

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr **INVOKAMET®**

canagliflozin and metformin hydrochloride tablets

Read this carefully before you start taking **INVOKAMET** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **INVOKAMET**.

Serious Warnings and Precautions

Lactic Acidosis

- **INVOKAMET** contains the medicinal ingredient metformin. Having too much metformin in your blood can cause lactic acidosis. Lactic acidosis is a rare but serious build-up of lactic acid in the blood. It can cause death and must be treated in a hospital setting.
- Alcohol may increase your risk of lactic acidosis. Do not drink a lot of alcohol while taking **INVOKAMET**. This means that you should not “binge” drink (have 5 or more drinks in a row by men, or 4 or more drinks in a row by women).

Diabetic Ketoacidosis (DKA)

- **DKA** may happen during or after stopping treatment with **INVOKAMET**. It is a serious and life-threatening condition, which may need urgent hospital care. Some cases of **DKA** have led to death. **DKA** is a complication of diabetes, where your body produces high levels of blood acids called ketones. It can happen in patients with type 2 diabetes mellitus (T2DM), with normal or high blood sugar (glucose) levels, who are treated with **INVOKAMET** or with other sodium-glucose co-transporter 2 (SGLT2) inhibitors.
- **Seek medical attention right away and stop taking INVOKAMET immediately** if you have any of the following symptoms (even if your blood sugar levels are normal): difficulty breathing, nausea, vomiting, stomach pain, loss of appetite, confusion, feeling very thirsty, feeling unusually tired or sleepy, a sweet smell to the breath, a sweet or metallic taste in the mouth, or a different odour to urine or sweat.
- Do NOT use **INVOKAMET** if you have:
 - type 1 diabetes
 - **DKA** or a history of **DKA**

Lower Limb Amputation

- **INVOKAMET** may increase your risk of lower limb amputations. Amputations have happened mainly on the toe or part of the foot, however, amputations involving the leg, below and above the knee have also occurred. Some people had more than one amputation, some on both sides of the body.
- Tell your healthcare professional if you have ever had an amputation, blood vessel disease, nerve disease, or a foot ulcer (sore) caused by diabetes.

- **Seek medical attention right away** if you have new pain or tenderness, any sores, ulcers, or infections in your leg or foot. Your healthcare professional may decide to stop your INVOKAMET if you have any of these signs or symptoms. Talk to your healthcare professional about proper foot care and keeping hydrated.

What is INVOKAMET used for?

INVOKAMET is used along with diet and exercise to improve blood sugar levels in adults with type 2 diabetes.

INVOKAMET can be used in patients:

- whose diabetes is not controlled on:
 - metformin alone
 - metformin in combination with a sulfonylurea
 - metformin in combination with pioglitazone
 - metformin in combination with insulin
- who are currently taking combination of separate tablets of:
 - metformin and INVOKANA (canagliflozin)
 - metformin, INVOKANA and a sulfonylurea
 - metformin, INVOKANA and pioglitazone
 - metformin, INVOKANA and insulin

How does INVOKAMET work?

INVOKAMET contains two different medicines, canagliflozin and metformin. They work together to help you better control your blood sugar level.

Canagliflozin is in a class of medicines called sodium-glucose co-transporter 2 (SGLT2) inhibitors. It lowers blood sugar by causing the kidneys to remove more sugar in the urine.

Metformin is in a class of medicines called biguanides. It helps your body respond better to insulin, a natural chemical that manage the amount of sugar in the blood. This lowers the amount of sugar made by the liver and the amount of sugar that moves from the food you eat to the blood.

What are the ingredients in INVOKAMET?

Medicinal ingredients: canagliflozin and metformin hydrochloride

Non-medicinal ingredients: croscarmellose sodium, hypromellose, iron oxide black (150/1000 mg tablets), iron oxide red (50 mg/1000 mg, 150 mg/500 mg and 150 mg/1000 mg tablets), iron oxide yellow (50 mg/1000 mg, and 150 mg/500 mg), macrogol (polyethylene glycol), magnesium stearate, microcrystalline cellulose, polyvinyl alcohol (partially hydrolyzed), talc, and titanium dioxide

INVOKAMET comes in the following dosage forms:

Tablets:

- 50 mg canagliflozin / 500 mg metformin hydrochloride
- 50 mg canagliflozin / 1000 mg metformin hydrochloride
- 150 mg canagliflozin / 500 mg metformin hydrochloride

- 150 mg canagliflozin / 1000 mg metformin hydrochloride

Do not use INVOKAMET if you:

- are allergic to canagliflozin, metformin or any other ingredients in INVOKAMET.
- have severe kidney problems or end-stage kidney disease.
- are on dialysis.
- do not know the health status of your kidneys.
- have or have had a condition called metabolic acidosis (including diabetic ketoacidosis, or lactic acidosis – too much acid in the blood).
- have type 1 diabetes (your body does not produce any insulin).
- drink alcohol very often or drink a lot of alcohol in a short-term “binge” drinking.
- have liver problems.
- have serious heart problems or heart failure.
- have lost a lot of water from your body (seriously dehydrated).
- are in shock.
- are under stress, have a serious infection, have recently had an injury.
- are going to have major surgery or are recovering from surgery.
- are going to have an exam or other tests such as an X-ray or scan with injectable dyes or contrast agents used. You will need to stop taking this medicine around the time of your procedure.
- are pregnant or are planning to become pregnant.
- are breastfeeding.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take INVOKAMET. Talk about any health conditions or problems you may have, including if you:

- **have any of the following conditions:**
 - are malnourished.
 - problems with your adrenal or pituitary glands (adrenal or pituitary insufficiency).
 - low vitamin B₁₂.
 - history of yeast infections of the vagina or penis.
 - current or history of low blood pressure (hypotension).
- are taking any of the medications listed in the drug interactions section below (see **The following may interact with INVOKAMET**).
- **have risk factors for DKA, such as if you:**
 - are dehydrated or suffer from excessive vomiting, diarrhea, or sweating;
 - are on a very low carbohydrate (sugar) diet;
 - have been fasting for a while;
 - are eating less, or there is a change in your diet;
 - drink a lot of alcohol;
 - have or have had problems with your pancreas, including pancreatitis or surgery on your pancreas;
 - are hospitalized for major surgery, or are about to have major surgery;
 - are hospitalized for serious infection or serious medical illnesses;
 - have an acute illness;
 - have sudden reduction in insulin dose;

- have diabetic kidney disease. This is when your kidneys are damaged as a result of your diabetes;
- have a history of DKA.
- **have risk factors for amputation, such as if you:**
 - have a history of amputation
 - have heart disease or are at risk for heart disease
 - have had blocked or narrowed blood vessels, usually in your leg
 - have damage to the nerves (neuropathy) in your leg
 - have had diabetic foot ulcers or sores
 - have a lower limb infection
 - are dehydrated.
- **have risk factors for lactic acidosis, such as if you:**
 - have severe kidney problems.
 - have liver problems.
 - have congestive heart failure that requires treatment with medicines.
 - have a heart attack, severe infection, or stroke.
 - drink a lot of alcohol (very often or short-term “binge” drinking).
 - are dehydrated. Dehydration can also happen when you sweat a lot with activity or exercise and don’t drink enough fluids. Tell your healthcare professional if this happens.
 - have certain x-ray tests with injectable dyes or contrast agents used.
 - have surgery.

Other warnings you should know about:

Vitamin B₁₂ levels

INVOKAMET can cause your vitamin B₁₂ levels to be low. This can cause peripheral neuropathy (nerve damage) or anemia (low red blood cells).

Children and adolescents (under 18 years of age)

INVOKAMET is not recommended for use in patients under 18 years of age.

Adults aged 65 years of age and older

You could have more side effects with INVOKAMET.

Check-ups and testing

You will have regular visits with your healthcare professional before and during treatment with INVOKAMET to monitor your health. They may check:

- your blood sugar levels. INVOKAMET will cause your urine to test positive for sugar.
- that your kidneys are working properly
- blood fat levels
- the amount of red blood cells in your blood; and
- the potassium levels in your blood
- ketone levels in your blood or urine. Ketones are a type of chemical that your liver produces when it breaks down fats for energy
- the levels of lithium in your blood.
- your blood levels of vitamin B₁₂

Broken bones (fracture)

Taking INVOKAMET may increase your risk of breaking a bone. Talk to your doctor about factors that increase the risk for broken bones.

Surgery and illnesses

Tell your healthcare professional if you:

- are going to have a surgery;
- are hospitalized for a serious infection
- have a serious medical illness; or
- had major surgery

Your healthcare professional may stop your INVOKAMET treatment before and after certain types of surgery, or when you are sick or injured.

If INVOKAMET is stopped, your healthcare professional will:

- continue to monitor for signs or symptoms of DKA.
- tell you when to start taking INVOKAMET again.

Driving and using machinery

INVOKAMET may cause dizziness or light-headedness. Do NOT drive or use machines until you know how the medicine affects you.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines

The following may interact with INVOKAMET:

- digoxin, used to treat heart problems.
- furosemide or other diuretics (water pills), used to treat high blood pressure and other heart problems.
- insulin or a sulfonylurea (such as glimepiride, gliclazide, or glyburide), used to help control blood sugar.
- carbamazepine or phenobarbital, used to treat seizures.
- barbiturates, used as sedatives and sleep-aids.
- efavirenz or ritonavir, used to treat HIV infection.
- rifampin, an antibiotic used to treat bacterial infections such as tuberculosis.
- lithium, used to treat bipolar disorder.
- St. John's wort, an herbal product used to treat depression.
- Angiotensin-Converting Enzyme (ACE) inhibitors, Angiotensin Receptor Blockers (ARB) used to treat high blood pressure.
- phenprocoumon and other drugs used prevent blood clots and thin the blood.
- other medicines that can cause high blood sugar, and may lead to a loss of blood sugar control, such as:
 - corticosteroids such as prednisone, used to treat a broad range of diseases
 - isoniazid, used to treat tuberculosis
 - phenothiazines, a group of medicines used to treat mental problems, including schizophrenia
 - thiazide (water pills), used to treat high blood pressure
 - thyroid medicines such as levothyroxine.

- birth control pills and other products containing estrogens
- a group of medicines known as calcium channel blockers, used to treat heart problems such as: nifedipine, amlodipine, felodipine, verapamil, diltiazem
- medicine used to treat epilepsy (seizures) such as phenytoin
- nicotinic acid, used to prevent and treat niacin deficiency
- bronchodilators (known as beta-2-agonists) medicines that make breathing easier, used to treat asthma like salbutamol or formoterol.
- alcohol.

How to take INVOKAMET:

- Take INVOKAMET exactly as your healthcare professional tells you. Check with your healthcare professional if you are not sure.
- Take twice per day with food. This is to reduce your chance of having an upset stomach.
- Swallow the tablet(s) whole.
- Continue taking INVOKAMET for as long as your healthcare professional tells you to.

Your healthcare professional may prescribe INVOKAMET alone or together with another medicine to help control your blood sugar.

Usual dose:

Your healthcare professional will decide the best dose that is right for you.

Overdose:

If you think you, or a person you are caring for, have taken too much INVOKAMET, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed dose:

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

What are possible side effects from using INVOKAMET?

These are not all the possible side effects you may feel when taking INVOKAMET. If you experience any side effects not listed here, contact your healthcare professional.

Side effects may include:

- Changes in taste or a metallic taste
- Changes in urination:
 - urinating more often or in larger amounts
 - an urgent need to urinate
 - a need to urinate at night
- Constipation, excess gas, abdominal discomfort
- Fatigue

- Feeling thirsty
- Headache
- Low vitamin B₁₂ (vitamin B₁₂ deficiency)
- Nausea, vomiting, diarrhea, indigestion, loss of appetite
- Rash, hives

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
VERY COMMON			
Vaginal yeast infection: vaginal odor, white or yellowish vaginal discharge, and/or itching		✓	
COMMON			
Balanitis (yeast infection of the penis): rash or redness of the penis or foreskin		✓	
Bone fracture (broken bone)		✓	
Skin ulcer (a break or sore on the skin with tissue breakdown) predominantly of the lower legs: It may start off red then get swollen and tender. Next, blisters can form with loss of skin layers. It can lead to an open round crater with a bad smell. Ulcers take a long time or may not heal.		✓	
Urinary tract infection: burning sensation when urinating, cloudy or bloody urine, strong odor		✓	
UNCOMMON			
Dehydration (not having enough water in your body): dry or sticky mouth, headache, dizziness or urinating less often than normal		✓	
Hypotension (low blood pressure): fainting, dizziness or light-headedness with standing		✓	
Kidney problems: any change in the amount, frequency or colour (pale or dark) of urine		✓	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Peripheral ischemia (blocked or narrow blood vessels): Leg pain with walking that gets better with rest. Poor circulation, bluish, cold skin, and poor nail and hair growth. It can lead to Skin Ulcers and Lower Leg or Toe Amputation .		✓	
RARE			
Acute kidney infection: painful, urgent or frequent urination, lower back (flank) pain, fever or chills, cloudy or foul smelling urine, blood in your urine			✓
Angioedema (swelling in deep layers of skin) and anaphylactic reaction (severe allergic reactions): rash, hives, swelling of the face, eyes, lips or throat, difficulty swallowing or breathing, wheezing, fever, stomach cramps, chest discomfort or tightness, unconsciousness			✓
Diabetic ketoacidosis (when your body produces high levels of blood acids called ketones): difficulty breathing, feeling very thirsty, vomiting, stomach pain, nausea, loss of appetite, confusion, and unusual tiredness, a sweet smell to the breath, a sweet or metallic taste in the mouth or a different odour to urine or sweat			✓

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Encephalopathy (disease of the brain that severely alters thinking): Possible neurological symptoms include: muscle weakness in one area, poor decision-making or concentration, involuntary twitching, trembling, difficulty speaking or swallowing, seizures.			✓
Fournier's gangrene (a serious infection affecting soft tissue around the groin): pain or tenderness, redness of the skin, or swelling in the genital or perineal area, with or without fever or feeling very weak, tired, or uncomfortable			✓
Hemolytic anemia (breakdown of red blood cells): symptoms may include fatigue, pale color, rapid heartbeat, shortness of breath, dark urine, chills, and backache.			✓
Severe hypoglycemia (severe low blood sugar): disorientation, loss of consciousness, seizure			✓
Lactic acidosis (a build-up of lactic acid in your blood): feeling cold or uncomfortable, severe nausea with or without vomiting, stomach pain, unexplained weight loss, rapid breathing			✓

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Peripheral neuropathy (a result of damage to your peripheral nerves): signs and symptoms might include gradual onset of numbness, prickling or tingling in your feet or hands, which can spread upward into your legs and arms, sharp, jabbing, throbbing, freezing or burning pain, extreme sensitivity to touch, lack of coordination and falling, muscle weakness or paralysis if motor nerves are affected.			✓
Urosepsis (severe infection that spreads from the urinary tract and throughout body): fever or low body temperature, rapid breathing, chills, rapid heartbeat, pain with urination, difficulty urinating, frequent urination			✓
VERY RARE			
Liver problems: yellowing of the skin or eyes, dark urine, abdominal pain, nausea, vomiting, loss of appetite		✓	
Pancreatitis (inflammation of the pancreas): severe stomach pain that lasts and gets worse when you lie down, nausea, vomiting		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Store INVOKAMET in the original container.
- Store at room temperature (15-30°C).
- Keep out of reach and sight of children.

Do not use INVOKAMET after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.

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.

If you want more information about INVOKAMET:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website www.janssen.com/canada or call 1-800-567-3331 or 1-800-387-8781.

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