

PART III: PATIENT MEDICATION INFORMATION**Pr PRO-METFORMIN****Metformin Hydrochloride Tablets, BP**

This leaflet is part III of a three-part "Product Monograph" published when PRO-METFORMIN was approved for sale in Canada and is designed specifically for Consumers. Read this leaflet carefully before you start taking PRO-METFORMIN 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 PRO-METFORMIN.

ABOUT THIS MEDICATION**What is PRO-METFORMIN used for?**

PRO-METFORMIN (metformin hydrochloride) is used, in addition to proper diet, exercise and weight reduction, to improve blood sugar levels in adults with type 2 diabetes mellitus.

How does PRO-METFORMIN work?

People with type 2 diabetes mellitus are not able to make enough insulin or respond normally to the insulin their bodies make. When this happens, sugar (glucose) builds up in the blood. This can lead to serious medical problems including kidney damage, amputations, and blindness. Diabetes is also closely linked to heart disease. The main goal of treating diabetes is to lower your blood sugar to a normal level.

High blood sugar can be lowered by diet and exercise, by a number of medicines taken by mouth, and by insulin shots. While you take your diabetes medicine, continue to exercise and follow the diet advised by your doctor for your diabetes.

No matter what your recommended diabetes management plan is, studies have shown that maintaining good blood sugar control can prevent or delay complications of diabetes, such as blindness.

PRO-METFORMIN helps to control your blood sugar.

Although the mode of action of PRO-METFORMIN is not fully understood, it is believed to help your body respond better to the insulin it makes naturally by:

- decreasing the amount of sugar your liver makes, and
- decreasing the amount of sugar your intestines absorb.

What are the ingredients in PRO-METFORMIN?**Medicinal ingredient**

Metformin hydrochloride.

Non-medicinal ingredients

Colloidal Silicon Dioxide, Croscarmellose Sodium, Hydroxypropyl Methylcellulose, Magnesium Stearate, Microcrystalline Cellulose, Polyethylene Glycol, Povidone and Pregelatinized Starch.

PRO-METFORMIN comes in the following dosage forms:

Tablets (film coated): 500 mg and 850 mg for oral administration.

Do not use PRO-METFORMIN if:

- You have unstable and/or insulin-dependent (Type I) diabetes mellitus.
- You have metabolic acidosis (including diabetic ketoacidosis, with or without coma, history of ketoacidosis with or without coma).
- You have a history of lactic acidosis (too much acid in the blood).
- You drink a lot of alcohol (regularly drink alcohol or sometimes drink a lot of alcohol, binge drinking).
- You have liver or kidney problems (severe liver dysfunction or liver disease, or kidney disease or impairment).
- You are going to have an x-ray procedure with injection of dyes (iodinated contrast materials).
- You are stressed, have a severe infection, or are experiencing trauma.
- Before surgery and during your recovery after your surgery.
- You suffer from severe dehydration (have lost a lot of water from your body).
- You are hypersensitive (have a high blood pressure) or allergic to metformin hydrochloride or any ingredient in the formulation or component of the container.
- You are pregnant or planning to become pregnant.
- You are breastfeeding (nursing a child).
- You have cardiovascular collapse (abrupt failure of blood circulation) or a disease that can cause hypoxemia (low oxygen in the blood) such as cardiorespiratory insufficiency.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

- PRO-METFORMIN may rarely cause a serious, life-threatening condition called lactic acidosis (see Lactic Acidosis section below).
- You should not drink a lot of alcohol if you take PRO-METFORMIN (see Lactic Acidosis section below).

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

Lactic Acidosis

PRO-METFORMIN may rarely cause a serious, life-threatening condition called lactic acidosis.

You should not take PRO-METFORMIN due to greater risk for lactic acidosis if you:

- have kidney problems or a history of kidney disease.
- are 80 years of age or older and you have NOT had your kidney function tested.
- are seriously dehydrated (have lost a lot of water from your body).
- have liver disease.
- have metabolic acidosis (e.g., diabetic ketoacidosis).
- drink a lot of alcohol (regularly drink alcohol or sometimes drink a lot of alcohol, binge drinking).
- have an x-ray procedure with injection of dyes (contrast agents).
- before surgery and during the recovery phase thereafter.
- develop a serious medical condition, such as heart attack, severe infection, or a stroke.

Due to greater risk for lactic acidosis, you should talk to your doctor if you take PRO-METFORMIN and if you:

- develop or experience a worsening of heart disease and particularly heart failure.

Signs and symptoms of lactic acidosis include: discomfort, muscle pain, difficult or fast breathing, extreme tiredness, weakness, upset stomach, stomach pain, feeling cold, low blood pressure or slow heartbeat.

If any of the above side effects occur, consult your doctor immediately.

Other warnings you should know about:

You should tell your doctor if you have any other medical condition, including: Vitamin B₁₂ deficiency or anemia, excessive alcohol use, allergies, or hypothyroidism (low levels of thyroid hormones).

Do not drive or operate machines if you develop hypoglycemia (low blood sugar levels).

Do not start or stop any medicine without the approval of your healthcare professional.

INTERACTIONS WITH THIS MEDICATION

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

The following drugs may interact with PRO-METFORMIN and require careful monitoring of your dose or condition:

- Other diabetes drugs such as glyburide
- Furosemide (diuretic [water pills]), used for oedema [fluid retention], and high blood pressure)
- Nifedipine (calcium-channel blocker used for high blood pressure; angina; Raynaud's phenomenon)

- Cationic drugs (e.g., amiloride, digoxin, morphine, procainamide, quinidine, quinine, ranitidine, triamterene, trimethoprim, and vancomycin)
- Certain “blood thinners” (phenprocoumon or other antivitamin K anticoagulants)
- Diuretics (water pills), especially loop diuretics, that may increase the risk of lactic acidosis (too much acid in the blood) due to their potential to decrease renal function
- Drugs that tend to produce hyperglycemia (high blood sugar) and may lead to a loss of blood sugar control. Some example of drugs that can increase the blood sugar include:
 - Thiazide and other diuretics (water pills)
 - Corticosteroids (such as prednisone)
 - Phenothiazines (antipsychotic medicine)
 - Thyroid hormone replacement drugs (e.g., Levothyroxine)
 - Estrogens or estrogens plus progestogen (female hormones)
 - Oral contraceptives
 - Phenytoin (medicine used to treat epilepsy)
 - Nicotinic Acid (medicine used to prevent and treat niacin deficiency)
 - Sympathomimetics
 - Calcium channel-blocking drugs (such as nifedipine, amlodipine, felodipine, verapamil, diltiazem)
 - Isoniazid (medicine used to treat active tuberculosis infections)
 - Medicines for asthma such as salbutamol or formoterol (Beta-2-agonists)
- ACE inhibitors (drugs used to treat hypertension [high blood pressure]) may lower blood glucose and the combination with metformin hydrochloride should be carefully monitored.

Before using any drugs or herbal products, consult your healthcare professional.

PROPER USE OF THIS MEDICATION

How to take PRO-METFORMIN:

PRO-METFORMIN tablets are to be taken orally (by mouth).

Usual dose:

Your doctor will tell you how much medicine to take and when to take it. Follow the directions provided by your doctor for using this medicine. Taking this medicine with food will decrease symptoms such as nausea and vomiting.

Overdose:

In general, an overdose may lead to increased symptoms as described under “SIDE EFFECTS AND WHAT TO DO ABOUT THEM”, including stomach discomfort, nausea, vomiting, diarrhea, drowsiness, weakness, dizziness, malaise and headache.

A serious, life-threatening condition called lactic acidosis may also occur (see WARNINGS AND PRECAUTIONS, Lactic Acidosis).

If you think you have taken too much PRO-METFORMIN, immediately see your doctor, contact your regional Poison Control Centre or go to the nearest hospital emergency department. Do this even if there is no signs of discomfort or poisoning.

Missed Dose:

If you forget to take PRO-METFORMIN tablets, do not take a double dose to make up for forgotten individual doses. Take the next dose at the usual time.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

What are possible side effects from using PRO-METFORMIN?

The side effects described below are not all the possible side effects you may feel when taking PRO-METFORMIN. If you experience any side effects not listed here, contact your healthcare professional. Please also see Warnings and Precautions.

Common side effects of PRO-METFORMIN include:

- diarrhea
- nausea
- upset stomach
- abdominal bloating
- gas
- loss of appetite

These side effects generally go away after you take the medicine for a while. Taking your medicine with meals can help reduce these side effects. Tell your doctor if the side effects bother you a lot, last for more than a few weeks, come back after they've gone away, or start later in treatment. You may need a lower dose of PRO-METFORMIN or need to stop taking the medicine for a short period or for good.

After you are on the same dose of PRO-METFORMIN for several days or weeks, if any of these side effects come back, tell your doctor immediately. A late reappearance of stomach symptoms may be due to a serious medical condition (lactic acidosis).

PRO-METFORMIN rarely causes hypoglycemia (low blood sugar) by itself; however, hypoglycemia can happen if you do not eat enough, if you drink alcohol, or if you take other medicines to lower blood sugar.

Lactic Acidosis

In rare cases, PRO-METFORMIN can cause a serious side effect called lactic acidosis. This is caused by a buildup of lactic acid in your blood. This build-up can cause serious damage.

Lactic acidosis caused by PRO-METFORMIN is rare and has occurred mostly in people whose kidneys were not working normally. Although rare, if lactic acidosis does occur, it can be fatal in up to half of the people who develop it.

It is also important for your liver to be working normally when you take PRO-METFORMIN. Your liver helps remove lactic acid from your blood.

Make sure you tell your doctor before you use PRO-METFORMIN if you have kidney or liver problems.

Your skin may be more sensitive to sunlight when you take PRO-METFORMIN. Protect your skin from the sun.

You should also **stop using PRO-METFORMIN and call your doctor right away if you have signs of lactic acidosis. Lactic acidosis is a medical emergency that must be treated in a hospital.**

If your medical condition suddenly changes, stop taking PRO-METFORMIN and call your doctor right away. This may be a sign of lactic acidosis or another serious side effect.

SERIOUS SIDE EFFECTS AND WHAT TO DO ABOUT THEM	
Symptom/effect	Stop taking drug and get immediate help
<u>UNCOMMON</u>	
Feeling very weak, tired or uncomfortable	✓
Unusual muscle pain	✓
Trouble breathing	✓
Unusual or unexpected stomach discomfort	✓
Feeling cold	✓
Feeling dizzy or lightheaded	✓
Suddenly developing a slow or irregular heartbeat	✓
<u>RARE</u>	
<p>Lactic Acidosis (a build up of lactic acid in the blood) that can cause death or cardiovascular mortality</p> <p>Symptoms include:</p> <ul style="list-style-type: none"> • Feeling very weak, tired, or uncomfortable • Unusual muscle pain • Trouble breathing • Unusual or unexpected stomach discomfort • Stomach pain with nausea and vomiting, or diarrhea • Feeling cold • Feeling dizzy or lightheaded • Suddenly developing a slow or irregular heartbeat 	✓
Pancreatitis (inflammation of the pancreas): prolonged severe abdominal pain which may be accompanied by vomiting; pain may spread out towards the back.	✓

SERIOUS SIDE EFFECTS AND WHAT TO DO ABOUT THEM	
Symptom/effect	Stop taking drug and get immediate help
Hemolytic anemia (when red blood cells are destroyed faster than bone marrow can replace them): symptoms may include fatigue, pale color, rapid heartbeat, shortness of breath, dark urine, chills, and backache.	✓
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.	✓
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.	✓

This is not a complete list of side effects. For any unexpected effects while taking PRO-METFORMIN, contact your healthcare professional. 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/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 health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

HOW TO STORE IT

Store between 15°C and 30°C.

Throw away any medication that is outdated or no longer needed. Talk to your pharmacist about the proper disposal of your medication.

Keep out of reach and sight of children.

MORE INFORMATION

If you want more information about PRO-METFORMIN:

- 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>) or by calling Pro Doc Ltée at 1-800-361-8559, www.prodoc.qc.ca or infoprodoc@prodoc.qc.ca.

This leaflet was prepared by:
Pro Doc Ltée
Laval, Québec
H7L 3W9

Last Revised: March 4, 2019