Invokamet® XR (canagliflozin/metformin extended-release) – New Formulation Approval

- On September 21, 2016, Janssen announced the FDA approval of Invokamet XR (canagliflozin/metformin extended-release), indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM) when treatment with both Invokana® (canagliflozin) and metformin is appropriate.
    - Invokamet XR is not for treatment of type 1 diabetes or diabetic ketoacidosis.
- According to the American Diabetes Association, approximately 29 million people in the U.S. have T2DM. Patients with diabetes are at higher risk for cardiovascular disease, kidney disease and blindness.
- Invokamet XR contains 2 diabetes medications: a sodium glucose co-transporter 2 (SGLT2) inhibitor, canagliflozin, and a biguanide, metformin. The combination medication helps to decrease the blood sugar levels in the body.
- The combination of canagliflozin and metformin is also available as Invokamet®. This combination contains regular release metformin and must be taken twice daily.
- No clinical efficacy studies have been conducted with Invokamet XR; however, bioequivalence of Invokamet XR to canagliflozin and metformin co-administered as individual tablets was demonstrated in healthy subjects.
    - In patients with T2DM, treatment with canagliflozin and metformin, co-administered as individual products, produced clinically and statistically significant improvements in HbA1c compared to placebo.
- Invokamet XR is contraindicated in patients with moderate to severe renal impairment (eGFR < 45 mL/min/1.73 m^2), end stage renal disease or dialysis; metabolic acidosis, including diabetic ketoacidosis; and history of serious hypersensitivity reaction to canagliflozin or metformin.
- Like other products with metformin, Invokamet XR carries a boxed warning regarding lactic acidosis.
- Other warnings and precautions of Invokamet XR include hypotension, ketoacidosis, acute kidney injury and impairment in renal function, hyperkalemia, urosepsis and pyelonephritis, hypoglycemia with concomitant use of sulfonylurea or insulin, genital mycotic infections, hypersensitivity reactions, bone fracture, vitamin B_{12} levels, increases in low-density lipoprotein, and macrovascular outcomes.
- The most common adverse events (≥ 5%) with canagliflozin use were female genital mycotic infections, urinary tract infection, and increased urination.
- The most common adverse events (≥ 5%) with metformin use were diarrhea, nausea, vomiting, flatulence, asthenia, indigestion, abdominal discomfort, and headache.
- The recommended dose of Invokamet XR in patients who currently are not treated with either canagliflozin or metformin is 2 tablets, each tablet containing canagliflozin 50 mg and metformin 500 mg, once daily with the morning meal. For patients currently taking canagliflozin and metformin, dosage should be individualized based on the patient's current regimen.
    - Tablets should be swallowed whole and never crushed, cut, or chewed.

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- Dose adjustments may be needed in patients with renal impairment.

- Janssen's launch plans for Invokamet XR are pending. Invokamet XR (canagliflozin/metformin extended-release) will be available as 50 mg/500 mg, 50 mg/1,000 mg, 150 mg/500 mg, and 150 mg/1,000 mg tablets.