraglutide) [prescribing information]. Plainsboro, NJ: Novo Nordisk; November 2020.
5. Tanzeum (albiglutide) [prescribing information]. Wilmington, DE: GlaxoSmithKline; December 2017.
6. Trulicity (dulaglutide) [prescribing information]. Indianapolis, IN: Eli Lilly and Company; September 2020.
7. Ozempic (semaglutide) [prescribing information]. Plainsboro, NJ: Novo Nordisk; September 2020.
8. American Diabetes Association. Standards of medical care in diabetes – 2021. *Diabetes Care*. 2021;44(Suppl. 1):S1-S222.
9. Rybelsus (semaglutide) [prescribing information]. Plainsboro, NJ: Novo Nordisk; January 2020.

APPROVAL HISTORY

May 9, 2017: Reviewed by Pharmacy & Therapeutics Committee.
Subsequent endorsements date(s) and changes made:

1. June 13, 2017: Added Adlyxin to Medical Necessity Guideline.
2. June 12, 2018: Administrative update, clarified a clinical rationale can be provided as to why Member cannot administer an additional generic antidiabetic agent.
3. April 9, 2019: Administrative changes made to template.
4. May 7, 2019: Added Ozempic (semaglutide) to Medical Necessity Guideline.
5. January 14, 2020: Added Rybelsus (semaglutide) to Medical Necessity Guideline.
6. January 12, 2021: Effective 2/1/2021, updated the criteria to include CVD and CVD risk factors.

BACKGROUND, PRODUCT AND DISCLAIMER INFORMATION

Pharmacy Medical Necessity Guidelines have been developed for determining coverage for plan benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. The plan makes coverage decisions on a case-by-case basis considering the individual member's health care needs. Pharmacy Medical Necessity Guidelines are developed for selected therapeutic classes or drugs found to be safe, but proven to be effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. The plan revises and updates Pharmacy Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Pharmacy Medical Necessity Guideline and a self-insured Member's benefit document, the provisions of the benefit document will govern.

Treating providers are solely responsible for the medical advice and treatment of members. The use of this policy is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to member eligibility and benefits on the date of service, coordination of benefits, referral/authorization and utilization management guidelines when applicable, and adherence to plan policies and procedures and claims editing logic.