STEP THERAPY POLICY

POLICY: Diabetes – Sodium Glucose Co-Transporter-2 Inhibitors Step Therapy Policy

- Brenzavvy™ (bexagliflozin tablets – TheracosBio)
- bexagliflozin tablets – GSMS
- Farxiga® (dapagliflozin tablets – Bristol-Myers Squibb, authorized generic)
- Invokana® (canagliflozin tablets – Janssen)
- Invokamet® (canagliflozin and metformin hydrochloride tablets Janssen)
- Invokamet® XR (canagliflozin and metformin hydrochloride extended-release tablets – Janssen)
- Jardiance® (empagliflozin tablets – Boehringer Ingelheim/Lilly)
- Segluromet® (ertugliflozin and metformin tablets – Merck)
- Steglatro® (ertugliflozin tablets – Merck)
- Synjardy® (empagliflozin/metformin hydrochloride tablets – Boehringer Ingleheim/ Lilly)
- Synjardy® XR (empagliflozin/metformin extended-release tablets – Boehringer Ingleheim/Lilly)
- Xigduo® XR (dapagliflozin/metformin extended-release tablets – Bristol-Meyers Squibb, authorized generic)

REVIEW DATE: 05/07/2025

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

Bexagliflozin, dapagliflozin, Invokana, Jardiance, and Steglatro are sodium glucose co-transporter-2 (SGLT-2) inhibitors indicated as an adjunct to diet and exercise to improve glycemic control in adults with **type 2 diabetes**.[1-4] Dapagliflozin, Invokana, and Jardiance are also indicated in pediatric patients ≥ 10 years of age with type 2 diabetes as an adjunct to diet and exercise to improve glycemic control.[1-3]

The SGLT-2 inhibitors also possess the following additional indications in patients with diabetes:

- **Jardiance**: To reduce the risk of cardiovascular (CV) death in adults with type 2 diabetes mellitus and established CV disease.
- **Invokana**: 1) To reduce the risk of major adverse CV events in adults with type 2 diabetes mellitus and established CV disease; AND 2) To reduce the risk of end-stage kidney disease, doubling of serum creatinine, CV death, and hospitalization for heart failure in adults with type 2 diabetes mellitus and diabetic nephropathy with albuminuria.
- **Dapagliflozin**: To reduce the risk of hospitalization for heart failure (HHF) in adults with type 2 diabetes mellitus and established CV disease or multiple CV risk factors.

In addition to indications in diabetes, **dapagliflozin and Jardiance** are indicated for the following indications in patients with and without diabetes:[1,3]

- **Heart failure,** to reduce the risk of CV death, HHF, and urgent heart failure visits in adults with heart failure (included both reduced and preserved ejection fraction).
- **Chronic kidney disease (CKD),** to reduce the risk of sustained estimated glomerular filtration rate (eGFR) decline, end-stage kidney disease, CV death, and hospitalization for heart failure in adults with chronic kidney disease at risk of progression.

Guidelines

Diabetes

The American Diabetes Association Standards of Care (2025) note that first-line therapy for 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 age indications for dapagliflozin and Invokana are not addressed). American Association of Clinical Endocrinology (AACE) Consensus Statement: Comprehensive Type 2 Diabetes Management Algorithm (2023) makes similar

recommendations.[12] It is noted that an agent with proven benefit should be utilized; with "proven benefit" referring to a label indication.

Heart Failure

The American College of Cardiology (ACC) Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment (2022) recommends SGLT-2 inhibitors (dapagliflozin or Jardiance) to reduce HHF and CV mortality, irrespective of the presence of type 2 diabetes in patients with symptomatic chronic heart failure with reduced ejection fraction (class 1 recommendation, level of evidence A).[6] In patients with heart failure with preserved ejection fraction, SGLT-2 inhibitors (Jardiance) can be beneficial in decreasing heart failure hospitalizations and CV mortality, irrespective of the presence of type 2 diabetes (class 2a recommendation, level of evidence B-R). Note: This does not reflect the updated indication for dapagliflozin in patients with preserved ejection fraction heart failure.

The ACC Expert Consensus Decision Pathway on Management of Heart Failure with Preserved Ejection Fraction (2023) recommends that all individuals with heart failure with preserved ejection fraction be started on an SGLT-2 inhibitor unless contraindicated.[10] SGLT-2 inhibitors are noted to have demonstrated significant CV benefits in individuals without type 2 diabetes, particularly in individuals with heart failure. In such patients, SGLT-2 inhibitors have significantly reduced the risk of HHF and CV death across all ejection fraction subgroups. Clinical trials with Jardiance and dapagliflozin are mentioned. For both agents, a significant decrease in HHF was observed.

The 2023 Focused Update of the 2021 European Society of Cardiology Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure recommend an SGLT-2 inhibitor (dapagliflozin or Jardiance) in patients with symptomatic HFmrEF or HFpEF to reduce the risk of HHF or CV death (Class I, Level A).[16] In patients with type 2 diabetes and CKD, SGLT-2 inhibitors (dapagliflozin or Jardiance) are recommended to reduce the risk of HHF or CV death (Class I, Level A).

According to the ACC Expert Consensus Decision Pathway for Treatment of Heart Failure with Reduced Ejection Fraction: a Report of the ACC Solution Set Oversight Committee (2024), guideline-directed medical therapy is the foundation of care in patients with heart failure and agents with the highest expected benefit should be prioritized.[15] The standard four-drug regimen includes renin-angiotensin inhibitors, beta-blockers, SGLT inhibitors (i.e., dapagliflozin, Inpefa® [sotaglitflozin tablets], Jardiance) and mineralocorticoid antagonists. These therapies should be initiated with a sense of urgency; the optimal time to initiate and/or optimize therapy is during hospitalization for heart failure with reduced ejection fraction.

Kidney Disease

Kidney Diseases Improving Global Outcomes (KDIGO) 2024 guidelines for the clinical evaluation and management of CKD recommend treating patients with type 2 diabetes, CKD, and an estimated glomerular filtration rate (eGFR) ≥ 20 mL/min/1.73 m^2 with an SGLT-2 inhibitor.[13] Once initiated, it is reasonable to continue the agent, even if the eGFR falls to < 20 mL/min/1.73 m^2.

In patients with diabetes and chronic kidney disease, the KDIGO guidelines for diabetes management in CKD (2022) recommend first-line pharmacotherapy with metformin and an SGLT-2 inhibitor with documented kidney or CV benefit (Invokana, dapagliflozin, and Jardiance).[7]

Peripheral Arterial Disease (PAD)
According to the Guideline for the Management of Lower Extremity PAD from the ACC/American Heart Association/American Association of Cardiovascular and Pulmonary Rehabilitation/American Podiatric Medical Association/Association of Black Cardiologists/Society for Cardiovascular Angiography and Interventions/Society for Vascular Medicine, Society for Vascular Nursing/Society for Vascular Surgery/Society of Interventional Radiology, and Vascular & Endovascular Surgery Society (2024), SGLT-2 inhibitors (dapagliflozin, Invokana, and Jardiance) and some GLP-1 agonists are noted to be effective to reduce the risk of MACE in patients with type 2 diabetes and PAD.[14]

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, and the use of a Step 2 Product prior to the use of a Step 3 Product. If the Step Therapy rule is not met for a Step 2 or Step 3 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.

- **Requests for a Step 2 Product:** 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, Kazano, alogliptin/metformin, Jentadueto, Jentadueto XR, Kombiglyze XR, saxagliptin/metformin extended-release, Janumet, Janumet XR, sitagliptin/metformin (authorized generic to Zituvimet), Zituvimet, Zituvimet XR; OR
  - One Step 2 Product; OR
  - One Step 3 Product.
- **Requests for a Step 3 Product:** A patient with a history of one Step 2 Product within the 130-day look-back period is excluded from Step Therapy.

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

Step 2: Farxiga, Jardiance, Synjardy, Synjardy XR, Xigduo XR

Step 3: Brenzavvy, bexagliflozin, Invokana, Invokamet, Invokamet XR, dapagliflozin (authorized generic to Farxiga), dapagliflozin/metformin

extended-release (authorized generic to Xigduo XR), Segluromet, Steglatro

***Diabetes – Sodium Glucose Co-Transporter-2 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

Step 2 Products

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: Fortamet ER (obsolete), Glucophage (obsolete), Glucophage XR (obsolete), Glumetza ER, 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), repaglinide/metformin (obsolete), Kazano, alogliptin/metformin, Jentadueto, Jentadueto XR, Kombiglyze XR, saxagliptin/metformin extended-release, Janumet, Janumet XR, sitagliptin/metformin (authorized generic to Zituvimet), Zituvimet, Zituvimet XR.

2. If the patient has tried one Step 2 Product, approve the requested Step 2 Product.

3. If the patient has tried one Step 3 Product, approve the requested Step 2 Product.

4. If the patient will be initiating dual therapy with metformin AND Farxiga or Jardiance, approve Farxiga or Jardiance.

5. If the patient has a contraindication to metformin, according to the prescriber, approve Farxiga, or Jardiance.
   Note: Examples of contraindications to metformin include acute or chronic metabolic acidosis, including diabetic ketoacidosis.

6. If the patient has heart failure, approve Farxiga or Jardiance.

7. If the patient has chronic kidney disease, approve Farxiga or Jardiance.

8. If the patient has atherosclerotic cardiovascular disease or, according to the prescriber, the patient has at least two risk factors for cardiovascular disease, approve Farxiga or Jardiance.

9. If the patient has type 2 diabetes AND peripheral arterial disease, approve Farxiga or Jardiance.

Step 3 Products

1. If the patient has tried one Step 2 Product, approve a Step 3 Product.
   Note: A trial of a Step 1 Product is required prior to a Step 2 Product, unless exception criteria are met.

REFERENCES

1. Farxiga® tablets [prescribing information]. Wilmington, DE: AstraZeneca; October 2024.
2. Invokana® tablets [prescribing information]. Titusville, NJ: Janssen; December 2024.
3. Jardiance® tablets [prescribing information]. Ridgefield, CT and Indianapolis, IN: Boehringer Ingelheim/Lilly; September 2023.
4. Steglatro® tablets [prescribing information]. Whitehouse Station, NJ: Merck; December 2024.
5. American Diabetes Association. Standards of care in diabetes – 2025. *Diabetes Care*. 2025;48(Suppl 1):S1-S359.
6. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2022;145(8):e153-e639.
7. Boer IH, Khunti K, Sadusky T, et al. Diabetes management in chronic kidney disease: a consensus report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney International.* 2022;102:974-989.
8. The EMPA-KIDNEY Collaborative group. Empagliflozin in patients with Chronic Kidney Disease. *N Engl J Med.* 2023; 388:117-127.
9. Solomon SD, McMurray JJV, Claggett B, et al.; DELIVER Trial Committees and Investigators. Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction. *N Engl J Med*. 2022;387(12):1089-109.
10. Kittleson MM, Panjrath GS, Amancherla K, et al. 2023 ACC expert consensus decision pathway on management of heart failure with preserved ejection fraction. *JACC*. 2023;81(18):1835-1878.
11. Brenzavvy™ tablets [prescribing information]. Marlborough, MA: TheracosBio; September 2023.
12. Samson SL, Vellanki P, Blonde L, et al. American Association of Clinical Endocrinology consensus statement: comprehensive type 2 diabetes management algorithm – 2023 update. *Endocr Pract.* 2023;29:305-340.
13. Kidney Diseases Improving Global Outcomes (KDIGO). KDIGO 2024 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int.* 2024;105(4S):S117-S314.
14. Gornik HL, Aronow HD, Goodney PP et al. 2024 ACC/AHA/AACVPR/APMA/ABC/SCAI/SVM/SVN/SVS/SIR/VESS guideline for the management of lower extremity peripheral artery disease: A report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. 2024;149(24):e1313-e1407.
15. Maddox TM, Januzzi JL Jr, Allen LA, et al. 2024 ACC expert consensus decision pathway for treatment of heart failure with reduced ejection fraction: a report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol.* 2024;3(15):1444-1488.
16. McDonagh TA, Metra M, Adamo M, et al; and the ESC Scientific Document Group. 2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2023;44(37):3627-3639.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Automation:** The following products were removed from the automation (obsolete): Glucophage, Glucophage XR,	05/03/2023

	repaglinide/metformin, Actoplus Met XR. Glumetza and Fortamet were clarified to be Glumetza ER and Fortamet ER. **Criteria Step 2 Products:** 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 requesting a Step 2 product with heart failure with preserved ejection fraction, Farxiga was added to the agent approved. Previously only Jardiance was approved. For patients requesting a Step 2 product with chronic kidney disease, Jardiance was added to the agent approved. Previously, only Farxiga was approved.	
Update	05/09/2023: Updated indication in the overview for Farxiga to include expanded heart failure indication.	NA
Selected Revision	**Automation:** Saxagliptin/metformin extended-release (generic to Kombiglyze XR) was added to the list of metformin-containing products. **Step 3 Products:** Benzavvy was added to Step 3.	09/27/2023
Selected Revision	**Step 3 Products:** Dapagliflozin (authorized generic to Farxiga) and dapagliflozin/metformin extended-release (authorized generic to Xigduo XR) were added to Step 3.	02/21/2024

HISTORY (CONTINUED)

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Automation:** Fortamet ER was removed from the list of metformin-containing products (obsolete). **Criteria Step 2 Products:** 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). Criteria for a patient with heart failure with reduced ejection fraction and a patient with heart failure with preserved ejection fraction were combined into one criterion (previously, each criterion approved Farxiga or Jardiance). For the new combined criterion, Farxiga or Jardiance is approved for a patient with heart failure.	05/01/2024
Update	06/13/2024: Updated indication in the overview for dapagliflozin to include expanded indication in pediatric patients.	NA
Selected Revision	**Automation:** Sitagliptin/metformin (authorized generic) was added to automation for one metformin-containing product. **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.	08/07/2024
Selected revision	The following changes are effective 01/01/2025: **Step 2 Products:** Steglatro and Segluromet were removed (moved to Step 3). **Step 3 Products:** Steglatro and Segluromet were added (previously, Step 2). **Criteria for Step 2 Products:** Steglatro was removed from the following criterion: In a patient initiating dual therapy with metformin AND Farxiga, Jardiance, or Steglatro, approve Farxiga, Jardiance, or Steglatro. The criterion continues to approve Farxiga or Jardiance in a patient initiating dual therapy with metformin and Farxiga or Jardiance.	09/18/2024 (effective 01/01/2025)

	Steglatro was removed from the following criterion: In a patient with a contraindication to metformin, according to the prescriber, approve Farxiga, or Jardiance, or Steglatro. The criterion continues to approve Farxiga or Jardiance in a patient with a contraindication to metformin, according to the prescriber.	
Selected Revision	**Automation:** Zituvimet and Zituvimet XR were added to automation for one metformin-containing product. **Criteria for Step 2 Products:** 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.	11/20/2024
Update	01/13/2025: Updated indication in the overview for Invokana to include expanded indication in pediatric patients.	NA
Annual Revision	**Automation:** Riomet ER was removed from the list of metformin-containing products (obsolete > 3 years). **Step 3 Products:** Bexagliflozin was added to Step 3 products. **Criteria for Step 2 Products:** 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 reflect that Riomet ER is obsolete (this still counts towards a trial of a Step 1 product). A new criterion was added to approve Farxiga or Jardiance if the patient has type 2 diabetes AND peripheral arterial disease (without a trial of a Step 1 product first).	05/07/2025

NA – Not applicable.