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Invokana (*canagliflozin*)

An overview of Invokana and why it is authorised in the EU

What is Invokana and what is it used for?

Invokana is a diabetes medicine that contains the active substance canagliflozin. It is used together with diet and exercise to treat adults with type 2 diabetes.

Invokana can be used on its own in patients who cannot take metformin (another diabetes medicine) or it can be used as an 'add-on' to other diabetes medicines.

How is Invokana used?

Invokana is available as tablets 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.

For more information about using Invokana, see the package leaflet or contact your doctor or pharmacist.

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 and other complications.

The active substance in Invokana, canagliflozin, works by blocking a protein in the kidneys called sodium-glucose co-transporter 2 (SGLT2). SGLT2 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.

SGLT2 also absorbs sodium from the urine into the bloodstream. Blocking the action of SGLT2 leads to a reduction of sodium in the blood reducing the pressure in the kidney and slowing the progression of diabetic kidney disease.

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What benefits of Invokana have been shown in studies?

Invokana's effects on blood glucose levels have been evaluated in 9 main studies involving a total of around 10,000 patients with type 2 diabetes. In all of the studies, the main measure of effectiveness was the reduction in 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 or 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 percentage points more than placebo after 26 weeks, while the 300 mg dose led to a reduction of 1.16 percentage points 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 percentage points to 0.92 percentage points with the 300 mg dose, and from 0.62 percentage points to 0.74 percentage points 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 percentage points more than placebo after 18 weeks, while the 100 mg dose led to a reduction of 0.65 percentage points 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 0.3 percentage points with the 100 mg dose.
- The study in older patients showed that Invokana had clinically relevant effects in patients above 75 years of age with HbA1c reductions compared with placebo of 0.70 percentage points and 0.57 percentage points with the 300 mg and 100 mg doses, respectively

In addition, Invokana's effects on the heart and diabetic kidney disease were studied in 3 main studies:

- In two studies involving over 10,000 patients who had heart disease or were at risk of developing it, treatment with Invokana for 149 weeks reduced the risk of heart problems or stroke: in the Invokana group there were 27 occurrences of a heart attack, stroke or death from problems in the heart and blood circulation per 1000 patient-years compared with 32 occurrences with placebo.
- Invokana was also shown to be effective in slowing the progression in diabetic kidney disease in patients with type 2 diabetes. In a study in 4,000 patients with mildly or moderately reduced kidney function, patients received either Invokana or placebo on top of standard treatment. With Invokana, 11% of patients (245 out of 2,202) had substantial worsening of kidney function or died from kidney and heart problems compared with 16% (340 out of 2,199) of patients on placebo. When compared to placebo, the effect on kidney function was largely independent from the blood-glucose-lowering effect of Invokana.

What are the risks associated with Invokana?

The most common side effects (which may affect more than 1 in 10 people) 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*) and urinary tract infection (infection of the structure that carries the urine).

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

Why is Invokana authorised in the EU?

The European Medicines Agency decided that Invokana's benefits are greater than its risks and it can be authorised for use in the EU. Invokana was shown to be effective at controlling blood glucose levels in patients with type 2 diabetes and at reducing diabetic kidney disease and heart complications. 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 manageable.

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

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Invokana have been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Invokana are continuously monitored. Side effects reported with Invokana are carefully evaluated and any necessary action taken to protect patients.

Other information about Invokana

Invokana received a marketing authorisation valid throughout the EU on 15 November 2013.

More information on Invokana can be found on the Agency's website: https://www.ema.europa.eu/en/medicines/human/EPAR/invokana

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