# GLP-1 (glucagon-like peptide-1) Agonists Step Therapy Program Summary

This program applies to Medicaid. It is implemented with auto-grandfathering.

Step Therapy only applies to the MN Medicaid Preferred Drug List (PDL) preferred drugs: Byetta, Bydureon pens, and Victoza.

The BCBS MN Step Therapy Supplement also applies to this program for Medicaid.

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 | Limitations for use | Dosage and Administration |
|---|---|---|---|
| **Adlyxin** (lixisenatide)<br><br>subcutaneous injection | 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.<br>• 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.<br>• The concurrent use of Adlyxin with short acting insulin has not been studied and is not recommended.<br>• 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.<br>• Increase the dose to the maintenance dose of 20 mcg once daily starting on Day 15. |
| **Bydureon** (exenatide extended-release)<br><br>subcutaneous injection | Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. | • Not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise.<br>• Not a substitute for insulin. Is not indicated for use in patients with type 1 diabetes mellitus or for the | • Inject subcutaneously 2 mg once every 7 days (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 |

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| | | treatment of diabetic ketoacidosis, as it would not be effective in these settings.<br>• Concurrent use with insulin has not been studied.<br>• Bydureon has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis. | was administered 3 or more days before.<br>• Injection should be in the abdomen, thigh or upper arm. |
| **Bydureon BCise** (exenatide extended release)<br><br>subcutaneous injection | Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. | • Not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise.<br>• Is not indicated for use in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.<br>• Concurrent use with prandial insulin has not been studied and is not recommended.<br>• Bydureon BCise is an extended-release formulation of exenatide. It should not be used with other products containing the active ingredient exenatide.<br>• 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.<br>• Administer immediately after the dose is prepared. |
| **Byetta** (exenatide)<br><br>subcutaneous injection | 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 for the treatment of type 1 diabetes or diabetic ketoacidosis, as it would not be effective in these settings.<br>• Concurrent use with prandial insulin has not been studied and cannot be recommended. | • 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).<br>• Initiate at 5 mcg per dose twice daily; increase to 10 mcg |

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| | | • Byetta has not been studied in patients with a history of pancreatitis. Other antidiabetic therapies should be considered in patients with a history of pancreatitis. | twice daily after 1 month based on clinical response. |
| **Ozempic** (semaglutide)<br><br>subcutaneous 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.<br>• Ozempic has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis<br>• Ozempic is not a substitute for insulin. Ozempic is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of patients with diabetic ketoacidosis, as it would not be effective in these settings. | • Administer once weekly at any time of day, with or without regard to meals.<br>• 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<br>• Inject subcutaneously in the abdomen, thigh, or upper arm. |
| **Rybelsus®** (semaglutide)<br><br>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<br>• Has not been studied in patients with a history of pancreatitis<br>• 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<br>• 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.<br>• 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) | Adjunct to diet and exercise to improve glycemic control in | • Not recommended as first-line therapy for patients inadequately controlled on diet and exercise. | • Administer once weekly at any time of day, without regard to meals. |

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| subcutaneous injection | adults with type 2 diabetes mellitus. | • Has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.<br>• Is not indicated in the treatment of patients with type 1 diabetes mellitus or for the treatment of patients with diabetic ketoacidosis. Tanzeum is not a substitute for insulin in these patients.<br>• 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.<br>• Has not been studied in combination with prandial insulin. | • Initiate at 30 mg subcutaneously once weekly. Dose can be increased to 50 mg once weekly if the glycemic response is inadequate.<br>• Inject subcutaneously in the abdomen, thigh, or upper arm. |
| **Trulicity** (dulaglutide)<br><br>subcutaneous injection | Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. | • Not recommended as first-line therapy for patients who have inadequate control on diet and exercise<br>• Has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis<br>• Should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. Trulicity is not a substitute for insulin.<br>• Has not been studied in patients with pre-existing severe gastrointestinal disease, including severe gastroparesis. Use is not recommended in patients with pre-existing severe gastrointestinal disease. | • Administer once weekly at any time of day<br>• Inject subcutaneously in the abdomen, thigh, or upper arm<br>• Initiate at 0.75 mg subcutaneously once weekly. Dose can be increased to 1.5 mg once weekly for additional glycemic control |

| GLP-1 Agonist | Indication | Limitations for use | Dosage and Administration |
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| | | • Has not been studied in combination with basal insulin | |
| **Victoza** (liraglutide)<br><br>subcutaneous injection | Adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.<br><br>To reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes mellitus and established cardiovascular disease | • Victoza should not be used in patients with type 1 diabetes mellitus or for the treatment of or diabetic ketoacidosis, as it would not be effective in these settings.<br>• Concurrent use with prandial insulin has not been studied. | • Administer once daily at any time of day.<br>• The injection site and timing can be changed without dose adjustment.<br>• 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 additional glycemic control is required, increase the dose to 1.8 mg daily after at least one week of treatments with the daily dose. |

## CLINICAL RATIONALE

Both the American Diabetes Association (ADA) and American Association of Clinical Endocrinologists (AACE) recommend metformin as the preferred first-line drug in type II diabetes mellitus.[4,5] Two-drug combinations should be considered if metformin fails to achieve A1c target after approximately 3 months. 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 and patient burden.[7, 8]

Bydureon, Bydureon BCise, Ozempic, Tanzeum, Trulicity, and Victoza all share the same black box warning:

- Causes thyroid C-cell tumors at clinically relevant exposures in rats. It is unknown whether these agents cause thyroid C-cell tumors, including medullary thyroid carcinoma (MTC) in humans, as the human relevance of induced rodent thyroid C-cell tumors has not been determined.
- Contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).[2,3,4,5,9,10]

## REFERENCES


1. Byetta prescribing information. AstraZeneca Pharmaceuticals, Inc. February 2015.
2. Victoza prescribing information. Novo Nordisk A/S. June 2019.
3. Bydureon prescribing information. AstraZeneca Pharmaceuticals, Inc. February 2019.
4. Tanzeum prescribing information. GlaxoSmithKline LLC. December 2017.
5. Trulicity prescribing information. Eli Lilly and Company. January 2019.
6. Adlyxin prescribing information. Sanofi-Aventis US. LLC. July 2016
7. American Diabetes Association. Standards of medical care in diabetes-2019. Accessed 8/27/2019. Available at: https://care.diabetesjournals.org/content/diacare/suppl/2018/12/17/42.Supplement_1.DC1/DC_42_S1_2019_UPDATED.pdf
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 – 2019 Executive Summary. Accessed 8/27/2019. Available at https://journals.aace.com/doi/pdf/10.4158/CS-2018-0535
9. Bydureon BCise prescribing information. AstraZeneca Pharmaceuticals, Inc. July 2019.
10. Ozempic prescribing information. Novo Nordisk. April 2019.
11. Rybelsus prescribing information. Novo Nordisk A/S. September 2019.

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

**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. Information has been provided that indicates that the patient is currently being treated with the requested agent
   **OR**
3. The prescriber states the patient is currently being treated with 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 Program Summary

This program applies to Medicaid.

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. BOTH of the following
    a. The patient's medication history includes the required prerequisite/preferred agent(s) or a drug in the same pharmacological class with the same mechanism of action as indicated by ONE of the following:
        i. Evidence of a paid claim(s) within the past 999 days
        **OR**
        ii. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days

    **AND**
    b. ONE of the following:
        i. The required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event
        **OR**
        ii. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over the prerequisite/preferred agent(s)

    **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