**PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986**

The medicine is dispensed with a doctor's prescription only

# Rivaroxaban Propharm 10 mg

**Film-coated Tablets**

**Active ingredient**
Each tablet contains:
rivaroxaban 10 mg

Inactive ingredients and allergens in the preparation: See section section 2 "Important information regarding some of the ingredients of the medicine" and section 6 "Further information".

**Read this leaflet carefully in its entirety before using the medicine.** This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.
This medicine has been prescribed for the treatment of your ailment. Do not pass it on to others. It may harm them even if it seems to you that their ailment is similar.

In addition to the leaflet, the Rivaroxaban Propharm 10 mg is provided with a patient safety information card.
This card contains important information that you must know and abide by before starting and during treatment with Rivaroxaban Propharm 10 mg.
Read the Patient Safety Information Card and the patient leaflet before starting to use the preparation.
Keep the card and leaflet for further reading if necessary.

## 1. WHAT IS THE MEDICINE INTENDED FOR?

Rivaroxaban Propharm 10 mg is intended for:
- preventing venous thrombosis in adults following elective hip or knee replacement surgery.
- preventing recurrence of blood clots in the veins of the legs (deep vein thrombosis) and in the blood vessels of the lungs (pulmonary embolism) following the completion of at least 6 months therapy for a previous deep vein thrombosis or pulmonary embolism.

**Therapeutic group:** Rivaroxaban Propharm 10 mg belongs to a group of medicines called antithrombotic agents and acts by lowering the tendency to form blood clots by blocking a factor involved in the blood-clotting process (Factor Xa).

## 2. BEFORE USING THE MEDICINE

**Do not use the medicine if:**

- you are sensitive (allergic) to rivaroxaban or to any of the other ingredients contained in the medicine. For the list of inactive ingredients, see section 6 "Further Information".
- you are suffering from excessive bleeding.
- you have a disease or a condition in an organ of the body that increases the risk of serious bleeding (e.g., stomach ulcer, brain injury or bleeding, recent brain or eye surgery).
- you are taking medicines to prevent blood clotting (e.g., warfarin, dabigatran, apixaban or heparin), except in cases of switching from one anticoagulant to another, or when you are receiving heparin through a venous or arterial catheter to keep it open.
- you are suffering from a liver disease that increases the risk of bleeding.
- you are pregnant or breastfeeding.

**Do not take Rivaroxaban Propharm 10 mg and tell your doctor** if any of the conditions described above applies to you.

**Special warnings regarding use of the medicine**
Before taking Rivaroxaban Propharm 10 mg, talk to the doctor or pharmacist.

**Special caution is required when using Rivaroxaban Propharm 10 mg. Before treatment with Rivaroxaban Propharm 10 mg, tell the doctor:**
- if you are at an increased risk of bleeding, as could be the case in any of the following situations:
  - a moderate or severe kidney disease, since kidney function may affect the amount of medicine acting in your body.
  - you are taking other medicines to prevent blood clotting (e.g., warfarin, dabigatran, apixaban or heparin), when you are switching from one anticoagulant to another, or when you are receiving heparin through a venous or arterial catheter to keep it open (see "Drug interactions" in section 2).
  - bleeding disorders.
  - very high blood pressure, not controlled by medicinal treatment.
  - a disease of the stomach or bowel that may cause bleeding, e.g., inflammation of the bowels or stomach, or inflammation of the esophagus as a result, for example, of gastroesophageal reflux disease (a disease in which acid from the stomach rises to the esophagus) or tumors located in the stomach or bowels or genital tract or urinary tract.
  - problems with the blood vessels of the retina (retinopathy).
  - a lung disease in which the bronchi are widened and filled with pus (bronchiectasis), or previous bleeding from the lung.
- if you have a prosthetic heart valve.
- if you know that you have a disease called antiphospholipid syndrome (a disorder of the immune system that causes an increased risk of blood clots), tell your doctor who will decide if the treatment may need to be changed.
- if the doctor determined that your blood pressure is unstable or a surgical or other treatment to remove a blood clot from your lungs is planned.

**If any of the above-mentioned conditions applies to you, tell the doctor** before taking the medicine. The doctor will decide if you should be treated with Rivaroxaban Propharm 10 mg and if you need close observation.

If the doctor thinks you are at increased risk of developing a stomach or intestinal ulcer, the doctor may also give you treatment to prevent it.

**If you are due to undergo surgery**
- it is very important that you take Rivaroxaban Propharm 10 mg before and after the surgery, exactly at the times determined for you by the doctor.
- If your operation involves a catheter or injection into your spinal column (e.g., for epidural or spinal anesthesia or pain reduction):
  - it is very important to take Rivaroxaban Propharm 10 mg exactly at the times determined for you by the doctor.
  - refer to the doctor immediately if you suffer from numbness or weakness of the legs or from problems with the bowel or bladder after the anesthesia has worn off, since urgent medical care will be necessary.

**Children and adolescents**
The medicine is not intended for children and adolescents under the age of 18. There is not enough information about the use in children and adolescents.

**Drug Interactions**
**If you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.** Especially if you are taking:
- certain medicines for fungal infections (e.g., fluconazole, itraconazole, voriconazole, posaconazole), with the exception of those intended for application to the skin only.

- tablets containing ketoconazole to treat Cushing's syndrome – a condition in which the body produces an excess of cortisol.
- certain medicines to treat bacterial infections (e.g., clarithromycin, erythromycin).
- certain antiviral medicines to treat infections of the AIDS virus (HIV) (e.g., ritonavir).
- other anticoagulants (e.g., enoxaparin, clopidogrel or vitamin K antagonists such as warfarin and acenocoumarol).
- anti-inflammatory and pain-relieving medicines (e.g., naproxen or acetylsalicylic acid [aspirin]).
- dronedarone, a medicine to treat abnormal heartbeat.
- certain medicines to treat depression (selective serotonin reuptake inhibitors [SSRIs] or serotonin norepinephrine reuptake inhibitors [SNRIs]).

**If any of the above-mentioned conditions applies to you, tell the doctor** before taking the medicine because these medicines may lead to increased activity of Rivaroxaban Propharm 10 mg. Your doctor will decide if you should be treated with Rivaroxaban Propharm 10 mg and if close medical supervision is necessary.

**Similarly, inform the doctor or pharmacist if you are taking:**
- certain medicines for treatment of epilepsy (e.g., phenytoin, carbamazepine, phenobarbital).
- the herbal preparation for treatment of depression, St. John's Wort (Hypericum).
- rifampicin (an antibiotic).

**If any of the above-mentioned conditions applies to you, tell the doctor** before taking the medicine because these medicines may lead to reduced activity of Rivaroxaban Propharm 10 mg. Your doctor will decide if you should be treated with Rivaroxaban Propharm 10 mg and if close medical supervision is necessary.

**Use of the medicine and food**
Rivaroxaban Propharm 10 mg can be taken with or without food.

**Pregnancy, breastfeeding and fertility**
Do not take Rivaroxaban Propharm 10 mg if you are pregnant or breastfeeding.
If there is a chance that you could become pregnant, use a reliable contraceptive while taking Rivaroxaban Propharm 10 mg.
If you become pregnant while taking the medicine, refer immediately to the doctor, who will decide upon the continuation of treatment.

**Driving and use of machines**
Rivaroxaban Propharm 10 mg may cause dizziness (a common side effect) or fainting (an uncommon side effect) (see section 4, "Side Effects"). Do not drive, ride a bicycle or use any tools or machines while using Rivaroxaban Propharm 10 mg if you are affected by these symptoms.

**Important information regarding some of the ingredients of the medicine**
The medicine contains lactose and sodium.
If you have been told by the doctor that you suffer from an intolerance to certain sugars, refer to the doctor before you start taking Rivaroxaban Propharm 10 mg.
The medicine contains less than 1 mmol sodium (23 mg) per tablet and is therefore considered essentially "sodium-free".

## 3. HOW SHOULD YOU USE THE MEDICINE?
Always use this preparation according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the preparation dosage and treatment regimen.
The dosage and treatment regimen will be determined by the doctor only.

The usual dosage for preventing formation of blood clots in the veins following hip or knee replacement surgery is generally One tablet (10 mg) once a day.
Take the first tablet 6-10 hours after the operation if the doctor determined that your condition is stable. Afterwards, take one tablet every day until the doctor instructs you to stop.

The usual dosage for preventing recurrence of blood clots in the veins of the legs (deep vein thrombosis) and in the blood vessels of the lungs (pulmonary embolism) after completion of 6 months of treatment for a previous deep vein thrombosis or pulmonary embolism is generally one tablet (10 mg) per day.

**Do not exceed the recommended dose.**

- Duration of treatment
  - For hip replacement surgery, the duration of treatment is generally 5 weeks.
  - For knee replacement surgery, the duration of treatment is generally 2 weeks.
  - The duration of treatment for prevention of recurrence of blood clots in the veins of the legs (deep vein thrombosis) and in the blood vessels of the lungs (pulmonary embolism) after completion of 6 months of treatment for a previous deep vein thrombosis or pulmonary embolism will be determined by the doctor.

- Form of administration

Swallow the medicine, preferably with water.

Taking the medicine at the same time every day will help you remember to take it.

If it is hard for you to swallow the tablet whole, talk to your doctor about other ways of taking Rivaroxaban Propharm 10 mg.
The tablet can be crushed and mixed with water or apple puree immediately before administration.
If necessary, your doctor will give you crushed Rivaroxaban Propharm 10 mg through a stomach feeding tube.
There is no information regarding halving/chewing.

**If you accidentally take too high a dosage,** refer to the doctor immediately. Taking too high a dose of Rivaroxaban Propharm 10 mg increases the risk of bleeding.
If you took an overdose, or if a child has accidentally swallowed some medicine, refer immediately to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

**If you forget to take this medicine at the required time,** take a dose as soon as you remember. Take the next tablet on the following day and continue treatment as usual. Never take a double dose!

Adhere to the treatment regimen as recommended by the doctor.

Even if there is an improvement in your health, do not stop treatment with the medicine before completing the treatment without consulting the doctor, since Rivaroxaban Propharm 10 mg prevents the development of a dangerous condition.

**Do not take medicines in the dark! Check the label and the dose <u>each time</u> you take medicine. Wear glasses if you need them.**

**If you have further questions regarding use of the medicine, consult the doctor or pharmacist.**

## 4. <u>SIDE EFFECTS</u>

As with any medicine, use of Rivaroxaban Propharm 10 mg may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Like other similar medicines to reduce the formation of blood clots, Rivaroxaban Propharm 10 mg can cause bleeding, which may be life-threatening. Excessive bleeding may lead to a sudden drop in blood pressure (shock). In some cases, the bleeding may not be obvious.

**Refer to the doctor immediately if** you suffer from any of the following side effects:
**Signs of bleeding:**
- brain bleeding or bleeding inside the skull (symptoms can include headache, one-sided weakness, vomiting, seizure, decreased level of consciousness, and neck stiffness. This is a serious medical emergency; seek medical attention immediately!).
- prolonged or excessive bleeding.
- exceptional weakness, tiredness, paleness, dizziness, headache, unexplained swelling, breathlessness, chest pain or angina pectoris.

Your doctor will decide whether close monitoring or a change in the treatment is necessary.

**Signs of a severe skin reaction:**
- spreading intense skin rash, blisters or mucosal lesions, e.g., in the mouth or eyes (Stevens-Johnson syndrome/toxic epidermal necrolysis).
- a drug reaction that causes rash, fever, inflammation of internal organs, blood abnormalities and systemic illness (DRESS syndrome).

The frequency of these side effects is very rare (up to one user in 10,000 users).

**Signs of a severe allergic reaction:**
- swelling of the face, lips, mouth, tongue or throat; difficulty swallowing; hives and breathing difficulties; sudden drop in blood pressure.
- The frequencies of severe allergic reactions are very rare (anaphylactic reactions, including anaphylactic shock; may affect up to one user in 10,000) and uncommon (angioedema and allergic edema; may affect up to one user in 100).

**Additional side effects**
Common side effects (effects that may affect up to one user in 10):
- reduction in red blood cells which can cause pallor, weakness or breathlessness
- bleeding in the stomach or bowel, urogenital bleeding (including blood in the urine and heavy menstrual bleeding), nosebleed, bleeding in the gums
- bleeding into the eye (including bleeding from the white of the eye)
- bleeding into tissue or a cavity of the body (haematoma, bruising)
- coughing up blood
- bleeding from the skin or under the skin
- bleeding following an operation
- oozing of blood or fluid from a surgical wound
- swelling of the limbs
- pain in the limbs
- impaired function of the kidneys (can be detected in tests performed by the doctor)
- fever
- abdominal pain, indigestion, nausea or vomiting, constipation, diarrhea
- low blood pressure (symptoms of this may be feeling dizzy or fainting when standing up)
- decreased general strength and energy (weakness, tiredness), headache, dizziness
- rash, itchy skin
- blood tests can indicate an increase in some liver enzymes

Uncommon side effects (effects that may affect up to one user in 100):
- bleeding into the brain or inside the skull (see above “signs of bleeding”)
- bleeding into a joint causing pain and swelling
- thrombocytopenia (a low number of platelets, which are cells that help blood to clot)
- allergic reactions, including allergic skin reactions
- impaired function of the liver (can be detected in tests performed by the doctor)
- blood tests may indicate an increase in bilirubin, some pancreatic or liver enzymes or in the number of platelets
- fainting
- generally feeling unwell
- faster heartbeat
- dry mouth

- hives (urticaria)

Rare side effects (effects that may affect up to one user in 1,000):
- bleeding into a muscle
- cholestasis (decreased bile flow), hepatitis including hepatocellular injury (inflamed liver including liver injury)
- yellowing of the skin and eyes (jaundice)
- localized swelling
- localized collection of blood (haematoma) in the groin resulting from a complication of a cardiac procedure where a catheter is inserted into a leg artery

Very rare side effects (effects that may affect up to one user in 10,000):
- accumulation of eosinophils, a type of white granulocytic blood cells that cause inflammation in the lungs (eosinophilic pneumonia)

Side effects of **unknown** frequency (the frequency cannot be estimated from the available data):
- kidney failure after severe bleeding
- Bleeding in the kidney, sometimes accompanied by blood in the urine, leading to inability of the kidneys to work properly (anticoagulant-related nephropathy)
- increased pressure within muscles of the legs or arms after bleeding, which leads to pain, swelling, altered sensation, numbness or paralysis (compartment syndrome after bleeding)

**If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor.**

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il

## 5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine and any other medicine must be kept in a safe place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- Do not store at a temperature above 25°C.
- 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. FURTHER INFORMATION

- **In addition to the active ingredient, the medicine also contains:**
  Tablet core:
  Cellulose microcrystalline, lactose monohydrate, hypromellose 2910, croscarmellose sodium, magnesium stearate, sodium laurilsulfate.
  Tablet coating:
  Hypromellose 2910, macrogol 3350, titanium dioxide, iron oxide red.
- **What does the medicine look like and what are the contents of the package:**
  Round, pink, biconvex, film-coated tablets marked with "10" on one side.
  The tablets come in trays (blisters) in packs of 30 tablets.
- **Registration holder and address:** Propharm Ltd., 23 Ben Gurion, Zichron Yaacov.

**Manufacturer and address:** Adalvo limited, Malta life sciences park, building 1, level 4, Sir Temi Zammit Buildings, San Gwann, Industrial estate, San Gwan, SGN 3000, Malta

Revised in October 2023 according to MOH guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:
175-28-36751-99