



Step Therapy Diabetes – Sodium Glucose Co-Transporter-2 and Dipeptidyl Peptidase-4 Inhibitors

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Product Identifier(s)

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National Formulary Medical Necessity

Drugs Affected

- Glyxambi® (empagliflozin and linagliptin tablets)
- Qtern® (dapagliflozin and saxagliptin tablets)
- Steglujan™ (ertugliflozin and sitagliptin tablets)
- Trijardy™ XR (empagliflozin, linagliptin, and metformin extended-release tablets)

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Step 1: generic metformin, generic metformin extended-release (generic to Glucophage XR only)

Step 2: Glyxambi, Qtern, Steglujan, Trijardy XR

Cigna covers Step 2 agents as medically necessary when the following criteria are met:

1. If the individual has tried one Step 1 Product, approve a Step 2 Product.
Note: A trial of one of the following metformin-containing products also satisfies the requirement: Glucophage, Glucophage XR, Glumetza, Fortamet, Riomet, metformin oral solution, Riomet ER, metformin extended-release (generics to Fortamet and Glumetza), metformin/glyburide, metformin/glipizide, Actoplus Met, pioglitazone/metformin, Actoplus Met XR, Janumet, Janumet XR, repaglinide/metformin, Kombiglyze XR, Jentadueto, Jentadueto XR, Kazano, alogliptin/metformin, Synjardy, Synjardy XR, Xigduo XR, Invokamet, Invokamet XR, Segluromet.
2. If the individual has tried a DPP-4 inhibitor (e.g., Januvia, Nesina, alogliptin, Onglyza, Tradjenta), DPP-4 inhibitor-containing product (e.g., Oseni, alogliptin/pioglitazone), or an SGLT-2 inhibitor (e.g., Farxiga, Invokana, Jardiance, Steglatro), other than Glyxambi, Qtern, Steglujan, or Trijardy XR, approve a Step 2 Product.
3. If the individual has a contraindication to metformin, according to the prescriber, approve Glyxambi, Qtern, or Steglujan.
Note: Examples of contraindications to metformin include acute or chronic metabolic acidosis, including diabetic ketoacidosis.

Conditions Not Covered

Any other exception is considered not medically necessary.

Background

Overview

Glyxambi, Qtern, Steglujan, and Trijardy XR are sodium glucose co-transporter-2 inhibitor (SGLT-2) and dipeptidyl peptidase-4 (DPP-4) inhibitor combination products indicated as an adjunct to diet and exercise to improve glycemic control in adults with **type 2 diabetes mellitus**; Trijardy XR also contains metformin.¹⁻⁴ Various single-entity SGLT-2 inhibitors and DPP-4 inhibitors are available. In addition to their indications for type 2 diabetes, Jardiance® (empagliflozin tablets), Invokana® (canagliflozin tablets), and Farxiga® (dapagliflozin tablets) possess indications related to cardiovascular, renal, and/or heart failure benefits. Efficacy of the SGLT-2 inhibitor combination products has not been established in these settings. Refer to Table 1 for a summary of the available products containing SGLT-2 and/or DPP-4 inhibitors.

Table 1. SGLT-2 and DPP-4 inhibitor-containing combination products.

	SGLT-2 Component				DPP-4 Inhibitor Component				Metformin
	CANA	DAPA	EMPA	ERTU	ALO	LINA	SAXA	SITA	
DPP-4 inhibitor and metformin									
Janumet								X	X
Janumet XR								X	X
Jentadueto						X			X
Jentadueto XR						X			X
Kazano, authorized generic					X				X
Kombiglyze XR							X		X
DPP-4 inhibitor and other									
Oseni (alogliptin/pioglitazone, authorized generic)					X				
SGLT-2 inhibitor and metformin									
Invokamet	X								X
Invokamet XR	X								X
Segluromet				X					X
Synjardy			X						X

Synjardy XR			X					X
Xigduo XR		X						X
SGLT-2 inhibitor and DPP-4 inhibitor								
Glyxambi			X			X		
Qtern		X					X	
Steglujan				X				X
Trijardy XR			X			X		X

SGLT-2 – Sodium glucose co-transporter-2; DPP-4 – Dipeptidyl peptidase-4; CANA – canagliflozin; DAPA – dapagliflozin; EMPA – empagliflozin; ERTU – ertugliflozin; ALO – alogliptin; LINA – linagliptin; SAXA – saxagliptin; SITA – sitagliptin; XR – extended-release.

Guidelines

The American Diabetes Association Standards of Care (2022) recommend metformin as initial therapy for most patients with type 2 diabetes, unless contraindications to metformin are present.⁵ Very high circulating levels of metformin have been associated with lactic acidosis. However, the occurrence of this complication is now known to be very rare. In patients with contraindications or intolerance to metformin, initial therapy should be based on patient factors. Metformin is contraindicated in patients with severe renal impairment (estimated glomerular filtration rate [eGFR] < 30 mL/min/1.73 m²) and in patients with acute or chronic metabolic acidosis, including diabetic ketoacidosis, with or without coma.⁷ DPP-4 inhibitors and SGLT-2 inhibitors are among the classes of medications recommended as add-on therapy after metformin (or as initial therapy if metformin cannot be used).⁵ Because type 2 diabetes is often a progressive disease, combination therapy may be needed for many patients over time to achieve glycemic targets. Other guidelines have similar recommendations.⁶

References

1. Glyxambi® tablets [prescribing information]. Ridgefield, CT: Boehringer Ingelheim; March 2022.
2. Qtern® tablets [prescribing information]. Wilmington, DE: AstraZeneca; March 2022.
3. Steglujan® tablets [prescribing information]. Whitehouse Station, NJ: Merck; September 2021.
4. Trijardy® XR tablets [prescribing information]. Ridgefield, CT: Boehringer Ingelheim; June 2021.
5. American Diabetes Association. Standards of medical care in diabetes – 2022. *Diabetes Care*. 2022;45(Suppl 1):S1-S258.
6. 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. *Endocr Pract*. 2020 Jan;26(1):107-139.
7. Metformin tablets [prescribing information]. Raleigh, NC: Indicus Pharma; June 2020.

Revision History

Type of Revision	Summary of Changes	Approval Date
Annual Revision	Step 1 Products: The Step 1 Products were revised such that only metformin and metformin extended-release (generic to Glucophage XR only) are listed in Step 1. A Note was added that the following metformin-containing products also satisfy the requirement for a Step 1 trial (previously, these products were also listed in Step 1): Glucophage, Glucophage XR, Glumetza, Fortamet, Riomet, metformin oral solution, Riomet ER, metformin extended-release (generics to Fortamet and Glumetza), metformin/glyburide, metformin/glipizide, Actoplus Met, pioglitazone/metformin, Actoplus Met XR, Janumet, Janumet XR, repaglinide/metformin, Kombiglyze XR, Jentadueto, Jentadueto XR, Kazano, aloglitpin/metformin, Synjardy, Synjardy XR, Xigduo XR, Invokamet, Invokamet XR, Segluromet. Of note, Glucovance was removed from this list (obsolete).	05/11/2022

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