



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)
 - Steglujan® (ertugliflozin and sitagliptin tablets – Merck)
 - Trijardy® XR (empagliflozin, linagliptin, and metformin extended-release tablets – Boehringer Ingelheim)

REVIEW DATE: 05/14/2025

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

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 (Farxiga®, authorized 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)								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.

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		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 (2025) note that therapy for patients with type 2 diabetes depends on comorbidities, patient-centered treatment factors, and management needs..⁵ The SGLT-2 inhibitors (with demonstrated

benefit) are recommended as initial therapy when pertinent comorbidities are present (atherosclerotic CV disease, or high CV risk, CKD, and heart failure), independent of metformin use. In pediatric patients with type 2 diabetes, metformin is the initial treatment of choice if HbA_{1c} is < 8.5%; if glycemic goals are no longer met, Jardiance may be considered in children ≥ 10 years of age (the updated cage indications for dapagliflozin and Invokana are not addressed). 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.

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.

- 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, 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: Januvia, Nesina, alogliptin, Onglyza, saxagliptin, Tradjenta, Oseni, alogliptin/pioglitazone, Zituvio, sitagliptin (authorized generic to Zituvio); OR
- One SGLT-2 inhibitor (Brenzavvy, bexagliflozin, Farxiga, dapagliflozin [authorized generic to Farxiga], Invokana, Jardiance, Steglatro).

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

Step 2: Glyxambi, Qtern, Steglujan, Trijardy XR

Diabetes – Sodium Glucose Co-Transporter-2 and Dipeptidyl Peptidase-4 Inhibitors Step Therapy Policy product(s) is(are) covered as medically necessary when the following step therapy criteria is(are) met. Any other exception is considered not medically necessary.

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, 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 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.
- 3.** 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.

REFERENCES

1. Glyxambi® tablets [prescribing information]. Ridgefield, CT: Boehringer Ingelheim; October 2023.
2. Qtern® tablets [prescribing information]. Wilmington, DE: AstraZeneca; September 2023.
3. Steglujan® tablets [prescribing information]. Whitehouse Station, NJ: Merck; December 2024.

4. Trijardy® XR tablets [prescribing information]. Ridgefield, CT: Boehringer Ingelheim; October 2023.
5. American Diabetes Association. Standards of care in diabetes – 2025. *Diabetes Care*. 2025;48(Suppl 1):S1-S359.
6. .Metformin tablets [prescribing information]. Raleigh, NC: Indicus; June 2020.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	<p>Automation: The following products were removed from the automation (obsolete): Glucophage, Glucophage XR, repaglinide/metformin, Actoplus Met XR. Glumetza and Fortamet were clarified to be Glumetza ER and Fortamet ER.</p> <p>Criteria: For a patient requesting a Step 2 product, the note was updated to reflect that Glucophage, Glucophage XR, repaglinide/metformin, and Actoplus Met XR are obsolete (these still count towards a trial of a Step 1 product). Additionally, Glumetza and Fortamet were clarified to be Glumetza ER and Fortamet ER. For a patient who has tried a DPP-4 inhibitor, a DPP-4 inhibitor-containing product, or an SGLT-2 inhibitor, examples of these products were moved to a note.</p>	05/03/2023
Selected Revision	<p>Automation: Brenzavvy was added to automation for one sodium glucose co-transporter-2 inhibitor, saxagliptin (generic for Onglyza) was added to automation for one dipeptidyl peptidase-4 inhibitor, and saxagliptin/metformin extended-release (generic to Kombiglyze XR) was added to automation for one metformin-containing product.</p>	09/13/2023
Selected Revision	<p>Automation: Zituvio was added to automation for one dipeptidyl peptidase-4 (DPP-4) inhibitor.</p>	02/07/2023
Selected Revision	<p>Automation: dapagliflozin/metformin extended-release (authorized generic to Xigduo XR) was added to automation for one metformin-containing product. Dapagliflozin (authorized generic to Farxiga) was added to automation for one sodium-glucose co-transporter-2 (SGLT-2) inhibitor product.</p>	02/21/2024
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>	05/14/2025

	<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>	
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