



## Glucagon-like Peptide-1 (GLP-1) Agonists Step Therapy and Quantity Limit Program Summary

### FDA APPROVED INDICATIONS AND DOSAGE<sup>1-8</sup>

Agent(s)	Indication(s)	Dosage
<b>Adlyxin<sup>®</sup></b> (lixisenatide)  Subcutaneous injection	Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus  Limitations of use: <ul style="list-style-type: none"> <li>• 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</li> <li>• Not for treatment of type 1 diabetes</li> <li>• Has not been studied in patients with gastroparesis and is not recommended in patients with gastroparesis</li> </ul>	<ul style="list-style-type: none"> <li>• Starting dose of 10 mcg subcutaneously once daily for 14 days</li> <li>• Increase the dose to the maintenance dose of 20 mcg once daily starting on Day 15</li> </ul>
<b>Bydureon<sup>®</sup></b> (exenatide extended release)  Subcutaneous injection	Adjunct to diet and exercise to improve glycemic control in adults and pediatric patients aged 10 years and older with type 2 diabetes mellitus  Limitations of use: <ul style="list-style-type: none"> <li>• Not recommended as first-line therapy for patients inadequately controlled on diet and exercise</li> <li>• Should not be used to treat type 1 diabetes</li> <li>• Bydureon is an extended-release formulation of exenatide and should not be used with other products containing exenatide</li> <li>• Has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis</li> </ul>	<ul style="list-style-type: none"> <li>• Administer 2 mg by subcutaneous injection once every 7 days (weekly) at any time of day, with or without meals</li> </ul>

Agent(s)	Indication(s)	Dosage
<p><b>Bydureon BCise®</b> (exenatide extended release)</p> <p>Subcutaneous injection</p>	<p>Adjunct to diet and exercise to improve glycemic control in adults and pediatric patients aged 10 years and older with type 2 diabetes mellitus.</p> <p>Limitations of use:</p> <ul style="list-style-type: none"> <li>• Not recommended as first-line therapy for patients inadequately controlled on diet and exercise</li> <li>• Should not be used to treat type 1 diabetes</li> <li>• Bydureon BCise is an extended-release formulation of exenatide. It should not be used with other products containing the active ingredient exenatide</li> <li>• Has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis</li> </ul>	<ul style="list-style-type: none"> <li>• Administer 2 mg by subcutaneous injection once every seven days (weekly), at any time of day and with or without meals.</li> </ul>
<p><b>Byetta®</b> (exenatide)</p> <p>Subcutaneous injection</p>	<p>Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus</p> <p>Limitations of use:</p> <ul style="list-style-type: none"> <li>• Not indicated for use in patients with type 1 diabetes</li> <li>• Byetta contains exenatide and should not be used with other products containing the active ingredient exenatide</li> <li>• Byetta has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis</li> </ul>	<ul style="list-style-type: none"> <li>• Initiate at 5 mcg per dose twice daily; increase to 10 mcg twice daily after 1 month based on clinical response</li> <li>• 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)</li> </ul>
<p><b>Ozempic®</b> (semaglutide)</p> <p>Subcutaneous injection</p>	<p>Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus</p> <p>To reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes mellitus and established cardiovascular disease</p> <p>Limitations of use:</p> <ul style="list-style-type: none"> <li>• Has not been studied in patients with a history of pancreatitis. Consider another antidiabetic therapy</li> <li>• Not indicated for use in type 1 diabetes mellitus</li> </ul>	<ul style="list-style-type: none"> <li>• Start at 0.25 mg subcutaneously once weekly for 4 weeks. The 0.25 mg dose is intended for treatment initiation and is not effective for glycemic control</li> <li>• After 4 weeks, increase to 0.5 mg once weekly</li> <li>• If additional glycemic control is needed after at least 4 weeks on the 0.5 mg dose, the dosage may be increased to 1 mg once weekly. The maximum recommended dosage is 1 mg once weekly</li> </ul>

Agent(s)	Indication(s)	Dosage
<b>Rybelsus®</b> (semaglutide)  Tablet	Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus  Limitations of use: <ul style="list-style-type: none"> <li>• Not recommended as first-line therapy for patients inadequately controlled on diet and exercise</li> <li>• Has not been studied in patients with a history of pancreatitis</li> <li>• Not indicated for use in patients with type 1 diabetes mellitus</li> </ul>	<ul style="list-style-type: none"> <li>• 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.</li> <li>• 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</li> </ul>
<b>Trulicity®</b> (dulaglutide)  Subcutaneous injection	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 who have established cardiovascular disease or multiple cardiovascular risk factors  Limitations of use: <ul style="list-style-type: none"> <li>• Has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in these patients</li> <li>• Not for treatment of type 1 diabetes</li> <li>• Not recommended in patients with severe gastrointestinal disease, including severe gastroparesis.</li> </ul>	<ul style="list-style-type: none"> <li>• Initiate at 0.75 mg subcutaneously once weekly. Increase to 1.5 mg once weekly for additional glycemic control. If additional glycemic control is needed, increase the dose to 3 mg once weekly after at least 4 weeks on the 1.5 mg dose. If additional glycemic control is needed, increase the dose to the maximum dose of 4.5 mg once weekly after at least 4 weeks on the 3 mg dose</li> </ul>
<b>Victoza®</b> (liraglutide)  Subcutaneous injection	Adjunct to diet and exercise to improve glycemic control in patients 10 years and older 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  Limitations of use: <ul style="list-style-type: none"> <li>• Not for treatment of type 1 diabetes mellitus or diabetic ketoacidosis.</li> <li>• Victoza contains liraglutide and should not be coadministered with other liraglutide-containing products</li> </ul>	<ul style="list-style-type: none"> <li>• Adult and pediatric dosage: Initiate with 0.6 mg daily for one week. The 0.6 mg dose is for titration and is not effective for glycemic control in adults. After one week at 0.6 mg daily, increase to 1.2 mg daily. If additional glycemic control is required, increase the dose to 1.8 mg daily after at least one week of treatment with the 1.2 mg dose</li> </ul>

## CLINICAL RATIONALE

### Overview

The American Diabetes Association (ADA) and American Association of Clinical Endocrinologists (AACE) recommend metformin as the preferred first-line drug in type 2

diabetes mellitus.<sup>9,10</sup> Metformin has a low risk of hypoglycemia, can promote modest weight loss, and has good antihyperglycemic efficacy at doses of 1000-2000 mg/day.<sup>10</sup> Two-drug combinations should be considered if A1c is greater than or equal to 1.5% to 2.0% above the glycemic target, or when metformin monotherapy 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 on drug-specific effects and patient factors.<sup>9</sup>

### **Safety**

Bydureon, Bydureon BCise, Ozempic, Rybelsus, 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).<sup>2-7</sup>

### **REFERENCES**

1. Byetta prescribing information. AstraZeneca Pharmaceuticals, Inc. June 2021.
2. Victoza prescribing information. Novo Nordisk A/S. November 2020.
3. Bydureon prescribing information. AstraZeneca Pharmaceuticals, Inc. July 2021.
4. Bydureon BCise prescribing information. AstraZeneca Pharmaceuticals, Inc. July 2021.
5. Ozempic prescribing information. Novo Nordisk. April 2021.
6. Rybelsus prescribing information. Novo Nordisk A/S. July 2021.
7. Trulicity prescribing information. Eli Lilly and Company. April 2021.
8. Adlyxin prescribing information. Sanofi-Aventis US. LLC. July 2021.
9. American Diabetes Association. Standards of medical care in diabetes-2021. Accessed 9/13/2021. Available at: [https://care.diabetesjournals.org/content/suppl/2020/12/09/44.Supplement\\_1.DC1](https://care.diabetesjournals.org/content/suppl/2020/12/09/44.Supplement_1.DC1)
10. Garber AJ, Handelsman Y, Grunberger G et, al. Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm-2020 Executive Summary. *Endocrine Practice*, 26 (1) January 2020. 107-139. Accessed 9/11/2020. Available at: <https://www.aace.com/disease-state-resources/diabetes/clinical-practice-guidelines-treatment-algorithms/comprehensive>

## Glucagon-like Peptide-1 (GLP-1) Agonists Step Therapy

### TARGET AGENT(S)

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

### PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

**Target Agent(s)** will be approved when ALL of the following are met:

1. The patient has a diagnosis of type 2 diabetes mellitus  
**AND**
2. ONE of the following:
  - A. Information has been provided that indicates the patient is currently being treated with the requested GLP-1 within the past 90 days  
**OR**
  - B. 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**
  - C. The patient's medication history includes use of one or more of the following: an agent containing metformin or insulin within the past 90 days  
**OR**
  - D. The patient has an intolerance or hypersensitivity to ONE of the following agents: metformin or insulin  
**OR**
  - E. The patient has an FDA labeled contraindication to ALL of the following agents: metformin AND insulin

**Length of Approval:** 12 months

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