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EPAR summary for the public

Invokana

canagliflozin

This is a summary of the European public assessment report (EPAR) for Invokana. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Invokana.

For practical information about using Invokana, patients should read the package leaflet or contact their doctor or pharmacist.

What is Invokana and what is it used for?

Invokana is a diabetes medicine that contains the active substance canagliflozin. It is used in adults with type 2 diabetes to control their blood glucose (sugar) level.

Invokana can be used on its own in patients whose blood glucose levels are not satisfactorily controlled on diet and exercise alone and who cannot take metformin (another diabetes medicine).

Invokana can also be used as an 'add-on' to other diabetes medicines, including insulin, when these medicines together with exercise and diet are not providing adequate control of the diabetes.

How is Invokana used?

Invokana is available as tablets (100 and 300 mg) and can only be obtained with a prescription. The tablets are taken once a day, preferably before the first meal of the day. The recommended starting dose is 100 mg once a day. If appropriate, the dose can be increased to 300 mg once a day.

As the effects of Invokana are dependent on kidney function, the effectiveness and tolerability of the medicine are reduced in patients with reduced kidney function. The use of Invokana is therefore not recommended in patients with severely reduced kidney function. In patients with moderately reduced kidney function the dose should be limited to 100 mg once a day.

For further information, see the package leaflet.



How does Invokana work?

Type-2 diabetes is a disease in which the pancreas does not make enough insulin to control the level of glucose in the blood or when the body is unable to use insulin effectively. This leads to high levels of glucose in the blood.

The active substance in Invokana, canagliflozin, works by blocking a protein in the kidneys called sodium-glucose co-transporter 2 (SGLT2). SGLT2 is a protein that absorbs glucose from the urine back into the bloodstream as the blood is filtered in the kidneys. By blocking the action of SGLT2, Invokana causes more glucose to be removed via the urine, thereby reducing the levels of glucose in the blood.

What benefits of Invokana have been shown in studies?

Invokana has been evaluated in 9 main studies involving a total of around 10,000 patients with type 2 diabetes. One of the studies compared Invokana with placebo (a dummy treatment) when used alone in patients whose blood glucose levels were not satisfactorily controlled on diet and exercise alone. Three studies looked at Invokana when used as add-on to one other diabetes medicine (metformin or insulin), and three further studies looked at Invokana when used as add-on to two other diabetes medicines (including metformin), when these medicines together with exercise and diet were not providing adequate control of the diabetes. A study was also performed in patients with moderately reduced kidney function, and one in older patients aged between 55 and 80 years. In all of the studies, the main measure of effectiveness was the level of a substance in the blood called glycosylated haemoglobin (HbA1c), which gives an indication of how well the blood glucose is controlled.

Invokana was shown to be more effective than placebo, and at least as effective as comparator medicines, at reducing the levels of HbA1c when used alone and in combination with other diabetes medicines:

- When Invokana was used on its own at a dose of 100 mg, it decreased HbA1c levels by 0.91% more than placebo after 26 weeks, while the 300 mg dose led to a reduction of 1.16% more than placebo.
- Across the studies that looked at Invokana when used as add-on to one or two other diabetes medicines, the reductions in HbA1c levels after 26 weeks compared with placebo ranged from 0.76% to 0.92% with the 300 mg dose, and from 0.62% to 0.74% with the 100 mg dose.
- When Invokana was used as add-on to insulin at a dose of 300 mg, it decreased HbA1c levels by 0.73% more than placebo after 18 weeks, while the 100 mg dose led to a reduction of 0.65% more than placebo.
- Invokana was also shown to be at least as effective as the diabetes medicines glimepiride and sitagliptin after 52 weeks of treatment.
- The study in patients with moderately reduced kidney function showed that the effects of Invokana were reduced in these patients, but still clinically relevant: the reduction of HbA1c levels compared with placebo was 0.30% with the 100 mg dose.
- The study in older patients showed that Invokana had clinically relevant effects also in patients above 75 years of age with HbA1c reductions compared with placebo of 0.70% and 0.57% with the 300 mg and 100 mg doses, respectively.

What are the risks associated with Invokana?

The most common side effects with Invokana are hypoglycaemia (low blood glucose levels) when used together with insulin or a sulphonylurea, vulvovaginal candidiasis (thrush, a fungal infection of the female genital area caused by *Candida*) urinary tract infection (infection of the structure that carries the urine) and polyuria (abnormally large production of urine) or pollakiuria (abnormally frequent urination).

For the full list of all side effects reported with Invokana, see the package leaflet.

Why is Invokana approved?

The Agency's Committee for Medicinal Products for Human Use (CHMP) decided that Invokana's benefits are greater than its risks and recommended that it be approved for use in the EU. The CHMP concluded that Invokana was shown to be effective at controlling blood glucose levels. Invokana treatment also led to weight loss and reductions in blood pressure, effects that are considered beneficial in patients with diabetes. Regarding its safety, this was considered similar to other medicines of the same class (SGLT2 inhibitors). Important side effects identified included dehydration and urinary tract infection, but these were considered to be manageable.

What measures are being taken to ensure the safe and effective use of Invokana?

A risk management plan has been developed to ensure that Invokana is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Invokana, including the appropriate precautions to be followed by healthcare professionals and patients.

Other information about Invokana

The European Commission granted a marketing authorisation valid throughout the European Union for Invokana on 15.11.2013.

The full EPAR for Invokana can be found on the Agency's website: ema.europa.eu/Find/medicine/Human_medicines/European_public_assessment_reports. For more information about treatment with Invokana, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 11-2013.