BlueCross BlueShield
Federal Employee Program

ANTIDIABETIC GLP-1, GIP-GLP-1 AGONISTS

Adlyxin injection* (lixisenatide)
Byetta injection*, Bydureon injection*, Bydureon BCise injection* (exenatide)
Mounjaro (tirzepatide)
Ozempic injection, Rybelsus tablets (semaglutide)
Trulicity injection (dulaglutide)
Victoza injection (liraglutide)

*Prior authorization for specific formulations applies only to formulary exceptions due to being a non-covered medication.

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Adlyxin, Byetta, Bydureon, Bydureon BCise, Ozempic, Rybelsus, Trulicity, and Victoza are glucagon-like peptide-1 receptor (GLP-1) agonists. Mounjaro is a glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 receptor agonist. These medications are designed to mimic the action of incretin hormones by stimulating insulin release after glucose is ingested, making them an additional avenue for treatment of type 2 diabetes mellitus, which has extensive guideline recommendations for treatment and diagnosis. Additionally, GLP-1, GIP-GLP-1 receptor agonists can decrease blood glucose through increasing feelings of satiety by delaying gastric emptying, stimulating the proliferation of pancreatic beta-cells, and inhibiting the production of glucagon (1-2).

Regulatory Status

FDA-approved indications: Bydureon, Bydureon BCise, Trulicity, and Victoza are indicated as an adjunct to diet and exercise to improve glycemic control in patients 10 years and older with type 2 diabetes mellitus and to reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes mellitus and established cardiovascular disease, or multiple cardiovascular risk factors (5-6, 10-11).

Adlyxin, Byetta, Mounjaro, Ozempic, and Rybelsus are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (3-4, 7-9).

<u>Limitations of Use:</u>

- Adlyxin, Byetta, Bydureon, Bydureon BCise, Mounjaro, Ozempic, Rybelsus, Trulicity, and Victoza are not indicated to treat type I diabetes mellitus (3-11).

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- Adlyxin, Byetta, Bydureon, Bydureon BCise, Mounjaro, Ozempic, Rybelsus, and Trulicity have not been studied in patients with a history of pancreatitis (3-10).
- Trulicity is not recommended in patients with severe gastrointestinal disease, including severe gastroparesis (10).
- Adlyxin has not been studied in patients with gastroparesis and is not recommended in patients with gastroparesis (3).

Bydureon, Bydureon BCise, Mounjaro, Ozempic, Trulicity, Victoza and Rybelsus have a boxed warning indicating that they have been shown to cause thyroid C-cell tumors in rats. It is unknown whether the GLP-1, GIP-GLP-1 agonists cause thyroid C-cell tumors, including medullary thyroid carcinoma (MTC) in humans. The use of GLP-1, GIP-GLP-1 agonists is contraindicated in patients with a personal or family history of MTC, or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Patients should be counseled on the potential risk of MTC and the symptoms of thyroid tumors (3-11).

The use of GLP-1, GIP-GLP-1 agonists has been associated with pancreatitis, acute kidney injury, acute gallbladder disease, and hypoglycemia. Patients should be monitored for these outcomes and the medication discontinued as medically indicated. Concomitant administration of a GLP-1 agonist with insulin or an insulin secretagogue may increase the risk of hypoglycemia and the dose of either insulin or insulin secretagogue may need to be reduced (3-12).

The safety and effectiveness of Bydureon, Bydureon BCise, Trulicity, and Victoza in pediatric patients less than 10 years of age have not been established (5-6,10 -11).

The safety and effectiveness of Adlyxin, Byetta, Mounjaro, Ozempic, and Rybelsus in pediatric

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patients less than 18 years of age have not been established (3-4, 7-9).

Summary

Adlyxin, Byetta, Bydureon, Bydureon BCise, Ozempic, Rybelsus, Trulicity, and Victoza are glucagon-like peptide-1 receptor (GLP-1) agonists. Mounjaro is a glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 receptor agonist. The medications are designed to mimic the action of incretin hormones by stimulating insulin release after glucose is ingested, making them an additional avenue for treatment of type 2 diabetes mellitus. They should not be used to treat type 1 diabetes. GLP-1, GIP-GLP-1 agonists have a boxed warning for causing thyroid c-cell tumors in rats. While unclear if this is applicable to humans, use of GLP-1s in patients who have a personal or family history of thyroid tumors is contraindicated (1-11).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Antidiabetic GLP-1, GIP-GLP-1 agonists while maintaining optimal therapeutic outcomes.

References

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