Invokana® (canagliflozin) – New indication

- On October 30, 2018, Janssen and Johnson & Johnson announced the FDA approval of Invokana (canagliflozin), to reduce the risk of major adverse cardiovascular events (MACE) (cardiovascular death, nonfatal myocardial infarction [MI] and nonfatal stroke) in adults with type 2 diabetes mellitus (T2DM) and established cardiovascular disease (CVD).
    - Previously, Invokana was only approved as an adjunct to diet and exercise to improve glycemic control in adults with T2DM.
    - Invokana is not recommended in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.
- This new indication for Invokana also applies to the fixed-dose combinations of Invokamet® (canagliflozin/metformin) and Invokamet XR (canagliflozin/metformin extended-release). However, the effectiveness of Invokamet/Invokamet XR on reducing the risk of major cardiovascular events in adults with T2DM and CVD has not been established.
    - In addition, Invokamet and Invokamet XR are also indicated as an adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with both canagliflozin and metformin is appropriate.
- Invokana is an inhibitor of sodium-glucose cotransporter 2 (SGLT2), the transporter responsible for reabsorbing the majority of glucose filtered by the kidney.
    - Jardiance® (empagliflozin), another SGLT2 inhibitor, was previously approved for risk reduction of cardiovascular death in adult patients with T2DM and established CVD.
- The new indication for Invokana was based on the CANVAS and CANVAS-R studies. These studies included 10,134 patients with T2DM who had either established CVD or were at risk for CVD. Patients received Invokana or placebo in addition to or concomitantly with standard of care treatments for T2DM and atherosclerotic CVD. The primary endpoint (MACE) was the time to first occurrence of a three-part composite outcome which included cardiovascular death, non-fatal MI and non-fatal stroke.
    - Overall, treatment with Invokana reduced the risk of first occurrence of MACE by 14% vs. placebo. The estimated hazard ratio for time to first MACE was 0.86 (95% CI: 0.75, 0.97; p = 0.0158 for superiority).
    - All three components of the primary outcome showed point estimates of effect that suggested benefit, although the individual effects did not reach statistical significance.
- In addition to the new indication, two warnings related to hyperkalemia and macrovascular outcomes were removed from the Invokana, Invokamet, and Invokamet XR labeling.
- Invokana carries a boxed warning for lower limb amputation.
- Invokamet and Invokamet XR carry boxed warnings for lactic acidosis and lower limb amputation.
- The recommended starting dose of Invokana is 100 mg once daily, taken before the first meal of the day. The dose can be increased to 300 mg once daily in patients tolerating Invokana 100 mg who have an estimated glomerular filtration rate of ≥ 60 mL/min/1.73 m^2 and require additional glycemic control.

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— Consult the Invokamet and Invokamet XR drug labels for dosing recommendations.