

About SGLT2 inhibitors

Type 2 diabetes and the unmet need

Despite the availability of many treatments for type 2 diabetes, approximately half of patients have not reached treatment goals at any given time. More treatment options are needed which provide strong, sustained efficacy in lowering excess blood glucose.^{1,2}

What are Sodium Glucose Co-Transporter 2 (SGLT2) inhibitors?

SGLT2 inhibitors are an exciting class of glucose-lowering agents for the treatment of type 2 diabetes, that are being developed with the aim of filling a gap for glucose-lowering treatments with a novel mechanism of action, compared to some existing therapies.^{3,4}

SGLT2 inhibitors are used to reduce blood glucose levels, either as a monotherapy or in addition to other glucose-lowering therapies, including insulin.^{3,4}

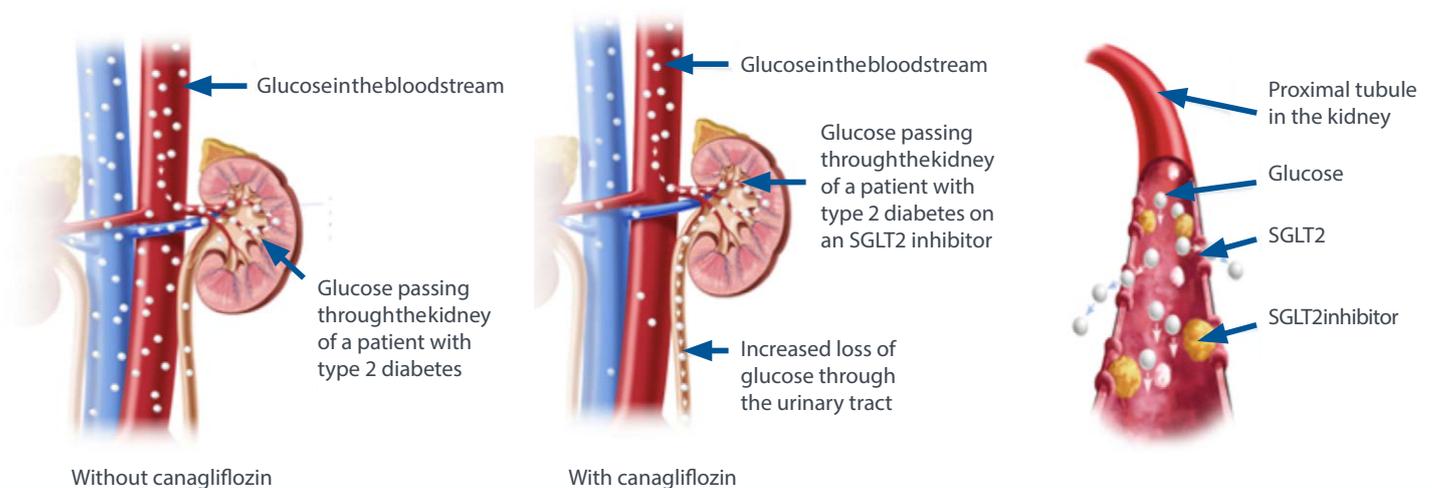
What is Sodium Glucose Co-Transporter 2 (SGLT2)?

The kidneys make an important contribution to balancing blood glucose. As glucose is filtered from the blood into the kidneys it is reabsorbed back into the bloodstream. A carrier responsible for most of this reabsorption is the kidney protein sodium glucose co-transporter 2 (SGLT2).^{3,4}

The kidneys of people with type 2 diabetes reabsorb greater amounts of glucose back into the body compared to people without type 2 diabetes, which may contribute to elevated blood glucose levels (hyperglycaemia).⁴ Therefore SGLT2 is a potential target for novel treatments for type 2 diabetes.^{3,4}

How do SGLT2 inhibitors work?

SGLT2 inhibitors work by blocking the SGLT2 protein. This reduces reabsorption of glucose in the kidney, leading to increased glucose excretion via the urine and lowering the level of glucose in the blood.³ This mechanism of action is independent of insulin.^{3,4}



What are the benefits of SGLT2 inhibitors?

The unique mechanism of action of SGLT2 inhibitors is independent of insulin, offering efficacy in lowering blood glucose with low risk of treatment-induced hypoglycaemia, when administered as a monotherapy or as an add on to other anti-diabetes medicines, such as metformin.^{3,4}

What is the safety and tolerability profile of SGLT2 inhibitors?

SGLT2 inhibitors are generally well-tolerated; however, the most commonly reported adverse reactions during treatment include hypoglycaemia when used in combination with insulin or a sulphonylurea.⁴

Due to the increased urinary glucose excretion, treatment with SGLT2 inhibitors can increase the risk of genital thrush ie. mycotic (fungal) infection or urinary tract infections (UTIs). The mycotic infections are generally mild to moderate and mainly simple to treat with topical creams and/or pessaries.^{3,4}

Diabetic ketoacidosis is a rare adverse reaction (affecting up to 1 in 1,000 patients). Patients taking these SGLT2 inhibitors should be aware of the symptoms of diabetic ketoacidosis and contact a doctor or visit the hospital immediately if they have any of the symptoms.⁵

Other side effects can include postural dizziness (associated with volume depletion) and urinary frequency and thirst (related to the mechanism of action).^{3,4}

In the CANVAS Program specifically, canagliflozin has been associated with an increased risk in lower limb amputation (primarily of the toe and midfoot). However, this risk is very low with an absolute risk of 6 per 1000 patient years (or equivalent) compared to 3 per 1000 patient years for the placebo arm. An underlying mechanism has not been established.

SGLT2 inhibitors when used as add-on to insulin, or insulin secretagogues, can cause hypoglycaemia.⁴

References

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