

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PRO-RIVAROXABAN

Rivaroxaban Tablets

Read this carefully before you start taking **PRO-RIVAROXABAN** 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-RIVAROXABAN**.

What is PRO-RIVAROXABAN used for?

PRO-RIVAROXABAN 10 mg, 15 mg and 20 mg tablets are used in adults to:

- prevent blood clots after major hip or knee surgery
- treat and prevent blood clots in the veins of the legs, arms or lungs
- prevent blood clots in the brain (stroke) and other blood vessels in the body of patients who have atrial fibrillation (irregular heart rhythm)

PRO-RIVAROXABAN 2.5 mg tablets are used in combination with acetylsalicylic acid (ASA) in adults to:

- prevent stroke, heart attack or severe leg or arm pain in patients with peripheral artery disease who are at high risk. This is a condition where the blood vessels that carry blood away from the heart to other parts of the body (arteries) are narrowing due to plaque buildup.
- prevent stroke, heart attack, severe leg or arm pain, or death in patients with coronary heart disease. This is a condition where the blood vessels supplying blood to the heart (coronary arteries) become narrow or blocked due to plaque buildup. This causes a lack of oxygen in the heart. These patients may also have peripheral artery disease.

PRO-RIVAROXABAN 15 mg and 20 mg tablets are used to treat and prevent blood clots in the veins of the arms or legs, or in the blood vessels of the lungs in:

- children and adolescents below 18 years of age who weigh from 30 kg to 50 kg (15 mg tablets)
- children and adolescents below 18 years of age who weigh more than 50 kg (20 mg tablets)

PRO-RIVAROXABAN will be given to your child once they complete at least 5 days of treatment with an injectable blood thinner.

How does PRO-RIVAROXABAN work?

PRO-RIVAROXABAN belongs to a group of medicines called anticoagulants (blood thinners). It helps prevent blood clots from forming by directly blocking the activity of a clotting factor called Factor-Xa.

What are the ingredients in PRO-RIVAROXABAN?

Medicinal ingredient: rivaroxaban

Non-medicinal ingredients: Microcrystalline Cellulose, Colloidal Silicon Dioxide, Croscarmellose Sodium, Hydroxypropyl Cellulose, Lactose Monohydrate, Magnesium Stearate, Sodium Lauryl Sulphate. The film-coating contains: FD & C Yellow #5 (for the 2.5 mg), Hypromellose, Iron Oxide Red (for the 10 mg, 15 mg and 20 mg), Iron Oxide Yellow (for the 2.5 mg), Polyethylene Glycol, Titanium Dioxide.

PRO-RIVAROXABAN comes in the following dosage forms:

Film-coated tablets: 2.5 mg, 10 mg, 15 mg and 20 mg.

Do not use PRO-RIVAROXABAN if you or the child:

- are allergic to rivaroxaban or to any other ingredients in PRO-RIVAROXABAN. PRO-RIVAROXABAN tablets contain lactose.
- are actively bleeding, especially if you are excessively bleeding
- have any injuries or conditions that may increase your risk of bleeding. This includes:
 - active or recent bleeding in the brain
 - active or recent bleeding in the stomach or gut
 - have difficulties to stop bleeding (bleeding disorder)
- take medicines to treat HIV/AIDS, such as cobicistat and ritonavir
- take medicines to treat fungal infections, such as ketoconazole, itraconazole and posaconazole
- take dronedarone, a medicine used to control an abnormal heart rhythm called atrial fibrillation
- take any other medicines used to prevent or treat blood clots. This includes:
 - warfarin, dabigatran, apixaban, edoxaban, heparin
 - low molecular weight heparin (LMWH), such as enoxaparin and dalteparin
 - heparin derivatives, such as fondaparinux
- have severe liver disease, which can lead to an increased risk of bleeding
- are pregnant, think you might be pregnant or plan on becoming pregnant
- are breastfeeding

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

- have an increased risk of bleeding. This includes if you:
 - have severe kidney problems or reduced kidney function
 - are taking Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), which are used to relieve pain and reduce inflammation, such as ibuprofen, naproxen and celecoxib
 - are taking acetylsalicylic acid (ASA, or ASPIRIN) or any other medicines used to prevent stroke or heart disease, such as clopidogrel, prasugrel and ticagrelor
 - are taking medicines to treat depression or other psychological conditions
 - have low levels of platelets in the blood or your platelets do not work properly
 - have very high blood pressure, not controlled by medical treatment
 - have or have had an ulcer in the stomach or bowel
 - have a problem with the blood vessels in the back of the eyes (retinopathy)
 - have problems with the blood vessels in the brain or spinal column
 - had surgery on the brain, spinal column or eyes
 - have bronchiectasis, which is a chronic disease where the bronchial tubes of the lungs become damaged, widened, and thickened
 - have a history of bleeding into the lungs
 - are older than 75 years of age
 - have been diagnosed with cancer, had a relapse of cancer or have been treated for cancer in the last 6 months
 - have liver problems

- are having surgery for any reason, including an operation that involves a catheter or injection into the spinal column (e.g. for epidural or spinal anesthesia or pain reduction)
- have damaged heart valves or heart valve disease
- have a prosthetic heart valve
- have antiphospholipid syndrome, also known as Hughes syndrome. This is a disorder of the immune system that causes an increased risk of blood clots.
- have a stent, which is a small metal coil inserted into a blocked blood vessel to restore blood flow by keeping it open
- have a history of stroke, with or without bleeding in the brain
- are taking rifampicin, a medicine used to treat bacterial infections, including tuberculosis
- are taking medicines used to prevent epilepsy or seizures, such as phenytoin, carbamazepine and phenobarbital
- are lactose intolerant. PRO-RIVAROXABAN tablets contain lactose.

Other warnings you should know about:

Do not stop taking or giving PRO-RIVAROXABAN to your child without first talking to your healthcare professional. If you or your child stop taking PRO-RIVAROXABAN, blood clots may form and cause a stroke, heart attack, or other serious complications. This can lead to severe disability or even death.

Risk of Bleeding: As with other blood thinners, taking PRO-RIVAROXABAN may increase the risk of bleeding from any part of the body, including internal organs. It may be serious or even life-threatening. Tell your healthcare professional **right away** if you or your child have any unusual bleeding or bruising. For examples of bleeding, see the **Serious side effects and what to do about them** table below.

Spinal or epidural blood clots (hematoma): People who take PRO-RIVAROXABAN and have medicine injected into their spinal or epidural area, or have a spinal puncture, have a risk of forming a spinal or epidural blood clot. This can cause long-term or permanent loss of the ability to move (paralysis). The risk of developing a spinal or epidural blood clot is higher if:

- A thin tube called an epidural catheter is placed in your/your child's back to give certain medicines
- You/your child take NSAIDs or a medicine to prevent blood from clotting
- You/your child have a history of difficult or repeated epidural or spinal punctures
- You/your child have a history of problems with the spinal column or have had surgery on the spinal column

If you or your child take PRO-RIVAROXABAN and receive spinal anesthesia or have a spinal puncture, your healthcare professional will watch you or your child closely for symptoms of spinal or epidural blood clots.

Tell your healthcare professional **right away** if you/your child develops the following symptoms after an epidural or a spinal procedure:

- back pain
- tingling
- numbness
- muscle weakness (especially in your legs and feet)
- or loss of control of the bowels or bladder (incontinence)

Surgery:

- Tell your healthcare professional if you or your child are going to have any surgeries, including dental procedures, while taking PRO-RIVAROXABAN. There is an increased risk of bleeding if you or your child take PRO-RIVAROXABAN during these procedures. It can be life-threatening.
- Your healthcare professional may ask you or your child to stop taking PRO-RIVAROXABAN before the surgery, and to resume taking PRO-RIVAROXABAN after the procedure. It is important that you or your child take PRO-RIVAROXABAN before and after the procedure exactly at the times the healthcare professional has instructed.

Anticoagulant-Related Nephropathy (ARN):

Some cases were reported in patients taking rivaroxaban. It is a type of serious kidney damage caused by anticoagulant medicines. ARN causes bleeding in the kidneys, sometimes with the presence of blood in the urine. This leads to the kidneys being unable to function properly. Your healthcare professional may monitor the health of your kidneys during your treatment with PRO-RIVAROXABAN. If you are experiencing symptoms of ARN during your treatment, tell your healthcare professional right away.

Children and adolescents:

- PRO-RIVAROXABAN 2.5 mg and 10 mg tablets are not to be used in children and adolescents under 18 years of age.
- PRO-RIVAROXABAN should **not** be used in children and adolescent under 18 years of age for any conditions other than the treatment and prevention of blood clots in the veins of the legs or arms, or blood vessels in the lungs.

Pregnancy:

- PRO-RIVAROXABAN should **not** be used during pregnancy. Taking it during pregnancy may harm an unborn baby.
- Your healthcare professional may ask you or your child (depending on their age), to use a highly effective birth control method while taking PRO-RIVAROXABAN.
- If you or your child discover that you/they are pregnant while taking PRO-RIVAROXABAN, contact your healthcare professional **as soon as possible**.

Breastfeeding: PRO-RIVAROXABAN should **not** be used while breastfeeding. It may pass into breast milk and harm a breastfed baby. PRO-RIVAROXABAN will only be given to you/your child once you/they have stopped breastfeeding.

Check-ups and testing: Your healthcare professional may:

- evaluate your/your child's risk of bleeding before starting PRO-RIVAROXABAN and regularly during treatment. This includes performing blood tests to check the amount of red blood cells in the blood, and monitoring blood pressure.
- do blood tests before you/your child start taking PRO-RIVAROXABAN and during treatment to check if your/your child's kidneys are working properly

Depending on the test results, your healthcare professional may discontinue your/your child's treatment with PRO-RIVAROXABAN.

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 PRO-RIVAROXABAN:

- Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), which are used to relieve pain and reduce inflammation, such as ibuprofen, naproxen and celecoxib
- Acetylsalicylic acid (ASA, or ASPIRIN), used to relieve fever and pain
- Medicines used to prevent stroke or heart disease, such as clopidogrel, prasugrel and ticagrelor
- Medicines used to prevent or treat blood clots. This includes:
 - warfarin, dabigatran, apixaban, edoxaban, heparin
 - low molecular weight heparin (LMWH), such as enoxaparin and dalteparin
 - heparin derivatives, such as fondaparinux
- Medicines used to treat HIV/AIDS, such as cobicistat and ritonavir
- Medicines used to treat fungal infections, such as ketoconazole, itraconazole and posaconazole
- Dronedarone, a medicine used to control an abnormal heart rhythm called atrial fibrillation
- Medicines used to treat bacterial infections, such as clarithromycin and rifampicin
- Medicines used to control epilepsy or seizures, such as phenytoin, carbamazepine and phenobarbital
- Medicines used to treat depression or other psychological conditions, such as Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)
- St. John's Wort (also known as *Hypericum perforatum*), a herbal remedy used to treat depression

PRO-RIVAROXABAN 2.5 mg tablets are prescribed with acetylsalicylic acid (ASA). Ask your healthcare professional first before taking any other NSAIDs. They will determine if it is beneficial for you to take it during your treatment with PRO-RIVAROXABAN and ASA.

How to take PRO-RIVAROXABAN:

- Take or give your child:
 - PRO-RIVAROXABAN tablets exactly as your healthcare professional tells you
 - PRO-RIVAROXABAN tablets at the same time every day to help you remember it
 - PRO-RIVAROXABAN 2.5 mg and 10 mg tablets with or without food
 - PRO-RIVAROXABAN 15 mg and 20 mg tablets **with** food
- Swallow tablet whole, preferably with water. Do **not** split tablets.
- Tell your child's healthcare professional if your child has trouble swallowing PRO-RIVAROXABAN tablets. They may prescribe your child another rivaroxaban product.
- PRO-RIVAROXABAN tablets may be crushed and mixed with apple sauce. Take the applesauce mixture right away after you have mixed it. A crushed 2.5 mg or 10 mg tablet can be taken with or without food. Eat food right after taking a crushed 15 mg or 20 mg tablet. The healthcare professional may give you or the child the crushed PRO-RIVAROXABAN tablet also via a tube.
- It is not recommended to crush and mix a 2.5 mg PRO-RIVAROXABAN tablet and an acetylsalicylic acid (ASA, or ASPIRIN) tablet together with applesauce.
- Do **not** stop taking or giving PRO-RIVAROXABAN to your child without talking to the healthcare professional first.
- **If you or the child spits up the dose or vomits:**
 - less than 30 minutes after taking PRO-RIVAROXABAN, take or give a new dose

- more than 30 minutes after taking PRO-RIVAROXABAN, do not take or give a new dose. In this case, take or give the next PRO-RIVAROXABAN dose at the usual time.

Contact the healthcare professional if you or the child repeatedly spits up the dose or vomits after taking PRO-RIVAROXABAN.

Usual dose:

- **Prevention of blood clots after major hip or knee surgery**

Usual adult dose: Take one 10 mg tablet once a day with or without food.

Take the first tablet 6 to 10 hours after your operation. Then take a tablet every day until your healthcare professional tells you to stop.

If you have had a major hip operation, you will usually take PRO-RIVAROXABAN for 35 days.

If you have had a major knee operation, you will usually take PRO-RIVAROXABAN for 14 days.

- **Treatment and prevention of blood clots in the veins of the legs or arms, or blood vessels of the lungs**

Adults:

- **Day 1 to 21:** Take one 15 mg tablet TWICE a day (in the morning and evening) with food.

- **Day 22 and onwards:** Take one 20 mg tablet ONCE a day with food.

After at least 6 months treatment, your healthcare professional may decide to continue treatment with either one 20 mg tablet once a day or one 10 mg tablet once a day.

The 10 mg tablet may be taken with or without food.

This is a long-term treatment and you should continue to take PRO-RIVAROXABAN until your healthcare professional says otherwise.

Children: PRO-RIVAROXABAN is available for children as tablets. Your child's healthcare professional will decide the right dose of PRO-RIVAROXABAN for your child depending on their body weight.

Always give PRO-RIVAROXABAN to your child exactly as the healthcare professional tells you to. You should check with your child's healthcare professional if you are not sure.

Children should keep scheduled visits with their healthcare professional. This is because their dose of PRO-RIVAROXABAN should be adjusted as their weight changes.

- **Prevention of blood clots in your brain (stroke) and in other blood vessels of your body if you have atrial fibrillation**

Usual adult dose: Take one 20 mg tablet once a day with food.

If your kidneys are not working properly, your healthcare professional may prescribe 15 mg once a day with food.

This is a long-term treatment and you should continue to take PRO-RIVAROXABAN until your healthcare professional says otherwise.

The recommended maximum daily dose is 20 mg.

- **Prevention of stroke, heart attack, severe leg or arm pain, or death if you have coronary artery disease and/or peripheral artery disease**

Usual adult dose: Take one 2.5 mg tablet twice a day with or without food. Take PRO-RIVAROXABAN around the same time every day (for example, one tablet in the morning and one in the evening).

Also take 1 tablet of 75 mg – 100 mg of acetylsalicylic acid (ASA, or ASPIRIN) once a day. Take the ASA tablet at the same time as one of your PRO-RIVAROXABAN doses.

This is long-term treatment and you should continue to take your treatment until your healthcare professional says otherwise.

Overdose:

Taking too much PRO-RIVAROXABAN may cause excessive bleeding.

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

Missed Dose:

- If you take PRO-RIVAROXABAN 2.5 mg tablets twice a day and miss a dose, skip the missed dose and take the next dose as usual.
- If you take PRO-RIVAROXABAN 15 mg tablets **twice** a day and miss a dose, take the missed dose as soon as you remember. If you forget to take a dose, you can take two 15 mg tablets at the same time to get a total of two tablets (30 mg) in one day. Do not take more than two 15 mg tablets in one day. The next day, take PRO-RIVAROXABAN as usual.
- If you or your child takes PRO-RIVAROXABAN 10 mg, 15 mg or 20 mg tablets **once** a day and miss a dose, take or give your child the missed dose as soon as you remember on the same day. If this is not possible, you or your child should skip the missed dose and take the next dose on the following day as usual. Do not take or give your child a double dose to make up for the one that was missed.

What are possible side effects from using PRO-RIVAROXABAN?

These are not all the possible side effects you may have when taking PRO-RIVAROXABAN. If you experience any side effects not listed here, tell your healthcare professional.

As PRO-RIVAROXABAN acts on the blood clotting system, most side effects are related to signs of bruising or bleeding.

In some cases, bleeding may not be obvious, such as unexplained swelling.

Patients treated with PRO-RIVAROXABAN may also experience the following side effects: Nausea, vomiting, stomach ache, constipation, diarrhea, indigestion, and decreased general strength and energy.

In general, the side effects observed in children treated with PRO-RIVAROXABAN were similar in type to

those observed in adults and were primarily mild to moderate in severity.

Side effects that were observed more often in children include: Very common: headache, fever, nose bleeding, vomiting.

Common: raised heartbeat, blood tests may show an increase in bilirubin, low number of platelets which are cells that help blood to clot, heavy menstrual bleeding observed in girls.

Uncommon: blood tests may show an increase in a subcategory of bilirubin (direct bilirubin).

PRO-RIVAROXABAN can cause abnormal blood test results. The healthcare professional may perform blood tests before you or your child take PRO-RIVAROXABAN and regularly during treatment. They will tell you if the test results are abnormal and if you or your child need treatment to correct these side effects.

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	
COMMON			
Anemia (decreased number of red blood cells): pale complexion, weakness, tiredness, dizziness, headache, breathlessness, unusually fast heartbeat, or chest pain		✓	
Bleeding from hemorrhoids	✓		
Bleeding from the surgical wound, an injury or other medical procedure		✓	
Bleeding gums for longer than 5 minutes when you brush your teeth		✓	
Bleeding in the eye	✓		
Bleeding under the skin	✓		
Blood in your urine, (red/pink tinge to urine)		✓	
Fever		✓	
Gastrointestinal (GI) bleeding (bleeding anywhere along the GI tract between mouth and anus): blood in vomit, black tarry stool, bright red blood in your stool or coming from rectum, rapid pulse, low blood pressure, low urine flow, confusion, weakness, dizziness		✓	
Genital bleeding in post-menopausal women		✓	
Hypotension (low blood pressure): dizziness, fainting, light-headedness, blurred vision, nausea, vomiting, fatigue (may occur when you go from lying or sitting to standing up)		✓	
Increased or more frequent menstrual bleeding	✓		
Itchy skin or rash		✓	
Localized swelling		✓	

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	
Nose bleed lasting more than 5 minutes		✓	
Pain or swelling in your limbs		✓	
Seizure (fit) reported in children: loss of consciousness with uncontrollable shaking			✓
Tachycardia (abnormally fast heartbeat)		✓	
Unexpected bruising		✓	
UNCOMMON			
Decreased urine output	✓		
Hemarthrosis (bleeding into a joint): joint pain, swelling		✓	
Hemoptysis : coughing up blood		✓	
Intracerebral hemorrhage (bleeding in the brain): sudden, severe headache; confusion; nausea and vomiting; seizures; loss of consciousness			✓
Oozing from the surgical wound		✓	
Seizure (fit) reported in adults: loss of consciousness with uncontrollable shaking			✓
Syncope (fainting): a temporary loss of consciousness due to a sudden drop in blood pressure		✓	
RARE			
Allergic Reaction : difficulty swallowing or breathing, wheezing; drop in blood pressure; feeling sick to your stomach and throwing up; hives or rash; swelling of the face, lips, tongue or throat			✓
Liver Disorder : yellowing of the skin or eyes, dark urine, pale stools abdominal pain, nausea, vomiting, loss of appetite		✓	
UNKNOWN FREQUENCY			
Agranulocytosis (decrease in white blood cells): frequent infection with fever, chills, sore throat		✓	
Anticoagulant-related nephropathy (ARN) (serious kidney damage caused by anticoagulant medicines): bleeding in the kidney sometimes with presence of blood in urine leading to inability of the kidneys to work properly		✓	
Compartment Syndrome : increased pressure within legs or arms after a bleed, with pain, swelling, numbness or paralysis		✓	
Eosinophilic Pneumonia (accumulation of a type of white blood cells that cause inflammation in the lung): shortness of breath, cough, wheezing, chest pain, fever, and unintended weight loss		✓	
Stevens-Johnson Syndrome (SJS) (severe skin rash): redness, blistering and/or peeling of the			✓

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 and/or inside of the lips, eyes, mouth, nasal passages or genitals, accompanied by fever, chills, headache, cough, body aches or swollen glands			

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

Storage:

- Keep PRO-RIVAROXABAN tablets at room temperature (15°C - 30°C).
- Keep out of the reach and sight of children.
- Do not use PRO-RIVAROXABAN after the expiry date which is stated on the bottle after EXP. The expiry date refers to the last day of that month.
- Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

If you want more information about PRO-RIVAROXABAN:

- 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 contacting Pro Doc Ltée : 1-800-361-8559, www.prodoc.qc.ca medinfo@prodoc.qc.ca

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