

**Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) – 1986**

The medicine is dispensed with a doctor's prescription only

## Apixaban Sandoz® 2.5 mg Apixaban Sandoz® 5 mg

### Film-coated tablets

Each tablet contains: apixaban 2.5 mg

### Film-coated tablets

Each tablet contains: apixaban 5 mg

For a list of inactive and allergens in this preparation, see section 2 under "Important information about some of this medicine's ingredients" and section 6 "Further information".

**Read the 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 the 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 to yours.

### In addition to the patient leaflet, Apixaban Sandoz also has a patient safety information card:

This card contains important safety information that you must be aware of and that you should follow, before starting treatment with **Apixaban Sandoz** and during treatment with **Apixaban Sandoz**. The card contains information intended for both the patient and the medical staff. It provides patient guidance as to how to minimize the risk of bleeding arising from treatment with each of the anticoagulants. In addition, the card contains personal patient information and information about **Apixaban Sandoz**.

Present this card to each medical staff member involved in your treatment. Carefully read the patient safety information card and patient leaflet before using this medicine. Keep the card in case you need to read it again.

## 1. What is the medicine intended for?

### Apixaban Sandoz 2.5 mg

For prevention of venous thrombotic events in adult patients following elective knee or hip replacement surgery.

For prevention of stroke and embolism in adult patients with atrial fibrillation (of a non-valvular source) and with at least one risk factor, such as: prior stroke or transient ischemic attack, aged 75 years and above, hypertension, diabetes mellitus, symptomatic heart failure.

For treatment of blood clots in the veins of the legs (deep-vein thrombosis) and in the blood vessels of the lungs (pulmonary embolism), and to prevent recurrence of blood clots in these blood vessels.

### Apixaban Sandoz 5 mg

For prevention of stroke and embolism in adult patients with atrial fibrillation (of a non-valvular source) and with at least one risk factor, such as: prior stroke or transient ischemic attack, aged 75 years and above, hypertension, diabetes mellitus, symptomatic heart failure.

For treatment of blood clots in the veins of the legs (deep-vein thrombosis) and in the blood vessels of the lungs (pulmonary embolism).

**Therapeutic group:** 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 additional ingredients contained in the medicine (detailed in section 6).
- You are suffering from significant active bleeding.
- You are suffering from a liver disease causing a coagulation disturbance and risk of bleeding.
- You are suffering from an injury or a medical condition with an increased risk of bleeding, e.g., active stomach or bowel ulcer or one that has recently occurred, a malignant tumour with increased risk of bleeding, recent brain injury or spinal cord injury, recent intracranial bleeding, known or suspected oesophageal varices, arteriovenous malformation, vascular aneurysm or major cerebral or spinal blood vessel abnormality.
- You have recently undergone brain, spine, or eye surgery.
- You are taking other anticoagulants, such as oral anticoagulants (e.g., warfarin, rivaroxaban, dabigatran), heparin, low-molecular weight heparin (e.g., enoxaparin, dalteparin), heparin derivatives (e.g., fondaparinux), excluding situations when switching from or to treatment with **Apixaban Sandoz** or if a venous or arterial line is installed and heparin needs to be administered through this line to keep it open.

### Special warnings regarding use of the medicine

- This medicine can cause changes in blood tests.

### Before treatment with Apixaban Sandoz, tell your doctor if:

- You are breast-feeding.
- You are suffering from a severe kidney disease or if you are undergoing dialysis.
- You are suffering, or have suffered in the past, from impaired liver function. Caution is required in patients with signs of altered liver function.
- You are suffering from a medical condition that may increase the risk of bleeding, such as: a bleeding disorder, including a reduction in the activity of platelets, severe hypertension that is not controlled by medicinal treatment.
- You are older than 75 years.
- You weigh 60 kg or less.
- You have had a catheter inserted or received an injection into the spine (for anaesthesia or analgesia) in proximity to administration of the medicine. The doctor will instruct you to take the medicine 5 or more hours after the removal of the catheter.
- You have a prosthetic heart valve.
- Your doctor has determined that your blood pressure is unstable or that another treatment or surgical procedure to remove the blood clot from your lungs is planned.
- You are suffering from a congenital problem of galactose intolerance, Lapp-lactase deficiency or glucose-galactose malabsorption.
- You are scheduled to undergo surgery or treatment that may cause bleeding. As a result, you may be asked by the doctor to stop treatment with this medicine for a short while. If you are uncertain whether the treatment can cause bleeding, consult the doctor.
- You are suffering from antiphospholipid syndrome (a disorder of the immune system that increases the risk of blood clots). Your doctor may decide to change the treatment.

### Children and adolescents

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

### Tests and follow-up

Before you start taking this medicine, your 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, tell the doctor, pharmacist or nurse.** In particular if you are taking:

- The following medicines may enhance the effect of **Apixaban Sandoz** and increase the chance of undesirable bleeding:
  - Certain medicines used to treat fungal infections (e.g., ketoconazole, itraconazole, voriconazole, and posaconazole).
  - Certain medicines used to treat acquired immunodeficiency syndrome (HIV/AIDS) (e.g., ritonavir).
  - Medicines that are used to treat hypertension or heart problems (e.g., diltiazem).
  - Other medicines that are used to reduce formation of blood clots (e.g., enoxaparin).
- Anti-inflammatory agents or pain-relief medicines such as: naproxen or aspirin, especially if you are older than 75 years of age and are taking aspirin, you are at increased risk for bleeding.
- Antidepressant from the selective serotonin reuptake inhibitor class (SSRIs) or serotonin-norepinephrine reuptake inhibitors (SNRIs).
- The following medicines may decrease the concentration of **Apixaban Sandoz** in the blood, and may thereby reduce its efficacy:
  - medicines for tuberculosis or other infections (e.g., rifampicin, an antibiotic).
  - medicines to prevent and to treat epilepsy or seizures (e.g., phenytoin, phenobarbital, and carbamazepine).
  - Hypericum (St. John's wort), a herbal remedy used for depression.

### Use of the medicine and food

This medicine can be taken with or without food.

### Pregnancy and breast-feeding

If you are pregnant or breast-feeding, suspect you are pregnant or are planning a pregnancy, consult the doctor before starting treatment with any medicine.

The effects of **Apixaban Sandoz** on pregnancy or on the unborn baby are unknown. Do not use **Apixaban Sandoz** if you are pregnant. If you become pregnant while using the medicine, **contact the doctor immediately**. If you are breast-feeding, consult a doctor, pharmacist or nurse before using **Apixaban Sandoz**. It is not known whether **Apixaban Sandoz** passes into breast milk. The medical staff will tell you to either stop breast-feeding or to stop/not to start treatment with **Apixaban Sandoz**.

### Important information about some of this medicine's ingredients

The tablet contains lactose (a type of sugar).

If you have been told by your doctor that you have an intolerance to certain sugars, consult with your doctor for advice before taking this medicine.

This medicine contains less than 1 millimole (23 mg) sodium per tablet, meaning it is considered 'sodium free'.

## 3. How should you use the medicine?

Always use the medicine according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain regarding the dosage and treatment regimen of the preparation.

- The dosage and treatment regimen will be determined by the doctor only.
- Manner of administration: swallow the medicine with water.
- If you have difficulty swallowing the tablet whole, talk to your doctor about other possible ways to take **Apixaban Sandoz**.

The tablet may be crushed and mixed with water, 5% glucose solution in water, apple juice or apple puree, immediately before you take it.

### Instructions for crushing:

- Crush the tablet with a pestle and mortar.
- Carefully transfer all the powder into a suitable container, and mix with a little liquid, approximately 30 mL (2 tablespoons) water or one of the other liquids mentioned above.
- Swallow the mixture.
- Rinse the pestle and mortar you used for crushing the tablet with a little water or one of the other liquids (e.g., 30 mL) into the container that contained the mixture, and swallow the rinse.

If necessary, your doctor may give you **Apixaban Sandoz** through a nasogastric tube.

### Do not exceed the recommended dose.

### Treatment for prevention of venous thrombotic events in adult patients following elective knee or hip replacement surgery:

The recommended dosage is one tablet of **Apixaban Sandoz 2.5 mg** twice a day. For example, one tablet in the morning and another tablet in the evening. Try to take the medicine at regular times every day, in order to obtain the optimal effect of the treatment. Start taking the medicine about 12–24 hours following the surgery. Do not stop taking the medicine unless you have been told to do so by the doctor. The standard duration of treatment is 32–38 days following hip surgery or 10–14 days following knee surgery.

### Treatment for prevention of stroke and embolism in adult patients with atrial fibrillation (of a non-valvular source) and with at least one risk factor, such as: previous stroke or transient ischemic event, 75 years of age and above, hypertension, diabetes mellitus, symptomatic heart failure:

The recommended dosage is one tablet of **Apixaban Sandoz 5 mg** twice a day. The recommended dose will be reduced to 2.5 mg twice a day if:

- you have severely reduced kidney function.
- two or more of the following criteria apply to you:
  - your blood tests indicate poor kidney function (value of serum creatinine is  $\geq 1.5$  mg/dL).
  - you are 80 years old or older.
  - your weight is 60 kg or lower.

The recommended dosage is one tablet twice a day. For example, one tablet in the morning and another tablet in the evening. Try to take the medicine at regular times every day, in order to obtain the optimal effect of the treatment. Your doctor will decide how long you should continue treatment.

### Treatment of blood clots in the veins of the legs and in the blood vessels of the lungs:

The recommended dosage is **two tablets of Apixaban Sandoz 5 mg** twice a day 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 Sandoz 5 mg** twice a day, for example, one tablet in the morning and another tablet in the evening. Try to take the medicine at regular times every day, in order to obtain the optimal effect of the treatment.

### For preventing blood clots from recurring following completion of 6 months of treatment:

The recommended dosage is **one tablet of Apixaban Sandoz 2.5 mg** twice a day.

For example, one tablet in the morning and another tablet in the evening. Try to take the medicine at regular times every day, in order to obtain the optimal effect of the treatment.

Your doctor will decide how long you should continue treatment.

Your doctor may prescribe the following changes in your anticoagulant treatment:

- Switching from treatment with **Apixaban Sandoz** to treatment with other anticoagulants:
  - Stop taking **Apixaban Sandoz** and start treatment with the other anticoagulant (e.g., heparin) at the time you would have taken the next dose of **Apixaban Sandoz**.
- Switching from another anticoagulant to treatment with **Apixaban Sandoz**:
  - Stop treatment with the anticoagulant and start treatment with **Apixaban Sandoz** at the time you would have had the next dose of the anticoagulant medicine you were taking. Then, continue as per the recommended dosage.
- Switching from treatment with vitamin K antagonists (e.g., warfarin) to treatment with **Apixaban Sandoz**:
  - Stop treatment with the vitamin K antagonists. The doctor must perform blood tests and instruct you when to start treatment with **Apixaban Sandoz**.
- Switching from **Apixaban Sandoz** to treatment with vitamin K antagonists (e.g., warfarin):
  - If your doctor instructs you to start treatment with vitamin K antagonists (e.g., warfarin), continue taking **Apixaban Sandoz** for at least 2 more days after taking the first dose of the vitamin K antagonist. The doctor must perform blood tests and tell you when treatment with **Apixaban Sandoz** should be terminated.

**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. An overdose may cause bleeding. In case of bleeding, you may need a blood transfusion or surgery.

**If you forgot to take this medicine** at the specified time, take a dose as soon as you remember and take the next dose at the regular time. Then continue as per the recommended dosage. If you are not sure what to do or have missed more than one dose, consult the doctor, pharmacist or nurse.

Adhere to 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 the pharmacist.

**If you stop taking the medicine too early**, you may suffer from the development of blood clots.

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

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

## 4. Side effects

As with any medicine, use of **Apixaban Sandoz** 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. Side effects and their frequency can vary between the different indications and are detailed below for each indication. The most common side effect of **Apixaban Sandoz** is bleeding, which can be life-threatening and therefore requires immediate referral to a doctor.

### Side effects characteristic of Apixaban Sandoz administration to prevent venous thrombotic events in adult patients following elective knee or hip replacement surgery:

#### Common side effects (may affect up to 1 in 10 people):

- Anaemia, which may cause tiredness and paleness.
- Bleeding, including bruising and swelling.
- Nausea.

#### Uncommon side effects (may affect up to 1 in 100 people):

- Reduced number of platelets in your blood (may affect clotting).
- Bleeding, including: bleeding occurring after a surgery, including bruising and swelling, blood or liquid leaking from the incision or injection site. Bleeding in the stomach, bowel or red/bright blood in the stools, blood in the urine, nosebleed, vaginal bleeding.
- A decrease in blood pressure that may cause a feeling of faintness or have a quicker heartbeat.
- Blood test changes that may show abnormal liver function results, increase in liver enzymes, increase in bilirubin - a breakdown product of red blood cells manifested by yellowing of the skin and eyes.
- Itching.

#### Rare side effects (may affect up to 1 in 1,000 people):

- Allergic reaction (hypersensitivity) which may cause swelling of the face, lips, mouth, tongue and/or throat and difficulty breathing. **Refer to the doctor immediately if you experience any of these symptoms.**
- Bleeding into the muscle, bleeding in the eye, bleeding from the gums and bloody cough, rectal bleeding, hair loss.

#### Side effects of unknown frequency (side effects whose frequency has not been established yet):

- Bleeding, including bleeding in the brain, intraspinal bleeding, bleeding in the lungs or throat, bleeding in the mouth, bleeding into the abdominal cavity or into the space behind the abdominal cavity, bleeding from haemorrhoids, tests that show blood in the stools or urine.
- Skin rash which may form blisters and looks like small targets (central dark spots surrounded by a paler area, with a dark ring around the edge) (erythema multiforme).
- Blood vessel inflammation (vasculitis) which may result in skin rash or pointed, flat, red, round spots under the skin's surface or bruising.

### Side effects characteristic of Apixaban sandoz administration to prevent stroke and embolism in adult patients with atrial fibrillation (of a non-valvular source) and with at least one additional risk factor:

#### Common side effects (may affect up to 1 in 10 people):

- Bleeding, including bleeding in the eyes, bleeding in the stomach or bowel, rectal bleeding, blood in the urine, nosebleed, bleeding from the gums, bruising and swelling.
- Anaemia, which may cause tiredness or paleness.
- Low blood pressure which may cause a feeling of faintness or a quicker heartbeat.
- Nausea.
- Blood tests which may show an increase in gamma-glutamyl transferase (GGT).

#### Uncommon side effects (may affect up to 1 in 100 people):

- Bleeding, including bleeding in the brain, intraspinal bleeding, bleeding in the mouth, bloody cough, bleeding into the abdominal cavity, vaginal bleeding, bright/red blood in the stools, bleeding occurring after a surgery, including bruising and swelling, blood or liquid leaking from the incision or injection site, bleeding from haemorrhoids, tests that show blood in the stools or urine.
- Reduced number of platelets in your blood (may affect clotting).
- Blood test changes that may show abnormal liver function results, increase in liver enzymes, increase in bilirubin - a breakdown product of red blood cells manifested by yellowing of the skin and eyes.

- Skin rash.

- Itching.

- Hair loss.

- Allergic reaction (hypersensitivity) which may cause swelling of the face, lips, mouth, tongue and/or throat and difficulty breathing. **Refer to the doctor immediately if you experience any of these symptoms.**

#### Rare side effects (may affect up to 1 in 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 affect up to 1 in 10,000 people):

- Skin rash which may form blisters and looks like small targets (central dark spots surrounded by a paler area, with a dark ring around the edge) (erythema multiforme).

#### Side effects of unknown frequency (side effects whose frequency has not been established yet):

- Blood vessel inflammation (vasculitis) which may result in skin rash or pointed, flat, red, round spots under the skin's surface or bruising.

### The following side effects are known if you take Apixaban Sandoz for treatment or prevention of recurrence of blood clots in the veins of the legs or in the blood vessels of the lungs:

#### Common side effects (may affect up to 1 in 10 people):

- Bleeding, including nosebleed, bleeding from the gums, blood in the urine, bruising and swelling, bleeding in the stomach, bleeding in the bowel and bleeding in the rectum, bleeding in the mouth, vaginal bleeding.
- Anaemia, which may cause tiredness or paleness.
- Reduced number of platelets in your blood (may affect clotting).
- Nausea.
- Skin rash.
- Blood tests which may show an increase in gamma-glutamyl transferase (GGT) or alanine aminotransferase (ALT).

#### Uncommon side effects (may affect up to 1 in 100 people):

- Low blood pressure, which may cause a feeling of faintness or a quicker heartbeat.
- Bleeding, including bleeding in the eyes, bleeding in the mouth or bloody cough, red/bright blood in the stools, tests showing blood in the stools or in the urine, bleeding as a result of surgery, including bruising and swelling, blood or liquid leaking from the incision or injection site, bleeding from haemorrhoids, bleeding into the muscle.
- Itching.
- Hair loss.
- Allergic reaction (hypersensitivity) which may cause swelling of the face, lips, mouth, tongue and/or throat and difficulty breathing. **Refer to the doctor immediately if you experience any of these symptoms.**
- Blood test changes that may show abnormal liver function results, increase in liver enzymes, increase in bilirubin - a breakdown product of red blood cells manifested by yellowing of the skin and eyes.

#### Rare side effects (may affect up to 1 in 1,000 people):

- Bleeding, including bleeding in the brain or in the spinal column, bleeding in the lungs.

#### Side effects of unknown frequency (side effects whose frequency has not been established yet):

- 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 (central dark spots surrounded by a paler area, with a dark ring around the edge) (erythema multiforme).
- Blood vessel inflammation (vasculitis) which may result in skin rash or pointed, flat, red, round spots under the skin's surface or bruising.

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

You can report side effects to the Ministry of Health by following the 'Reporting Side Effects of Drug Treatment' link on the Ministry of Health home page ([www.health.gov.il](https://www.health.gov.il)), which opens an online form for reporting side effects, or you can also use this 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 closed place out of the reach and sight of children and/or infants in order 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) appearing on the package. The expiry date refers to the last day of that month.
- Storage conditions:** Do not store above 25°C.

## 6. Further information

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

**Tablet core:** lactose monohydrate, cellulose, microcrystalline, croscarmellose sodium, sodium laurylsulfate, magnesium stearate

### 2.5 mg:

**Film coat:** hypromellose, hydroxypropylcellulose, macrogol 6000, titanium dioxide (E171), iron oxide, yellow (E172).

### 5 mg:

**Film coat:** hypromellose, hydroxypropylcellulose, macrogol 6000, titanium dioxide (E171), iron oxide, red (E172), iron oxide, yellow (E172).

### What the film-coated tablets look like and contents of the pack

**Apixaban Sandoz 2.5 mg:** yellow, round, biconvex, film-coated tablets, marked with AX on one side and 2.5 on the other side.

**Apixaban Sandoz 5 mg:** pink, oval, biconvex, film-coated tablets, marked with AX on one side and 5 on the other side.

This product is available in blister packs of 10, 14, 20, 28, 30, 56, 60 film-coated tablets.

Not all pack sizes may be marketed.

**License Holder and Importer's name and address:** Sandoz Pharmaceuticals Israel Ltd., P.O.Box 9015, Tel Aviv, Israel.

**Registration numbers of the medicine in the Ministry of Health's National Drug Registry:**

**Apixaban Sandoz 2.5 mg: 176-26-37166-99**

**Apixaban Sandoz 5 mg: 176-27-37167-99**

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