Sodium-Glucose Co-Transporter-2 (SGLT-2) Inhibitors and Combination Products

Policy # 00385
Original Effective Date: 08/21/2013
Current Effective Date: 01/08/2024

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Sodium-Glucose Co-Transporter-2 (SGLT-2) Inhibitors, SGLT-2 Inhibitor/Metformin Combination Products

Based on review of available data, the Company may consider Invokana™‡ (canagliflozin), Invokamet™‡ (canagliflozin/metformin), Invokamet XR (canagliflozin/metformin extended release), Brenzavvy™‡ (bexagliflozin), or Inpefa™‡ (sotagliflozin) to be **eligible for coverage**** when the below patient selection criterion is met:

Patient Selection Criteria

Coverage eligibility will be considered when the below patient selection criteria is met for the requested drug:

- For Invokana (canagliflozin), Invokamet (canagliflozin/metformin), Invokamet XR (canagliflozin/metformin extended release), or Brenzavvy (bexagliflozin) requests:
    - There is clinical evidence or patient history that suggests the use of Farxiga™‡ (dapagliflozin), Jardiance®‡ (empagliflozin), Steglatro™‡ (ertugliflozin), Synjardy®‡ (empagliflozin/metformin), Synjardy XR (empagliflozin/metformin extended release), Xigduo XR™‡ (dapagliflozin/metformin extended release), or Segluromet™‡ (ertugliflozin/metformin) will be ineffective or cause an adverse reaction to the patient.
- For Inpefa (sotagliflozin) requests:

- There is clinical evidence or patient history that suggests the use of Farxiga (dapagliflozin) and Jardiance (empagliflozin) will be ineffective or cause an adverse reaction to the patient.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of Invokana (canagliflozin), Invokamet (canagliflozin/metformin), Invokamet XR (canagliflozin/metformin extended release), Brenzavvy (bexagliflozin), or Inpefa (sotagliflozin) when there is an absence of clinical evidence or patient history that suggests the preferred alternatives for the requested drug will be ineffective or cause an adverse reaction to the patient to be **not medically necessary**.**

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

SGLT-2/DPP4 (Dipeptidyl Peptidase 4) Inhibitor/ +/- Metformin Combination Products

Based on review of available data, the Company may consider Qtern®‡ (dapagliflozin/saxagliptin) or Steglujan™‡ (ertugliflozin/sitagliptin) to be **eligible for coverage**** when the below patient selection criterion is met:

Patient Selection Criteria

Coverage eligibility will be considered for Qtern (dapagliflozin/saxagliptin) or Steglujan (ertugliflozin/sitagliptin) when the below patient selection criterion is met:

- There is clinical evidence or patient history that suggests the use of Glyxambi®‡ (empagliflozin/linagliptin) or Trijardy XR®‡ (empagliflozin/linagliptin/metformin extended release) will be ineffective or cause an adverse reaction to the patient.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of Qtern (dapagliflozin/saxagliptin) or Steglujan (ertugliflozin/sitagliptin) when there is an absence of clinical

evidence or patient history that suggests the use of Glyxambi (empagliflozin/linagliptin) or Trijardy XR (empagliflozin/linagliptin/metformin extended release) will be ineffective or cause an adverse reaction to the patient to be **not medically necessary**.**

Schematic

Class	Preferred	Non-Preferred
SGLT-2 Inhibitors, SGLT-2 Inhibitor/Metformin Combination Products	Farxiga Jardiance Steglatro Synjardy Synjardy XR Xigduo XR Segluromet	Invokana Invokamet Invokamet XR Brenzavvy Inpefa
SGLT-2 Inhibitor/DPP4 Inhibitor/ +/- Metformin Combination Products	Glyxambi Trijardy XR	Qtern Steglujan

Background/Overview

SGLT-2 inhibitors are indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus. They also have several cardiorenal indications, including CV risk reduction and heart failure, but these vary between drugs. Inpefa is the only SGLT-2 inhibitor that is not indicated to improve glycemic control in patients with type 2 diabetes mellitus. SGLT-2, expressed in the proximal renal tubules, is responsible for the majority of the reabsorption of filtered glucose from the tubular lumen. The inhibition of SGLT-2 reduces reabsorption of filtered glucose and lowers the renal threshold for glucose, and thereby increases urinary glucose excretion.

The active ingredients in the non-preferred products have not been studied head to head versus the preferred products and therefore no superiority claims can be made between preferred and non-preferred products.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

All of these products, except Inpefa are indicated for the treatment of type 2 diabetes mellitus. Inpefa is indicated to reduce the risk of cardiovascular death, hospitalization for heart failure, and urgent heart failure visit in adults with heart failure or type 2 diabetes mellitus, chronic kidney disease, and other cardiovascular risk factors. In addition to Inpefa, Farxiga, Jardiance, and Invokana also carry cardiorenal indications.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Based on a review of the available data and in the absence of any of the caveats mentioned, there is no advantage of using Invokana (canagliflozin), Invokamet (canagliflozin/metformin), Invokamet XR (canagliflozin/metformin extended release), or Brenzavvy™‡ (bexagliflozin), over Farxiga (dapagliflozin), Jardiance (empagliflozin), Steglatro (ertugliflozin), Synjardy (empagliflozin/metformin), Synjardy XR (empagliflozin/metformin extended release), Xigduo XR (dapagliflozin/metformin extended release), or Segluromet (ertugliflozin/metformin). Based on a review of the available data and in the absence of any of the caveats mentioned, there is no advantage of using Inpefa (sotagliflozin) over Farxiga (dapagliflozin) or Jardiance (empagliflozin). Based on a review of the available data and in the absence of any of the caveats mentioned, there is no advantage of using Qtern (dapagliflozin/saxagliptin) or Steglujan (ertugliflozin/sitagliptin) over Glyxambi (empagliflozin/linagliptin) or Trijardy XR (empagliflozin/linagliptin/metformin extended release).

References

1. Invokana [package insert]. Jannsen Pharmaceuticals, Inc. Titusville, NJ.
2. Farxiga [package insert], Bristol Myers Squibb. Princeton, NJ.
3. Xigduo XR tablets [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; October 2014.

4. Invokamet tablets [prescribing information]. Titusville, NJ: Janssen; August 2014.
5. Jardiance tablets [prescribing information]. Ridgefield, CT and Indianapolis, IN: Boehringer Ingelheim Pharmaceuticals, Inc and Eli Lilly and Company; August 2014.
6. SGLT-2 Step Therapy Policy. Express Scripts. Updated 06/2105.
7. Synjardy/XR [package insert]. Boehringer Ingelheim, Eli Lilly and Company. Ridgefield, Connecticut and Indianapolis, Indiana. Updated 7/2016.
8. Steglatro [package insert]. Merck. Whitehouse Station, New Jersey. Updated 12/2017.
9. Segluromet [package insert]. Merck. Whitehouse Station, New Jersey. Updated 12/2017.
10. Steglujan [package insert]. Merck. Whitehouse Station, New Jersey. Updated 12/2017.
11. Qtern [package insert]. Astra Zeneca. Wilmington, Delaware. Updated February 2017.
12. Trijardy XR [package insert]. Boehringer Ingelheim. Ridgefield, Connecticut. Updated January 2020.
13. Inpefa [package insert]. Lexicon Pharmaceuticals, Inc. The Woodlands, Texas. Updated May 2023.
14. Inpefa Drug Evaluation. Express Scripts. June 2023.
15. Brenzavvy [package insert]. TheracosBio, LLC. Marlborough, Massachusetts. Updated September 2023.

Policy History

Original Effective Date: 08/21/2013
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08/07/2013	Medical Policy Committee review
08/21/2013	Medical Policy Implementation Committee approval. New Pharmacy step-therapy policy.
08/07/2014	Medical Policy Committee review
08/20/2014	Medical Policy Implementation Committee approval. Added new drugs (Farxiga) and empagliflozin (Jardiance) to the description of the included products that may be eligible for coverage.
08/06/2015	Medical Policy Committee review
08/19/2015	Medical Policy Implementation Committee approval. Added new drugs (canagliflozin/metformin (Invokamet), and dapagliflozin/metformin extended release (Xigduo XR) to the description of the included products that may be eligible for coverage.

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08/04/2016	Medical Policy Committee review
08/17/2016	Medical Policy Implementation Committee approval. Added a new brand, Synjardy, to the policy.
10/06/2016	Medical Policy Committee review
10/19/2016	Medical Policy Implementation Committee approval. Chose preferred products in this class (Invokana, Invokamet, Invokamet XR, Jardiance, Synjardy).
08/03/2017	Medical Policy Committee review
08/23/2017	Medical Policy Implementation Committee approval. Removed the PA and PA/step sections to revert this back to a step only policy.
07/05/2018	Medical Policy Committee review
07/11/2018	Medical Policy Implementation Committee approval. Added Steglujan, Steglatro, Segluromet, and Qtern to the policy.
09/06/2018	Medical Policy Committee review
09/19/2018	Medical Policy Implementation Committee approval. Removed generic before brand
09/05/2019	Medical Policy Committee review
09/11/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/06/2020	Medical Policy Committee review
08/12/2020	Medical Policy Implementation Committee approval. Added Trijardy as a preferred product to the combination portion of the policy.
08/05/2021	Medical Policy Committee review
08/11/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/04/2022	Medical Policy Committee review
08/10/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/03/2023	Medical Policy Committee review
08/09/2023	Medical Policy Implementation Committee approval. Added Inpefa to policy as a non-preferred agent.
12/07/2023	Medical Policy Committee review
12/13/2023	Medical Policy Implementation Committee approval. Added Brenzavvy to policy as a non-preferred agent.

Next Scheduled Review Date: 12/2024

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.