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5.30.074

Section:	Prescription Drugs	**Effective Date:**	April 1, 2025
Subsection:	Endocrine and Metabolic Agents	**Original Policy Date:**	January 29, 2021
Subject:	Trijardy XR	**Page:**	1 of 6

Last Review Date: March 7, 2025

Trijardy XR

Description

Trijardy XR (empagliflozin, linagliptin, & metformin)

Background
Trijardy XR is a combination of empagliflozin, a sodium-glucose co-transporter 2 (SGLT2) inhibitor, linagliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor, and metformin hydrochloride, a biguanide. Empagliflozin works by blocking the reabsorption of glucose by the kidney, increasing glucose excretion, and lowering blood glucose levels. Linagliptin increases the concentrations of active incretin hormones, stimulating the release of insulin in a glucose-dependent manner and decreasing the levels of glucagon in the circulation. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization (1).

Regulatory Status
FDA-approved indication: Trijardy XR is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (1).

Empagliflozin is also indicated to reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease (1).

Limitations of Use:
Trijardy XR is not recommended in patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients. Trijardy XR has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at an increased risk for the development of pancreatitis while using Trijardy XR (1).

Metformin has a boxed warning for lactic acidosis which can occur due to metformin accumulation. The risk increases with conditions such as renal impairment, concomitant use of certain drugs, age 65 years old or greater, excess alcohol intake, and hepatic impairment (1).

Trijardy XR is contraindicated in patients with severe renal impairment, end-stage renal disease (ESRD), or dialysis (1).

Trijardy XR should not be initiated or continued in patients with an eGFR less than 45 mL/min/1.73m^2. Trijardy XR is contraindicated in patients with an eGFR less than 30 mL/min/1.73m^2 (1).

Safety and effectiveness of Trijardy XR in pediatric patients under 18 years of age have not been established (1).

FDA safety review has resulted in adding warnings to the labels of a specific class of type 2 diabetes medicines called sodium-glucose cotransporter-2 (SGLT2) inhibitors about the risks of too much acid in the blood and of serious urinary tract infections. Both conditions can result in hospitalization. Health care professionals should assess for ketoacidosis and urinary tract infections in patients taking SGLT2 inhibitors who present with suggestive symptoms. Ketoacidosis associated with the use of SGLT2 inhibitors can occur even if the blood sugar level is not very high. FDA also identified 19 cases of life-threatening blood infections (urosepsis) and kidney infections (pyelonephritis) that started as urinary tract infections with the SGLT2 inhibitors (2).

Off-label and alternative uses of Trijardy XR such as enhancement of weight loss and diabetes prevention are not approved by the FDA.

Related policies

GLP-1 Agonists, Insulin GLP-1 Combinations, Metformin, Mounjaro, SGLT2 Inhibitors, SGLT2 Step Policy

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Trijardy XR may be considered **medically necessary** if the conditions indicated below are met.

Trijardy XR may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Type 2 diabetes mellitus

AND ALL of the following:

1. Inadequate treatment response, intolerance, or contraindication to metformin **AND ONE** of the drugs from the following drug classes:
    a. Alpha-glucosidase inhibitor
    b. Dipeptidyl peptidase 4 inhibitors (DPP-4)
    c. Thiazolidinedione
    d. Glucagon-like peptide-1 receptor agonists (GLP-1)
2. Inadequate treatment response, intolerance, or contraindication to **TWO** SGLT2 inhibitors (see Appendix 1)
3. Patient must have a HgbA1C greater than 7.0%
4. Patient has an eGFR ≥ 45 mL/min/1.73m^2
5. **NO** dual therapy with another SGLT2 inhibitor (see Appendix 1)

AND NOT to be used for the following:

1. Diabetic ketoacidosis (DKA)
2. Prevention of diabetes
3. Exclusively used for weight loss

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Type 2 diabetes mellitus

AND ALL of the following:

1. Condition has improved or stabilized on the therapy
2. **NO** dual therapy with another SGLT2 inhibitor (see Appendix 1)
3. Patient has an eGFR ≥ 45 mL/min/1.73m^2

AND NOT to be used for the following:

1. Diabetic ketoacidosis (DKA)
2. Prevention of diabetes
3. Exclusively used for weight loss

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Trijardy XR is a combination of empagliflozin, a sodium-glucose co-transporter 2 (SGLT2) inhibitor, linagliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor, and metformin hydrochloride, a biguanide. Empagliflozin works by blocking the reabsorption of glucose by the kidney, increasing glucose excretion, and lowering blood glucose levels. Linagliptin increases the concentrations of active incretin hormones, stimulating the release of insulin in a glucose-dependent manner and decreasing the levels of glucagon in the circulation. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Trijardy XR while maintaining optimal therapeutic outcomes.

References

1. Trijardy XR [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; October 2023.
2. FDA News Release. FDA Drug Safety Communication: FDA revises labels of SGLT2 inhibitors for diabetes to include warnings about too much acid in the blood and serious urinary tract infections. December 4, 2015.

Policy History

Date	Action
January 2021	Addition to PA
March 2021	Annual review
December 2022	Annual review and reference update. Changed policy number to 5.30.074
September 2023	Annual review
September 2024	Annual review and reference update
March 2025	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 7, 2025 and is effective on April 1, 2025.

Appendix 1 - List of SGLT2 Inhibitors

Generic Name	Brand Name
canagliflozin	Invokana
canagliflozin/metformin	Invokamet/Invokamet XR
dapagliflozin	Farxiga
dapagliflozin/metformin	Xigduo XR
dapagliflozin/saxagliptin	Qtern
empagliflozin	Jardiance
empagliflozin/linagliptin	Glyxambi
empagliflozin/linagliptin/metformin	Trijardy XR
empagliflozin/metformin	Synjardy/Synjardy XR
ertugliflozin	Steglatro
ertugliflozin/metformin	Segluromet
ertugliflozin/sitagliptin	Steglujan
sotagliflozin	Inpefa