PATIENT LEAFLET IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Rivar Teva 15 mg
Rivar Teva 20 mg

Film-coated tablets

Each film-coated tablet contains:
Rivaroxaban 15 mg
Rivaroxaban 20 mg
For information regarding inactive ingredients, see section 2 – "Important information about some of the ingredients of the medicine" and section 6 – "Additional information".

Read the entire leaflet carefully before using the medicine. This leaflet contains concise information about the medicine. If you have additional questions, refer to the doctor or the pharmacist.

In addition to the leaflet, there is a patient safety information card for Rivar Teva. This card contains important information that you must know and act accordingly before starting treatment with Rivar Teva and during the treatment.
Please review the patient safety information card and the patient leaflet before starting to use the preparation.
You should keep the leaflet and the card for further review, if necessary.

This medicine has been prescribed for your treatment. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

1. What is the medicine intended for?

Rivar Teva 15 mg and Rivar Teva 20 mg are intended for:
- Prevention of blood clots in the brain (stroke) and other blood vessels in the body, in adult patients with irregular heartbeat called non-valvular atrial fibrillation, who have one or more of the following risk factors: heart failure, hypertension, age (75 or older), diabetes, prior stroke or transient ischemic attack.
- Treatment of blood clots in the veins of the legs (deep vein thrombosis, DVT) and in pulmonary blood vessels (pulmonary embolism, PE), and prevention of the recurrence of blood clots in the veins of the legs and/or lungs in adults.

Therapeutic class: Rivar Teva belongs to a class of medicines called anticoagulants, and acts by reducing the tendency to produce blood clots by blocking a factor involved in the clotting process (factor Xa).

2. Before using the medicine

Do not use this medicine if:

- You are sensitive (allergic) to rivaroxaban or to any of the other ingredients the medicine contains. (For information regarding inactive ingredients, see section 2 – "Important information about some of the ingredients of the medicine" and section 6 – "Additional information").
- You suffer from excessive bleeding.
- You have a disease or condition in an organ of the body that increases the risk of serious bleeding (such as: stomach ulcer, injury or bleeding in the brain, recent surgery of the brain or eyes).
- You are taking anticoagulants (e.g. warfarin, dabigatran, apixaban or heparin), except when changing from one anticoagulant to another or while receiving heparin through a venous or arterial line to keep it open.
- You have a liver disease which leads to an increased risk of bleeding.
- You are pregnant or breastfeeding.

Do not take Rivar Teva and inform your doctor if any of the abovementioned conditions apply to you.

Special warnings regarding the use of the medicine

Talk to the doctor or pharmacist before taking Rivar Teva.

Special caution is required when using Rivar Teva. Before treatment with Rivar Teva, tell the doctor:
- If you have an increased risk of bleeding, as could be the case in any of the following situations:
  - Severe kidney disease, since your kidney function may affect the amount of medicine that works in your body (see section 3 – "How should you use the medicine?" regarding the recommended dosage in the case of a kidney disease).
  - You are taking other anticoagulants (e.g. warfarin, dabigatran, apixaban or heparin), when changing from one anticoagulant to another, or while receiving heparin through a venous or arterial line to keep it open (see below in section 2 – "Drug interactions").
  - You have bleeding disorders.
  - Very high blood pressure, which is not controlled by medicinal treatment.
  - Diseases of the stomach or bowel that might result in bleeding, such as: inflammation of the bowels or stomach, or inflammation of the esophagus, e.g. due to gastroesophageal reflux disease (a disease in which stomach acid goes upwards into the esophagus) or tumors located in the stomach or bowels or genitals or urinary tract.
  - Problems with the blood vessels of the retina (retinopathy).
  - A lung disease where the bronchi are enlarged and filled with purulent secretions (bronchiectasis), or previous bleeding from your 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 whether the treatment should be changed.
- If your doctor determines that your blood pressure is unstable or if another treatment or surgical procedure to remove the blood clot from your lungs is planned.

If any of the abovementioned conditions apply to you, tell your doctor before you take the medicine. Your doctor will decide whether you should be treated with Rivar Teva and whether you should be kept under close observation.
- If the doctor thinks that you have an increased risk for developing a stomach or intestinal ulcer, he may also prescribe you with a treatment to prevent it.

If you need to undergo surgery <u>or an invasive procedure</u>
- It is highly important to take Rivar Teva before and after the surgery or invasive procedure at the exact times your doctor has scheduled for you.
- If your surgery involves an intraspinal catheter or injection (e.g., for epidural or spinal anesthesia or for pain relief):
  - It is highly important to take Rivar Teva before and after the injection or the removal of the catheter at the exact times your doctor has scheduled for you.
  - Refer to your treating doctor immediately if you experience numbness or weakness in the legs or intestinal problems or bladder problems after the anesthesia wears off, as this requires urgent medical intervention.

Children and adolescents

The medicine is not intended for use in children and adolescents under the age of 18.

Information regarding the use in children and adolescents is insufficient.

Drug interactions

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or the pharmacist. Especially if you are taking:
- Certain anti-fungal medicines (such as: fluconazole, itraconazole, voriconazole, posaconazole), except for those only intended for topical application.
- Tablets containing ketoconazole for treatment of Cushing's syndrome – a condition in which the body produces an excess of cortisol.
- Certain medicines for the treatment of bacterial infections (such as: clarithromycin, erythromycin).
- Certain anti-viral medicines for treatment of human immunodeficiency virus (HIV) infections/AIDS (such as: ritonavir).
- Other anticoagulants (such as: enoxaparin, clopidogrel or vitamin K antagonists, such as warfarin and acenocoumarol).
- Anti-inflammatory and analgesic medicines (such as: naproxen or acetylsalicylic acid [aspirin]).
- Dronedarone, a medicine for treatment of irregular heartbeat.
- Certain medicines for treatment of depression (selective serotonin reuptake inhibitors [SSRIs] or serotonin-norepinephrine reuptake inhibitors [SNRIs]).

If any of the abovementioned conditions apply to you, tell your doctor before taking the medicine, as these medicines may increase the activity of Rivar Teva. Your doctor will decide whether to treat you with Rivar Teva and whether close medical supervision is required.

Moreover, the doctor or pharmacist should be informed if you are taking:
- Certain medicines for treatment of epilepsy (such as: phenytoin, carbamazepine, phenobarbital).
- The herbal preparation for treatment of depression St. John's wort (hypericum).
- Rifampicin (an antibiotic).

If any of the above apply to you, tell your doctor before taking the medicine, as these medicines may decrease the activity of Rivar Teva. Your doctor will decide whether to treat you with Rivar Teva and whether close medical supervision is required.

Use of the medicine and food

Rivar Teva 15 mg and Rivar Teva 20 mg must be taken with food and swallowed with water.

Pregnancy, breastfeeding and fertility

Do not take Rivar Teva if you are pregnant or breastfeeding.
If there is a chance that you might become pregnant, you must use a reliable contraceptive while taking Rivar Teva.
If you become pregnant while taking the medicine, inform the treating doctor immediately, who will decide how to continue the treatment.

Driving and operating machinery

Rivar Teva may cause dizziness (a common side effect) or fainting (an uncommon side effect) (see section 4 – "side effects"). Do not drive, ride a bicycle, use tools or operate machinery while using Rivar Teva if you experience these symptoms.

Important information about some of the ingredients of the medicine

The medicine contains lactose and sodium.
If you have been told by your doctor that you have an intolerance to certain sugars, speak to your doctor before starting to take Rivar Teva.
The medicine contains less than 1 mmol of sodium (23 mg) per tablet, and is thus considered to be "sodium-free".

3. How should you use the medicine?

Always use the preparation according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and how to use the preparation.
The dosage and treatment regimen will be determined only by the doctor.
- To prevent blood clots in the brain (stroke) and in other blood vessels in your body, the generally accepted dose is one tablet of Rivar Teva 20 mg once a day.
  If you have kidney impairment, the dosage may be reduced to one tablet of Rivar Teva 15 mg once a day.
  If you need to undergo a procedure to treat blocked blood vessels in your heart (a procedure called a percutaneous coronary intervention – PCI with an insertion of a stent), there is limited information about reducing the dosage to one tablet of Rivar Teva 15 mg once a day, in addition to an antiplatelet medicine, such as clopidogrel.
- To treat blood clots in the veins of your legs and in the blood vessels of your lungs, and to prevent blood clots from reoccurring, the generally accepted dosage is one tablet of Rivar Teva 15 mg twice a day for the first 3 weeks, and then one tablet of Rivar Teva 20 mg once a day. After completing at least 6 months of treatment, your doctor may decide to continue treatment with Rivar Teva 10 mg, one tablet a day.
  If you have kidney impairment and take Rivar Teva 20 mg once a day, your doctor may decide to reduce the dosage after 3 weeks to one tablet of Rivar Teva 15 mg once a day, if the risk for bleeding is higher than the risk of another blood clot forming.

Do not exceed the recommended dose.

Duration of treatment

Rivar Teva should be taken every day until the doctor instructs you to stop.
The doctor will decide about the duration of treatment with the medicine.

How to take the medicine

The medicine must be taken with food and it is recommended to swallow the tablet with water.
If you have difficulty swallowing the tablet whole, speak to your doctor about other ways to take Rivar Teva.
The tablet may be crushed and mixed with water or apple puree immediately before it is taken.
You should eat immediately after taking the crushed medicine.
If necessary, your doctor will administer crushed Rivar Teva through a feeding tube into your stomach.
No information is available regarding halving/chewing.
Taking the medicine at the same time every day will help you remember to take it.

If you accidentally take a higher dosage you should refer to your treating doctor immediately. Taking too much Rivar Teva increases your risk for bleeding.
If you took an overdose or a child accidentally swallowed this medicine, go to the doctor or the emergency room of the hospital immediately and take the package of the medicine with you.

If you forget to take this medicine at the required time
- If your dosage is one tablet of Rivar Teva 15 mg or Rivar Teva 20 mg <u>once a day</u>, take a dose as soon as you remember, but under no circumstances should you take a double dose or two doses on the same day! Take the next dose on the following day and then once a day as usual, and consult your doctor.
- If your dosage is one tablet of Rivar Teva 15 mg <u>twice</u> a day, take a dose as soon as you remember. Do not take more than two tablets of Rivar Teva 15 mg in one day. You can take two tablets of Rivar Teva 15 mg together to make a dose of 30 mg for one day. On the following day continue taking one tablet of Rivar Teva 15 mg twice a day.

Follow the treatment as recommended by the doctor.
Even if there is an improvement in your health, do not stop the treatment with the medicine without consulting the doctor, since Rivar Teva treats and prevents severe conditions.

If you stop taking the medicine you compromise its therapeutic and preventive capacity.

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

If you have any other questions regarding use of the medicine, consult the doctor or the pharmacist.

4. Side effects

As with any medicine, using Rivar Teva may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.

Like other similar medicines for reducing the formation of blood clots, Rivar Teva may cause potentially life-threatening bleeding. Heavy bleeding may cause a sudden drop in blood pressure (shock). In certain cases the bleeding may be occult.

Refer to the doctor immediately if you experience any of the following side effects:

Signs of bleeding:
- Cerebral or intracranial bleeding (symptoms may include headache, one-sided weakness, vomiting, convulsions, decreased level of consciousness and neck stiffness. This is a serious medical emergency, seek immediate medical attention!).
- Prolonged or heavy bleeding.
- Abnormal weakness, tiredness, pallor, dizziness, headache, unexplained swelling, shortness of breath, chest pain or angina pectoris.

Your doctor will decide whether to keep you under close observation or change the treatment.

Signs of severe skin reactions:
- Spreading intense skin rash, blisters or mucosal lesions, e.g. in the mouth or eyes (Toxic Epidermal Necrolysis/Stevens-Johnson syndrome).
- 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 1 in 10,000 users).

Signs of severe allergic reactions:
- 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 1 in 10,000 users) or uncommon (angioedema and allergic edema; may affect up to 1 in 100 users).

Additional side effects

Common side effects (effects that may affect up to 1 in 10 users):
- Reduction in red blood cells which can cause pallor, weakness or breathlessness
- Gastric or intestinal bleeding, urogenital bleeding (including blood in the urine and heavy menstrual bleeding), nose bleeding, bleeding in the gums
- Bleeding into the eye (including bleeding from the whites of the eyes)
- Bleeding into tissue or a cavity of the body (local hematoma, bruising)
- Coughing blood
- Bleeding from the skin or under the skin
- Post-operative bleeding
- Oozing of blood or fluid from a surgical wound
- Limb swelling
- Pain in the limbs
- Impaired function of the kidneys (may be seen in tests performed by your doctor)
- Fever
- Abdominal pain, digestive difficulties, nausea or vomiting, constipation, diarrhea
- Low blood pressure (symptoms may be feeling dizzy or fainting when standing up)
- General decrease in strength and energy (weakness, tiredness), headache, dizziness
- Rash, itching of the skin
- Blood tests may show an increase in some liver enzymes

Uncommon side effects (effects that may affect up to 1 in 100 users):
- Bleeding into the brain or inside the skull (see above, 'Signs of bleeding')
- Bleeding into a joint causing pain and swelling
- Thrombocytopenia (low number of platelets, which are cells that help blood to clot)
- Allergic reactions, including allergic skin reactions
- Impaired liver function (can be discovered in tests performed by the doctor)
- Blood tests may show an increase in bilirubin, some pancreatic or liver enzymes or in the number of platelets
- Fainting
- General malaise
- Rapid heartbeat
- Dry mouth
- Hives (urticaria)

Rare side effects (effects that can affect up to 1 in 1,000 users):
- Bleeding into a muscle
- Cholestasis (decreased bile flow), inflammation of the liver (hepatitis), including hepatocellular injury (inflamed liver, including liver injury)
- Yellowing of the skin and the eyes (jaundice)
- Localized swelling
- Local hematoma in the groin as a complication of the cardiac procedure where a catheter is inserted into your leg artery

Side effects with unknown frequency (frequency cannot be estimated from the available data):
- Kidney failure after a severe bleeding
- Increased pressure within muscles of the legs or arms after a bleeding, which leads to pain, swelling, altered sensation, numbness or paralysis (compartment syndrome after a bleeding)

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

Reporting side effects

Side effects may be reported to the Ministry of Health by clicking on the link "Report side effects due to medicinal treatment" found on the Ministry of Health website homepage (www.health.gov.il), which will direct you to the online form for reporting side effects, or by clicking on the following link: https://sideeffects.health.gov.il.

5. How to store the medicine?

- Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting without an explicit instruction from the doctor.
- Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.
- **Store in a dry place below 25°C.**

6. Additional information

In addition to the active ingredient, the medicine also contains:

Rivar Teva 15 mg:
Lactose monohydrate, croscarmellose sodium, hypromellose, sodium lauryl sulfate, polyvinyl alcohol (part. hydrolyzed), magnesium stearate, macrogol, titanium dioxide, talc, iron oxide yellow, iron oxide red.

Rivar Teva 20 mg:
Lactose monohydrate, croscarmellose sodium, hypromellose, sodium lauryl sulfate, polyvinyl alcohol (part. hydrolyzed), magnesium stearate, iron oxide red, macrogol, talc.

What does the medicine look like and what are the contents of the package?

Rivar Teva 15 mg: A round, orange, film-coated tablet, debossed with "T" on one side of the tablet and with "3R" on the other side.
Rivar Teva 20 mg: A round, red, film-coated tablet, debossed with "T" on one side of the tablet and with "7R" on the other side.
The tablets come in blister packs in packages of 28, 30, 56 or 60 tablets.
Not all package sizes may be marketed.

Name and address of marketing authorization holder and manufacturer:
Teva Israel Ltd.,
124 Dvora HaNevi'a St., Tel Aviv 6944020.

The leaflet was revised in December 2021 in accordance with the Ministry of Health guidelines.

Registration numbers of the medicines in the national drug registry of the Ministry of Health:
Rivar Teva 15 mg: 168.09.36159
Rivar Teva 20 mg: 168.10.36160

teva