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Sodium Glucose Co-Transporter-2 (SGLT-2) Inhibitors and SGLT-2 / Metformin Combinations

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INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for formulary exceptions for the following Sodium Glucose Co-Transporter-2 (SGLT-2) Inhibitors and SGLT-2 / Metformin Combination products:

- **Brenzavvy™** (bexagliflozin tablets)
- **Bexagliflozin tablets**
- **Dapagliflozin tablets**
- **Dapagliflozin and metformin extended-release tablets**
- **Invokana®** (canagliflozin tablets)
- **Invokamet®** (canagliflozin and metformin hydrochloride tablets)
- **Invokamet® XR** (canagliflozin and metformin hydrochloride extended-release tablets)
- **Jardiance®** (empagliflozin tablets)
- **Segluromet®** (ertugliflozin and metformin tablets)
- **Steglatro®** (ertugliflozin tablets)
- **Synjardy®** (empagliflozin/metformin hydrochloride tablets)
- **Synjardy® XR** (empagliflozin/metformin extended-release tablets)

Receipt of sample product does not satisfy any criteria requirements for coverage.

Click here for Individual and Family Plan criteria.

Medical Necessity Criteria

Coverage criteria are listed for products **in below table:**

Employer Plans:

Product	Criteria
Brenzavvy (bexagliflozin)	**Brenzavvy (bexagliflozin) is considered medically necessary when the individual meets the following:** 1. **Type 2 diabetes.** Individual meets **ALL** of the following criteria are met: A. **ONE** of the following: i. Unable to achieve goal HbA1C despite metformin or metformin-containing regimen (meglitides, sulfonylureas, or thiazolidinediones) at greater than or equal to 1,500 mg per day ii. Intolerance to metformin 1,500 mg per day despite appropriate dose titration duration (for example, period of 8-12 weeks) iii. Contraindication to metformin (for example, acute/chronic metabolic acidosis, severe renal dysfunction) iv. Not a candidate for metformin (for example, hepatic impairment, moderate renal dysfunction, unstable heart failure, individual is using an agent for a non-diabetic FDA-approved indication) v. Initial metformin combination therapy is clinically appropriate for elevated HbA1C (for example; HbA1C greater than 1.5% above goal) vi. Initial metformin combination therapy is clinically appropriate in an individual with co-morbid conditions (such as ASCVD, heart failure, or CKD) B. Individual will continue maximally tolerated metformin therapy, if not contraindicated or intolerant C. **ONE** of the following: i. Contraindication or intolerance to **BOTH** of the following: a. Farxiga (dapagliflozin) [step therapy may apply] b. Jardiance (empagliflozin) [step therapy may apply] ii. Estimated glomerular filtration rate is less than 45 mL/minute **AND** contraindication or intolerance to Jardiance (empagliflozin) [step therapy may apply]
Bexagliflozin	**Bexagliflozin is considered medically necessary when the individual meets the following:** 1. **Type 2 diabetes.** Individual meets **ALL** of the following criteria are met: A. **ONE** of the following: i. Unable to achieve goal HbA1C despite metformin or metformin-containing regimen (meglitides, sulfonylureas, or thiazolidinediones) at greater than or equal to 1,500 mg per day

Product	Criteria
	ii. Intolerance to metformin 1,500 mg per day despite appropriate dose titration duration (for example, period of 8-12 weeks) iii. Contraindication to metformin (for example, acute/chronic metabolic acidosis, severe renal dysfunction) iv. Not a candidate for metformin (for example, hepatic impairment, moderate renal dysfunction, unstable heart failure, individual is using an agent for a non-diabetic FDA-approved indication) v. Initial metformin combination therapy is clinically appropriate for elevated HbA1C (for example; HbA1C greater than 1.5% above goal) vi. Initial metformin combination therapy is clinically appropriate in an individual with co-morbid conditions (such as ASCVD, heart failure, or CKD) B. Individual will continue maximally tolerated metformin therapy, if not contraindicated or intolerant C. **ONE** of the following: i. Contraindication or intolerance to **BOTH** of the following: a. Farxiga (dapagliflozin) [step therapy may apply] b. Jardiance (empagliflozin) [step therapy may apply] ii. Estimated glomerular filtration rate is less than 45 mL/minute **AND** contraindication or intolerance to Jardiance (empagliflozin) [step therapy may apply]
dapagliflozin tablets	**Dapagliflozin** is considered medically necessary when there is documented inability to obtain Farxiga® (the brand name product) due to market availability
dapagliflozin and metformin extended-release tablets	**Dapagliflozin and metformin ER** is considered medically necessary when there is documented inability to obtain Xigduo® XR (the brand name product) due to market availability
Invokana (canagliflozin)	**Invokana (canagliflozin) is considered medically necessary when the individual meets the following:** 1. **Type 2 Diabetes.** Individual meets **ALL** of the following criteria: A. **ONE** of the following: i. Unable to achieve goal HbA1C despite metformin or metformin-containing regimen (meglitides, sulfonylureas, or thiazolidinediones) at greater than or equal to 1,500 mg per day ii. Intolerance to metformin 1,500 mg per day despite appropriate dose titration duration (for example, period of 8-12 weeks) iii. Contraindication to metformin (for example, acute/chronic metabolic acidosis, severe renal dysfunction) iv. Not a candidate for metformin (for example, hepatic impairment, moderate renal dysfunction, unstable heart failure, individual is using an agent for a non-diabetic FDA-approved indication) v. Initial metformin combination therapy is clinically appropriate for elevated HbA1C (for example; HbA1C greater than 1.5% above goal)

Product	Criteria
	vi. Initial metformin combination therapy is clinically appropriate in an individual with co-morbid conditions (such as ASCVD, heart failure, or CKD) B. Individual will continue maximally tolerated metformin therapy, if not contraindicated or intolerant C. **ONE** of the following: i. Contraindication or intolerance to **BOTH** of the following: a. Farxiga (dapagliflozin) [step therapy may apply] b. Jardiance (empagliflozin) [step therapy may apply] ii. Invokana is being used for glycemic control and **BOTH** of the following: a. Estimated glomerular filtration rate is less than 45 mL/minute b. Contraindication or intolerance to Jardiance (empagliflozin) [step therapy may apply] iii. Diabetic kidney disease AND documented contraindication or intolerance to Farxiga [step therapy may apply]
Invokamet (canagliflozin-metformin)	**Invokamet (canagliflozin-metformin) is considered medically necessary when the individual meets the following:** 1. **Type 2 Diabetes.** Individual meets **ALL** of the following criteria: A. **ONE** of the following: i. Unable to achieve goal HbA1C despite metformin or metformin-containing regimen (meglitides, sulfonylureas, or thiazolidinediones) at greater than or equal to 1,500 mg per day ii. Intolerance to metformin 1,500 mg per day despite appropriate dose titration duration (for example, period of 8-12 weeks) iii. Contraindication to metformin (for example, acute/chronic metabolic acidosis, severe renal dysfunction) iv. Not a candidate for metformin (for example, hepatic impairment, moderate renal dysfunction, unstable heart failure, individual is using an agent for a non-diabetic FDA-approved indication) v. Initial metformin combination therapy is clinically appropriate for elevated HbA1C (for example; HbA1C greater than 1.5% above goal) vi. Initial metformin combination therapy is clinically appropriate in an individual with co-morbid conditions (such as ASCVD, heart failure, or CKD) B. Individual will continue maximally tolerated metformin therapy, if not contraindicated or intolerant C. Contraindication or intolerance to **BOTH** of the following: i. Synjardy **OR** Synjardy XR (empagliflozin/ metformin) [step therapy may apply] ii. Xigduo XR (dapagliflozin/ metformin) [step therapy may apply]
Invokamet XR	**Invokamet XR (canagliflozin-metformin) is considered medically necessary when the individual meets the following:**

Product	Criteria
(canagliflozin - metformin)	1. **Type 2 Diabetes.** Individual meets **ALL** of the following criteria: A. **ONE** of the following: i. Unable to achieve goal HbA1C despite metformin or metformin-containing regimen (meglitides, sulfonylureas, or thiazolidinediones) at greater than or equal to 1,500 mg per day ii. Intolerance to metformin 1,500 mg per day despite appropriate dose titration duration (for example, period of 8-12 weeks) iii. Contraindication to metformin (for example, acute/chronic metabolic acidosis, severe renal dysfunction) iv. Not a candidate for metformin (for example, hepatic impairment, moderate renal dysfunction, unstable heart failure, individual is using an agent for a non-diabetic FDA-approved indication) v. Initial metformin combination therapy is clinically appropriate for elevated HbA1C (for example; HbA1C greater than 1.5% above goal) vi. Initial metformin combination therapy is clinically appropriate in an individual with co-morbid conditions (such as ASCVD, heart failure, or CKD) B. Individual will continue maximally tolerated metformin therapy, if not contraindicated or intolerant C. Contraindication or intolerance to **BOTH** of the following: i. Synjardy **OR** Synjardy XR (empagliflozin/ metformin) [step therapy may apply] ii. Xigduo XR (dapagliflozin/ metformin) [step therapy may apply]
Segluromet (ertugliflozin - metformin)	**Segluromet (ertugliflozin - metformin) is considered medically necessary when the individual meets the following:** 1. **Type 2 Diabetes.** Individual meets **ALL** of the following criteria: A. **ONE** of the following: i. Unable to achieve goal HbA1C despite metformin or metformin-containing regimen (meglitides, sulfonylureas, or thiazolidinediones) at greater than or equal to 1,500 mg per day ii. Intolerance to metformin 1,500 mg per day despite appropriate dose titration duration (for example, period of 8-12 weeks) iii. Contraindication to metformin (for example, acute/chronic metabolic acidosis, severe renal dysfunction) iv. Not a candidate for metformin (for example, hepatic impairment, moderate renal dysfunction, unstable heart failure, individual is using an agent for a non-diabetic FDA-approved indication) v. Initial metformin combination therapy is clinically appropriate for elevated HbA1C (for example; HbA1C greater than 1.5% above goal) vi. Initial metformin combination therapy is clinically appropriate in an individual with co-morbid conditions (such as ASCVD, heart failure, or CKD)

Product	Criteria
	B. Individual will continue maximally tolerated metformin therapy, if not contraindicated or intolerant C. Contraindication or intolerance to **BOTH** of the following: i. Synjardy **OR** Synjardy XR (empagliflozin/ metformin) [step therapy may apply] ii. Xigduo XR (dapagliflozin/ metformin) [step therapy may apply]
Steglatro (ertugliflozin)	**Steglatro (ertugliflozin) is considered medically necessary when the individual meets the following:** 1. **Type 2 Diabetes.** Individual meets **ALL** of the following criteria: A. **ONE** of the following: i. Unable to achieve goal HbA1C despite metformin or metformin-containing regimen (meglitides, sulfonylureas, or thiazolidinediones) at greater than or equal to 1,500 mg per day ii. Intolerance to metformin 1,500 mg per day despite appropriate dose titration duration (for example, period of 8-12 weeks) iii. Contraindication to metformin (for example, acute/chronic metabolic acidosis, severe renal dysfunction) iv. Not a candidate for metformin (for example, hepatic impairment, moderate renal dysfunction, unstable heart failure, individual is using an agent for a non-diabetic FDA-approved indication) v. Initial metformin combination therapy is clinically appropriate for elevated HbA1C (for example; HbA1C greater than 1.5% above goal) vi. Initial metformin combination therapy is clinically appropriate in an individual with co-morbid conditions (such as ASCVD, heart failure, or CKD) B. Individual will continue maximally tolerated metformin therapy, if not contraindicated or intolerant C. Contraindication or intolerance to **BOTH** of the following: i. Farxiga (dapagliflozin) [step therapy may apply] ii. Jardiance (empagliflozin) [step therapy may apply]

For Individual and Family Plans

Product	Criteria
Brenzavvy (bexagliflozin)	**Brenzavvy (bexagliflozin) is considered medically necessary when the individual meets BOTH of the following:** A. Documented diagnosis of Type 2 diabetes B. **ONE** of the following: i. Contraindication or intolerance to Farxiga (dapagliflozin) ii. Estimated glomerular filtration rate is less than 45 mL/minute
dapagliflozin tablets	**Dapagliflozin** is considered medically necessary when there is documented inability to obtain Farxiga® (the brand name product) due to market availability

Product	Criteria
dapagliflozin and metformin extended-release tablets	**Dapagliflozin and metformin ER** is considered medically necessary when there is documented inability to obtain Xigduo® XR (the brand name product) due to market availability
Invokana (canagliflozin)	**Invokana (canagliflozin) is considered medically necessary when the individual meets ONE of the following criteria:** A. Contraindication or intolerance to Farxiga (dapagliflozin) B. Invokana is being used for glycemic control in an individual with an estimated glomerular filtration (eGFR) is less than 45 mL/minute
Invokamet (canagliflozin-metformin)	**Invokamet** (canagliflozin-metformin) is considered medically necessary when there is documentation of contraindication or intolerance to Xigduo XR (dapagliflozin/ metformin)
Invokamet XR (canagliflozin - metformin)	**Invokamet XR** (canagliflozin-metformin) is considered medically necessary when there is documentation of contraindication or intolerance to Xigduo XR (dapagliflozin/ metformin)
Jardiance (empagliflozin)	**Jardiance (empagliflozin) is considered medically necessary when ONE of the following is met:** 1. **Type 2 Diabetes.** Individual meets **ONE** of the following criteria: A. Age 10 years to less than 18 years B. Jardiance is being used for glycemic control in an individual with an estimated glomerular filtration (eGFR) is less than 45 mL/minute C. Contraindication or intolerance to Farxiga (dapagliflozin) 2. **Heart Failure. To reduce the risk of CV death, HHF, and urgent heart failure visits in adults with heart failure (included both reduced and preserved ejection fraction).** Individual meets the following criteria: A. Contraindication or intolerance to Farxiga (dapagliflozin) 3. **Chronic Kidney Disease**. **To reduce the risk of sustained estimated glomerular filtration rate (eGFR) decline, end-stage kidney disease, CV death, and hospitalization for heart failure in adults with chronic kidney disease at risk of progression.** Individual meets the following criteria: A. Contraindication or intolerance to Farxiga (dapagliflozin)
Segluromet (ertugliflozin - metformin)	**Segluromet** (ertugliflozin-metformin) is considered medically necessary when there is documentation of contraindication or intolerance to Xigduo XR (dapagliflozin/ metformin)
Steglatro (ertugliflozin)	**Steglatro** (ertugliflozin) is considered medically necessary when there is documentation of contraindication or intolerance to Farxiga (dapagliflozin)
Synjardy (empagliflozin - metformin)	**Synjardy (empagliflozin-metformin) is considered medically necessary when there is documentation of ONE of the following:** A. Contraindication or intolerance to Xigduo XR (dapagliflozin/ metformin) B. **BOTH** of the following: i. Age 10 years to 17 years ii. Diagnosis of Type 2 Diabetes
Synjardy XR (empagliflozin - metformin)	**Synjardy XR** (empagliflozin -metformin) is considered medically necessary when there is documentation of contraindication or intolerance to Xigduo XR (dapagliflozin/ metformin)

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of Sodium Glucose Co-Transporter-2 (SGLT-2) Inhibitors and SGLT-2 / Metformin Combination products is considered medically necessary when the above medical necessity criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration: up to 12 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational or unproven.

Background

OVERVIEW
Brenzavvy, Farxiga, Invokana, Jardiance, and Steglatro are sodium glucose co-transporter-2 (SGLT-2) inhibitors indicated as an adjunct to diet and exercise to improve glycemic control in adults with **type 2 diabetes**.[1-4] Jardiance is also indicated in pediatric patients ≥ 10 years of age with type 2 diabetes as an adjunct to diet and exercise to improve glycemic control.[3]

The SGLT-2 inhibitors also possess the following additional indications in patients with diabetes:

- Jardiance: To reduce the risk of cardiovascular (CV) death in adults with type 2 diabetes mellitus and established CV disease.
- Invokana: 1) To reduce the risk of major adverse CV events in adults with type 2 diabetes mellitus and established CV disease; AND 2) To reduce the risk of end-stage kidney disease, doubling of serum creatinine, CV death, and hospitalization for heart failure in adults with type 2 diabetes mellitus and diabetic nephropathy with albuminuria.
- Farxiga: To reduce the risk of hospitalization for heart failure (HHF) in adults with type 2 diabetes mellitus and established CV disease or multiple CV risk factors.

In addition to indications in diabetes, Farxiga and Jardiance are indicated for the following indications in patients with and without diabetes:[1,3]

- **Heart failure,** to reduce the risk of CV death, HHF, and urgent heart failure visits in adults with heart failure (included both reduced and preserved ejection fraction).
- **Chronic kidney disease,** to reduce the risk of sustained estimated glomerular filtration rate (eGFR) decline, end-stage kidney disease, CV death, and hospitalization for heart failure in adults with chronic kidney disease at risk of progression.

Guidelines
Diabetes
The American Diabetes Association Standards of Care (2023) note that first-line therapy for type 2 diabetes depends on comorbidities, patient-centered treatment factors, and management needs; it generally includes metformin and comprehensive lifestyle modification.[5] Other medications (glucagon-like peptide-1 receptor agonists, SGLT-2 inhibitors), with or without metformin based on glycemic needs, are appropriate initial therapy for individuals with type 2 diabetes with or at high risk of atherosclerotic CV disease, heart failure, and/or chronic kidney disease. It is noted that an agent with proven benefit should be utilized; with “proven benefit” referring to a label indication.

Heart Failure
The American College of Cardiology (ACC) Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment was updated in 2022.[6] In patients with symptomatic chronic heart failure with reduced ejection fraction, SGLT-2 inhibitors (Farxiga or Jardiance) are recommended to reduce hospitalization for heart failure and CV mortality, irrespective of the presence of type 2 diabetes (class 1 recommendation, level of evidence A). In patients with heart failure with preserved ejection fraction, SGLT-2 inhibitors (Jardiance) can be beneficial in decreasing heart failure hospitalizations and CV mortality, irrespective of the presence of type 2 diabetes (class 2a recommendation, level of evidence B-R).

The ACC Expert Consensus Decision Pathway on Management of Heart Failure with Preserved Ejection Fraction (2023) recommends that all individuals with heart failure with preserved ejection fraction be started on an SGLT-2 inhibitor unless contraindicated.[10] SGLT-2 inhibitors are noted to have demonstrated significant CV benefits in individuals without type 2 diabetes, particularly in individuals with HF. In such patients, SGLT-2 inhibitors have significantly reduced the risk of hospitalization for HF and CV death across all ejection fraction subgroups. Clinical trials with Jardiance and Farmiga are mentioned. For both agents, a significant decrease in HHF was observed.

Kidney Disease
In patients with diabetes and CKD, the Kidney Diseases – Improving Global Outcomes (KDIGO) guidelines for diabetes management in CKD (2022) recommend first-line pharmacotherapy with metformin and an SGLT-2 inhibitor with documented kidney or CV benefit (Invokana, Farxiga, and Jardiance).[7]

References

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