Clinical Policy: Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors
Reference Number: CP.PPA.##
Effective Date: 09/17
Last Review Date: 08/17 Revision Log
Line of Business: Medicaid

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

Description
The following are sodium-glucose co-transporter 2 (SGLT2) inhibitors requiring prior authorization: *PDL*: empagliflozin (Jardiance®); *non-PDL*: canagliflozin (Invokana®), canagliflozin/metformin (Invokamet®, Invokamet® XR), dapagliflozin (Farxiga®), dapagliflozin/metformin (Xigduo® XR), empagliflozin/linagliptin (Glyxambi®), and empagliflozin/metformin (Synjardy®, Synjardy® XR).

FDA approved indication
SGLT2 inhibitors are indicated as adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Jardiance is also indicated to reduce the risk of cardiovascular death in adult patients with type 2 diabetes mellitus and established cardiovascular disease.

Limitation of use: SGLT2 inhibitors should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) 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. Member meets one of the following (a or b):
   a. Failure of ≥ 3 consecutive months of metformin at doses ≥ 2000 mg/day unless contraindicated or clinically significant adverse effects are experienced;
   b. Both (i and ii):
      i. HbA1c drawn within the past 3 months is > 7%;
      ii. Failure of ≥ 3 consecutive months of metformin at doses ≥ 1500 mg/day unless contraindicated or clinically significant adverse effects are experienced;
3. If request is for a non-PDL SGLT2 inhibitor, failure of ≥ 3 consecutive months of a PDL SGLT2 inhibitor at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed the FDA approved maximum recommended dose.

Approval duration: 12 months

B. Other diagnoses/indications
1. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

Authorization is automatically renewed if there is a claims history of ≥ 90 day supply of the requested agent in the last 120 days

A. Type 2 Diabetes Mellitus (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. If request is for a dose increase, new dose does not exceed the FDA approved maximum recommended dose.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to CP.PMN.53 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 – CP.PMN.53 or evidence of coverage documents

B. Type 1 diabetes mellitus

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AACE: American Association of Clinical Endocrinologists
ACE: American College of Endocrinology
ADA: American Diabetes Association
DPP-4: dipeptidyl peptidase-4
FDA: Food and Drug Administration
GLP-1: glucagon-like peptide 1
HbA1c: glycated hemoglobin
PDL: preferred drug list
SGLT2: sodium-glucose co-transporter

Appendix B: 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 2000 mg. However, the difference in adjusted mean change in HbA1c between the 1500 and 2000 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 American Diabetes Association (ADA) and American Association of Clinical Endocrinologists and American College of Endocrinology (AACE/ACE) 2017 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 ≥ 9% per the ADA (≥ 7.5% per the AACE/ACE).
  - Starting with combination injectable therapy (i.e., with GLP-1 receptor agonist or 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 injectable therapy should be initiated. Each non-insulin agent added to initial therapy can lower HbA1c by 0.9-1.1%.

V. Dosage and Administration

Drug	Dosing Regimen	Maximum Dose
PDL		
Jardiance (empagliflozin)	10 mg once daily	25 mg/day
Non-PDL		
Farxiga (dapagliflozin)	5 mg once daily	10 mg/day
Glyxambi (empagliflozin/linagliptin)	10/5 mg once daily	25/5 mg/day
Invokamet (canagliflozin/metformin)	One 50/500 mg tablet twice daily	300/2000 mg/day
Invokamet XR (canagliflozin/metformin)	Two 50/500 mg tablets once daily	300/2000 mg/day
Invokana (canagliflozin)	100 mg once daily	300 mg/day
Synjardy (empagliflozin/metformin)	Individualized dose twice daily	25/2000 mg/day
Synjardy XR (empagliflozin/metformin)	Individualized dose once daily	25/2000 mg/day
Xigduo XR (dapagliflozin/metformin)	Individualized dose once daily	10/2000 mg/day

VI. Product Availability

Drug	Availability
PDL	
Jardiance (empagliflozin)	Tablets: 10 mg, 25 mg
Non-PDL	
Farxiga (dapagliflozin)	Tablets: 5 mg, 10 mg
Glyxambi (empagliflozin/linagliptin)	Tablets: 10/5 mg, 25/5 mg

Invokamet (canagliflozin/metformin)	Tablets: 50/500 mg, 50/1000 mg, 150/500 mg, 150/1000 mg
Invokamet XR (canagliflozin/metformin)	Tablets: 50/500 mg, 50/1000 mg, 150/500 mg, 150/1000 mg
Invokana (canagliflozin)	Tablets: 100 mg, 300 mg
Synjardy (empagliflozin/metformin)	Tablets: 5/500 mg, 5/1000 mg, 12.5/500 mg, 12.5/1000 mg
Synjardy XR (empagliflozin/metformin)	Tablets: 5/1000 mg, 10/1000 mg, 12.5/1000 mg, 25/1000 mg
Xigduo XR (dapagliflozin/metformin)	Tablets: 5/500 mg, 5/1000 mg, 10/500 mg, 10/1000 mg

VII. References

1. American Diabetes Association. Standards of medical care in diabetes—2017. Diabetes Care. 2017; 40(suppl 1): S1-S135.
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10. Xigduo XR Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; March 2017. Available at: www.xigduoxr.com. Accessed April 10, 2017.
11. 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.
12. Garber AJ, Abrahamson MJ, Barzilay, JI, et al. Consensus statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the comprehensive type 2 diabetes management algorithm – 2017 executive summary. Endocr Pract. 2017; 23(2): 207-238.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	04/17	08/17

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.

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.