

PATIENT INFORMATION LEAFLET

VENMIX® 15 mg Film Coated Tablet

It is applied externally.

- **Active ingredient:** Each film-coated tablet contains 15 mg rivaroxaban.
- **Excipients:** Lactose monohydrate (lactose 200 mesh) (bovine origin), microcrystalline cellulose pH 101, croscarmellose sodium, hydroxypropylmethylcellulose E5 premium LV, sodium lauryl sulfate, magnesium stearate, polyvinyl alcohol, polyethylene glycol, talc, FD&C Yellow #6/Sunset yellow FCF aluminum lacquer, titanium dioxide, iron oxide red and iron oxide yellow.

▼ This medicine is subject to additional monitoring. This triangle will allow new safety information to be identified quickly. You can help by reporting any side effects that occur. See the end of Chapter 4 for how to report side effects.

Please read this INSTRUCTIONS FOR USE carefully before you start using this medicine, because it contains important information for you.

- *Keep these instructions for use. You may need to read it again later.*
- *If you have any additional questions, please consult your doctor or pharmacist.*
- *This medicine has been prescribed for you personally, do not give it to others.*
- *During the use of this medicine, tell your doctor that you are using this medicine when you go to the doctor or hospital.*
- *Follow exactly what is written in this instruction. Do not use **high or low** doses other than the dose recommended to you about the drug.*

In This Leaflet:

1. **What VENMIX is and what it is used for?**
2. **What you need to know before you use VENMIX?**
3. **How to use VENMIX?**
4. **Possible side effects**
5. **How to store VENMIX?**

1. What VENMIX is and what it is used for?

Each VENMIX film-coated tablet contains 15 mg of active substance (rivaroxaban).

VENMIX contains lactose monohydrate (bovine origin). Rivaroxaban belongs to a group of medicines called anticoagulants and works by inhibiting factor Xa, which is involved in blood clotting, thereby reducing the tendency of blood to form clots.

VENMIX is available in packs of 28 and 42 film-coated tablets. The tablets in the package are brown-red, round, biconvex film-coated tablets.

VENMIX is used in adult patients in the following cases:

- Treatment of a type of heart rhythm disorder (non-valvular atrial fibrillation), prevention of blood clots in the brain (stroke) or other vessels of the body,
- Treatment of blood clots in the veins of the legs (deep vein thrombosis) and treatment of blood clots in the veins of the lungs (pulmonary embolism) and prevention of re-occurrence of blood clots in the veins of the legs and lungs.

2. What you need to know before you use VENMIX?

DO NOT use VENMIX if:

If

- If you are allergic to rivaroxaban or any of the excipients in this medicine,
- If you have excessive bleeding,
- You have a disease or condition that increases the risk of serious bleeding in any organ in your body (e.g. stomach ulcer, brain damage or bleeding, recent brain or eye surgery),
- If you are taking medicines to prevent blood clotting (e.g. warfarin, dabigatran, apixaban, edoxaban or heparin), except when changing anticoagulant therapy or when heparin is administered to keep a vein or artery line open,
- If you have liver disease with an increased risk of bleeding,
- If you are pregnant or breastfeeding.

If any of the above applies to you, do not use VENMIX and tell your doctor.

Take special care with VENMIX with caution in the following situations

If,

- You have one of the following conditions that increase the risk of bleeding:
 - Serious kidney disease as kidney function can affect the amount of medicine that will work in your body,
 - If you are taking other medicines to prevent blood clotting (e.g. warfarin, dabigatran, apixaban, edoxaban or heparin) during a change of anticoagulant treatment or if heparin is administered to keep a vein or artery line open (see “Concomitant use with other medicines”),
 - Bleeding disorders,
 - İlaç tedavisi ile kontrol altına alınamayan çok yüksek kan basıncı,
 - Diseases that can cause bleeding in the stomach or intestines, e.g. inflammation of the intestines or stomach or inflammation of the esophagus and pharynx (esophageal inflammation) due to gastroesophageal reflux disease (a disease in which stomach acid moves up into the esophagus) or tumors in the stomach, intestines, reproductive tract or urinary tract,
 - Problems with the blood vessels at the back of the eye (retinopathy),
 - A history of lung disease (bronchiectasis), in which the bronchi enlarge and fill with pus, or a history of pulmonary hemorrhage,
- If you have a prosthetic heart valve,

- If you know you have a condition called antiphospholipid antibody syndrome (a disease of the immune system that increases the risk of blood clots), tell your doctor. your doctor will decide if your treatment needs to be changed.
- If your doctor decides that your blood pressure is not under control or if another treatment or surgical procedure to remove the blood clot from your lungs is planned.

If any of the above conditions apply to you, tell your doctor before taking VENMIX. Your doctor will decide whether you should be treated with this medicine and kept under close supervision.

If you need an operation:

- It is very important that you take VENMIX before and after operation at exactly the times specified by your doctor.
 - If your operation will involve a catheter or an injection into your spine (e.g. for epidural or spinal anesthesia or to reduce your pain):
 - Tell your doctor immediately if you have numbness or weakness in your legs after the end of the anesthesia or if you have bowel or bladder problems; in such cases, emergency treatment is needed.

Children and adolescents

There is insufficient information on the use of VENMIX in children and adolescents. VENMIX is not recommended for people under the age of 18.

If these warnings apply to you at any time in the past, please consult your doctor.

Use of VENMIX with food and beverage

VENMIX should be used with meals.

Pregnancy

Consult your doctor or pharmacist before using the medicine.

It should not be used in pregnant women.

It can only be used in women of childbearing potential in combination with an effective contraceptive method.

If you notice that you are pregnant during your treatment, consult your doctor or pharmacist immediately.

Lactation

Consult your doctor or pharmacist before using the medicine.

VENMIX should not be used in during breastfeeding.

Driving and using machines

VENMIX may cause dizziness (common side effect) or fainting (uncommon side effect) (see section 4. “What are the possible side effects?”). Do not drive a car, ride a bicycle, use any tools or machinery when these side effects occur.

Important information about some excipients contained in VENMIX

VENMIX contains lactose. If you have been told by your doctor that you are intolerant to certain sugars, contact your doctor before taking this medicinal product.

This medicine contains less than 1 mmol (23 milligrams) of sodium per film-coated tablet, so it is essentially “sodium-free”.

Concomitant use with other drugs

If you are taking the following medicines:

- Some medicines used to treat fungus (e.g. fluconazole, itraconazole, voriconazole, posaconazole), except when applied only to the skin,
- Ketoconazole tablets (used to treat Cushing's syndrome, where the body produces excessive amounts of cortisol),
- Some medicines used for bacterial infections (e.g. clarithromycin, erythromycin),
- Some antiviral drugs used to treat HIV/AIDS (e.g. ritonavir),
- Other medicines used to reduce blood clotting (e.g. enoxaparin, clopidogrel or warfarin and vitamin K antagonists such as acenocoumarol),
- Anti-inflammatory and painkillers (e.g. naproxen or acetylsalicylic acid),
- Dronedarone used to treat arrhythmia in the heart,
- Some medicines used to treat depression [selective serotonin reuptake inhibitors (SSRIs) or serotonin norepinephrine reuptake inhibitors (SNRIs)].

If you are currently using or have recently used any prescription or over-the-counter medication, please tell your doctor or pharmacist about them.

If your doctor thinks you are at high risk of developing ulcers in your stomach or intestine, he or she may also decide to use preventive ulcer treatment.

If you are taking the following medicines:

- Some medicines used in epilepsy (phenytoin, carbamazepine, phenobarbital),
- St. John's Wort (*Hypericum perforatum*), an herbal product used in the treatment of depression,
- Rifampicin used as an antibiotic.

If you are taking any of these medicines that may reduce the effect of VENMIX, consult your doctor before using VENMIX.

Your doctor will decide whether you will be treated with VENMIX and whether you will be kept under close supervision.

Please tell your doctor or pharmacist if you are currently taking or have recently taken any prescription or non-prescription medicines.

3. How to use VENMIX?

Instructions for proper use and dose/frequency of administration:

When VENMIX is used to prevent stroke or blood clots in other vessels of the body, the recommended dose is one tablet of VENMIX 20 mg once a day. If you have kidney problems, the dose may be reduced to one VENMIX 15 mg tablet once a day.

If you need a procedure to treat blocked arteries in your heart (stent placement during percutaneous coronary intervention (PCI)), there is limited data on lowering the dose to VENMIX 15 mg tablets once daily (or 10 mg rivaroxaban tablets once daily if your kidneys are not working properly) in addition to an anticoagulant such as clopidogrel.

When VENMIX is used for the treatment of blood clots in the veins of the legs and for the treatment of blood clots in the veins of the lungs and for the prevention of re-formation of blood clots; the recommended dose is one VENMIX 15 mg tablet twice daily for the first 3 weeks. For treatment after 3 weeks, the recommended dose is one VENMIX 20 mg tablet once daily.

After at least 6 months of blood clot treatment, your doctor may decide to continue treatment with one 10 mg tablet once daily or one 20 mg tablet once daily.

If you have kidney problems and are taking VENMIX 20 mg tablets once daily, your doctor may decide to reduce the treatment dose to VENMIX 15 mg tablets once daily after 3 weeks if the risk of bleeding is higher than the risk of another blood clot.

To prevent blood clots in the brain (stroke) or blood clots in other vessels in your body: If your heart rate needs to be normalized with a procedure called cardioversion, take VENMIX when your doctor tells you to.

Route and method of administration:

VENMIX should be taken with meals. Take the tablet(s) preferably with water.

If you have difficulty swallowing the tablet whole, ask your doctor about other ways to take VENMIX. The tablet can be crushed and mixed with water or applesauce just before use. This mixture should be eaten immediately afterwards.

If necessary, your doctor can also give you the crushed VENMIX tablet through a stomach tube. Take the tablets every day until your doctor tells you to stop.

Try to take the tablets at the same time every day so that you do not forget to take the medicine. Your doctor will decide how long you should continue treatment.

If you spit out or vomit the dose

Take a new dose less than 30 minutes after taking VENMIX.

Do not take a new dose more than 30 minutes after taking VENMIX. In this case, take the next dose of VENMIX at the usual time.

If you spit up or vomit the dose repeatedly after taking VENMIX, consult a doctor.

Different age groups:**Use in children:**

VENMIX is not recommended for persons under 18 years of age. Use in children and adolescents There is insufficient information on the issue.

Use in the elderly:

No dose adjustment is required in elderly patients.

Specific use cases:**Renal impairment:**

When VENMIX is used to prevent a type of heart rhythm disorder (non-valvular atrial fibrillation), stroke or blood clots in other vessels of the body; the recommended dose in moderate and severe renal impairment is 15 mg once daily.

When VENMIX is used for the treatment of blood clots in the veins of the legs (deep vein thrombosis), the treatment of blood clots in the veins of the lungs (pulmonary embolism) and the prevention of recurrent blood clots in the veins of the legs and blood clots in the veins of the lungs (pulmonary embolism), the recommended dose in moderate and severe renal impairment is 15 mg twice daily for the first 3 weeks and 20 mg once daily thereafter. If the patient's assessed risk of bleeding is greater than the risk of recurrent blood clots in the veins of the legs (deep vein thrombosis) and blood clots in the veins of the lungs (pulmonary embolism), a dose reduction from 20 mg once daily to 15 mg once daily should be considered. The recommendation to use the 15 mg dose is based on pharmacokinetic modeling and has not been studied in this clinical setting.

No dose adjustment is required in patients with mild renal impairment.

It should be used with caution in patients with severe renal impairment.

If you have very severe renal impairment, VENMIX should not be used.

Hepatic impairment:

It should not be used in patients with liver disease that may cause bleeding risk.

If you have an impression that the effect of VENMIX is too strong or weak, talk to your doctor or pharmacist.

If you have used more VENMIX than you should:

If you have used more VENMIX than you should, talk to a doctor or pharmacist.

Taking more VENMIX than you should increases the risk of bleeding.

If you forget to use VENMIX:

If you miss a dose during the 20 mg once daily or 15 mg once daily treatment phase, take the missed dose immediately. Do not take more than one tablet in one day to make up the missed dose.

Take the next tablet the next day and then continue your treatment with one tablet once daily. If you miss a dose during the 15 mg twice daily treatment phase, take the missed dose immediately. Do not take more than two 15 mg tablets in one day. If you forget to take a dose, two 15 mg tablets can be taken together at the same time to get a total of two tablets (30 mg) in one day. The next day, continue your treatment with one 15 mg tablet twice a day.

Do not take double doses to compensate for forgotten doses.

Possible effects when treatment with VENMIX is discontinued

Do not stop taking VENMIX without talking to your doctor first because VENMIX treats and prevents serious conditions.

4. Possible side effects

Like all medicines, people who are sensitive to the ingredients in VENMIX may have side effects.

If you notice any of the following, stop taking VENMIX and IMMEDIATELY inform your doctor or contact the emergency department of the nearest hospital:

Like other similar medicines (blood clotting inhibitors), VENMIX can cause life-threatening bleeding. Excessive bleeding can cause sudden drops in blood pressure (shock). Sometimes this bleeding may not be obvious.

Symptom of bleeding

- Bleeding into the brain or skull (Symptoms may include headache, unilateral weakness, vomiting, seizures, decreased level of consciousness and neck stiffness. This is a serious medical emergency. Medical attention should be sought immediately.)
- Prolonged or excessive bleeding,
- Symptoms such as unusual weakness, tiredness, pallor, dizziness, headache, unexplained swelling in one part of the body, trouble breathing, chest pain or angina pectoris.

Your doctor may keep you under closer observation or change your treatment.

Symptom of serious skin reaction

- A spreading intense skin rash, blisters or mucosal lesions (e.g. in the mouth or eyes) (Stevens-Johnson syndrome/toxic epidermal necrolysis).
- A drug reaction leading to rash, fever, inflammation of internal organs, blood abnormalities and systemic disease (DRESS syndrome).

The incidence of these side effects is very rare (less than one in 10,000 patients).

Symptom of severe allergic reaction

Swelling of the face, lips, mouth, tongue or throat; difficulty swallowing, hives, breathing difficulties, sudden drop in blood pressure. The incidence of these serious allergic reactions is very rare for anaphylactic reactions including anaphylactic shock (less than one in 10,000 patients) and uncommon for angioedema and allergic oedema (less than one in 100 patients but more than one in 1,000 patients).

These are all very serious side effects. If you have any of these, you are seriously allergic to VENMIX. You may need urgent medical attention or hospitalization.

The side effects you will feel while using VENMIX are usually mild. However, if any of the following side effects bother you, consult your doctor.

Side effects are listed as shown in the categories below:

Very common: Occurs in at least one in 10 patients.

Common: Less than one in 10 patients, but more than one in 100 patients.

Uncommon: Less than one in 100 patients, but more than one in 1,000 patients.

Rare: Less than one in 1,000 patients but more than one in 10,000 patients.

Very rare: Less than one in 10,000 patients.

Unknown: It may occur in too few patients to be determined with the available data.

Common:

- Reduced red blood cells causing pale skin and weakness or shortness of breath,
- Bleeding in the stomach or intestines, urogenital bleeding (including blood in the urine and severe menstrual bleeding), nosebleeds, bleeding gums,
- Intraocular bleeding (including bleeding in the white part of the eye),
- Bleeding into tissue or body cavity (hematoma, bruise),
- Coughing up blood,
- Bleeding through the skin or subcutaneously,
- Postoperative bleeding,
- Leakage of blood or fluid at the surgical wound site,
- Swelling in the arms and legs,
- Pain in the arms and legs,
- Fire,
- Impairment of kidney function (visible in tests performed by your doctor),
- Stomach pain, indigestion, feeling or being sick, constipation, diarrhea,
- Low blood pressure (symptoms may include dizziness or feeling faint when standing up),
- General decrease in strength and energy (fatigue, exhaustion), headache, dizziness,
- Skin itching, rash,

- Blood tests may show an increase in some liver enzymes.

Uncommon

- Bleeding into the brain or skull (see section Signs of bleeding),
- Intra-articular bleeding causing pain or swelling,
- Thrombocytopenia (low numbers of platelets - blood platelets - the cells that help the blood to clot),
- Allergic reactions including allergic skin reactions,
- Impaired liver function (visible in tests performed by your doctor),
- Blood tests may show an increase in bilirubin, some pancreatic or liver enzymes or an increase in the number of blood platelets,
- Feeling faint,
- Not feeling well,
- Increased heart rate,
- Dry mouth,
- Hives.

Rare:

Intramuscular bleeding,

- Cholestasis (decreased bile flow), hepatitis (inflammation of the liver, including hepatocellular injury),
- Yellowing of the skin or eyes (jaundice),
- Regional swelling,
- A collection of blood in the groin (hematoma) as a complication of a heart-related procedure (pseudoaneurysm) involving the insertion of a catheter into an artery in your leg.

Very Rare:

- Accumulation of eosinophils, a type of white granulocytic blood cell that causes inflammation in the lung (eosinophilic pneumonia)

Unknown:

- Renal failure after severe bleeding.
- Increased pressure in the leg or arm muscles after bleeding causing pain, swelling, changes in sensation, numbness or paralysis (post-bleeding compartment syndrome).

If you experience any side effects not listed in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

Talk to your doctor, pharmacist or nurse in case of any side effects that may or may not be included in the instructions for use. In addition, report the side effects you encounter to the Turkish Pharmacovigilance Center (TÜFAM) by clicking on the "Drug Side Effect Notification" icon on the www.titck.gov.tr website or by calling the side effect reporting line at

0 800 314 00 08. By reporting the side effects that occur, you will contribute to learning more about the safety of the drug you are using.

5. How to store VENMIX?

Keep VENMIX out of sight and reach of children and in its packaging.

Store below 25 °C.

Use in accordance with the expiry date.

Do not use VENMIX after the expiry date on the packaging.

If you notice defects in the product and/or its packaging, do not use VENMIX.

Do not throw away expired or unused medicines! Give it to the collection system determined by the Ministry of Environment and Urbanization

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