

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

Reference Number: CP.PST.19

Effective Date: 03.01.18

Last Review Date: 05.18

Line of Business: Medicaid

[Revision Log](#)

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 step therapy: canagliflozin (Invokana[®]), canagliflozin/metformin (Invokamet[®], Invokamet[®] XR), dapagliflozin (Farxiga[®]), dapagliflozin/metformin (Xigduo[®] XR), empagliflozin (Jardiance[®]), empagliflozin/linagliptin (Glyxambi[®]), 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.

Jardiance is also indicated to reduce the risk of cardiovascular death in adult patients with type 2 diabetes mellitus and established cardiovascular disease.

Limitation(s) 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 (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. Electronic Step Therapy for SGLT2 Inhibitors (must meet all):

1. Age \geq 18 years;
2. Member meets one of the following (a or b):
 - a. Previous use of \geq 3 consecutive months of metformin, unless contraindicated or clinically significant adverse effects are experienced;
 - b. HbA1c drawn within the past 3 months is \geq 9% and concurrent use of metformin, unless contraindicated or clinically significant adverse effects are experienced;
3. If request is for a non-preferred SGLT2 inhibitor, member meets one of the following (a or b):
 - a. For Glyxambi and Steglujan: Previous use of \geq 3 consecutive months of a preferred SGLT2 inhibitor OR a preferred dipeptidyl peptidase-4 (DPP-4)

inhibitor, unless all are contraindicated or clinically significant adverse effects are experienced;

- b. For all other non-preferred SGLT2 inhibitors: Previous use of ≥ 3 consecutive months of a preferred SGLT2 inhibitor, 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: Not applicable

II. Continued Therapy

A. Electronic Step Therapy for SGLT2 Inhibitors (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: Not applicable

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

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

ER: extended-release

FDA: Food and Drug Administration

GLP-1: glucagon-like peptide-1

HbA1c: glycated hemoglobin

IR: immediate-release

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 (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: 1000 mg PO QD; increase as needed in increments of 500 mg/week 	Regular-release: 2550 mg/day Extended-release <ul style="list-style-type: none"> • Fortamet: 2500 mg/day • Glucophage XR, Glumetza: 2000 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	<ul style="list-style-type: none"> Glucophage XR: 500 mg PO QD; increase as needed in increments of 500 mg/week 	

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: 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 2018 American Diabetes Association (ADA) and 2017 American Association of Clinical Endocrinologists and American College of Endocrinology (AAACE/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 \geq 9% per the ADA (\geq 7.5% per the AAACE/ACE).
 - Starting with combination injectable therapy (i.e., with GLP-1 receptor agonist or insulin) may be considered for patients with baseline HbA1c \geq 10% per the ADA (\geq 9% if symptoms are present per the AAACE/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 Name	Dosing Regimen	Maximum Dose
Farxiga (dapagliflozin)	5 mg PO once daily	10 mg/day
Glyxambi (empagliflozin/linagliptin)	10/5 mg PO once daily	25/5 mg/day
Invokamet (canagliflozin/metformin)	One 50/500 mg tablet PO twice daily	300/2000 mg/day
Invokamet XR (canagliflozin/metformin)	Two 50/500 mg tablets PO once daily	300/2000 mg/day
Invokana (canagliflozin)	100 mg PO once daily	300 mg/day
Jardiance (empagliflozin)	10 mg PO once daily	25 mg/day
Segluromet (ertugliflozin/metformin)	Individualized dose PO twice daily	15/2000 mg/day
Steglatro (ertugliflozin)	5 mg PO once daily	15 mg/day

Drug Name	Dosing Regimen	Maximum Dose
Steglujan (ertugliflozin/sitagliptin)	One 5/100 mg tablet PO once daily	15/100 mg/day
Synjardy (empagliflozin/metformin)	Individualized dose PO twice daily	25/2000 mg/day
Synjardy XR (empagliflozin/metformin)	Individualized dose PO once daily	25/2000 mg/day
Xigduo XR (dapagliflozin/metformin)	Individualized dose PO once daily	10/2000 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, 50/1000 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
Jardiance (empagliflozin)	Tablets: 10 mg, 25 mg
Segluromet (ertugliflozin/metformin)	Tablets: 2.5/500 mg, 2.5/1000 mg, 7.5/500 mg, 7.5/1000mg
Steglatro (ertugliflozin)	Tablets: 5 mg, 15 mg
Steglujan (ertugliflozin/sitagliptin)	Tablets: 5/100 mg, 15/100 mg
Synjardy (empagliflozin/metformin)	Tablets: 5/500 mg, 5/1000 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: 2.5/1000 mg, 5/500 mg, 5/1000 mg, 10/500 mg, 10/1000 mg

VII. References

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15. Steglujan Prescribing Information. Whitehouse Station, NJ: Merck & Co., Inc.; December 2017. Available at www.steglujan.com. Accessed January 8, 2018.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	11.07.17	02.18
Added new FDA-approved drugs: Steglatro, Segluromet, Steglujan. Added requirement for Steglujan to step-through a preferred SGLT2 or DPP-4 inhibitor.	02.06.18	05.18

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.

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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.

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