

Canagliflozin: New Medication for Type 2 Diabetes Mellitus

Canagliflozin (trade name Invokana) has been approved for monotherapy or combination therapy with other oral hypoglycemics and insulin for the treatment of type 2 diabetes.

Canagliflozin is the first in the class of sodium-glucose co-transporter 2 (SGLT2) inhibitors to be marketed in Canada. Dapagliflozin is available in the USA and Europe and two others, ipragliflozin and empagliflozin, are currently in development. The SGLT2 inhibitors reduce resorption of glucose in the kidney, resulting in increased urinary glucose excretion, which causes lowering of plasma glucose levels as well as weight loss.

Dosage: Start with 100mg po daily. May be increased to 300mg daily to achieve effect if eGFR > 60 ml/min. Tablets are available in 100mg and 300mg strengths. Take before the first meal of the day. Some diuretic effect is seen, therefore, morning dosing is preferred. Initial response is within 24 hours.

Adverse Reactions: The most common adverse reactions are vulvovaginal candidiasis (10-11%) and urinary tract infections (4.3-5.9%). Others include penile candidiasis, hyperkalemia, hypotension, hypovolemia, hypermagnesemia, hyperphosphatemia, increased thirst, nausea and constipation. *Caution is needed in the elderly due to increased risk of hypotension, hypovolemia and hyperkalemia.*

Interactions: Concurrent use of canagliflozin and

- Digoxin may result in increased digoxin levels.
- UDP-glucuronosyltransferase (UGT) enzyme inducers (phenytoin, phenobarbital, rifampin, etc) may result in decreased canagliflozin levels.
- Loop diuretics may increase risk of hypotension and hypovolemia.

Comparison with other oral hypoglycemics: Canagliflozin has been studied as monotherapy, in combination with metformin, sulfonylurea, with both metformin and sulfonylurea, with metformin and thiazolidinedione and in combination with insulin. HbA1C lowering is seen as early as week 12 of therapy and may continue to improve up to week 26. HbA1C is lowered between 0.5-1.1% with an average of 0.7-0.8% making canagliflozin similar in efficacy to the DPP-4 inhibitors. The major advantage of canagliflozin is that it provides statistically significant and clinically relevant weight loss in overweight patients (1.9-2.9 kg). Reductions in systolic blood pressure are also seen (3.7-5.4 mm Hg). It causes minimal hypoglycemia on its own and is relatively well tolerated.

Place in Therapy: Useful as an add-on agent to current type 2 diabetes treatments where glycemic control is inadequate. Please keep in mind that patients over the age of 65 will have lower reductions in HbA1C than younger patients and that, in addition to the increased risk of hypotension, hypovolemia and hyperkalemia, may limit the usefulness of canagliflozin in the elderly.

Monitor:

- Lab values: HbA1c; eGFR; potassium (especially for those at increased risk of hyperkalemia e.g. decreased kidney function or concurrent therapy with ACE-inhibitors, ARBs, potassium-sparing diuretics)
- Symptoms of UTIs, genital yeast infections
- Blood pressure

Cost and Coverage: The wholesale price of Invokana is approximately \$85.00/30 tablets for both the 100mg or 300mg strengths. It is not currently listed on the Saskatchewan Drug Plan formulary and Exception Drug Status is not available at this time either.

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References:

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