

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

Reference Number: CP.PMN.14

Effective Date: 03.01.19 Last Review Date: 02.21 Line of Business: Medicaid

Revision Log

See <u>Important Reminder</u> 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®), dapagliflozin/saxagliptin/metformin (Qternmet® XR), empagliflozin (Jardiance®), empagliflozin/linagliptin (Glyxambi®), empagliflozin/linagliptin/metformin (Trijardy™ XR), empagliflozin/metformin (Synjardy®, Synjardy® XR), 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 (CV) disease (or multiple CV 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).

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.
- Qternmet XR initiation is intended only for patients currently taking metformin.

^{*}If formulary status is step therapy only, refer to CP.PST.01 Step Therapy for ertugliflozin (SteglatroTM) and ertugliflozin/metformin (SeglurometTM).



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.

It is the policy of health plans affiliated with Centene Corporation[®] 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 ≥ 3 consecutive months of metformin, unless contraindicated or clinically significant adverse effects are experienced;
 - b. For medication-naïve members, requested agent is approvable if intended for concurrent use with metformin due to HbA1c ≥ 8.5% (drawn within the past 3 months);
- 4. Request meets one of the following (a, b, or c):
 - a. Failure of ≥ 3 consecutive months of Steglatro or Segluromet, unless both are contraindicated or clinically significant adverse effects are experienced;
 - b. Member has established CV disease (e.g., ASCVD or HF) or diabetic nephropathy, and request is for a formulary empagliflozin-containing product, unless contraindicated or clinically significant adverse effects are experienced;
 - c. Member has multiple risk factors for CV disease (*see Appendix D*), and request is for a formulary canagliflozin- or dapaglifozin-containing product, 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 HFrEF of NYHA Class II, III, or IV;
- 2. Request is for Farxiga;
- 3. Prescribed by or in consultation with a cardiologist;
- 4. Age > 18 years:
- 5. Left ventricular ejection fraction (LVEF) is $\leq 40\%$;
- 6. Member does not have a diagnosis of type 1 diabetes mellitus;
- 7. Member is currently receiving standard HF drug therapy at target doses for ≥ 4 weeks, including both of the following (a and b) unless clinically significant adverse effects are experienced or all are contraindicated:
 - a. Angiotensin converting enzyme inhibitor, angiotensin receptor blocker, or Entresto[®];
 - b. Beta blocker;
- 8. Dose does not exceed 10 mg (1 tablet) per day.

Approval duration: 12 months



C. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

II. Continued Therapy

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

- 1. Currently receiving medication via Centene benefit 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 Centene benefit, or documentation supports that member is currently receiving Farxiga for HFrEF and has received this medication for at least 30 days;
- 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

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

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

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

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 policies – CP.PMN.53 for Medicaid 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

CV: cardiovascular

DPP-4: dipeptidyl peptidase-4

ER: extended-release

FDA: Food and Drug Administration

GLP-1: glucagon-like peptide-1

HbA1c: glycated hemoglobin

HF: heart failure

HFrEF: heart failure with reduced ejection

fraction

IR: immediate-release



LVEF: left ventricular ejection fraction

SGLT2: sodium-glucose co-transporter 2

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 for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/
		Maximum Dose
metformin	Regular-release (Glucophage): 500 mg PO	Regular-release:
(Fortamet [®] ,	BID or 850 mg PO QD; increase as needed in	2,550 mg/day
Glucophage®,	increments of 500 mg/week or 850 mg every 2	
Glucophage® XR,	weeks	
Glumetza®)		
	Extended-release:	Extended-release:
	• Fortamet, Glumetza: 1,000 mg PO QD;	2,000 mg/day
	increase as needed in increments of 500	
	mg/week	
	• Glucophage XR: 500 mg PO QD; increase	
	as needed in increments of 500 mg/week	
Segluromet	Individualized dose PO BID	15/2,000 mg/day
(ertugliflozin/		
metformin)		
Steglatro	5 mg PO QD	15 mg/day
(ertugliflozin)		
ACEIs		
captopril	Initially, 6.25 mg PO 3 times daily, then	450 mg/day
(Capoten®)	increase to 50 mg PO 3 times daily if tolerated.	
enalapril (Vasotec®,	Initially, 2.5 mg PO twice daily, then increase	40 mg/day
Epaned®)	to 10 to 20 mg PO twice daily if tolerated.	
fosinopril	Initially, 5 to 10 mg PO once daily, then	80 mg/day
(Monopril®)	increase to 40 mg/day if tolerated.	
lisinopril (Prinivil®,	Initially, 2.5 to 5 mg PO once daily, then	80 mg/day
Zestril [®] , Qbrelis [®])	increase to 20 to 40 mg/day if tolerated.	
perindopril	Initially, 4 mg PO once daily for 2 weeks, then	16 mg/day
(Aceon®)	increase to 8 mg PO once daily if tolerated.	
quinapril	Initially, 5 mg PO twice daily, then increase to	80 mg/day
(Accupril®)	20 mg PO twice daily of tolerated.	
ramipril (Altace®)	Initially, 2.5 mg PO once daily. Gradually	20 mg/day
	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.	
trandolapril	Initially, 1 mg PO once daily, then increase to	8 mg/day
(Mavik®)	4 mg/day if tolerated.	
ARBs		
candesartan	Initially, 4 to 8 mg PO once daily, then	32 mg/day
(Atacand [®])	increase to 32 mg/day if tolerated.	



Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
losartan (Cozaar®)	Initially, 25 to 50 mg PO once daily, then	100 mg/day
iosarian (Cozaar)	increase to 50 to 150 mg/day if tolerated.	100 mg/day
telmisartan	<u> </u>	90 m a/day
(Micardis [®])	80 mg PO once daily	80 mg/day
valsartan (Diovan®)	Initially, 20 to 40 mg PO twice daily, then	320 mg/day
vaisartaii (Biovaii)	increase dose to 160 mg PO twice daily if	320 mg/day
	tolerated.	
ARNI/ARB		
Entresto®	The recommended starting dose is 49/51 mg	194/206 mg/day
(sacubitril/valsartan)	(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.	
Beta-Blockers Recon	imended for HF	
bisoprolol (Zebeta®)	HF	10 mg/day
	Initially, 1.25 mg PO QD for 48 hours, then	
	2.5 mg QD for the first month, then 5 mg QD.	
carvedilol (Coreg®,	HF	Immediate-
Coreg CR®)	Immediate-release: Initially, 3.125 mg PO BID	release: 100
	for 2 weeks. Dosage may be subsequently	mg/day
	increased to 6.25, 12.5, and then 25 mg PO	
	BID over successive intervals of at least 2	Extended-release:
	weeks.	80 mg/day
	Extended-release: 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.	
metoprolol	HF	200 mg/day
succinate extended	25 mg PO QD for 2 weeks in patients with	
release (Toprol	NYHA class II HF, or 12.5 mg PO QD in	
$\mathrm{XL}^{\scriptscriptstyle{\circledR}}$)	patients with more severe HF. Double the dose	
	every 2 weeks as tolerated, up to the target	
	dosage of 200 mg PO QD.	

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):
 - o 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
 - Metabolic acidosis, including diabetic ketoacidosis (metformin-containing products only)
- Boxed warning(s): lactic acidosis (*metformin-containing products only*)



Appendix D: General Information

- A double-blind, placebo-controlled dose-response trial by Garber et al. found the maximal efficacy of metformin to occur at doses of 2,000 mg. However, the difference in adjusted mean change in HbA1c between the 1,500 and 2,000 mg doses was 0.3%, suggesting that the improvement in glycemic control provided by the additional 500 mg may be insufficient when HbA1c is > 7%.
- Per the 2020 American Diabetes Association (ADA) and 2020 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, dipeptidyl peptidase-4 [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).</p>
 - 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).
 - o 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 2020 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).
 - o 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, 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.
- 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 2020 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.
 - o 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).
 - o 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)	5 mg PO QD	10 mg/day	
	To reduce the risk of hospitalization for HF in T2DM patients and the risk		
	of CV death and hospitalization in adults with		
	HFrEF, the recommended dose is 10 mg PO QD		
Glyxambi (empagliflozin/linagliptin)	One 10/5 mg tablet PO QD	25/5 mg/day	
Invokamet (canagliflozin/metformin)	One 50/500 mg tablet PO BID	300/2,000 mg/day	
Invokamet XR	Two 50/500 mg tablets PO	300/2,000 mg/day	
(canagliflozin/metformin)	QD	_ ,	
Invokana (canagliflozin)	100 mg PO QD	300 mg/day	



Drug Name	Dosing Regimen	Maximum Dose	
Jardiance (empagliflozin)	10 mg PO QD	25 mg/day	
Qtern (dapagliflozin/saxagliptin)	One 5/5 mg tablet PO QD	10/5 mg/day	
Qternmet XR	Individualized dose PO QD	10/5/2,000 mg/day	
(dapagliflozin/saxagliptin/metformin)			
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	Individualized dose PO QD	25/2,000 mg/day	
(empagliflozin/metformin)			
Trijardy XR	Individualized dose PO QD	25/5/2,000 mg/day	
(empagliflozin/linagliptin/			
metformin)			
Xigduo XR	Individualized dose PO QD	10/2,000 mg/day	
(dapagliflozin/metformin)			

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	Tablets: 50/500 mg, 50/1,000 mg, 150/500 mg,
(canagliflozin/metformin)	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
Qternmet XR	Tablets: 2.5/2.5/1,000 mg, 5/2.5/1,000 mg,
(dapagliflozin/saxagliptin/metformin)	5/5/1000 mg, 10/5/1,000 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	Tablets: 5/1,000 mg, 10/1,000 mg, 12.5/1,000 mg,
(empagliflozin/metformin)	25/1,000 mg
Trijardy XR	Tablets: 5/2.5/1,000 mg, 10/5/1,000 mg,
(empagliflozin/linagliptin/	12.5/2.5/1,000 mg, 25/5/1,000 mg
metformin)	
Xigduo XR	Tablets: 2.5/1,000 mg, 5/500 mg, 5/1,000 mg,
(dapagliflozin/metformin)	10/500 mg, 10/1,000 mg

VII. References

- 1. American Diabetes Association. Standards of medical care in diabetes—2020. Diabetes Care. 2020;43 (suppl 1): S1-S212. Updated June 5, 2020. Accessed October 26, 2020.
- 2. Farxiga Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; May 2020. Available at: www.farxiga.com. Accessed October 28, 2020.

CLINICAL POLICY

Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors



- 3. Qtern Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; January 2020. Available at: www.qtern.com. Accessed October 27, 2020.
- Qternmet XR Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; January 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/210874s000lbl.pdf. Accessed October 27, 2020.
- 5. Xigduo XR Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; January 2020. Available at: www.xigduoxr.com. Accessed October 28, 2020.
- 6. Invokana Prescribing Information. Titusville, NJ: Janssen Pharmaceuticals, Inc.; August 2020. Available at: www.invokana.com. Accessed October 28, 2020.
- 7. Invokamet/Invokamet XR Prescribing Information. Titusville, NJ: Janssen Pharmaceuticals, Inc.; August 2020. Available at: www.invokamet.com. Accessed October 28, 2020.
- 8. Jardiance Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; January 2020. Available at: www.jardiance.com. Accessed October 28, 2020.
- 9. Glyxambi Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; March 2020. Available at: www.glyxambi.com. Accessed October 27, 2020.
- 10. Synjardy Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; January 2020. Available at: www.synjardy.com. Accessed October 28, 2020.
- 11. Synjardy XR Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; January 2020. Available at: www.synjardyxr.com. Accessed October 28, 2020.
- 12. Trijardy XR Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; January 2020. Available at: www.trijardy.com. Accessed October 27, 2020.
- 13. Steglatro Prescribing Information. Whitehouse Station, NJ: Merck & Co., Inc.; January 2020. Available at www.steglatro.com. Accessed October 28, 2020.
- 14. Segluromet Prescribing Information. Whitehouse Station, NJ: Merck & Co., Inc.; January 2020. Available at www.segluromet.com. Accessed October 28, 2020.
- 15. Steglujan Prescribing Information. Whitehouse Station, NJ: Merck & Co., Inc.; January 2020. Available at www.steglujan.com. Accessed October 27, 2020.
- 16. Garber AJ, Duncan TG, Goodman AM, et al. Efficacy of metformin in type II diabetes: results of a double-blind, placebo-controlled, dose-response trial. Am J Med. 1997; 102: 491-497.
- 17. 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.
- 18. 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
- 19. 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
- 20. 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/NEJMoa1504720



21. 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2019 Policy created per SDC recommendation based on previously approved clinical guidance: adapted from previously corporate approved policy CP.PST.19; modified to reflect that all SGLT2 inhibitors (except for Steglatro and Segluromet) now require PA (instead of ST), added diagnosis, and added re-direction to Steglatro/Segluromet (with exception for members with ASCVD requesting Jardiance); removed Steglatro and Segluromet from policy (added to CP.PST.01 Step Therapy); added updated indication for ASCVD for Invokana; modified minimum A1c related for concurrent use of metformin from 9% to 8.5% based on 2019 ADA guidelines.	10.17.18	02.19
Added Qtern and Qternmet XR with re-direction to the preferred SGLT2 inhibitor Steglatro/Segluromet.	05.08.19	
1Q 2020 annual review: policy updated to include Invokana's new FDA indication: diabetic nephropathy and 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 modified to allow Jardiance for diabetic nephropathy/HF as supported by ADA guidelines/published data (Farxiga and Invokana are not allowed due to formulary status); clarified that established cardiovascular disease can mean ASCVD or HF; added criteria to allow Invokana for patients with multiple cardiovascular risk factors as supported by CANVAS Program trials; added Trijardy XR with re-direction to Steglatro or Segluromet per SDC; references reviewed and updated.	12.03.19	02.20
Modified references to parent products (Farxiga, Invokana, and Jardiance) to allow formulary combination products (e.g., dapagliflozin-, canagliflozin-, and empagliflozin-containing products) per previously approved clinical guidance and SDC clarification.	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

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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 clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.



©2018 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation 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 Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene® and Centene Corporation® are registered trademarks exclusively owned by Centene Corporation.