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, KeyRx, FocusRx, and Health Insurance Marketplace.

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.

**FDA APPROVED INDICATIONS AND DOSAGE**

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<thead>
<tr>
<th>GLP-1 Agonist</th>
<th>Indication</th>
<th>Limitations for use</th>
<th>Dosage and Administration</th>
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</table>
| Adlyxin (lixisenatide)        | 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. |
| Subcutaneous injection        |                                                                           | • 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. |
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<td><strong>Bydureon</strong> (exenatide extended-release) subcutaneous injection</td>
<td>Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.</td>
<td>• Not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise.</td>
<td>• 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 was administered 3 or more days before.</td>
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<td>• Not a substitute for insulin. Is not indicated for use in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.</td>
<td>• Injection should be in the abdomen, thigh or upper arm.</td>
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| **Byetta** (exenatide) | 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.  
• Concurrent use with prandial insulin has not been studied and cannot be recommended.  
• 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. | • 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) | 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.  
• 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 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.  
• 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. |
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| 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) 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 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.  
 • 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.  
 • 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 if the glycemic response is inadequate.  
 • Inject subcutaneously in the abdomen, thigh, or upper arm. |
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| **Trulicity** (dulaglutide) 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  
• Has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis  
• 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.  
• 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.  
• 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) subcutaneous injection | Adjunct to diet and exercise to improve glycemic control in patients 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 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.  
• 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 additional glycemic control is required, increase the dose to 1.8 mg daily after at least one week of treatments with the daily dose. |
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.\textsuperscript{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.\textsuperscript{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).\textsuperscript{2,3,4,5,9,10}

REFERENCES

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 has a diagnosis of type 2 diabetes mellitus AND ONE of the following:
   a. The patient’s medication history includes use of one or more of the following: an agent containing metformin, sulfonylurea, or insulin within the past 999 days
      OR
   b. BOTH of the following:
      1. The prescriber has stated that the patient has tried insulin or an agent containing metformin or sulfonylurea
         AND
      2. Insulin or an agent containing metformin or sulfonylurea agent was discontinued due to lack of effectiveness or an adverse event
         OR
   c. The patient has an intolerance or hypersensitivity to ONE of the following agents: metformin, sulfonylurea, or insulin
      OR
   d. The patient has an FDA labeled contraindication to ALL of the following agents: metformin, sulfonylurea, AND insulin
      OR
   e. The prescriber has provided documentation that ALL of the following agents: metformin, sulfonylurea, and insulin 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
      OR

2. Information has been provided that indicates that the patient is currently being treated with the requested GLP-1 within the past 90 days
   OR

3. The prescriber states the patient is currently being treated with the requested GLP-1 within the past 90 days AND is at risk if therapy is changed
   OR

4. 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

**Length of approval:** 12 months

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