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

Reference Number: IL.PMN.14
Effective Date: 1.1.20
Last Review Date: 3.30.23
Line of Business: 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: bexagliflozin (Brenzavvy™), canagliflozin (Invokana®), canagliflozin/metformin (Invokamet®, Invokamet® XR), dapagliflozin (Farxiga®), empagliflozin (Jardiance®), dapagliflozin/metformin (Xigduo® XR), dapagliflozin/saxagliptin (Qtern®), dapagliflozin/saxagliptin/metformin (Qternmet® XR), 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 (HHF) 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 HHF in adults with HF 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 HHF in adults with chronic kidney disease (CKD) at risk of progression

Jardiance is additionally indicated to:

- Reduce the risk of CV death plus HHF in adults with HF.

Empagliflozin, when used as a component of Synjardy or Synjardy XR, is additionally indicated in adults with type 2 diabetes mellitus to reduce the risk of cardiovascular death and HHF 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 m^2. Farxiga is likely to be ineffective in this setting based upon its mechanism of action.
- Farxiga is 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 is 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 m^2. 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.
- Because of the metformin component, Synjardy and Synjardy XR are not recommended for use in patients with heart failure without type 2 diabetes mellitus.

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 ≥ 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 antidiabetic 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. Member meets one of the following (a, b, or c):
   a. Failure of ≥ 3 consecutive months of Farxiga, Jardiance or Invokana, unless all are contraindicated or clinically significant adverse effects are experienced.
   b. Member has established CV disease (e.g., ASCVD or HF) or diabetic

nephropathy/CKD, and request is for a formulary dapagliflozin, empagliflozin or canagliflozin containing product, unless clinically significant adverse effects are experienced or
all are contraindicated;

c. Member has multiple risk factors for CV disease (*see Appendix D)*, and request is for a formulary 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 HF of NYHA Class II, III, or IV;
2. Request is for Farxiga or Jardiance;*
   **If request is for Synjardy, Synjardy XR, or Xigduo XR, please refer to criteria set I.A above.*
3. Prescribed by or in consultation with a cardiologist;
4. Age ≥ 18 years;
5. If request is for Farxiga, member has HFrEF as evidenced by left ventricular ejection fraction (LVEF) ≤ 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*;
   **If request is for Xigduo XR, please refer to criteria set I.A above.*
3. Age ≥ 18 years;
4. Both of the following (a and b):
   a. eGFR between 25 and 75 mL/min/1.73 m^2;
   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 standard CKD drug therapy (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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
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 or Jardiance for HFrEF and has received this medication for at least 30 days;
2. Request is for Farxiga or Jardiance*;
   **If request is for Synjardy, Synjardy XR, or Xigduo XR, please refer to criteria set II.A above*
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 Centene benefit or member has previously met initial approval criteria;
2. Request is for Farxiga;*
   **If request is for Xigduo XR, please refer to criteria set II.A above.*
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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

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

Appendix B: 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 C: 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, 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).
    - 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, 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
Brenzavvy (bexagliflozin)	20 mg PO QD	20 mg/day
Farxiga (dapagliflozin)	Diabetes: 5 mg PO QD HFrEF, CKD: 10 mg PO QD	10 mg/day
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 (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
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

Drug Name	Dosing Regimen	Maximum Dose
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
Brenzavvy (bexagliflozin)	Tablets: 20 mg
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
Qternmet XR (dapagliflozin/saxagliptin/metformin)	Tablets: 2.5/2.5/1,000 mg, 5/2.5/1,000 mg, 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 (empagliflozin/metformin)	Tablets: 5/1,000 mg, 10/1,000 mg, 12.5/1,000 mg, 25/1,000 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

1. 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.
2. Farxiga Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; April 2021. Available at: www.farxiga.com. Accessed September 20, 2021.
3. Brenzavvy Prescribing Information. Marlborough, MA: TheracosBio, LLC; January 2023. Available at: www.accessdata.fda.gov/drugsatfda_docs/label/2023/214373s000lbl.pdf. Accessed February 2, 2023.
4. Qtern Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; January 2020. Available at: www.qtern.com. Accessed September 20, 2021.
5. Xigduo XR Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; February 2022. Available at: www.xigduoxr.com. Accessed February 18, 2022.
6. Invokana Prescribing Information. Titusville, NJ: Janssen Pharmaceuticals, Inc.; August 2020. Available at: www.invokana.com. Accessed September 20, 2021.
7. Invokamet/Invokamet XR Prescribing Information. Titusville, NJ: Janssen Pharmaceuticals, Inc.; August 2020. Available at: www.invokamet.com. Accessed September 20, 2021.
8. Jardiance Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; February 2022. Available at: www.jardiance.com. Accessed March 11, 2022.
9. Glyxambi Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; June 2021. Available at: www.glyxambi.com. Accessed September 20, 2021.
10. Synjardy Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; February 2023. Available at: www.synjardy.com. Accessed February 23, 2023.
11. Synjardy XR Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; February 2023. Available at: www.synjardyxr.com. Accessed February 23, 2023.
12. Trijardy XR Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; June 2021. Available at: www.trijardy.com. Accessed September 20, 2021.
13. Steglatro Prescribing Information. Whitehouse Station, NJ: Merck & Co., Inc.; February 2021. Available at www.steglatro.com. Accessed September 20, 2021.
14. Segluromet Prescribing Information. Whitehouse Station, NJ: Merck & Co., Inc.; February 2021. Available at www.segluromet.com. Accessed September 20, 2021.
15. Steglujan Prescribing Information. Whitehouse Station, NJ: Merck & Co., Inc.; February 2021. Available at www.steglujan.com. Accessed September 20, 2021.
16. 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.
17. 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

18. 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
19. 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
20. 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.
21. 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.
22. 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.
23.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
New policy created, adapted from CP.PMN.14 SGLT2 inhibitors policy.	11.21.19	
1Q 2020 annual review: policy updated to include Invokana's new FDA indication: diabetic nephropathy: 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 and Invokana for diabetic nephropathy/HF as supported by ADA guidelines/published data (Farxiga not allowed due to formulary status); clarified that established cardiovascular disease can mean ASCVD or HF; added criteria to allow Jardiance and Invokana for patients with multiple cardiovascular risk factors as supported trials; references reviewed and updated.	12.30.19	1.7.20
Criteria added for Farxiga's new FDA indication: heart failure with reduced ejection fraction.	7.11.20	7.22.20
Q1 2021 Annual Review. For continued therapy request added heart failure . Updated Appendix C general information. Removed from initial approval criteria: Member has established cardiovascular disease (e.g., ASCVD or HF) or diabetic nephropathy, and request is for Invokana or Jardiance, unless contraindicated or clinically significant adverse effects are experienced. Member has multiple risk factors for cardiovascular disease (*see Appendix C)*, and request is for Invokana or Jardiance,	12.29.20	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
unless contraindicated or clinically significant adverse effects are experienced;		
Changes: **Removed** lower limb amputation boxed warning for canagliflozin from Appendix C per updated PI; references reviewed and updated; Criteria added for Farxiga's new FDA indication CKD; updated policy to reflect the new FDA approval of Jardiance for HFrEF, for which criteria were previously already added based on guidelines	4.20.21	
Changes: Criteria added for Farxiga's new FDA indication CKD; updated policy to reflect the new FDA approval of Jardiance for HFrEF, for which criteria were previously already added based on guidelines; added request is for Jardiance for HFrEF	9.22.2021	
1Q 2022 Annual Review - updated FDA Approved Indication(s) section; Updated HF criteria per Jardiance's revised indication for HF regardless of ejection fraction; added preferred product Farixga; updated Appendix C: General Information; updated section Dosage and Administration; references reviewed and updated	3.23.2022	
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.	6.28.22	
2Q2022 Annual review: template changes applied; added bypass of metformin for members with ASCVD, indicators of high ASCVD risk, HF, or CKD per ADA guidelines; added Brenzavvy to policy; updated FDA Approved Indication(s) section with Synjardy/Synjardy XR's updated indication in heart failure for the empagliflozin component and new limitation of use per revised PI; references reviewed and updated	3.30.23	

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.