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

The medicine is dispensed with a doctor's prescription only

Apixaban Teva 2.5 mg Film-coated tablets

Composition
Each film-coated tablet contains:
Apixaban 2.5 mg

Apixaban Teva 5 mg Film-coated tablets

Composition
Each film-coated tablet contains:
Apixaban 5 mg

For information regarding inactive ingredients and allergens in the preparation 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.

This medicine has been prescribed for treatment of your illness, do not pass it on to others, it may harm them even if it seems to you that their illness is similar to yours.

This medicine is not intended for treatment of children and adolescents under the age of 18 years.

Patient safety information card:
This card contains important safety information, which you need to know before starting treatment with **Apixaban Teva** and during the treatment with **Apixaban Teva**. The card contains information intended for both the patient and the healthcare staff. It provides guidance for patients on how to minimize the risk of bleeding, which results from treatment with any of the anticoagulant preparations.
In addition, the card contains personal details of the patient and information regarding the preparation **Apixaban Teva**.
Present this card to any healthcare professional involved in your treatment.

1. WHAT IS THE MEDICINE INTENDED FOR?

Apixaban Teva 2.5 mg
For the prevention of venous thromboembolism in adult patients following elective hip or knee replacement surgery.
For the prevention of stroke and embolism in adult patients with (non-valvular) atrial fibrillation, with at least one risk factor, such as prior stroke or transient ischemic attack, age 75 years and above, hypertension, diabetes, symptomatic heart failure.
For the treatment of blood clots in the leg veins (deep vein thrombosis) and in the lung blood vessels (pulmonary embolism), and to prevent the recurrence of blood clots in these blood vessels.

Apixaban Teva 5 mg
For the prevention of stroke and embolism in adult patients with (non-valvular) atrial fibrillation, with at least one risk factor, such as prior stroke or transient ischemic attack, age 75 years and above, hypertension, diabetes, symptomatic heart failure.
For the treatment of blood clots in the leg veins (deep vein thrombosis) and in the lung blood vessels (pulmonary embolism).

Therapeutic class
Anticoagulant

2. BEFORE USING THE MEDICINE

Do not use the medicine if:
- You are sensitive (allergic) to the active ingredient or to any of the other ingredients this medicine contains (see section 6 – "Additional information").
- You suffer from a significant active bleeding.
- You suffer from a liver disease leading to a clotting disorder and a risk of bleeding.
- You suffer from a disorder or a medical condition that increases the risk of bleeding, such as an active or recent stomach or intestinal ulcer, a malignant tumor with increased risk of bleeding, recent spinal or brain injury, recent intracranial bleeding, known or suspected esophageal varices, arteriovenous malformation, vascular aneurysm or major intraspinal or intracerebral vascular abnormalities.
- You have recently had a brain, spinal or eye surgery.
- You are taking other anticoagulant preparations, for example oral anticoagulants (such as warfarin, rivaroxaban, dabigatran), heparin, low molecular weight heparin (such as enoxaparin, dalteparin), heparin derivatives (such as fondaparinux), except when switching from or to treatment with **Apixaban Teva** or if an intra-venous or intra-arterial catheter is installed, through which heparin must be administered to keep it open.

Special warnings regarding the use of the medicine
This medicine may cause changes in blood tests.

Before treatment with Apixaban Teva, inform the doctor if:
- You are breastfeeding.
- You suffer from a severe kidney disease or you are treated with dialysis.
- You suffer or have suffered in the past from impaired liver function. Caution must be exercised in patients with changes in liver function.
- You suffer from a medical condition that may increase the risk of bleeding, such as a bleeding disorder including platelet dysfunction, severe hypertension which is not controlled by pharmacological treatment.
- You are over 75 years of age, if your weight is 60 kg or less.
- You had a catheter inserted or received an injection into your spine (to perform anesthesia or to relieve pain) in close proximity to the medicine administration. The doctor will instruct you to take the medicine 5 hours or more after the catheter is removed.
- You have a prosthetic heart valve.
- Your doctor has determined that your blood pressure is not stable or that another treatment or surgical procedure is planned to remove the blood clot from the lungs.
- You are sensitive to any type of food or medicine.
- You suffer from a congenital problem of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption.
- You are about to undergo a surgery or treatment that may cause bleeding. This may lead the doctor to ask you to stop the treatment with the medicine for a short period. Consult the doctor if you are not certain whether the surgery may cause bleeding.
- You suffer from antiphospholipid syndrome (a disorder of the immune system which increases the risk of blood clots). Your doctor may decide to change the treatment.

Tests and follow-up
Before starting to use the medicine, the doctor will refer you for a liver function test.

Drug interactions
If you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements, inform the doctor, pharmacist or nurse. In particular, inform the doctor, pharmacist or nurse if you are taking:
- The following medicines may increase the effect of **Apixaban Teva** and increase the risk of undesirable bleeding:
  - Some medicines used for treatment of fungal infection (such as ketoconazole, itraconazole, voriconazole and posaconazole).
  - Some medicines used for treatment of acquired immunodeficiency syndrome (HIV/AIDS) (such as ritonavir).
  - Medicines used for treatment of high blood pressure or heart problems (such as diltiazem).
  - Other medicines used for reducing the formation of blood clots (such as enoxaparin).
  - Anti-inflammatory medicines or analgesics, such as naproxen or aspirin. You are at an increased risk of bleeding, especially if you are above 75 years of age and taking aspirin.
  - Antidepressants from the group of selective serotonin reuptake inhibitors (SSRI) or from the group of serotonin-norepinephrine reuptake inhibitors (SNRI).
- The following medicines may reduce the concentration of **Apixaban Teva** in the blood and therefore may decrease its efficacy: medicines for treatment of tuberculosis or other infections (such as rifampin – an antibiotic), medicines for treatment of epilepsy or seizures (such as phenytoin, phenobarbital and carbamazepine), hypericum (St. John's Wort), a herbal remedy used for treatment of depression.

Use of the medicine and food
The medicine may be taken with or without food.

Pregnancy and breastfeeding
Consult the doctor before starting treatment with any medicine if you are pregnant or breastfeeding, suspect you may be pregnant or are planning to become pregnant.
The effects of **Apixaban Teva** on the pregnancy or the fetus are not known. Do not use **Apixaban Teva** if you are pregnant. If you become pregnant while using the medicine, **contact the doctor immediately.**
If you are breastfeeding, consult the doctor, pharmacist or nurse before using **Apixaban Teva**. It is unknown whether **Apixaban Teva** passes into breastmilk.
The medical staff will recommend whether to stop breastfeeding or whether to stop/not start the treatment with **Apixaban Teva**.

Important information about some of the ingredients of the medicine
- **Apixaban Teva** contains lactose (a type of sugar). If you have been told by your doctor that you have an intolerance (sensitivity) to some sugars, consult with your doctor before taking this medicine.
- This medicine contains less than 23 mg of sodium in a tablet, and is therefore considered 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.

Dosage
The dosage and treatment regimen will be determined only by the doctor.
- Swallow the medicine with water.
- Do not halve the tablets in the absence of a score line.
- If you have a difficulty swallowing the tablet whole, talk to your doctor about other possible administration routes for **Apixaban Teva**. The tablet can be crushed and mixed with water, 5% glucose in water, apple juice or apple sauce, immediately before taking.
  Directions for crushing:
  - Crush the tablet with a mortar and pestle.
  - Transfer all the powder carefully into a suitable vessel and mix with a little liquid, about 30 ml (two spoons) of water or any of the above-mentioned liquids.
  - Swallow the mixture.
  - Rinse the mortar and pestle you used to crush the tablet with a little water or any of the other liquids (30 ml) into the vessel that contained the mixture, and swallow the rinsing fluid.
- If necessary, your doctor can give you **Apixaban Teva** through a nasogastric tube.
- **Treatment for the prevention of venous thromboembolism in adult patients following elective hip or knee replacement surgery:**
  The recommended dosage is one tablet of **Apixaban Teva 2.5 mg** twice daily, for example, one tablet in the morning and another tablet in the evening. Try taking the medicine at regular times every day, to get the optimal effect of the treatment.
  Start taking the medicine about 12-24 hours after the surgery. Do not stop taking the medicine unless your doctor has told you to.
  The accepted duration of treatment is 32-38 days following hip surgery, or 10-14 days following knee surgery.
- **Treatment for the prevention of stroke and embolism in adult patients with (non-valvular) atrial fibrillation, with at least one risk factor** such as a prior stroke or transient ischemic attack, age 75 years and above, hypertension, diabetes, symptomatic heart failure:
  The recommended dosage is one tablet of **Apixaban Teva 5 mg** twice daily.
  The recommended dosage will be reduced to **2.5 mg** twice daily if:
  - You suffer from severely reduced kidney function.
  - At least two of the following criteria are met:
    - Your blood tests indicate low kidney function (creatinine serum value ≥ 1.5 mg/dL).
    - You are 80 years or older.
    - Your body weight is 60 kg or less.

  The recommended dosage is one tablet twice daily, for example, one tablet in the morning and another tablet in the evening. Try taking the medicine at regular times every day, to get the optimal effect of the treatment.
  Your doctor will decide how long you should continue with the treatment.
- **Treatment of blood clots in the leg veins and in the lung blood vessels:**
  The recommended dosage is **two tablets** of **Apixaban Teva 5 mg** twice daily for the first 7 days, for example, two tablets in the morning and two tablets in the evening.
  After the first 7 days of treatment, the recommended dosage is **one tablet** of **Apixaban Teva 5 mg** twice daily, for example, one tablet in the morning and another tablet in the evening. Try taking the medicine at regular times every day, to get the optimal effect of the treatment.
- **Prevention of recurrent blood clots following 6 months of treatment:**
  The recommended dosage is one tablet of **Apixaban Teva 2.5 mg** twice daily, for example, one tablet in the morning and another tablet in the evening. Try taking the medicine at regular times every day, to get the optimal effect of the treatment.
  Your doctor will decide how long you should continue with the treatment.

Do not exceed the recommended dose.
Your doctor may make the following changes in the anticoagulation treatment you are receiving:
- Switching from treatment with **Apixaban Teva** to treatment with other anticoagulant preparations:
  Stop taking **Apixaban Teva** and start the treatment with the other anticoagulant preparation (such as heparin) at the time you were supposed to take the next dose of **Apixaban Teva**.
- Switching from treatment with another anticoagulant preparation to treatment with **Apixaban Teva**:
  Stop taking the anticoagulant preparation and start the treatment with **Apixaban Teva** at the time you were supposed to take the next dose of the anticoagulant preparation. Afterwards, continue according to the recommended dosage.
- Switching from treatment with vitamin K antagonists (such as warfarin) to treatment with **Apixaban Teva**:
  Stop the treatment with the vitamin K antagonists. The doctor has to perform blood tests and to instruct you regarding the time of starting treatment with **Apixaban Teva**.
- Switching from treatment with **Apixaban Teva** to treatment with vitamin K antagonists (such as warfarin):
  If your doctor instructs you to start treatment with vitamin K antagonists, continue taking **Apixaban Teva** for at least two additional days after taking the first dose of the vitamin K antagonist. The doctor has to perform blood tests and to instruct you regarding the time of stopping treatment with **Apixaban Teva**.

If you took an overdose, or if a child accidentally swallowed the medicine, refer immediately to the doctor or to a hospital emergency room and take the package of the medicine with you. An overdose may cause bleeding. In case of bleeding, you may need blood transfusion or surgery.

If you forgot to take this medicine at the appointed time, take a dose as soon as you remember and take the next dose at the usual time. Afterwards, continue according to the recommended dosage as usual. If you are uncertain about what you should do, or if you forgot more than one dose, consult the doctor, pharmacist or nurse.
Follow the treatment as recommended by the doctor.
Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor or pharmacist.

If you stop taking the medicine too early, you may develop blood clots.

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

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

4. SIDE EFFECTS

As with any medicine, using **Apixaban 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. The side effects and their frequency may be different for the different indications and are detailed below for each indication. The most common side effect of **Apixaban Teva** is bleeding, which may be life-threatening and therefore requires you to immediately refer to the doctor.

Typical side effects of treatment with Apixaban Teva for the prevention of venous thromboembolism in adult patients following elective hip or knee replacement surgery:

Common side effects (may occur in up to 1 out of 10 people):
- Anemia that may lead to tiredness or pallor
- Bleeding that includes bruising and swelling
- Nausea (feeling sick)

Uncommon side effects (may occur in up to 1 out of 100 people):
- Decreased blood platelet count (may affect blood clotting)
- Bleeding, including: bleeding following surgery including bruising and swelling, blood or liquid excretion from the incision or from the place of injection; bleeding in the stomach, intestine or red/light blood in the stool, blood in the urine, nose bleeding, vaginal bleeding
- Decrease in blood pressure which may cause a feeling of fainting or rapid heartbeat
- Changes in blood tests which may demonstrate: abnormal liver function results, increased liver enzymes, increased bilirubin (a product of the metabolism of red blood cells which is manifested by yellowing of the skin and eyes)
- Itch

Rare side effects (may occur in up to 1 out of 1,000 people):
- Allergic reaction (hypersensitivity) which may cause swelling of the face, lips, mouth, tongue and/or throat and breathing difficulties. **Refer to a doctor immediately if you experience any of these symptoms.**
- Bleeding into the muscle, bleeding in the eye, bleeding gums and bloody cough, anal bleeding
- Hair loss

Side effects with unknown frequency (frequency cannot be estimated from the available data):
- Bleeding, including: cerebral bleeding, spinal bleeding, bleeding in the lungs or throat, mouth bleeding, bleeding into the abdominal cavity or bleeding into the space behind the abdominal cavity, hemorrhoidal bleeding, tests that show blood in the stool or urine
- Skin rash which may form blisters and looks like small targets (a dark central spot surrounded by a pale area, with a dark ring around the margins) (*erythema multiforme*)
- Inflammation of the blood vessels (vasculitis) which may cause skin rash or pointed, flat, red, round spots below the skin surface or bruising

Typical side effects of treatment with Apixaban Teva for the prevention of stroke and embolism in adult patients with (non-valvular) atrial fibrillation, with at least one additional risk factor:

Common side effects (may occur in up to 1 out of 10 people):
- Bleeding, including: bleeding in the eyes, gastric or intestinal bleeding, anal bleeding, blood in the urine, nose bleeding, bleeding gums, swelling and bruising
- Anemia that may lead to tiredness or pallor
- Low blood pressure which may lead to a feeling of fainting or rapid heartbeat
- Nausea (feeling sick)
- Blood tests that may demonstrate an elevation in gamma-glutamyl transferase (GGT)

Uncommon side effects (may occur in up to 1 out of 100 people):
- Bleeding, including: cerebral bleeding, spinal bleeding, mouth bleeding or bloody cough, bleeding into the abdominal cavity, vaginal bleeding, red/light blood in the stool, bleeding following surgery including bruising and swelling, blood or liquid excretion from the incision or from the place of injection; hemorrhoidal bleeding, tests that show blood in the stool or urine
- Decreased blood platelet count (may affect blood clotting)
- Changes in blood tests which may demonstrate: abnormal liver function results, increased liver enzymes, increased bilirubin (a product of the metabolism of red blood cells which is manifested by yellowing of the skin and eyes)
- Skin rash
- Itch
- Hair loss
- Allergic reaction (hypersensitivity) which may cause swelling of the face, lips, mouth, tongue and/or throat and breathing difficulties. **Refer to a doctor immediately if you experience any of these symptoms.**

Rare side effects (may occur in up to 1 out of 1,000 people):
- Bleeding in the lungs or throat, bleeding into the space behind the abdominal cavity, bleeding into the muscle

Very rare side effects (may occur in up to 1 out of 10,000 people):
- Skin rash which may form blisters and looks like small targets (a dark central spot surrounded by a pale area, with a dark ring around the margins) (*erythema multiforme*)

Side effects with unknown frequency (frequency cannot be estimated from the available data):
- Inflammation of the blood vessels (vasculitis) which may cause skin rash or pointed, flat, red, round spots below the skin surface or bruising

The following side effects are known if you take Apixaban Teva for the treatment or the prevention of the recurrence of blood clots in the leg veins or in the lung blood vessels:

Common side effects (may occur in up to 1 out of 10 people):
- Bleeding, including: nose bleeding, bleeding gums, blood in the urine, bruising and swelling, abdominal bleeding, intestinal bleeding and anal bleeding, mouth bleeding, vaginal bleeding
- Anemia that may lead to tiredness or pallor
- Decreased blood platelet count (may affect blood clotting)
- Nausea (feeling sick)
- Skin rash
- Blood tests that may demonstrate an elevation in gamma-glutamyl transferase (GGT) or in alanine aminotransferase (ALT)

Uncommon side effects (may occur in up to 1 out of 100 people):
- Low blood pressure which may lead to a feeling of fainting or rapid heartbeat
- Bleeding, including: bleeding in the eyes, mouth bleeding or bloody cough, red/light blood in the stool, tests that show blood in the stool or urine, bleeding following surgery, including bruising and swelling, blood or liquid excretion from the incision or from the place of injection; hemorrhoidal bleeding, bleeding into the muscle
- Itch
- Hair loss
- Allergic reaction (hypersensitivity) which may cause swelling of the face, lips, mouth, tongue and/or throat and breathing difficulties. **Refer to the doctor if you experience any of these symptoms.**
- Changes in blood tests which may demonstrate: abnormal liver function results, increased liver enzymes, increased bilirubin (a product of the metabolism of red blood cells which is manifested by yellowing of the skin and eyes)

Rare side effects (may occur in up to 1 out of 1,000 people):
- Bleeding, including: cerebral bleeding, spinal bleeding, bleeding in the lungs

Side effects with unknown frequency (frequency cannot be estimated from the available data):
- Bleeding, including: bleeding into the abdominal cavity or into the space behind the abdominal cavity
- Skin rash which may form blisters and looks like small targets (a dark central spot surrounded by a pale area, with a dark ring around the margins) (*erythema multiforme*)
- Inflammation of the blood vessels (vasculitis) which may cause skin rash or pointed, flat, red, round spots below the skin surface or bruising

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 below 25°C.**

6. ADDITIONAL INFORMATION

In addition to the active ingredient, the medicine also contains:
Lactose (anhydrous), microcrystalline cellulose, croscarmellose sodium, hypromellose, magnesium stearate, titanium dioxide, lactose monohydrate, sodium lauryl sulfate, polyethylene glycol, triacetin, iron oxide red
2.5 mg - iron oxide yellow.

What does the medicine look like and what are the contents of the package?
Apixaban Teva 2.5 mg: light yellow, film coated, round tablet, debossed with "TV" on one side and with "G1" on the other side of the tablet.
Apixaban Teva 5 mg: light pink, film coated, oval shape tablet, debossed with "TV" on one side and with "G2" on the other side of the tablet.
The packages contain 30, 60 or 100 tablets.
Not all package sizes may be marketed.

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

The leaflet was revised in February 2023 in accordance with the Ministry of Health guidelines.

Registration numbers of the medicine in the national drug registry of the Ministry of Health
Apixaban Teva 2.5 mg: 164.92.35374
Apixaban Teva 5 mg: 164.93.35375

Apixaban PIL MW0223

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