EMA/119828/2014
EMEA/H/C/002656

EPAR summary for the public

Vokanamet

canagliflozin / metformin

This is a summary of the European public assessment report (EPAR) for Vokanamet. 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 Vokanamet.

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

What is Vokanamet and what is it used for?

Vokanamet is a diabetes medicine that contains the active substances canagliflozin and metformin. It is used, together with diet and exercise, to control the blood glucose (sugar) levels in adults with type 2 diabetes whose disease is not satisfactorily controlled with metformin alone, or in combination with other diabetes medicines, including insulin, when these medicines together with metformin are not providing adequate control of the diabetes. Vokanamet can also be used to replace canagliflozin and metformin given separately.

How is Vokanamet used?

Vokanamet is available as tablets containing canagliflozin and metformin in various strengths (50/850 mg, 150/850 mg, 50/1000 mg and 150/1000 mg) and can only be obtained with a prescription.

The recommended dose is one tablet taken twice a day. The tablet strength depends on the patient's treatment before starting Vokanamet. Patients should start Vokanamet at a strength that provides 50 mg canagliflozin and the dose of metformin they were previously taking (or a close approximation of it). The dose of canagliflozin can then be increased if needed.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

When Vokanamet is used as an add-on to insulin or medicines that stimulate the secretion of insulin (e.g. sulphonylureas) the dose of these other medicines may need to be reduced to lower the risk of the patient's blood glucose becoming too low.

For further information, see the package leaflet.

How does Vokanamet 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.

Vokanamet contains two different active substances, which work in different ways:

- canagliflozin works by blocking a protein in the kidneys called sodium glucose co-transporter 2 (SGLT2). SGLT2 absorbs glucose back into the bloodstream as the blood is filtered in the kidneys. By blocking the action of SGLT2, canagliflozin causes more glucose to be removed via the urine, thereby reducing the levels of glucose in the blood. Canagliflozin as separate tablets has been authorised in the EU under the brand name Invokana since 15 November 2013.
- Metformin works mainly by inhibiting glucose production and reducing its absorption in the gut. It has been available in the EU since the 1950s.

As a result of the action of both active substances, the blood glucose is reduced and this helps to control type 2 diabetes.

What benefits of Vokanamet have been shown in studies?

The benefits of canagliflozin used in combination with metformin have been shown in several main studies that were evaluated at the time of the authorisation of Invokana. The studies, involving over 5,000 adults with type 2 diabetes, studied canagliflozin at daily doses of 100 and 300 mg and looked mainly at how they reduced the level of a substance in the blood called glycosylated haemoglobin (HbA1c), which gives an indication of how well the blood glucose is controlled.

In two studies evaluating canagliflozin as an add-on to metformin, the reductions in HbA1c levels after 26 weeks was 0.91 to 1.16 percentage points higher with canagliflozin than with placebo (a dummy treatment) when added to metformin and canagliflozin achieved similar reductions to two other diabetes medicines, glimepiride and sitagliptin, after 52 weeks of treatment.

Three further studies evaluated canagliflozin as an add-on to combined treatment with metformin and either a sulphonylurea or pioglitazone. Added to metformin and a sulphonylurea, canagliflozin led to reductions in HbA1c that were between 0.71 and 0.92percentage points more than those seen with placebo after 26 weeks and similar to those seen with sitagliptin (another diabetes medicine) after 52 weeks. Added to metformin and pioglitazone, canagliflozin was also superior to placebo, leading to HbA1c reductions that were 0.62 and 0.76 points more than was seen by adding placebo.

Canagliflozin was also studied as an add-on treatment in patients who were taking insulin alone, or insulin in combination with other diabetes medicines including metformin and in patients who were taking a sulphonylurea. Adding canagliflozin to treatment was shown to be effective at reducing HbA1c compared with placebo by 0.65 to 0.73 points after 18 weeks in patients receiving insulin and by 0.74 to 0.83 points in patients receiving a sulphonylurea.

What are the risks associated with Vokanamet?

The most common side effects with Vokanamet (which may affect more than 1 in 10 people) are hypoglycaemia (low blood glucose levels) when used in combination with insulin or a sulphonylurea and vulvovaginal candidiasis (thrush, a fungal infection of the female genital area caused by *Candida*).

Vokanamet must not be used in:

- patients with diabetic ketoacidosis or pre-coma (dangerous complications of diabetes),
- patients with moderately or severely reduced kidney function or with severe conditions that could affect the kidneys such as dehydration or severe infection.
- patients with a condition that could lead to body tissues being deprived of oxygen (e.g. heart or respiratory failure)
- patients who have liver impairment or are suffering from alcoholism or are intoxicated.

For the full list of restrictions, see the package leaflet.

Why is Vokanamet approved?

The Agency's Committee for Medicinal Products for Human Use (CHMP) decided that Vokanamet's benefits are greater than its risks and recommended that it be approved for use in the EU. The benefits of metformin are well established and the added advantage of adding canagliflozin to metformin to control blood sugar has been shown in the studies. It also leads to weight loss, which is considered beneficial in patients with diabetes. The CHMP also noted that giving the combination of canagliflozin and metformin as a single tablet could provide an additional treatment option for patients with type 2 diabetes, and may improve adherence to treatment.

Concerning its safety, the CHMP considered that the side effects seen with Vokanamet are acceptable and can be managed in clinical practice.

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

A risk management plan has been developed to ensure that Vokanamet 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 Vokanamet, including the appropriate precautions to be followed by healthcare professionals and patients.

Further information can be found in the summary of the risk management plan.

Other information about Vokanamet

The European Commission granted a marketing authorisation valid throughout the European Union for Vokanamet on 23 April 2014.

The full EPAR and risk management plan summary for Vokanamet 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 Vokanamet, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 05-2014.