

Clinical Policy: Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors

Reference Number: ERX.NPA.136

Effective Date: 03.01.20

Last Review Date: 08.22

Line of Business: Commercial, Medicaid

[Revision Log](#)

See **Important Reminder** at the end of this policy for important regulatory and legal information.

Description

The following agents contain a sodium-glucose co-transporter 2 (SGLT2) inhibitor and require prior authorization: canagliflozin (Invokana®), canagliflozin/metformin (Invokamet®, Invokamet® XR), dapagliflozin (Farxiga®), dapagliflozin/metformin (Xigduo® XR), dapagliflozin/saxagliptin (Qtern®), empagliflozin (Jardiance®), empagliflozin/linagliptin (Glyxambi®), empagliflozin/linagliptin/metformin (Trijardy™ XR), empagliflozin/metformin (Synjardy®, Synjardy® XR), ertugliflozin (Steglatro™), ertugliflozin/metformin (Segluromet™), and ertugliflozin/sitagliptin (Steglujan™).

FDA Approved Indication(s)

SGLT2 inhibitors are indicated as adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Dapagliflozin-, canagliflozin-, and empagliflozin-containing products are also indicated in adult patients with type 2 diabetes mellitus and established cardiovascular disease (CV) (or multiple cardiovascular risk factors [*dapagliflozin only*]) to:

- Reduce the risk of hospitalization for heart failure (HF) (*dapagliflozin*)
- Reduce the risk of major adverse CV events: CV death, nonfatal myocardial infarction, and nonfatal stroke (*canagliflozin*)
- Reduce the risk of CV death (*empagliflozin*)

Canagliflozin-containing products are additionally indicated to reduce the risk of end-stage kidney disease, doubling of serum creatinine, CV death, and hospitalization for HF in adults with type 2 diabetes mellitus and diabetic nephropathy with albuminuria > 300 mg/day.

Farxiga is additionally indicated to:

- Reduce the risk of CV death and hospitalization for HF in adults with heart failure with reduced ejection fraction (HFrEF) (New York Heart Association [NYHA] class II-IV)
- Reduce the risk of sustained estimated glomerular filtration rate (eGFR) decline, end stage kidney disease, cardiovascular death, and hospitalization for heart failure in adults with chronic kidney disease (CKD) at risk of progression

Jardiance is additionally indicated to reduce the risk of CV death and hospitalization for HF in adults with HF.

Limitation(s) of use:

- SGLT2 inhibitors should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. SGLT2 inhibitors may increase the risk of diabetic ketoacidosis.
- Farxiga is not recommended for use to improve glycemic control in adults with type 2 diabetes mellitus with an eGFR less than 45 mL/min/1.73 m². Farxiga is likely to be ineffective in this setting based upon its mechanism of action.
- Farxiga and Xigduo XR are not recommended for the treatment of CKD in patients with polycystic kidney disease or patients requiring or with a recent history of immunosuppressive therapy for the treatment of kidney disease. Farxiga and Xigduo XR are not expected to be effective in these populations.
- Jardiance and Glyxambi are not recommended for use to improve glycemic control in adults with type 2 diabetes mellitus with an eGFR less than 30 mL/min/1.73 m². They are likely to be ineffective in this setting based upon their mechanism of action.

- Steglujan has not been studied in patients with a history of pancreatitis.
- Because of the metformin component, the use of Xigduo XR is limited to adults with type 2 diabetes mellitus for all indications.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that SGLT2 inhibitors are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Type 2 Diabetes Mellitus (must meet all):

1. Diagnosis of type 2 diabetes mellitus;
2. Age \geq 18 years;
3. Member meets one of the following (a or b):
 - a. Failure of \geq 3 consecutive months of metformin, unless contraindicated or clinically significant adverse effects are experienced;
 - b. For antidiabetic medication-naïve members, requested agent is approvable if intended for concurrent use with metformin due to HbA1c \geq 8.5% (drawn within the past 3 months);
4. If request is for a non-preferred SGLT2 inhibitor, member meets one of the following (a, b, c, or d):
 - a. For empagliflozin-containing products: Member has established CV disease (e.g., ASCVD or HF) or diabetic nephropathy;
 - b. For canagliflozin- or dapagliflozin-containing products: Member has established CV disease (e.g., ASCVD or HF), diabetic nephropathy/CKD, or multiple risk factors for cardiovascular disease (*see Appendix D*);
 - c. For Glyxambi, Qtern, Steglujan, and Trijardy XR: Failure of \geq 3 consecutive months of a preferred SGLT2 inhibitor OR a preferred dipeptidyl peptidase-4 (DPP-4) inhibitor, unless clinically significant adverse effects are experienced or all are contraindicated;
 - d. For all other non-preferred SGLT2 inhibitors: Failure of \geq 3 consecutive months of a preferred SGLT2 inhibitor, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed the FDA-approved maximum recommended dose (*see Section V*).

Approval duration: 12 months

B. Heart Failure (must meet all):

1. Diagnosis of HF of NYHA Class II, III, or IV;
2. Request is for Farxiga or Jardiance;
3. Prescribed by or in consultation with a cardiologist;
4. Age \geq 18 years;
5. If request is for Farxiga, member has HFrEF as evidenced by left ventricular ejection fraction (LVEF) \leq 40%;
6. Member does not have a diagnosis of type 1 diabetes mellitus;
7. Dose does not exceed 10 mg (1 tablet) per day.

Approval duration: 12 months

C. Chronic Kidney Disease (must meet all):

1. Diagnosis of CKD;
2. Request is for Farxiga;
3. Age \geq 18 years;

4. Both of the following (a and b):
 - a. eGFR between 25 and 75 mL/min/1.73 m²;
 - b. Urine albumin creatinine ratio (UACR) ≥ 200 mg/g;
5. Member does not have a diagnosis of type 1 diabetes mellitus or polycystic kidney disease;
6. Member has not received immunosuppressive therapy for the treatment of kidney disease in the past 6 months;
7. Member is currently receiving an angiotensin converting enzyme inhibitor or angiotensin receptor blocker at maximally tolerated doses for ≥ 4 weeks, unless clinically significant adverse effects are experienced or all are contraindicated;
8. Dose does not exceed 10 mg (1 tablet) per day.

Approval duration: 12 months

D. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Type 2 Diabetes Mellitus (must meet all):

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed the FDA-approved maximum recommended dose (*see Section V*).

Approval duration: 12 months

B. Heart Failure (must meet all):

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Farxiga or Jardiance for HFrEF and has received this medication for at least 30 days;
2. Request is for Farxiga or Jardiance;
3. Member is responding positively to therapy;
4. If request is for a dose increase, new dose does not exceed 10 mg (1 tablet) per day.

Approval duration: 12 months

C. Chronic Kidney Disease (must meet all):

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Request is for Farxiga;
3. Member is responding positively to therapy;
4. If request is for a dose increase, new dose does not exceed 10 mg (1 tablet) per day.

Approval duration: 12 months

D. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.

Approval duration: Duration of request or 12 months (whichever is less); or

2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

- A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AACE: American Association of Clinical Endocrinologists
ACE: American College of Endocrinology
ADA: American Diabetes Association
ASCVD: atherosclerotic cardiovascular disease
CKD: chronic kidney disease
CV: cardiovascular
DPP-4: dipeptidyl peptidase-4
eGFR: estimated glomerular filtration rate

ER: extended-release
FDA: Food and Drug Administration
GLP-1: glucagon-like peptide-1
HbA1c: glycated hemoglobin
HFrEF: heart failure with reduced ejection fraction
IR: immediate-release
LVEF: left ventricular ejection fraction
SGLT2: sodium-glucose co-transporter 2
UACR: urine albumin creatinine ratio

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
metformin (Fortamet [®] , Glucophage [®] , Glucophage [®] XR, Glumetza [®])	Regular-release (Glucophage): 500 mg PO BID or 850 mg PO QD; increase as needed in increments of 500 mg/week or 850 mg every 2 weeks Extended-release: <ul style="list-style-type: none"> Fortamet, Glumetza: 1,000 mg PO QD; increase as needed in increments of 500 mg/week Glucophage XR: 500 mg PO QD; increase as needed in increments of 500 mg/week 	Regular-release: 2,550 mg/day Extended-release: 2,000 mg/day
Angiotensin Converting Enzyme Inhibitors		
captopril (Capoten [®])	Initially, 6.25 mg PO 3 times daily, then increase to 50 mg PO 3 times daily if tolerated.	450 mg/day
enalapril (Vasotec [®] , Epaned [®])	Initially, 2.5 mg PO twice daily, then increase to 10 to 20 mg PO twice daily if tolerated.	40 mg/day
fosinopril (Monopril [®])	Initially, 5 to 10 mg PO once daily, then increase to 40 mg/day if tolerated.	80 mg/day
lisinopril (Prinivil [®] , Zestril [®] , Qbrelis [®])	Initially, 2.5 to 5 mg PO once daily, then increase to 20 to 40 mg/day if tolerated.	80 mg/day
perindopril (Aceon [®])	Initially, 4 mg PO once daily for 2 weeks, then increase to 8 mg PO once daily if tolerated.	16 mg/day
quinapril (Accupril [®])	Initially, 5 mg PO twice daily, then increase to 20 mg PO twice daily if tolerated.	80 mg/day
ramipril (Altace [®])	Initially, 2.5 mg PO once daily. Gradually titrate to 5 mg/day PO, then increase if tolerated to the target dosage of 10 mg/day PO, given in 1 to 2 divided doses.	20 mg/day
trandolapril (Mavik [®])	Initially, 1 mg PO once daily, then increase to 4 mg/day if tolerated.	8 mg/day
Angiotensin Receptor Blockers		
candesartan (Atacand [®])	Initially, 4 to 8 mg PO once daily, then increase to 32 mg/day if tolerated.	32 mg/day
losartan (Cozaar [®])	Initially, 25 to 50 mg PO once daily, then increase to 50 to 150 mg/day if tolerated.	100 mg/day
telmisartan (Micardis [®])	80 mg PO once daily	80 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
valsartan (Diovan®)	Initially, 20 to 40 mg PO twice daily, then increase dose to 160 mg PO twice daily if tolerated.	320 mg/day
Angiotensin Receptor-Neprilysin Inhibitor/Angiotensin Receptor Blocker		
Entresto® (sacubitril/valsartan)	The recommended starting dose is 49/51 mg (sacubitril/valsartan) PO BID. Double the dose after 2 to 4 weeks to the target maintenance dose of 97/103 mg (sacubitril/valsartan) BID, as tolerated by the patient.	194/206 mg/day
Beta Blockers Recommended for HF		
bisoprolol (Zebeta®)	Initially, 1.25 mg PO QD for 48 hours, then 2.5 mg QD for the first month, then 5 mg QD.	10 mg/day
carvedilol (Coreg®, Coreg CR®)	<u>Immediate-release:</u> Initially, 3.125 mg PO BID for 2 weeks. Dosage may be subsequently increased to 6.25, 12.5, and then 25 mg PO BID over successive intervals of at least 2 weeks. <u>Extended-release:</u> Initially, 10 mg PO QD for 2 weeks. Dosage may be subsequently increased to 20, 40, and then 80 mg PO QD over successive intervals of at least 2 weeks.	Immediate-release: 100 mg/day Extended-release: 80 mg/day
metoprolol succinate extended release (Toprol XL®)	25 mg PO QD for 2 weeks in patients with NYHA class II HF, or 12.5 mg PO QD in patients with more severe HF. Double the dose every 2 weeks as tolerated, up to the target dosage of 200 mg PO QD.	200 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
 - History of serious hypersensitivity reaction to the requested drug product
 - Moderate to severe renal impairment*, end-stage renal disease, or dialysis
*Minimum degree of renal impairment varies per agent; refer to individual prescribing information
 - Acute or chronic metabolic acidosis, including diabetic ketoacidosis (*metformin-containing products only*)
- Boxed warning(s): lactic acidosis (*metformin-containing products only*)

Appendix D: General Information

- Per the American Diabetes Association (ADA) and American Association of Clinical Endocrinologists and American College of Endocrinology (AACE/ACE) guidelines:
 - Metformin is recommended for all patients with type 2 diabetes. Monotherapy is recommended for most patients; however:
 - Starting with dual therapy (i.e., metformin plus another agent, such as a sulfonylurea, thiazolidinedione, DPP-4 inhibitor, SGLT2 inhibitor, glucagon-like peptide 1 [GLP-1] receptor agonist, or basal insulin) may be considered for patients with baseline HbA1c ≥ 1.5% above their target per the ADA (≥ 7.5% per the AACE/ACE). According to the ADA, a reasonable HbA1c target for many non-pregnant adults is < 7% (≤ 6.5% per the AACE/ACE).
 - Starting with combination therapy with insulin may be considered for patients with baseline HbA1c > 10% per the ADA (> 9% if symptoms are present per the AACE/ACE).
 - If the target HbA1c is not achieved after approximately 3 months of monotherapy, dual therapy should be initiated. If dual therapy is inadequate after 3 months, triple therapy should be initiated. Finally, if triple therapy fails to bring a patient to goal, combination therapy with

- insulin should be initiated. Each non-insulin agent added to initial therapy can lower HbA1c by 0.7-1%.
- Although Invokana is currently the only SGLT2 inhibitor with a labeled indication for diabetic nephropathy, Farxiga and Jardiance have also demonstrated renal protective effects. The ADA guidelines recommend SGLT2 inhibitors be considered when treating type 2 diabetic patients with renal concerns, noting that Farxiga, Jardiance, and Invokana all confer renal benefit, with no preference for one over the other
 - Farxiga DECLARE-TIMI 58: The cardiorenal secondary composite outcome (sustained decline of at least 40% in eGFR to less than 60 mL/min/1.73 m², end stage renal disease (ESRD), or death from renal or CV causes) was significantly reduced with Farxiga compared to placebo (HR 0.76, 95% CI 0.67-0.87; p < 0.0001); excluding death from CV causes, the HR for the renal-specific outcome was 0.53 (95% CI 0.43-0.66; p < 0.0001). There was a 46% reduction in sustained decline in eGFR by at least 40% to less than 60 mL/min/1.73 m² (120 [1.4% vs 221 [2.6%]; HR 0.54 [95% CI 0.43-0.67]; p < 0.0001). The risk of ESRD or renal death was also lower in the Farxiga group than in the placebo group (11 [0.1%] vs 27 [0.3%]; HR 0.41 [95% CI 0.20-0.82]; p = 0.012).
 - Jardiance EMPA-REG Outcome: Analysis of secondary outcomes yielded a reduction of risk for incident of or worsening nephropathy (HR 0.61 [95% CI 0.53-0.70]), progression to urine albumin to creatinine ratio (UACR) > 300 mg/g (HR 0.62 [95% CI 0.54-0.72]), composite consisting doubling of serum creatinine, initiation of renal replacement therapy, and death from ESRD (HR 0.54 [95% CI 0.40-0.75]).
 - Examples of CV risk factors may include but are not limited to: dyslipidemia, hypertension, obesity/overweight, a family history of premature coronary disease, and smoking.
 - According to the ADA, ASCVD includes coronary heart disease, cerebrovascular disease, or peripheral arterial disease presumed to be of atherosclerotic origin. Indicators of high ASCVD risk are age ≥ 65 years with coronary, carotid, or lower-extremity artery stenosis > 50% or left ventricular hypertrophy.
 - Although Farxiga and Invokana are the only SGLT2 inhibitors with labeled indications for reducing the risk of HHF, Jardiance has also been shown to reduce the risk of HHF. The ADA guidelines acknowledge Farxiga along with Jardiance and Invokana as agents which reduce the risk of HHF, without a preference for one agent over the other. Any of the three can be used in T2DM patients with established HF; however, the guidelines recommend only Jardiance or Invokana for patients with established ASCVD.
 - Jardiance EMPA-REG Outcome, patients with established ASCVD: The primary outcome (composite of death from CV causes, nonfatal MI, or non-fatal stroke) was reduced with Jardiance compared to placebo (HR 0.86, 95% CI 0.74 – 0.99; p = 0.04). Analysis of secondary outcomes yielded a reduction in hospitalization for heart failure when treated with Jardiance compared to placebo (HR 0.65, 95% CI 0.50 – 0.85; p = 0.002).
 - Invokana CANVAS Program, patients with established ASCVD or multiple ASCVD risk factors: The primary outcome (composite of death from CV causes, nonfatal MI or nonfatal stroke) was reduced with Invokana compared to placebo (HR 0.86, 95% CI 0.75 – 0.97; p = 0.02). Analysis of secondary outcomes yielded a reduction in hospitalization for heart failure when treated with Invokana compared to placebo (HR 0.67, 95% CI 0.52 – 0.87).
 - In August 2020, the FDA removed the boxed warning regarding the risk of leg and foot amputations from the canagliflozin prescribing information. Although the risk is still present (and continues to be described in the Warnings and Precautions section of the prescribing information), the FDA notes the significantly enhanced benefit of canagliflozin (e.g., effects in heart and kidney disease) relative to said risk, which safety information from recent trials suggest is lower than previously described.

V. Dosage and Administration

Drug Name	Dosing regimen	Maximum Dose
Farxiga (dapagliflozin)	Diabetes: 5 mg PO QD HFrEF, CKD: 10 mg PO QD	10 mg/day
Glyxambi (empagliflozin/linagliptin)	10/5 mg PO QD	25/5 mg/day

Drug Name	Dosing regimen	Maximum Dose
Invokamet (canagliflozin/metformin)	One 50/500 mg tablet PO BID	300/2,000 mg/day
Invokamet XR (canagliflozin/metformin)	Two 50/500 mg tablets PO QD	300/2,000 mg/day
Invokana (canagliflozin)	100 mg PO QD	300 mg/day
Jardiance (empagliflozin)	10 mg PO QD	Diabetes: 25 mg/day HF: 10 mg/day
Qtern (dapagliflozin/saxagliptin)	One 5/5 mg tablet PO QD	10/5 mg/day
Segluromet (ertugliflozin/metformin)	Individualized dose PO BID	15/2,000 mg/day
Steglatro (ertugliflozin)	5 mg PO QD	15 mg/day
Steglujan (ertugliflozin/sitagliptin)	One 5/100 mg tablet PO QD	15/100 mg/day
Synjardy (empagliflozin/metformin)	Individualized dose PO BID	25/2,000 mg/day
Synjardy XR (empagliflozin/metformin)	Individualized dose PO QD	25/2,000 mg/day
Trijardy XR (empagliflozin/linagliptin/metformin)	Individualized dose PO QD	25/5/2,000 mg/day
Xigduo XR (dapagliflozin/metformin)	Individualized dose PO QD	10/2,000 mg/day

VI. Product Availability

Drug Name	Availability
Farxiga (dapagliflozin)	Tablets: 5 mg, 10 mg
Glyxambi (empagliflozin/linagliptin)	Tablets: 10/5 mg, 25/5 mg
Invokamet (canagliflozin/metformin)	Tablets: 50/500 mg, 50/1,000 mg, 150/500 mg, 150/1,000 mg
Invokamet XR (canagliflozin/metformin)	Tablets: 50/500 mg, 50/1,000 mg, 150/500 mg, 150/1,000 mg
Invokana (canagliflozin)	Tablets: 100 mg, 300 mg
Jardiance (empagliflozin)	Tablets: 10 mg, 25 mg
Qtern (dapagliflozin/saxagliptin)	Tablet: 5/5 mg, 10/5 mg
Segluromet (ertugliflozin/metformin)	Tablets: 2.5/500 mg, 2.5/1,000mg, 7.5/500 mg, 7.5/1,000mg
Steglatro (ertugliflozin)	Tablets: 5 mg, 15 mg
Steglujan (ertugliflozin/sitagliptin)	Tablets: 5/100 mg, 15/100 mg
Synjardy (empagliflozin/metformin)	Tablets: 5/500 mg, 5/1,000 mg, 12.5/500 mg, 12.5/1,000 mg
Synjardy XR (empagliflozin/metformin)	Tablets: 5/1,000 mg, 10/1,000 mg, 12.5/1,000 mg, 25/1,000 mg
Trijardy XR (empagliflozin/linagliptin/ metformin)	Tablets: 5/2.5/1,000 mg, 10/5/1,000 mg, 12.5/2.5/1,000 mg, 25/5/1,000 mg
Xigduo XR (dapagliflozin/metformin)	Tablets: 2.5/1,000 mg, 5/500 mg, 5/1,000 mg, 10/500 mg, 10/1,000 mg

VII. References

- American Diabetes Association. Standards of medical care in diabetes—2021. Diabetes Care. 2021; 44(suppl 1): S1-S232. Updated June 16, 2021. Accessed September 16, 2021.
- Farxiga Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; April 2021. Available at: www.farxiga.com. Accessed September 20, 2021.
- Qtern Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; January 2020. Available at: www.qtern.com. Accessed September 20, 2021.
- Xigduo XR Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; April 2022. Available at: www.xigduoxr.com. Accessed May 3, 2022.
- Invokana Prescribing Information. Titusville, NJ: Janssen Pharmaceuticals, Inc.; August 2020. Available at: www.invokana.com. Accessed September 20, 2021.
- Invokamet/Invokamet XR Prescribing Information. Titusville, NJ: Janssen Pharmaceuticals, Inc.; August 2020. Available at: www.invokamet.com. Accessed September 20, 2021.

7. Jardiance Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; February 2022. Available at: www.jardiance.com. Accessed March 11, 2022.
8. Glyxambi Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; June 2021. Available at: www.glyxambi.com. Accessed September 20, 2021.
9. Synjardy Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; June 2021. Available at: www.synjardy.com. Accessed September 20, 2021.
10. Synjardy XR Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; June 2021. Available at: www.synjardyxr.com. Accessed September 20, 2021.
11. Trijardy XR Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; June 2021. Available at: www.trijardy.com. Accessed September 20, 2021.
12. Steglatro Prescribing Information. Whitehouse Station, NJ: Merck & Co., Inc.; February 2021. Available at www.steglatro.com. Accessed September 20, 2021.
13. Segluromet Prescribing Information. Whitehouse Station, NJ: Merck & Co., Inc.; February 2021. Available at www.segluromet.com. Accessed September 20, 2021.
14. Steglujan Prescribing Information. Whitehouse Station, NJ: Merck & Co., Inc.; February 2021. Available at www.steglujan.com. Accessed September 20, 2021.
15. 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; 26(1): 107-139.
16. Patorno E, Pawar A, Franklin JM, et al. Empagliflozin and the Risk of Heart Failure Hospitalization in Routine Clinical Care. *Circulation* *AHA*; 2019 Jun 18;139(25):2822-2830. doi: 10.1161/CIRCULATIONAHA.118.039177
17. Neal B, Perkovic V, Mahaffey KW, et al. Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes. *N Engl J Med* 2017; 377:644-657. DOI: 10.1056/NEJMoa1611925
18. Zinman B, Wanner C, Lachin JM, et al. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. *N Engl J Med* 2015; 373:2117-2128. DOI:10.1056/NEJMoa150472
19. Yancy C, Jessup M, Bozkurt B, et al. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure. *J Am Coll Cardiol.* 2017 Aug, 70 (6) 776-803.
20. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney inter., Suppl.* 2013; 3: 1–150.
21. Maddox TM, Januzzi JL, Allen LA, et al. 2021 update to the 2017 ACC expert consensus decision pathway for optimization of heart failure treatment: Answers to 10 pivotal issues about heart failure with reduced ejection fraction: A report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol.* 2021 Feb; 77(6): 772-810. Available at: <https://www.jacc.org/doi/10.1016/j.jacc.2020.11.022>. Accessed October 28, 2021.
22. 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: e895-e1032.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created: adapted from ERX.ST.01 SGLT2 inhibitors; added diagnosis, age, and positive response requirements; criteria added for Invokana’s new FDA indication: diabetic nephropathy; criteria added for Farxiga’s new FDA indication: reduction in risk of hospitalization due to HF in patients with established cardiovascular disease or with multiple cardiovascular risk factors; criteria added for Farxiga/Jardiance for diabetic nephropathy and Invokana/Jardiance for HF as supported by ADA guidelines and published data; criteria added for Invokana for multiple cardiovascular risk factors references as supported by CANVAS Program trials; added Trijardy XR; references reviewed and updated.	12.03.19	02.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Modified references to parent products (Farxiga, Invokana, and Jardiance) to allow combination products (e.g., dapagliflozin-, canagliflozin-, and empagliflozin-containing products) per previously approved clinical guidance.	04.01.20	
Criteria added for Farxiga's new FDA indication: heart failure with reduced ejection fraction.	06.02.20	08.20
1Q 2021 annual review: no significant changes; removed lower limb amputation boxed warning for canagliflozin from Appendix C per updated PI; references reviewed and updated.	10.28.20	02.21
RT4: criteria added for Farxiga's new FDA indication: CKD. Ad hoc: allowed off-label use of Jardiance for HFrEF per ADA/ACC guidelines and specialist feedback.	07.07.21	08.21
RT4: updated policy to reflect the new FDA approval of Jardiance for HFrEF, for which criteria were previously already added based on guidelines and specialist feedback.	09.08.21	
1Q 2022 annual review: no significant changes; removed Qternmet XR as it is no longer on market; references reviewed and updated.	09.16.21	02.22
RT4: updated FDA Approved Indication(s) section with Xigduo XR's new limitation of use per revised PI, and updated HF criteria per Jardiance's revised indication for HF regardless of ejection fraction.	03.11.22	
RT4: updated FDA Approved Indication(s) section with Xigduo XR's new limitation of use for CKD per revised PI; for diabetes, clarified that canagliflozin- or dapagliflozin-containing products may also be used for CKD in addition to diabetic nephropathy.	05.05.22	
For HFrEF, removed requirement for prior use of standard HF therapy as SGLT2 inhibitors are now a recommended first line therapy per 2022 AHA/ACC/HFSA guidelines.	06.01.22	08.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

This policy is the property of Envolve Pharmacy Solutions. Unauthorized copying, use, and distribution of this Policy or any information contained herein is strictly prohibited. By accessing this policy, you agree to be bound by the foregoing terms and conditions, in addition to the Site Use Agreement for Health Plans associated with Envolve Pharmacy Solutions.

©2020 Envolve Pharmacy Solutions. All rights reserved. All materials are exclusively owned by Envolve Pharmacy Solutions and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Envolve Pharmacy Solutions. You may not alter or remove any trademark, copyright or other notice contained herein.