

**READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE
PATIENT MEDICATION INFORMATION**

**PrINVOKAMET®
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 metformin and it can rarely cause a serious condition that can cause death called lactic acidosis.
- Alcohol may increase the risk of lactic acidosis. Do not drink a lot of alcohol while taking INVOKAMET®.

Diabetic Ketoacidosis (DKA)

- Diabetic ketoacidosis (DKA) is a serious and life-threatening condition that requires urgent hospitalization. DKA has been reported in patients with type 2 diabetes mellitus (T2DM) with normal or high blood sugar levels, who are treated with canagliflozin or with other sodium-glucose co-transporter 2 (SGLT2) inhibitors. Some cases of DKA have led to death.
- 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.
- INVOKAMET® should not be used in patients with type 1 diabetes
- INVOKAMET® should not be used in patients with DKA or a history of DKA

Lower Limb Amputation

- INVOKAMET® may increase your risk of lower limb amputations. Amputations mainly involve removal of 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.
- Seek medical attention if you have new pain or tenderness, any sores, ulcers, or infections in your leg or foot. Your doctor may decide to stop your INVOKAMET® if you have any of these signs or symptoms. Talk to your doctor 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 who are not controlled on metformin alone or on a combination of metformin with:
 - a sulfonylurea
 - pioglitazone
 - insulin

- in patients who are currently treated with combinations of separate tablets of metformin and canagliflozin (INVOKANA®), or a combination of metformin and canagliflozin (INVOKANA®) with:
 - a sulfonylurea
 - pioglitazone
 - insulin

How does INVOKAMET® work?

INVOKAMET® is a tablet containing two different medicines, canagliflozin and metformin.

Canagliflozin removes excess glucose from the body through the urine.

Metformin helps your body respond better to the insulin it makes naturally. It helps to lower the amount of sugar made by the liver and lower the amount of sugar moved from the gut into the blood.

What are the ingredients in INVOKAMET®?

Medicinal ingredients: anhydrous 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 of the nonmedicinal ingredients in INVOKAMET®.
- have kidney problems.
- have or have had a condition called metabolic acidosis, lactic acidosis or diabetic ketoacidosis (a complication of diabetes with high blood sugar, rapid weight loss, nausea, or vomiting). INVOKAMET® should not be used to treat these conditions.
- have type 1 diabetes (your body does not produce any insulin). INVOKAMET® is not recommended for use in patients with type 1 diabetes.
- drink alcohol very often or drink a lot of alcohol in a short-term “binge” drinking.
- have liver problems.
- have severe heart problems or heart failure.
- are under stress, have a serious infection, have recently had a trauma, are about to have surgery or are recovering from surgery.
- are severely dehydrated.
- need to have major surgery or if you need an examination such as an X-ray or scan involving injection of dye or contrast agents into your bloodstream. INVOKAMET® will need to be stopped for a short time. Talk to your healthcare professional about when you should stop INVOKAMET® and when you should start INVOKAMET® again.
- are pregnant or are planning to become pregnant. INVOKAMET® should not be used during pregnancy.
- are breastfeeding. INVOKAMET® should not be used while 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 an increased chance of developing DKA, including if you:
 - are dehydrated or suffer from excessive vomiting, diarrhea, or sweating;
 - are on a very low carbohydrate diet;
 - have been fasting for a while;
 - are eating less, or there is a change in your diet;
 - drink a lot of alcohol;
 - have/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 an increased chance of needing an amputation, including 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
- if you have or have had low pressure (hypotension) or are taking medicines to:
 - remove excess water from your body. These are called diuretics or water pills. An example is furosemide.
 - lower your blood pressure. Examples are angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB).

Taking INVOKAMET[®] with any of these medicines may increase your risk for dehydration and/or low blood pressure.

- are older than 65 years of age.
- are malnourished or have problems with your adrenal or pituitary glands (adrenal or pituitary insufficiency).
- have low B₁₂.
- have a history of yeast infections of the vagina or penis.
- are taking medicines to lower your blood sugar such as glyburide, gliclazide or glimepiride (sulfonylureas) or insulin. Taking INVOKAMET[®] with any of these medicines can increase the risk of having low blood sugar (hypoglycemia). Take precautions to avoid the potential for low blood sugar while driving or using heavy machinery.
- are taking medicines used to treat pain and reduce inflammation and fever known as NSAIDs (nonsteroidal anti-inflammatory drugs). Taking INVOKAMET[®] with these medicines can increase the risk for kidney problems.

Other warnings you should know about:

Stop taking INVOKAMET[®] and tell your healthcare professional if you get the following symptoms of lactic acidosis:

- You feel very weak and tired.
- You have unusual (not normal) muscle pain.
- You have trouble breathing or fast breathing.
- You have stomach pain with nausea and vomiting, or diarrhea.
- You feel cold, especially in your arms and legs.
- You feel dizzy or lightheaded.
- You feel unusual fatigue and drowsiness.
- You have a slow or irregular heartbeat.
- Your medical condition suddenly changes.
- You develop or experience a worsening of heart problems and particularly heart failure.

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

INVOKAMET[®] will cause your urine to test positive for sugar (glucose).

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

While taking INVOKAMET[®] your healthcare professional may order blood tests to check your kidney function, blood fat levels (Low-Density Lipoprotein cholesterol or LDL-C), the amount of red blood cells in your blood (haematocrit), and potassium blood levels.

INVOKAMET[®] may cause necrotizing fasciitis of the perineum (area between and around the anus and genitals). This is a rare but serious and potentially life-threatening infection that can affect both men and women. It is also known as Fournier's gangrene and requires urgent treatment. If you experience tenderness, redness, or swelling of the genitals or the area from the genitals back to the rectum, especially if you also have fever or are feeling very weak, tired, or uncomfortable, seek medical attention immediately. These may be signs of Fournier's gangrene.

Your doctor may stop your INVOKAMET[®] if you:

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

Talk to your doctor about when to stop taking INVOKAMET[®] and when to start it again. Your doctor will check for ketones in your blood or urine.

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, phenytoin or phenobarbital, used to treat seizures.
- barbituates, 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.
- St. John's wort, an herbal product used to treat depression.
- nifedipine, a Calcium Channel Blocker used to treat heart problems.
- 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.
- Birth control pills and other products containing estrogens.

- Alcohol.

How to take INVOKAMET®:

- Take the dose prescribed for you by your healthcare professional. Your healthcare professional will prescribe the strength that is right for you.
- Take INVOKAMET® twice a day with meals to lower your chance of having an upset stomach. Swallow the tablet whole.
- Your healthcare professional may prescribe INVOKAMET® together with another medicine to help control your blood sugar.
- Always take INVOKAMET® and all other medicines prescribed to you exactly as your healthcare professional has told you. Check with your doctor or pharmacist if you are not sure.
- Before starting INVOKAMET®, your doctor will do tests to see how well your kidneys are working.

Overdose:

If you think you have taken too much INVOKAMET®, contact your 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 urination:
 - urinating more often or in larger amounts
 - an urgent need to urinate
 - a need to urinate at night
- Constipation, excess gas, abdominal discomfort
- Nausea, vomiting, diarrhea, indigestion, loss of appetite
- Changes in taste or a metallic taste
- Feeling thirsty
- Rash, hives
- Headache
- Fatigue

Diabetic Ketoacidosis (DKA) is a serious, life-threatening medical condition that may lead to death. DKA can occur with normal or high blood glucose levels. DKA has happened in people with diabetes who were sick or who had surgery, during treatment with INVOKAMET®. DKA requires immediate treatment in a hospital. DKA can happen with INVOKAMET® even if your blood sugar is at normal or near normal levels. **Stop taking INVOKAMET® immediately and get** medical help right away if you have any of the symptoms in the table below under DKA, even if your blood glucose levels are normal.

Tell your doctor if you are hospitalized for major surgery, serious infection or serious medical illness.

Increased need for lower leg or toe amputation (removal) especially if you are at high risk of heart disease. Talk to your doctor if you experience symptoms including leg pain, poor circulation, bluish, cold skin, and poor hair and toe nail growth. Good foot care and adequate amount of fluid are recommended.

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.

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)		✓	
Urinary tract infection: burning sensation when urinating, cloudy or bloody urine, strong odor		✓	

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	
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.		✓	
UNCOMMON 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.		✓	
Hypotension (low blood pressure): fainting, dizziness or light-headedness with standing		✓	
Dehydration (not having enough water in your body): dry or sticky mouth, headache, dizziness or urinating less often than normal		✓	
Kidney problems: any change in the amount, frequency or colour (pale or dark) of urine		✓	
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			✓

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	
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			✓
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			✓
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			✓
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			✓

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	
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			✓
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		✓	

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/adverse-reaction-reporting.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 healthcare 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).
- 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.

- Keep out of reach and sight of children.

If you want more information about INVOKAMET®:

- Talk to your healthcare professional
- For questions or concerns, or the product monograph go to www.janssen.com/canada or call 1-800-567-3331 or 1-800-387-8781.

This leaflet was prepared by: JANSSEN Inc., Toronto, Ontario, M3C 1L9

Last Revised: September 2, 2022

All trademarks used under license.