GLP-1 (glucagon-like peptide-1) Agonists Step Therapy and Quantity Limit Program Summary

This program applies to FlexRx Open, FlexRx Closed, GenRx Open, GenRx Closed, and Health Insurance Marketplace. It is implemented with auto-grandfathering.

This is a FlexRx standard and GenRx standard step therapy program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

Program specific denial language for prerequisite step therapy component does not apply. Instead, supplemental program denial language will apply.

FDA APPROVED INDICATIONS AND DOSAGE[1-6,9-11]

GLP-1 Agonist	Indication	Important limitations for use	Dosage and Administration
Adlyxin (lixisenatide) **Available as:** Starter Pack: For treatment initiation, 1 prefilled green pen of 10 mcg and 1 prefilled burgundy pen of 20 mcg Maintenance Pack: 2 prefilled burgundy pens of 20 mcg	Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.	• Adlyxin has not been studied in patients with chronic pancreatitis or a history of unexplained pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis. • Adlyxin is not a substitute for insulin. Adlyxin is not indicated for use in patients with type 1 diabetes mellitus or for treatment of diabetic ketoacidosis. • The concurrent use of Adlyxin with short acting insulin has not been studied and is not recommended. • Adlyxin has not been studied in patients with gastroparesis and is not recommended in patients with gastroparesis.	• Starting dose of 10 mcg subcutaneously once daily for 14 days. • Increase the dose to the maintenance dose of 20 mcg once daily starting on Day 15.

GLP-1 Agonist	Indication	Important limitations for use	Dosage and Administration
Bydureon (exenatide extended-release) Injection **Available as**: 2 mg vial in single-dose tray with syringe of diluent and needle; 4 trays per carton 2 mg single-dose pen supplied in cartons with 4 pens and needle	Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.	• Not recommended as first-line therapy for patients inadequately controlled on diet and exercise. • Not a substitute for insulin. Should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. • Concurrent use with insulin has not been studied and cannot be recommended. • Bydureon has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.	• Inject subcutaneously 2 mg once weekly at any time of day, with or without meals. The day of weekly administration can be changed if necessary as long as the last dose was administered 3 or more days before. • Injection should be in the abdomen, thigh or upper arm.
Bydureon BCise (exenatide extended release) Injection **Available as:** 2 mg single dose auto-injector supplied in cartons with 4 auto-injectors	Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.	• Not recommended as first-line therapy for patients inadequately controlled on diet and exercise. • Should not be used to treat type 1 diabetes or diabetic ketoacidosis. • Use with insulin has not been studied and is not recommended. • Bydureon BCise is an extended-release formulation of exenatide. Do not coadminister with other exenatide containing products. • Has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.	• Administer 2 mg by subcutaneous injection once every seven days (weekly), at any time of day and with or without meals. • Administer immediately after the dose is prepared.

GLP-1 Agonist	Indication	Important limitations for use	Dosage and Administration
Byetta (exenatide) Injection **Available as**: 250 mcg/mL in: 5 mcg per dose, 60 doses, 1.2 mL prefilled pen 10 mcg per dose, 60 doses, 2.4 mL prefilled pen	Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.	• Not a substitute for insulin. Should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. • Concurrent use with insulin has not been studied and cannot be recommended. • Byetta has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.	• Inject subcutaneously within 60 minutes prior to morning and evening meals (or before the 2 main meals of the day, approximately 6 hours or more apart). • Initiate at 5 mcg per dose twice daily; increase to 10 mcg twice daily after 1 month based on clinical response.
Ozempic (semaglutide) **Available as:** Single-patient-use-pen, in cartons of one 2 mg pen delivering doses 0.25-0.5 mg per injection; and in cartons of two 2 mg pens delivering 1 mg per injection	Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus	• Ozempic is not recommended as a first-line therapy for patients who have inadequate glycemic control on diet and exercise because of the uncertain relevance of rodent C-cell tumor findings to humans • Ozempic has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis • OZEMPIC is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of patients with diabetic ketoacidosis.	• Administer once weekly at any time of day, with or without regard to meals. • Initiate at 0.25 mg subcutaneously once weekly. Dose can be increased to 0.5 mg once weekly after 4 weeks, and the increased to 1 mg once weekly after 4 weeks of 0.5 mg once weekly therapy • Inject subcutaneously in the abdomen, thigh, or upper arm.

GLP-1 Agonist	Indication	Important limitations for use	Dosage and Administration
Rybelsus® (semaglutide) tablet	Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus	• Not recommended as first-line therapy for patients inadequately controlled on diet and exercise • Has not been studied in patients with a history of pancreatitis • Not indicated for use in patients with type 1 diabetes mellitus or treatment of diabetic ketoacidosis	• Take 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 • Start with 3 mg once daily for 30 days. After 30 days on the 3 mg dose, increase the dose to 7 mg once daily. • 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
Tanzeum (albiglutide for injection, for subcutaneous (SC) use **Available as:** single-dose pens for injection, in cartons of 4 syringes plus needles, in doses of 30 mg and 50 mg	Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.	• Tanzeum is not indicated in the treatment of patients with type 1 diabetes mellitus or for the treatment of patients with diabetic ketoacidosis • Not recommended as first-line therapy for patients inadequately controlled on diet and exercise. • Has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis. • Has not been studied in patients with severe gastrointestinal disease, including severe gastroparesis. Use is not recommended in patients with pre-existing severe gastrointestinal disease. • Has not been studied in combination with prandial insulin.	• Administer once weekly at any time of day, without regard to meals. • Initiate at 30 mg subcutaneously once weekly. Dose can be increased to 50 mg once weekly in patients requiring additional glycemic control. • Inject subcutaneously in the abdomen, thigh, or upper arm.

GLP-1 Agonist	Indication	Important limitations for use	Dosage and Administration
Trulicity (dulaglutide for SC injection) **Available as:** Single dose pens and prefilled syringes	Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.	• Not recommended as first-line therapy for patients inadequately • controlled on diet and exercise • Has not been studied in patients with a history of pancreatitis. • Consider another antidiabetic therapy in patients with a history of pancreatitis • Not for treatment of type 1 diabetes mellitus or diabetic ketoacidosis. • Not for patients with pre-existing severe gastrointestinal disease. • Has not been studied in combination with basal insulin	• Administer once weekly at any time of day • Inject subcutaneously in the abdomen, thigh, or upper arm • Initiate at 0.75 mg subcutaneously once weekly. Dose can be increased to 1.5 mg once weekly for additional glycemic control
Victoza (liraglutide [rDNA origin] injection), solution for subcutaneous (SC) use **Available as:** Solution for subcutaneous injection, pre-filled, multi-dose pen that delivers doses of 0.6 mg, 1.2 mg, or 1.8 mg (6 mg/mL, 3 mL)	Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. To reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes mellitus and established cardiovascular disease	• Victoza is not a substitute for insulin. Victoza should not be used in patients with type 1 diabetes mellitus or for the treatment of or diabetic ketoacidosis • Concurrent use with prandial insulin has not been studied.	• Administer once daily at any time of day. • The injection site and timing can be changed without dose adjustment. • Initiate at 0.6 mg per day for one week. This dose is intended to reduce GI symptoms during initial titration, and is not effective for glycemic control. After 1 week, increase the dose to 1.2 mg. If 1.2 mg dose does not result in acceptable glycemic control, dose can be increased to 1.8 mg. • When initiating, consider reducing the dose of concomitantly-administered insulin secretagogues to reduce the risk of hypoglycemia.

CLINICAL RATIONALE

Both the American Diabetes Association (ADA) and American Association of Clinical Endocrinologists (AACE) recommend metformin as the optimal non-insulin first-line drug in type II diabetes mellitus.[7,8] Two-drug combinations should be used if metformin fails to achieve A1c target after approximately 3 months.[7,8] The choice of the second agent (sulfonylurea, thiazolidinedione, dipeptidyl peptidase-4 inhibitors, sodium-glucose cotransporter 2 inhibitor, basal insulin, glucagon-like peptide-1 agonist) is based upon patient and drug characteristics, with the goal of improving glycemic control while minimizing side effects.[7,8]

REFERENCES

1. Byetta prescribing information. AstraZeneca Pharmaceuticals, Inc. February 2015.
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4. Tanzeum prescribing information. GlaxoSmithKline LLC. August 2017.
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7. American Diabetes Association. Standards of medical care in diabetes 2018. Accessed 9/10/2018. Available at https://professional.diabetes.org/content/clinical-practice-recommendations.
8. Garber AJ, Abrahamson MB, Barzilay J, et al. Consensus statement by the American association of clinical endocrinologists and American college of endocrinology on the comprehensive type 2 diabetes management algorithm 2018 executive summary. Accessed 09/10/2018. Available at https://www.aace.com/publications/guidelines.
9. Bydureon BCise prescribing information. AstraZeneca Pharmaceuticals, Inc. October 2017.
10. Ozempic prescribing information. Novo Nordisk. December 2017.
11. Rybelsus prescribing information. Novo Nordisk A/S. September 2019.

GLP-1 (glucagon-like peptide-1) Agonists Step Therapy

OBJECTIVE
The intent of the GLP-1 (glucagon-like peptide-1) Agonists Step Therapy (ST) program is to promote appropriate selection of patients based on product labeling, and/or clinical guidelines, and/or clinical studies. Appropriate patients for GLP-1 agonist therapy are those who are concurrently receiving or have tried an agent containing metformin or sulfonylurea, insulin, or insulin/GLP-1. The step edit allows continuation of therapy when patients are currently receiving the requested agent. Patients without prerequisite agents in claims history or those who are unable to take a prerequisite agent due to documented intolerance, FDA labeled contraindication, or hypersensitivity will be reviewed when patient-specific documentation has been provided.

TARGET AGENTS
Adlyxin™ (lixisenatide)
Byetta® (exenatide)
Bydureon™ (exenatide extended-release)
Bydureon BCise™ (exenatide extended-release)
Ozempic® (semaglutide)
Rybelsus® (semaglutide)
Tanzeum™ (albiglutide)
Trulicity™ (dulaglutide)
Victoza® (liraglutide)

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Target Agents will be approved when ONE of the following is met:
1. The patient's medication history includes one or more of the following antidiabetic agents (an agent containing metformin or sulfonylurea, insulin, or insulin/GLP-1) in the past 90 days
   OR
2. There is documentation that the patient is currently using the requested agent
   OR
3. The prescriber states the patient is using the requested agent AND is at risk if therapy is changed
   OR
4. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to at least one of the following agents: metformin, sulfonylurea, or insulin

Length of approval: 12 months

NOTE: If Quantity Limit program also applies, please refer to Quantity Limit documents.

Step Therapy Supplement

This program applies to FlexRx Closed, FlexRx Open, GenRx Closed, GenRx Open, Health Insurance Marketplace, FocusRx and KeyRx formularies.

Please note, this does not include or apply to quantity limit questions.

STEP THERAPY SUPPLEMENT
OBJECTIVE
The intent of the Step Therapy Supplement is to provide additional questions, to ensure compliance to MN Statute 62Q.184. These questions will apply if the step therapy component within a Prior Authorization or Step Therapy program is not able to be approved.

CONDITIONS FOR APPROVAL
The requested agent will be approved when ONE of the following are met:

1. The patient is currently being treated with the requested agent as indicated by ALL of the following:
    a. A statement by the prescriber that the patient is currently taking the requested agent
    AND
    b. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
    AND
    c. The prescriber states that a change in therapy is expected to be ineffective or cause harm

    OR
2. The patient's medication history include the required prerequisite/preferred agent(s) as indicated by:
    a. Evidence of a paid claim(s) within the past 999 days
    OR
    b. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days AND the required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event

    OR
3. The prescriber has provided documentation that the required prerequisite/preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

Length of Approval: As per program specific criteria