STEP THERAPY POLICY

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

- Farxiga® (dapagliflozin tablets – Bristol-Myers Squibb)
- 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)

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OVERVIEW

Farxiga, 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] 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.
- Farxiga: 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, Farxiga is indicated for the following indications in patients with and without diabetes:[1]

- **Heart failure,** to reduce the risk of CV death and HHF in adults with heart failure with reduced ejection fraction (New York Heart Association [NYHA] class II through IV).
- **Chronic kidney disease,** 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.

In addition to indications in diabetes, Jardiance is indicated to reduce the risk of CV death plus HHF in adults with heart failure (includes both reduced and preserved ejection fraction).[3]

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Guidelines

Diabetes

The American Diabetes Association Standards of Care (2022) note that first-line therapy for type 2 diabetes depends on comorbidities, patient-centered treatment factors, and management needs and generally includes metformin and comprehensive lifestyle modification.[5] Other medications (glucagon-like peptide-1 receptor agonists, SGLT-2 inhibitors), with or without metformin based on glycemic needs, are appropriate initial therapy for individuals with type 2 diabetes with or at high risk of atherosclerotic CV disease, heart failure, and/or chronic kidney disease. 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 Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment was updated in 2022.[6] In patients with symptomatic chronic heart failure with reduced ejection fraction, SGLT-2 inhibitors are recommended to reduce hospitalization for heart failure and CV mortality, irrespective of the presence of type 2 diabetes (class 1 recommendation, level of evidence A). In patients with heart failure with preserved ejection fraction, SGLT-2 inhibitors can be beneficial in decreasing heart failure hospitalizations and CV mortality (class 2a recommendation, level of evidence B-R).

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.

Automation: The following automation is applied in this policy:

- **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: Fortamet, Glucophage, Glucophage XR, Glumetza, Riomet, metformin oral solution, Riomet ER, metformin extended-release (generics to Fortamet and Glumetza), glyburide/metformin, glipizide/metformin, Actoplus Met, pioglitazone/metformin, Actoplus Met XR, repaglinide/metformin, Kazano, alogliptin/metformin, Jentadueto, Jentadueto XR, Kombiglyze XR, Janumet, Janumet 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.

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

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

Step 3: Invokana, Invokamet, Invokamet XR

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, Glucophage, Glucophage XR, Glumetza, Riomet, metformin oral solution, Riomet ER, metformin extended-release (generics to Fortamet and Glumetza), glyburide/metformin, glipizide/metformin, Actoplus Met, pioglitazone/metformin, Actoplus Met XR, repaglinide/metformin, Kazano, alogliptin/metformin, Jentadueto, Jentadueto XR, Kombiglyze XR, Janumet, Janumet 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, Jardiance, or Steglatro, approve Farxiga, Jardiance, or Steglatro.

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

6. If the patient has heart failure with reduced ejection fraction, approve Farxiga or Jardiance.

7. If the patient has heart failure with preserved ejection fraction, approve Jardiance.

8. If the patient has chronic kidney disease, approve Farxiga.

9. 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.

10. No other exceptions are recommended.

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.

No other exceptions are recommended.

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REFERENCES

1. Farxiga® tablets [prescribing information]. Wilmington, DE: AstraZeneca; April 2021.
2. Invokana® tablets [prescribing information]. Titusville, NJ: Janssen; August 2020.
3. Jardiance® tablets [prescribing information]. Ridgefield, CT and Indianapolis, IN: Boehringer Ingelheim/Lilly; March 2022.
4. Steglatro® tablets [prescribing information]. Whitehouse Station, NJ: Merck; September 2021.
5. American Diabetes Association. Standards of medical care in diabetes – 2022. *Diabetes Care*. 2022;45(Suppl 1):S1-S258.
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 Apr 1. [Epub ahead of print].

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