

Package leaflet: Information for the patient

Vokanamet 50 mg/850 mg film-coated tablets
Vokanamet 50 mg/1000 mg film-coated tablets
Vokanamet 150 mg/850 mg film-coated tablets
Vokanamet 150 mg/1000 mg film-coated tablets

canagliflozin/metformin hydrochloride

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Vokanamet is and what it is used for
2. What you need to know before you take Vokanamet
3. How to take Vokanamet
4. Possible side effects
5. How to store Vokanamet
6. Contents of the pack and other information

1. What Vokanamet is and what it is used for

Vokanamet contains two different active substances, canagliflozin and metformin. These are two medicines that work together in different ways to lower blood glucose (sugar) levels and can help prevent heart disease in adults with type 2 diabetes.

This medicine can be used by itself or along with other medicines you may be using to treat your type 2 diabetes (such as insulin, a DPP-4 inhibitor [such as sitagliptin, saxagliptin, or linagliptin], a sulphonylurea [such as glimepiride or glipizide], or pioglitazone) that lower blood sugar levels. You may already be taking one or more of these to treat your type 2 diabetes. Vokanamet is used when your blood sugar cannot be adequately controlled by metformin alone or together with other diabetes medicines. If you are already taking both canagliflozin and metformin as single tablets, Vokanamet can replace them in one tablet.

It is important to keep following advice about diet and exercise given by your doctor or nurse.

What is type 2 diabetes?

Type 2 diabetes is a condition in which your body does not make enough insulin, and the insulin that your body produces does not work as well as it should. Your body can also make too much sugar. When this happens, sugar (glucose) builds up in the blood. This can lead to serious medical conditions such as heart disease, kidney disease, blindness, and amputation.

2. What you need to know before you take Vokanamet

Do not take Vokanamet

- if you are allergic to canagliflozin, metformin or any of the other ingredients of this medicine (listed in section 6)
- if you have liver problems
- if you have severely reduced kidney function

- if you have uncontrolled diabetes, with, for example, severe hyperglycaemia (high blood glucose), nausea, vomiting, diarrhoea, rapid weight loss, lactic acidosis (see “Risk of lactic acidosis” below) or ketoacidosis. Ketoacidosis is a condition in which substances called 'ketone bodies' accumulate in the blood and which can lead to diabetic pre-coma. Symptoms include stomach pain, fast and deep breathing, sleepiness or your breath developing an unusual fruity smell.
- if you have a severe infection
- if you have lost a lot of water from your body (dehydration), e.g. due to long-lasting or severe diarrhoea, or if you have vomited several times in a row
- if you have a diabetic pre-coma
- if you have recently had a heart attack or have severe blood circulation problems, such as ‘shock’ or breathing difficulties
- if you drink alcohol to excess (either every day or from time to time)
- if you have or have recently had heart failure.

Warnings and precautions

Risk of lactic acidosis

Vokanamet may cause a very rare, but very serious side effect called lactic acidosis, particularly if your kidneys are not working properly. The risk of developing lactic acidosis is also increased with uncontrolled diabetes, serious infections, prolonged fasting or alcohol intake, dehydration (see further information below), liver problems and any medical conditions in which a part of the body has a reduced supply of oxygen (such as acute severe heart disease).

If any of the above applies to you, talk to your doctor for further instructions.

Temporarily stop taking Vokanamet if you have a condition that may be associated with dehydration (significant loss of body fluids) such as severe vomiting, diarrhoea, fever, exposure to heat or if you drink less fluid than normal. Talk to your doctor for further instructions.

Stop taking Vokanamet and talk to a doctor or go to the nearest hospital immediately if you experience some of the symptoms of lactic acidosis, as this condition may lead to coma.

Symptoms of lactic acidosis include:

- vomiting
- stomach ache (abdominal pain)
- muscle cramps
- a general feeling of not being well with severe tiredness
- difficulty in breathing
- reduced body temperature and heartbeat

Lactic acidosis is a medical emergency and must be treated in a hospital.

Talk to your doctor, pharmacist or nurse before taking Vokanamet, and during treatment:

- about what you can do to prevent dehydration (see section 4 for signs of dehydration).
- if you have type 1 diabetes because Vokanamet should not be used to treat this condition.
- if you experience rapid weight loss, feeling sick or being sick, stomach pain, excessive thirst, fast and deep breathing, confusion, unusual sleepiness or tiredness, a sweet smell to your breath, a sweet or metallic taste in your mouth or a different odour to your urine or sweat, talk to a doctor or go to the nearest hospital immediately. These symptoms could be a sign of “diabetic ketoacidosis” – a rare but serious, sometimes life-threatening problem you can get with diabetes because of increased levels of “ketone bodies” in your urine or blood, seen in tests. The risk of developing diabetic ketoacidosis may be increased with prolonged fasting, excessive alcohol consumption, dehydration, sudden reductions in insulin dose, or a higher need of insulin due to major surgery or serious illness.
- if you have ever had serious heart disease or if you have had a stroke
- if you are on medicines to lower your blood pressure (anti-hypertensives) or have ever had low blood pressure (hypotension). More information is given below in "Other medicines and Vokanamet".

- if you have had a lower limb amputation.
- It is important to check your feet regularly and adhere to any other advice regarding foot care and adequate hydration given by your healthcare professional. You should notify your doctor immediately if you notice any wounds or discolouration, or if you experience any tenderness or pain in your feet. Some studies indicate that taking canagliflozin may have contributed to the risk of lower limb amputation (mainly toe and midfoot amputations).
- if you have signs of a genital yeast infection such as irritation, itching, unusual discharge or odour

Kidney function

Your kidneys will be tested by a blood test before you start taking and during treatment with Vokanamet. Your doctor will check your kidney function at least once a year or more frequently if you are elderly and/or if you have worsening kidney function.

Surgery

If you need to have major surgery you must stop taking Vokanamet during and for some time after the procedure. Your doctor will decide when you must stop and when to restart your treatment with Vokanamet.

Your doctor will decide whether you need any other treatment to control your blood sugar while you have stopped taking Vokanamet. It is important that you follow your doctor's instructions carefully.

Urine glucose

Because of the way canagliflozin works, your urine will test positive for sugar (glucose) while you are taking this medicine.

Children and adolescents

Vokanamet is not recommended for children and adolescents under 18 years, because data are not available in these patients.

Other medicines and Vokanamet

If you need to have an injection of a contrast medium that contains iodine into your bloodstream, for example in the context of an X-ray or scan, you must stop taking Vokanamet before or at the time of the injection. Your doctor will decide when you must stop and when to restart your treatment with Vokanamet.

Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines. This is because this medicine can affect the way some other medicines work. Also, some other medicines can affect the way this medicine works. You may need more frequent blood glucose and kidney function tests, or your doctor may need to adjust the dose of Vokanamet. It is especially important to mention the following:

- insulin or a sulphonylurea (such as glimepiride or glipizide) for diabetes – your doctor may want to reduce your dose in order to avoid your blood sugar level from getting too low (hypoglycaemia)
- medicines which increase urine production (diuretics)
- St. John's wort (a herbal medicine used to treat depression)
- carbamazepine, phenytoin, or phenobarbital (medicines used to control seizures)
- efavirenz or ritonavir (medicines used to treat HIV infection)
- rifampicin (an antibiotic used to treat tuberculosis)
- cholestyramine (medicine used to reduce cholesterol levels in the blood). See section 3, "Taking this medicine".
- digoxin or digitoxin (medicines used for certain heart problems). The level of digoxin or digitoxin in your blood may need to be checked if taken with Vokanamet.
- dabigatran (blood thinner medicine that lowers the risk of blood clot formation)
- medicines that contain alcohol. See section "Vokanamet with alcohol".
- cimetidine (medicine used to treat stomach problems)

- corticosteroids (used to treat a variety of conditions, such as severe inflammation of the skin or in asthma) that are given by mouth, as an injection, or inhaled
- beta-2 agonists (such as salbutamol or terbutaline) used to treat asthma.
- medicines used to treat pain and inflammation (NSAID and COX-2-inhibitors, such as ibuprofen and celecoxib)
- certain medicines for the treatment of high blood pressure (ACE inhibitors and angiotensin II receptor antagonists)

Vokanamet with alcohol

Avoid excessive alcohol intake while taking this medicine since this may increase the risk of lactic acidosis. See section “Warning and precautions”.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking or continuing to take this medicine.

Canagliflozin, one of the ingredients in Vokanamet, should not be used during pregnancy. Talk to your doctor about the best way to control your blood sugar without Vokanamet as soon as you know that you are pregnant.

You should not take this medicine if you are breast-feeding. Talk to your doctor about whether to stop taking this medicine or to stop breast-feeding.

Driving and using machines

Vokanamet has no or negligible influence on the ability to drive, cycle, and use tools or machines. However, dizziness or lightheadedness has been reported, which may affect your ability to drive, cycle, or use tools or machines.

Taking Vokanamet with other medicines for diabetes called sulphonylureas (such as glimepiride or glipizide) or insulin can increase the risk of having low blood sugar (hypoglycaemia). Signs include blurred vision, tingling lips, trembling, sweating, pale looking, a change in mood, or feeling anxious or confused. This may affect your ability to drive, cycle, and use any tools or machines. Tell your doctor as soon as possible if you get any signs of low blood sugar.

Vokanamet contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially ‘sodium free’.

3. How to take Vokanamet

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

How much to take

- The dose of Vokanamet is one tablet twice a day.
- The strength of Vokanamet that you will take varies depending on your condition and the amount of canagliflozin and metformin needed to control your blood sugar.
- Your doctor will prescribe the strength that is right for you.

Taking this medicine

- Swallow the tablet whole with water.
- It is best to take your tablet with a meal. This will lower your chance of having an upset stomach.
- Try to take it at the same times each day. This will help you remember to take it.

- If your doctor has prescribed this medicine along with any medicine for lowering cholesterol such as cholestyramine you should take this medicine at least 1 hour before or 4 hours to 6 hours after the cholesterol-lowering medicine.

Your doctor may prescribe Vokanamet together with another glucose-lowering medicine. Remember to take all medicines as directed by your doctor to achieve the best results for your health.

Diet and exercise

To help control your diabetes, you still need to follow the advice about diet and exercise from your doctor, pharmacist or nurse. In particular, if you are following a diabetic weight control diet, continue to follow it while you are taking this medicine.

If you take more Vokanamet than you should

As Vokanamet contains metformin, if you take more of this medicine, you may experience lactic acidosis. If this happens to you, you may need immediate hospital treatment, as lactic acidosis may lead to coma. Symptoms of lactic acidosis include vomiting, stomach ache, muscle cramps, a general feeling of not being well with severe tiredness, or difficulty breathing. Further symptoms are reduced body temperature and heartbeat. Stop taking this medicine immediately and contact a doctor or the nearest hospital straight away (see section 2). Take the medicine pack with you.

If you forget to take Vokanamet

- If you forget to take a dose, take it as soon as you remember. However, if it is time for the next dose, skip the missed dose.
- Do not take a double dose to make up for a forgotten dose.

If you stop taking Vokanamet

Your blood sugar levels may rise if you stop taking this medicine. Do not stop taking this medicine without talking to your doctor first.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Stop taking Vokanamet and talk to a doctor or go to the nearest hospital immediately if you have any of the following serious side effects:

Severe allergic reaction (rare, may affect up to 1 in 1,000 people)

Possible signs of severe allergic reaction may include:

- swelling of the face, lips, mouth, tongue, or throat that may lead to difficulty breathing or swallowing.

Lactic acidosis (very rare, may affect up to 1 in 10,000 people)

Vokanamet may cause a very rare but very serious side effect called lactic acidosis (see section “Warnings and precautions”). If this happens, you must **stop taking Vokanamet and talk to a doctor or go to the nearest hospital immediately**, as lactic acidosis may lead to coma.

Diabetic ketoacidosis (rare, may affect up to 1 in 1,000 people)

These are the signs of diabetic ketoacidosis (see also section 2):

- increased levels of “ketone bodies” in your urine or blood
- rapid weight loss
- feeling sick or being sick
- stomach pain
- excessive thirst
- fast and deep breathing

- confusion
- unusual sleepiness or tiredness
- a sweet smell to your breath, a sweet or metallic taste in your mouth or a different odour to your urine or sweat.

This may occur regardless of blood glucose level. The doctor may decide to temporarily or permanently stop the treatment with Vokanamet.

Dehydration (uncommon, may affect up to 1 in 100 people)

- loss of too much fluid from your body (dehydration). This happens more often in elderly people (aged 75 and over), people with kidney problems, and people taking water tablets (diuretics). Possible signs of dehydration are:
 - feeling light-headed or dizzy
 - passing out (fainting) or feeling dizzy or faint when you stand up
 - very dry or sticky mouth, feeling very thirsty
 - feeling very weak or tired
 - passing little or no urine
 - fast heartbeat.

Tell your doctor as soon as possible if you have any of the following side effects:

Hypoglycaemia (very common, may affect more than 1 in 10 people)

- low blood sugar levels (hypoglycaemia) - when taking this medicine with insulin or a sulphonylurea (such as glimepiride or glipizide). Possible signs of low blood sugar are:
 - blurred vision
 - tingling lips
 - trembling, sweating, looking pale
 - a change in mood or feeling anxious or confused.

Your doctor will tell you how to treat low blood sugar levels and what to do if you have any of the signs above.

Other side effects when taking canagliflozin alone:

Very common (may affect more than 1 in 10 people)

- vaginal yeast infection.

Common (may affect up to 1 in 10 people)

- rash or redness of the penis or foreskin (yeast infection)
- urinary tract infections
- changes in urination (including urinating more frequently or in larger amounts, urgent need to urinate, need to urinate at night)
- constipation
- feeling thirsty
- feeling sick (nausea)
- blood tests may show changes in blood fat (cholesterol) levels and increases in the amount of red blood cells in your blood (haematocrit).

Uncommon (may affect up to 1 in 100 people)

- rash or red skin - this may be itchy and include raised bumps, oozing fluid or blisters.
- hives
- blood tests may show changes related to kidney function (increased creatinine or urea) or increased potassium
- blood tests may show increases in your blood phosphate level
- bone fracture
- kidney failure (mainly as a consequence of loss of too much fluid from your body).
- lower limb amputations (mainly of the toe) especially if you are at high risk of heart disease.

- phimosis – difficulty pulling back the foreskin around the tip of the penis.

Side effects when taking metformin alone that were not described for canagliflozin:

- very common: feeling sick (nausea), being sick (vomiting), diarrhoea, stomach ache, and loss of appetite
- common: a metallic taste (taste disturbance)
- very rare: decreased vitamin B₁₂ levels (may cause anaemia – low count of red blood cells), liver function test disorders, hepatitis (a problem with your liver), and itching.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

In the UK, you can also report side effects directly via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Vokanamet

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the bottle and carton after EXP. The expiry date refers to the last day of that month.

Do not store above 30°C.

Do not use Vokanamet if the packaging is damaged or shows signs of tampering.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Vokanamet contains

- The active substances are canagliflozin and metformin hydrochloride.
 - Each 50 mg/850 mg tablet contains canagliflozin hemihydrate, equivalent to 50 mg of canagliflozin and 850 mg of metformin hydrochloride.
 - Each 50 mg/1000 mg tablet contains canagliflozin hemihydrate, equivalent to 50 mg of canagliflozin and 1000 mg of metformin hydrochloride.
 - Each 150 mg/850 mg tablet contains canagliflozin hemihydrate, equivalent to 150 mg of canagliflozin and 850 mg of metformin hydrochloride.
 - Each 150 mg/1000 mg tablet contains canagliflozin hemihydrate, equivalent to 150 mg of canagliflozin and 1000 mg of metformin hydrochloride.
- The other ingredients are:
 - Tablet core: microcrystalline cellulose, hypromellose, croscarmellose sodium, and magnesium stearate.
 - Film-coating:
 - 50 mg/850 mg tablets: macrogol 3350, poly(vinylalcohol), talc, titanium dioxide (E171), iron oxide red (E172) and iron oxide black (E172).
 - 50 mg/1000 mg tablets: macrogol 3350, poly(vinylalcohol), talc, titanium dioxide (E171), iron oxide yellow (E172), and iron oxide red (E172).
 - 150 mg/850 mg tablets: macrogol 3350, poly(vinylalcohol), talc, titanium dioxide (E171), and iron oxide yellow (E172).

- 150 mg/1000 mg tablets: macrogol 3350, poly(vinylalcohol), talc, titanium dioxide (E171), iron oxide red (E172) and iron oxide black (E172).

What Vokanamet looks like and contents of the pack

- Vokanamet 50 mg/850 mg film-coated tablets (tablets) are pink, capsule-shaped, 20 mm in length, and debossed with “CM” on one side and “358” on the other side.
- Vokanamet 50 mg/1000 mg film-coated tablets (tablets) are beige, capsule-shaped, 21 mm in length, and debossed with “CM” on one side and “551” on the other side.
- Vokanamet 150 mg/850 mg film-coated tablets (tablets) are light yellow, capsule-shaped, 21 mm in length, and debossed with “CM” on one side and “418” on the other side.
- Vokanamet 150 mg/1000 mg film-coated tablets (tablets) are purple, capsule-shaped, 22 mm in length, and debossed with “CM” on one side and “611” on the other side.

Vokanamet is available in HDPE bottles with child-resistant closure. The pack sizes are cartons of 20 and 60 tablets, and multipack cartons of 180 tablets (3 bottles containing 60 tablets each).

Not all pack sizes may be marketed.

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site:
<http://www.ema.europa.eu>.