BlueCross BlueShield
Federal Employee Program

SGLT2 INHIBITORS

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

*Prior authorization for certain formulations applies only to formulary exceptions due to being a non-covered medication. Please review plan formulary options.

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Brenzavvy (bexagliflozin), 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, 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).

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).

<u>Limitation of Use:</u>

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^2. The use of Steglatro, Steglujan, and Segluromet is not recommended in patients with an eGFR is below 45 mL/min/1.73m^2. Invokana should not be initiated in patients with an eGFR less than 30 mL/min/1.73 m^2, 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^2. 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^2 (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 hospitalization. Health care professionals should assess for ketoacidosis and urinary tract

BlueCross BlueShield
Federal Employee Program

SGLT2 INHIBITORS

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

*Prior authorization for certain formulations applies only to formulary exceptions due to being a non-covered medication. Please review plan formulary options.

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.

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.