

STEP THERAPY POLICY

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

- Glyxambi® (empagliflozin and linagliptin tablets – Boehringer Ingelheim)
- Qtern® (dapagliflozin and saxagliptin tablets – AstraZeneca [*obsolete 05/31/2025*])
- Steglujan® (ertugliflozin and sitagliptin tablets – Merck)
- Trijardy® XR (empagliflozin, linagliptin, and metformin extended-release tablets – Boehringer Ingelheim)

REVIEW DATE: 05/06/2026

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 dapagliflozin tablets (Farxiga®, generic) possess indications related to cardiovascular, renal, and/or heart failure benefits. Efficacy of the SGLT-2/DPP-4 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 (saxagliptin/metformin XR, generic)							X		X
Zituvimet (sitagliptin/metformin, authorized generic)								X	X
Zituvimet XR (sitagliptin/metformin XR, authorized generic)								X	X
DPP-4 inhibitor and other									
Oseni (alogliptin/pioglitazone, authorized generic)					X				

Table 1 (continued). 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	
SGLT-2 inhibitor and metformin									
Invokamet	X								X
Invokamet XR	X								X
Segluromet				X					X
Synjardy			X						X
Synjardy XR			X						X
Xigduo XR, authorized generic and generic		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; * alogliptin/metformin is available as the authorized generic to Kazano and as a branded product (no trade name).

GUIDELINES

The American Diabetes Association Standards of Care in Diabetes (2026) note that therapy for patients with type 2 diabetes depends on comorbidities and patient-centered treatment factors.⁵ The SGLT-2 inhibitors with demonstrated benefit (noted to be dapagliflozin, Invokana, and Jardiance) are recommended as initial therapy when pertinent comorbidities are present (atherosclerotic cardiovascular [CV] disease, or high CV risk, chronic kidney disease, and heart failure), independent of metformin use. In pediatric patients with type 2 diabetes, dapagliflozin, Invokana, or Jardiance may be used for patients ages 10 to 17 years who have not met glycemic goals with metformin with or without insulin. DPP-4 inhibitors do not carry indications for cardiorenal benefit and have lower glycemic efficacy than metformin.

Because type 2 diabetes is a progressive disease, maintenance of glycemic goals often requires combination therapy. Traditional recommendations have called for the use of stepwise addition of medications to metformin to maintain glycemic goals. 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.⁶

Initial combination therapy should be considered in people presenting with HbA_{1c} levels 1.5% to 2.0% above their individualized goal. Incorporation of high-glycemic-efficacy therapies or therapies for cardiorenal risk reduction (e.g., glucagon-like peptide-1 agonists, dual GLP-1/GIP agonists, and SGLT-2 inhibitors) may reduce the need for agents that increase the risks of hypoglycemia and weight gain or are less well tolerated.

The American Association of Clinical Endocrinology Consensus Statement: Algorithm for Management of Adults With Type 2 Diabetes (2026) recommends that pharmacologic therapy for adults with type 2 diabetes be selected using a comorbidities- and complications-centric approach, rather than a glucose-centric sequencing strategy alone.⁷ Recommendations are similar to the American Diabetes Association Standards of Care in Diabetes.

POLICY STATEMENT

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.

Automation: A patient with a history of one of the following within the 130-day look-back period is excluded from Step Therapy:

- One Step 1 Product; OR
- One of the following metformin-containing products: Glumetza ER, Riomet, metformin oral solution, metformin extended-release (generics to Fortamet ER and Glumetza ER), glyburide/metformin, glipizide/metformin, Actoplus Met, pioglitazone/metformin, Janumet, Janumet XR, sitagliptin/metformin (authorized generic to Zituvimet), Zituvimet, sitagliptin/metformin extended-release (authorized generic to Zituvimet XR), Zituvimet XR, Kombiglyze XR, saxagliptin/metformin extended-release, Jentadueto, Jentadueto XR, Kazano, aloglitpin/metformin, Synjardy, Synjardy XR, Xigduo XR, dapagliflozin/metformin extended-release, Invokamet, Invokamet XR, Segluromet; OR
- One of the following DPP-4 inhibitor products: Brynovin, Januvia, Nesina, alogliptin, Onglyza, saxagliptin, Tradjenta, Oseni, alogliptin/pioglitazone, Zituvio, sitagliptin (authorized generic to Zituvio); OR
- One SGLT-2 inhibitor (Brenzavvy, bexagliflozin, Farxiga, dapagliflozin, Invokana, Jardiance, Steglatro).

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

Step 2: Glyxambi, Qtern, Steglujan, Trijardy XR

CRITERIA

1. If the patient 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 (obsolete), Glucophage XR (obsolete), Glumetza ER, Fortamet ER (obsolete), Riomet, metformin oral solution, Riomet ER (obsolete), metformin extended-release (generics to Fortamet ER and Glumetza ER), glyburide/metformin, glipizide/metformin, Actoplus Met, pioglitazone/metformin, Actoplus Met XR (obsolete), Janumet, Janumet XR, Zituvimet, sitagliptin/metformin (authorized generic to Zituvimet), Zituvimet XR, sitagliptin/metformin extended-release (authorized generic to Zituvimet XR), repaglinide/metformin (obsolete), Kombiglyze XR, saxagliptin/metformin extended-release, Jentadueto, Jentadueto XR, Kazano, aloglitpin/metformin, Synjardy, Synjardy XR, Xigduo XR, dapagliflozin/metformin extended-release, Invokamet, Invokamet XR, Segluromet.

2. If the patient has tried a DPP-4 inhibitor, a DPP-4 inhibitor-containing product, OR an SGLT-2 inhibitor, other than Glyxambi, Qtern, Steglujan, or Trijardy XR, approve a Step 2 Product.

Note: Examples of DPP-4 inhibitors include but are not limited to Brynovin, Januvia, Nesina, alogliptin, Onglyza, saxagliptin, Tradjenta, Zituvio, and sitagliptin (authorized generic to Zituvio). Examples of DPP-4 inhibitor-containing products include but are not limited to Oseni and alogliptin/pioglitazone. Examples of SGLT-2 inhibitors include but are not limited to Brenzavvy, bexagliflozin, Farxiga, dapagliflozin, Invokana, Jardiance, Steglatro.

- If the patient 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.

- No other exceptions are recommended.

REFERENCES

- Glyxambi® tablets [prescribing information]. Ridgefield, CT: Boehringer Ingelheim; October 2025.
- Qtern® tablets [prescribing information]. Wilmington, DE: AstraZeneca; September 2023.
- Steglujan® tablets [prescribing information]. Whitehouse Station, NJ: Merck; December 2024.
- Trijardy® XR tablets [prescribing information]. Ridgefield, CT: Boehringer Ingelheim; October 2025.
- American Diabetes Association. Standards of care in diabetes – 2026. *Diabetes Care*. 2026;49(Suppl 1):S1-S371.
- .Metformin tablets [prescribing information]. Raleigh, NC: Indicus; June 2020.
- Samson SL, Vellanki P, Blonde L, et al. American Association of Clinical Endocrinology consensus statement: algorithm for management of adults with type 2 diabetes – 2026 update. *Endocr Pract*. 2026;32:473-518

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	<p>Automation: Fortamet ER was removed from the list of metformin-containing products (obsolete). Sitagliptin (authorized generic to Zituvio) was added to the list of DPP-4 inhibitor products.</p> <p>Criteria: For a patient requesting a Step 2 product, the note was updated to reflect that Fortamet ER is obsolete (this still counts towards a trial of a Step 1 product). For a patient that has tried a DPP-4 inhibitor, a DPP-4 inhibitor-containing product, or an SGLT-2 inhibitor, other than Glyxambi, Qtern, Steglujan, or Trijardy XR, the note was updated to add sitagliptin (authorized generic to Zituvio).</p>	05/22/2024
Selected Revision	<p>Automation: Sitagliptin/metformin (authorized generic) was added to automation for one metformin-containing product.</p> <p>Criteria: For a patient requesting a Step 2 product, the note was updated to add sitagliptin/metformin (authorized generic) to the list of metformin-containing products.</p>	08/07/2024
Selected Revision	<p>Automation: Zituvimet and Zituvimet XR were added to automation for one metformin-containing product.</p> <p>Criteria: For a patient requesting a Step 2 product, the note was updated to add Zituvimet and Zituvimet XR to the list of metformin-containing products.</p>	11/20/2024
Annual Revision	<p>Automation: Riomet ER was removed from the list of metformin-containing product (obsolete > 3 years). Bexagliflozin was added to automation for one sodium glucose co-transporter-2 (SGLT-2) inhibitor.</p> <p>Criteria: For a patient requesting a Step 2 product, the note listing metformin-containing products was updated to reflect that Riomet ER is obsolete (this still counts towards a trial of a Step 1 product). For a patient requesting a Step 2 product that has tried a dipeptidyl peptidase-4 (DPP-4) inhibitor, a DPP-4 inhibitor-containing product, OR an SGLT-2 inhibitor, other than Glyxambi, Qtern, Steglujan, or Trijardy XR, the note was updated to add bexagliflozin as an example of an SGLT-2 inhibitor.</p>	05/14/2025

HISTORY (CONTINUED)

Type of Revision	Summary of Changes	Review Date
Selected Revision	<p>Automation: Sitagliptin/metformin extended-release (authorized generic to Zituvinet XR) was added to the list of metformin-containing products.</p> <p>Criteria: For a patient requesting a Step 2 product that has tried a Step 1 product, the note listing metformin or metformin-containing products was updated to add sitagliptin/metformin extended-release (authorized generic to Zituvinet XR).</p>	08/06/2025
Selected Revision	<p>Automation: Brynovin was added to the list of dipeptidyl-peptidase-4 inhibitor-products.</p> <p>Criteria: For a patient that has tried a DPP-4 inhibitor, a DPP-4 inhibitor-containing product, OR an SGLT-2 inhibitor, other than Glyxambi, Qtern, Steglujan, or Trijardy XR, Brynovin was added to the note listing examples of DPP-4 inhibitors.</p>	10/22/2025
Annual Revision	<p>Automation: For the automation applied to one sodium glucose co-transporter-2 (SGLT-2) inhibitor, reference to dapagliflozin was revised to remove “authorized generic to Farxiga” due to the availability of both an authorized generic and true generic. Automation applies to both products.</p>	05/06/2026