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IN BRIEF

***Trijardy XR* – A New 3-Drug Combination for Type 2 Diabetes**

The FDA has approved *Trijardy XR* (Boehringer Ingelheim/Lilly), a fixed-dose combination of the sodium-glucose cotransporter 2 (SGLT2) inhibitor empagliflozin,¹ the dipeptidyl peptidase-4 (DPP-4) inhibitor linagliptin,² and extended-release metformin, for oral treatment of type 2 diabetes in adults. Empagliflozin and linagliptin have been available in a fixed-dose combination as *Glyxambi* since 2015,³ and both have been available in 2-drug combinations with extended-release metformin for years (see Table 1).

Pronunciation Key

Trijardy: try jar' dee

Used alone, oral antihyperglycemic drugs usually lower glycated hemoglobin (A1C) by 0.5-1.5%. Metformin is generally the drug of choice for initial treatment of type 2 diabetes. If metformin alone does not achieve the desired A1C goal, comorbidities or cost may determine the choice of a second drug: options include an SGLT2 inhibitor or a GLP-1 receptor agonist for patients with cardiovascular disease or chronic kidney disease, an SGLT2 inhibitor for patients with heart failure, or a sulfonylurea if cost is an issue. If glycemic control is not achieved with maximum doses of 2 drugs, insulin or another drug can be added.⁴

Two randomized, open-label, crossover studies in a total of 60 healthy adults found that the 3-drug combination tablet was bioequivalent to individual tablets of empagliflozin, linagliptin, and extended-release metformin taken together.⁵

No new efficacy trials were required for approval of *Trijardy XR*. Approval of the 3-drug combination was based on the results of earlier trials in which addition of empagliflozin/linagliptin to metformin reduced A1C significantly more than addition of either drug alone.

The labeling of *Trijardy XR* includes a long list of warnings and precautions about adverse effects, including lactic acidosis associated with metformin, acute pancreatitis with DPP-4 inhibitors, and euglycemic ketoacidosis with SGLT2 inhibitors.

As might be expected with a 3-drug combination available in 4 different strengths, the dosing instructions for starting treatment are complex. ■

1. Empagliflozin (Jardiance) for diabetes. Med Lett Drugs Ther 2014; 56:99.
2. Linagliptin (Tradjenta) – a new DPP-4 inhibitor for type 2 diabetes. Med Lett Drugs Ther 2011; 53:49.
3. Glyxambi – a new combination for type 2 diabetes. Med Lett Drugs Ther 2015; 57:65.
4. Drugs for type 2 diabetes. Med Lett Drugs Ther 2019; 61:169.
5. I Lingvay et al. Triple fixed-dose combination of empagliflozin, linagliptin, and metformin for patients with type 2 diabetes. Postgrad Med 2020 May 4 (epub).

Table 1. *Trijardy XR* and Its Components

Drug	Some Formulations	Usual Adult Dosage	Cost ¹
Metformin ER ² – generic	500, 750, 1000 mg ER tabs ³	1500-2000 mg PO once/day	\$8.10
<i>Glucophage XR</i> (BMS)	500, 750 mg ER tabs ³		90.60
<i>Glumetza</i> (Bausch) generic	500, 1000 mg ER tabs ³		4884.30
Empagliflozin – <i>Jardiance</i> (Boehringer Ingelheim/Lilly)	10, 25 mg tabs	10-25 mg PO once/day ⁴	522.40
Linagliptin – <i>Tradjenta</i> (Boehringer Ingelheim)	5 mg tabs	5 mg PO once/day	462.30
Empagliflozin/metformin ER ² – <i>Synjardy XR</i> (Boehringer Ingelheim/Lilly)	5/1000, 10/1000, 12.5/1000, 25/1000 mg ER tabs ³	5/1000-25/1000 mg PO once/day ⁵	261.20
Linagliptin/metformin ER ² – <i>Jentadueto XR</i> (Boehringer Ingelheim/Lilly)	2.5/1000, 5/1000 mg ER tabs ³	5/1000-5/2000 mg PO once/day	462.30
Empagliflozin/linagliptin – <i>Glyxambi</i> (Boehringer Ingelheim/Lilly)	10/5, 25/5 mg tabs	10/5-25/5 mg PO once/day ⁴	539.30
Empagliflozin/linagliptin/metformin ER ² – <i>Trijardy XR</i> (Boehringer Ingelheim/Lilly)	5/2.5/1000, 10/5/1000, 12.5/2.5/1000, 25/5/1000 mg ER tabs ³	10/5/1000-25/5/2000 mg PO once/day ^{4,6}	522.30

ER = extended-release

1. Approximate WAC for 30 days' treatment at the lowest usual adult dosage. Approximate WAC. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. May 5, 2020. Reprinted with permission by First Databank, Inc. All rights reserved. ©2020. www.fdbhealth.com/drug-pricing-policy.
2. Metformin is contraindicated in patients with an eGFR <30 mL/min/1.73 m². Starting metformin therapy in patients with an eGFR of 30-45 mL/min/1.73 m² is not recommended. If the eGFR falls below 45 mL/min/1.73 m² in patients already taking metformin, the benefits and risk of continuing treatment should be assessed.
3. Tablets should not be crushed, chewed, or divided.
4. Should not be started in patients with an eGFR <45 mL/min/1.73 m² and should be discontinued if eGFR persistently falls below 45 mL/min/1.73 m².
5. Contraindicated in patients with an eGFR <45 mL/min/1.73 m².
6. Patients already taking metformin, with or without linagliptin, should start with a similar total daily dose of metformin and total daily doses of 10 mg of empagliflozin and 5 mg of linagliptin. Patients already taking metformin and empagliflozin, with or without linagliptin, should start with similar total daily doses of metformin and empagliflozin and a total daily dose of linagliptin 5 mg. The maximum recommended daily dose is 25/5/2000 mg. When doses of 2000 mg of metformin are needed, two tablets of 5/2.5/1000 mg or 12.5/2.5/1000 mg should be used.

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