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**5.30.019**

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<b>Subsection:</b>	Endocrine and Metabolic Agents	<b>Original Policy Date:</b>	September 18, 2015
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**Last Review Date:** December 12, 2025

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## SGLT2 Inhibitors

### Description

Brenzavvy (bexagliflozin), dapagliflozin, dapagliflozin & metformin, Invokana (canagliflozin), Invokamet, Invokamet XR (canagliflozin & metformin), Segluromet (ertugliflozin & metformin), Steglatro (ertugliflozin), Steglujan (ertugliflozin & sitagliptin)

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### Background

Brenzavvy (bexagliflozin), dapagliflozin, dapagliflozin and metformin, Invokana (canagliflozin), Invokamet, Invokamet XR (canagliflozin and metformin), Steglatro (ertugliflozin), Steglujan (ertugliflozin and sitagliptin), and Segluromet (ertugliflozin and metformin) are oral sodium-glucose co-transporter 2 (SGLT2) inhibitors indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. They should not be used to treat type 1 diabetes; in those who have increased ketones in their blood or urine (diabetic ketoacidosis); or in those with severe renal impairment, end stage renal disease, or in patients on dialysis. They work by blocking the reabsorption of glucose by the kidney, increasing glucose excretion, and lowering blood glucose levels in patients with diabetes who have elevated blood glucose levels (1-7).

### Regulatory Status

FDA-approved indications for SGLT2 Inhibitors: Brenzavvy, dapagliflozin, dapagliflozin and metformin Invokana, Invokamet, Invokamet XR, Steglatro, Steglujan, and Segluromet: They are sodium-glucose co-transporter 2 (SGLT2) inhibitors indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (1-7,9-10).

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Invokana, Invokamet, and Invokamet XR are also indicated to reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes mellitus and established cardiovascular disease (1-3).

Invokana, Invokamet, and Invokamet XR are also indicated to reduce the risk of end-stage kidney disease, doubling of serum creatinine, cardiovascular death, and hospitalization for heart failure in adults with type 2 diabetes mellitus and diabetic nephropathy with albuminuria (1-3).

Limitation of Use:

SGLT2 Inhibitors should not be used for treatment of type 1 diabetes mellitus or diabetic ketoacidosis (1-7).

Metformin has a boxed warning for lactic acidosis which can occur due to metformin accumulation. The risk increases with conditions such as renal impairment, sepsis, dehydration, excess alcohol intake, hepatic impairment, and acute congestive heart failure (2).

SGLT2 inhibitors are contraindicated in patients with severe renal impairment, end-stage renal disease (ESRD), or dialysis. SGLT2 inhibitors increase serum creatinine and decrease eGFR. Renal function should be evaluated prior to initiating SGLT2 inhibitor therapy and periodically thereafter (1-7).

Renal function and eGFR have an effect on the SGLT2 inhibitor dosing. Brenzavvy is not recommended in patients with an eGFR less than 30 mL/min/1.73m<sup>2</sup>. The use of Steglatro, Steglujan, and Segluromet is not recommended in patients with an eGFR is below 45 mL/min/1.73m<sup>2</sup>. Invokana should not be initiated in patients with an eGFR less than 30 mL/min/1.73 m<sup>2</sup>, however patients with albuminuria greater than 300 mg/day may continue 100 mg once daily to reduce the risk of ESKD, doubling of serum creatinine, CV death, and hospitalization for heart failure. Invokamet and Invokamet XR should not be continued in patients with eGFR less than 30 mL/min/1.73 m<sup>2</sup>. A dose reduction is limited to no more than 50mg twice daily for Invokamet and Invokamet XR if the eGFR is between 30 to less than 60 mL/min/1.73m<sup>2</sup> (1-7).

Safety and effectiveness of SGLT2 inhibitors in patients under 18 years of age have not been established (1-7).

FDA safety review has resulted in adding warnings to the labels of a specific class of type 2 diabetes medicines called sodium-glucose cotransporter-2 (SGLT2) inhibitors about the risks of too much acid in the blood and of serious urinary tract infections. Both conditions can result in

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hospitalization. Health care professionals should assess for ketoacidosis and urinary tract infections in patients taking SGLT2 inhibitors who present with suggestive symptoms. Ketoacidosis associated with the use of SGLT2 inhibitors can occur even if the blood sugar level is not very high. FDA also identified 19 cases of life-threatening blood infections (urosepsis) and kidney infections (pyelonephritis) that started as urinary tract infections with the SGLT2 inhibitors (8).

Off-label and alternative uses of Brenzavvy, Invokana, Invokamet, Invokamet XR, Steglatro, Steglujan, and Segluromet such as enhancement of weight loss and diabetes prevention are not approved by the FDA.

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#### Related policies

GLP-1 Agonists, Insulin GLP-1 Combinations, Metformin, Mounjaro, SGLT2 Step Policy, Trijardy XR

#### Policy

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

SGLT2 inhibitors may be considered **medically necessary** if the conditions indicated below are met.

SGLT2 inhibitors may be considered **investigational** for all other indications.

### Prior-Approval Requirements

**Age** 18 years of age or older

#### Diagnosis

Patient must have the following with provided documentation (e.g., medical records, laboratory reports):

Type 2 diabetes mellitus

**AND ALL** of the following:

1. Inadequate treatment response, intolerance, or contraindication to metformin **AND ONE** of the drugs from the following drug classes:
  - a. Alpha-glucosidase inhibitor

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- b. Dipeptidyl peptidase 4 inhibitors (DPP-4)
  - c. Thiazolidinedione
  - d. Glucagon-like peptide-1 receptor agonists (GLP-1)
- 2. Patient must have a HgbA1C greater than 7.0%
- 3. Patient has an eGFR greater than or equal to **ONE** of the following:
  - a. Patients on **Brenzavvy**:  $\geq 30$  mL/min/1.73m<sup>2</sup>
  - b. Patients on **Steglatro**, **Steglujan**, and **Segluromet**:  $\geq 45$  mL/min/1.73m<sup>2</sup>
  - c. Patients on **Invokana 100mg**:  $\geq 30$  mL/min/1.73m<sup>2</sup> **OR** patient has albuminuria greater than 300 mg/day
  - d. Patients on **Invokana > 100mg**:  $\geq 60$  mL/min/1.73m<sup>2</sup>
  - e. Patients on **Invokamet or Invokamet XR 50mg**:  $\geq 30$  mL/min/1.73m<sup>2</sup>
  - f. Patients on **Invokamet or Invokamet XR > 50mg**:  $\geq 60$  mL/min/1.73m<sup>2</sup>
- 4. **NO** dual therapy with other SGLT2 inhibitors (see Appendix 1)
- 5. Patient **MUST** have tried the preferred product(s) (see Appendix 2) unless the patient has a valid medical exception (e.g., inadequate treatment response, intolerance, contraindication)

**AND NOT** to be used for the following:

- 1. Diabetic ketoacidosis (DKA)
- 2. Prevention of diabetes
- 3. Exclusively used for weight loss

All approved requests are subject to review by a clinical specialist for final validation and coverage determination once all required documentation has been received. Current utilization, including samples, does not guarantee approval of coverage.

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## Prior – Approval *Renewal* Requirements

**Age** 18 years of age or older

### Diagnosis

Patient must have the following with provided documentation (e.g., medical records, laboratory reports):

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Type 2 diabetes mellitus

**AND ALL** of the following:

1. Condition has improved or stabilized on the therapy
2. **NO** dual therapy with other SGLT2 inhibitors (see Appendix 1)
3. Patient has an eGFR greater than or equal to **ONE** of the following:
  - a. Patients on **Brenzavvy**:  $\geq 30$  mL/min/1.73m<sup>2</sup>
  - b. Patients on **Steglatro**, **Steglujan**, or **Segluromet**:  $\geq 45$  mL/min/1.73m<sup>2</sup>
  - c. Patients on **Invokana 100mg**:  $\geq 30$  mL/min/1.73m<sup>2</sup> **OR** patient has albuminuria greater than 300 mg/day
  - d. Patients on **Invokana > 100mg**:  $\geq 60$  mL/min/1.73m<sup>2</sup>
  - e. Patients on **Invokamet** or **Invokamet XR 50mg**:  $\geq 30$  mL/min/1.73m<sup>2</sup>
  - f. Patients on **Invokamet** or **Invokamet XR > 50mg**:  $\geq 60$  mL/min/1.73m<sup>2</sup>
  - g. Patients on **dapagliflozin** or **dapagliflozin and metformin**:  $\geq 30$  mL/min/1.73m<sup>2</sup>
4. Patient **MUST** have tried the preferred product(s) (see Appendix 2) unless the patient has a valid medical exception (e.g., inadequate treatment response, intolerance, contraindication)

**AND NOT** to be used for the following:

1. Diabetic ketoacidosis (DKA)
2. Prevention of diabetes
3. Exclusively used for weight loss

All approved requests are subject to review by a clinical specialist for final validation and coverage determination once all required documentation has been received. Current utilization, including samples, does not guarantee approval of coverage.

### Policy Guidelines

#### Pre - PA Allowance

None

#### Prior - Approval Limits

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**Duration** 12 months

### **Prior – Approval *Renewal* Limits**

Same as above

### **Rationale**

#### **Summary**

SGLT2 inhibitors are indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Renal function should be monitored during SGLT2s therapy. SGLT2 Inhibitors should not be used for treatment of type 1 diabetes mellitus or diabetic ketoacidosis (1-7).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of SGLT2 inhibitors while maintaining optimal therapeutic outcomes.

#### **References**

1. Invokana [package insert] Titusville, NJ: Janssen Pharmaceuticals, Inc.; July 2023.
2. Invokamet [package insert] Titusville, NJ: Janssen Pharmaceuticals, Inc.; January 2024.
3. Invokamet XR [package insert] Titusville, NJ: Janssen Pharmaceuticals, Inc.; January 2024.
4. Steglatro [package insert] Whitehouse Station, NJ: Merck & Co., Inc.; June 2024.
5. Steglujan [package insert] Whitehouse Station, NJ: Merck & Co., Inc.; June 2024.
6. Segluromet [package insert] Whitehouse Station, NJ: Merck & Co., Inc.; June 2024.
7. Brenzavvy [package insert]. Marlborough, MA: TheracosBio, LLC; September 2023.
8. FDA News Release. FDA Drug Safety Communication: FDA revises labels of SGLT2 inhibitors for diabetes to include warnings about too much acid in the blood and serious urinary tract infections. December 4, 2015.
9. Dapagliflozin [package insert]. Mason, OH: Prasco Laboratories. December 2024.
10. Dapagliflozin and metformin [package insert]. Mason, OH: Prasco Laboratories. December 2024.

### **Policy History**

Date	Action
September 2015	New addition to PA
December 2015	Annual editorial review and reference update

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March 2016	Annual editorial review Addition of inadequate treatment response, intolerance, or contraindication to one of the following: alpha-glucosidase inhibitor, sulfonylurea, or thiazolidinedione; addition of eGFR 's for the different medications Changed the wording of weight loss to exclusively used for weight loss Policy number change from 5.07.19
September 2016	Annual editorial review and reference update
October 2016	Addition of Invokamet XR
December 2016	Annual review
January 2017	Addition of Synjardy XR
March 2017	Annual editorial review and reference update Addition of Qtern and the age requirement in the renewal section
June 2017	Annual editorial review Addition of dipeptidyl peptidase 4 inhibitors (DPP-4) and glucagon-like peptide-1 receptor agonists (GLP-1) to the tried and failed requirement Removal of sulfonylurea from the tried and failed requirement
January 2018	Addition of Steglatro, Steglujan, and Segluromet
March 2018	Annual editorial review Change in initiation criteria from: inadequate treatment response, intolerance, or contraindication to metformin monotherapy, to inadequate treatment response, intolerance, or contraindication to metformin.
June 2018	Annual review and reference update Addition of eGFR requirement to the renewal section and the removal of no severe renal impairment, ESRD, or on dialysis
November 2018	Annual editorial review and reference update. Updated Invokana, Invokamet, and Invokamet XR indications. Removed Step Edit SGLT2s from policy: Farxiga, Qtern, Jardiance, Glyxambi, Synjardy, Synjardy XR, Xigduo XR
November 2019	Reduced Invokana 100 mg required eGFR from $\geq 45$ to $\geq 30$
December 2019	Annual review and reference update. Addition of requirement to trial preferred products
June 2020	Annual review and reference update
September 2020	Annual review. Revised eGFR limits for Invokana, Invokamet, and Invokamet XR and added the option of albuminuria $> 300$ mg/day for Invokana 100 mg. Also removed boxed warning statement for lower limb amputation for Invokana, Invokamet, and Invokamet XR
November 2020	Addition of Trijardy XR

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January 2021	Removal of Trijardy XR to its own policy
March 2021	Annual review
October 2021	Revised eGFR limit for Steglatro, Steglujan, and Segluromet to $\geq 45$ mL/min/1.73m <sup>2</sup>
December 2021	Annual review
September 2022	Annual review and reference update. Addition of Appendix 1
September 2023	Annual review. Added Inpefa to Appendix 1
December 2023	Annual editorial review. Addition of Brenzavvy to policy
September 2024	Annual review and reference update
March 2025	Annual review
December 2025	Annual review. Added documentation requirement and dapagliflozin and dapagliflozin and metformin. Revised Appendix 2

### Keywords

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**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 12, 2025 and is effective on January 1, 2026.**



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### Appendix 1 - List of SGLT2 Inhibitors

Generic Name	Brand Name
bexagliflozin	Brenzavvy
canagliflozin	Invokana
canagliflozin/metformin	Invokamet/Invokamet XR
dapagliflozin	Farxiga
dapagliflozin/metformin	Xigduo XR
dapagliflozin/saxagliptin	Qtern
empagliflozin	Jardiance
empagliflozin/linagliptin	Glyxambi
empagliflozin/linagliptin/metformin	Trijardy XR
empagliflozin/metformin	Synjardy/Synjardy XR
ertugliflozin	Steglatro
ertugliflozin/metformin	Segluromet
ertugliflozin/sitagliptin	Steglujan
sotagliflozin	Inpefa

### Appendix 2 - List of Preferred Products

List of preferred products:

[https://info.caremark.com/content/dam/enterprise/caremark/microsites/dig/pdfs/pa-fep/fep-misc/FEP\\_ProductMedChx.pdf](https://info.caremark.com/content/dam/enterprise/caremark/microsites/dig/pdfs/pa-fep/fep-misc/FEP_ProductMedChx.pdf)

Refer to formulary documents for confirmation of coverage:

<https://www.fepblue.org/pharmacy/prescriptions#drug-lists>