SGLT2 INHIBITORS
Invokana (canagliflozin), Invokamet, Invokamet XR (canagliflozin & metformin)
Farxiga (dapagliflozin), Qtern (dapagliflozin & saxagliptin), Xigduo XR (dapagliflozin & metformin)
Jardiance (empagliflozin), Glyxambi (empagliflozin & linagliptin), Synjardy, Synjardy XR (empagliflozin & metformin)
Steglatro* (ertugliflozin), Steglujan* (ertugliflozin & sitagliptin), Segluromet* (ertugliflozin & metformin)

*These medications are included in this policy but are not available in the market as of yet.

RATIONALE FOR INCLUSION IN PA PROGRAM

Background
Invokana (canagliflozin), Invokamet, Invokamet XR (canagliflozin and metformin), Farxiga (dapagliflozin), Xigduo XR (dapagliflozin and metformin), Qtern (dapagliflozin and saxagliptin), Jardiance (empagliflozin), Glyxambi (empagliflozin and linagliptin), Synjardy, Synjardy XR (empagliflozin 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 diabetics who have elevated blood glucose levels (1-13).

Regulatory Status
FDA-approved indications for SGLT2 Inhibitors – Invokana, Invokamet, Invokamet XR, Farxiga, Xigduo XR, Qtern, Jardiance, Glyxambi, Synjardy, Synjardy 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 (1-13).

Limitation of Use:
SGLT2 Inhibitors should not be used for treatment of type 1 diabetes mellitus or diabetic ketoacidosis (1-13).
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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, 4, 7-9, 13).

Invokana, Invokamet, and Invokamet XR have boxed warnings for lower limb amputations, most frequently of the toe and midfoot. Before initiating therapy, prescribers must consider factors that may increase the risk of amputations and during therapy monitor patients for ulcers or infections of the lower limbs, and discontinue these medications if they complications occur (1-2, 8).

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 (1-13).

Renal function and eGFR have an effect on the SGLT2 inhibitor dosing. Farxiga, Xigduo XR, Qtern, Steglatro, Steglujan, and Segluromet should not be initiated if the eGFR is below 60 ml/min/1.73m². Glyxambi, Invokana, Invokamet, Jardiance, Synjardy and Synjardy XR should not be initiated in patients with an eGFR less than 45 mL/min/1.73 m² and should not be continued if the eGFR is less than 30 mL/min/1.73 m². A dose reduction is limited to no more than 50mg twice daily for Invokamet and Invokamet XR, and 100mg once daily for Invokana if the eGFR is between 45 to less than 60 ml/min/1.73m² (1-13).

Safety and effectiveness of SGLT2 inhibitors in patients under 18 years of age have not been established (1-13).
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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 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 (14).

Off-label and alternative uses of Invokana, Invokamet, Farxiga, Xigduo XR, Qtern, Jardiance, Glyxambi, Synjardy XR, Synjardy, 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. Invokana, Invokamet, Farxiga, Xigduo XR, Qtern, Jardiance, Glyxambi Synjardy, Synjardy XR, Steglatro, Steglujan, and Segluromet are contraindicated in setting of severe renal impairment, ESRD, or dialysis particularly in patients with eGFR less than 45 to 60 mL/min/1.73m². Renal function should be monitored during SGLT2s therapy. SGLT2 Inhibitors should not be used for treatment of type 1 diabetes mellitus or diabetic ketoacidosis (1-13).

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