Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986
This medicine is dispensed with a doctor's prescription only

ELIQUIS® 2.5 mg
Film-coated tablets
Apixaban 2.5 mg

ELIQUIS® 5 mg
Film-coated tablets
Apixaban 5 mg

Inactive ingredients and allergens: See section 2 under 'Important information about some of this medicine's ingredients' and section 6 'Further information'.

Read the entire leaflet carefully before using this medicine. This leaflet contains concise information about this medicine. If you have further questions, consult your doctor or pharmacist.

This medicine has been prescribed to treat 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.

In addition to the patient information leaflet, **Eliquis** also has a patient safety information card.
This card contains important safety information that you need to know and that you should follow before you start and during treatment with **Eliquis**. The card contains information intended for both the patient and the medical staff. It provides patient guidance on 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 **Eliquis**.
Present this card to each medical staff member involved in your treatment.
Carefully read the patient safety information card and patient information leaflet before using this medicine. Keep the card in case you need to read it again.

1. WHAT IS THIS MEDICINE INTENDED FOR?

Eliquis 2.5 mg
For prevention of venous thrombotic events in adult patients following elective hip or knee replacement surgery.
For prevention of stroke and systemic 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.

Eliquis 5 mg
For prevention of stroke and systemic 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 THIS MEDICINE

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredient or to any of the other ingredients in this medicine (listed in section 6).
- You are suffering from significant active bleeding.
- You are suffering from an injury or a medical condition in an organ of the body that increases the risk of serious bleeding (e.g., an active or recent stomach or bowel ulcer, recent bleeding in your brain).
- You are suffering from a liver disease which leads to an increased risk of bleeding (hepatic coagulopathy).
- You are taking medicines to prevent blood clotting (e.g., warfarin, rivaroxaban, dabigatran or heparin), except when changing anticoagulant treatment, while a venous or arterial line has been inserted and administration of heparin through it is necessary to keep it open, or if a tube was inserted into your blood vessel (catheter ablation) to treat an irregular heartbeat (arrhythmia).

Special warnings regarding use of the medicine
Before treatment with Eliquis, tell the doctor if:

- You are suffering from an increased risk of bleeding such as:
    - bleeding disorders, including conditions resulting in reduced platelet activity
    - very high blood pressure, not controlled by medical treatment
    - you are older than 75 years
    - you weigh 60 kg or less.
- You are suffering from a severe kidney disease or if you are treated with dialysis.
- You are suffering from a liver problem or a history of liver problems. This medicine will be administered with caution in patients with signs of impaired liver function.
- You have had a tube (catheter) inserted or received an injection into the spine (for anesthesia or analgesia).
  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.

Take special care with **Eliquis**

- 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 you are scheduled to undergo surgery or a procedure which may cause bleeding, your doctor may ask you to stop taking this medicine temporarily for a short while. If you are uncertain whether a certain procedure may cause bleeding, consult the doctor.

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

Drug interactions
If you are taking, or have recently taken, other medicines, including nonprescription medicines and dietary supplements, tell the doctor, pharmacist or nurse.

Some medicines may increase the effects of Eliquis and others may decrease its effects. Your doctor will decide if you should receive treatment with Eliquis when taking these medicines and how closely you should be monitored.

- The following medicines may enhance the effect of **Eliquis** and increase the chance of undesirable bleeding:
  - Certain medicines used to treat fungal infections (e.g., ketoconazole, etc.).
  - Certain medicines used to treat acquired immunodeficiency syndrome (HIV/AIDS) (e.g., ritonavir).
  - Other medicines that are used to reduce formation of blood clots (e.g., enoxaparin, etc.).
  - Anti-inflammatory or pain medicines (e.g., aspirin or naproxen), especially if you are older than 75 years of age and are taking aspirin, you may have an increased chance of bleeding.
  - Medicines that are used to treat hypertension or heart problems (e.g., diltiazem).
  - Antidepressants from the selective serotonin reuptake inhibitor class (SSRIs) or serotonin-norepinephrine reuptake inhibitors (SNRIs).
- The following medicines may reduce the ability of **Eliquis** to help prevent blood clots from forming:
  - Medicines to prevent epilepsy or seizures (e.g., phenytoin, etc.).
  - St. John's wort, (a herbal supplement used for depression).
  - Medicines to treat tuberculosis or other infections (e.g., rifampicin).

Using this medicine and food
The medicine can be taken with or without food.

Pregnancy and breastfeeding
If you are pregnant or breastfeeding, suspect you are pregnant or are planning a pregnancy, consult the doctor before starting treatment with any medicine.

The effects of **Eliquis** on pregnancy or on the unborn baby are unknown.
Do not use **Eliquis** if you are pregnant. If you become pregnant while using the medicine, **contact the doctor immediately.**

If you are breastfeeding, consult a doctor, pharmacist or nurse before using **Eliquis**. It is not known whether **Eliquis** passes into breast milk. The medical staff will tell you to either stop breastfeeding or to stop / not to start treatment with **Eliquis**.

Driving and using machines
Eliquis has not been shown to impair your ability to drive or use machines.

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 before taking this medicine.
This medicine contains less than 1 mmol (23 mg) of sodium per tablet, meaning it is considered 'sodium free'.

3. HOW TO USE THIS MEDICINE?

Always use this medicine according to your doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the medicine.
- The dosage and treatment regimen will be determined by your doctor only.
- Try to take the tablets at the same times every day to have the best treatment effect.
- 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 **Eliquis**. The tablet may be crushed and mixed with water, 5% glucose 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 (30 mL), into the container that contained the mixture, and swallow the rinse.

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

Do not exceed the recommended dose.

- **Treatment for prevention of venous thrombotic events in adult patients following elective hip or knee replacement surgery:**
  The recommended dosage is **one tablet** of **Eliquis** 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.
  If you have had a major hip operation, you will usually take the tablets for 32 to 38 days.
  If you have had a major knee operation, you will usually take the tablets for 10 to 14 days.

- **Treatment for prevention of stroke and systemic 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 **Eliquis** 5 mg, twice a day.
  The recommended dosage 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 1.5 mg/dL (133 micromole/L) or greater).
    - 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.
  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 **Eliquis 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 **Eliquis 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 **Eliquis 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 **Eliquis** to treatment with other anticoagulants:
  Stop taking **Eliquis** and start treatment with the other anticoagulant (e.g., heparin) at the time you would have taken the next dose of **Eliquis**.
- Switching from another anticoagulant to treatment with **Eliquis**:
  Stop treatment with the anticoagulant and start treatment with **Eliquis** 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 **Eliquis**:
  Stop treatment with the vitamin K antagonists. The doctor must perform blood tests and instruct you when to start treatment with **Eliquis**.
- Switching from **Eliquis** treatment 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 **Eliquis** for at least two more days after taking the first dose of the vitamin K antagonist. The doctor must perform blood tests and tell you when treatment with **Eliquis** should be terminated.

Patients undergoing cardioversion
If your abnormal heartbeat needs to be restored to normal by a medical procedure called cardioversion, take **Eliquis** at the times your doctor tells you, to prevent blood clots in blood vessels in your brain and other blood vessels in your body.

If you took an overdose or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you, even if there are no tablets left.
If you take more than the recommended dose, you may have an increased risk of bleeding. If bleeding occurs, surgery, blood transfusions, or other treatments that may reverse anti factor Xa activity may be required.
If you forget to take the medicine at the scheduled time, take the dose as soon as possible on the same day and continue taking the medicine twice daily (and no more). Do not double the dose to make up for the missed dose.

Adhere to the treatment regimen as recommended by your doctor.

Even if your health improves, do not stop treatment with the medicine without consulting the doctor or the pharmacist.

Do not stop using this medicine without consulting your doctor first, because the risk of developing a blood clot could be higher if you stop treatment too early.

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

If you have further questions about using this medicine, consult the doctor, pharmacist or nurse.

4. SIDE EFFECTS
As with any medicine, use of **Eliquis** may cause side effects in some users.
Do not be alarmed by this list of side effects; you may not experience any of them. The side effects and their frequency can vary between the different indications and are detailed below

for each indication. The most common side effect of **Eliquis** is bleeding, which can be life-threatening and therefore requires immediate referral to a doctor.

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

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

- Anemia, which may cause tiredness and paleness.
- Bleeding, including bruising and swelling.
- Nausea (feeling sick).

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 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 (their frequency cannot be estimated from the existing data):

- 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 hemorrhoids, 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.
- Bleeding in the kidney sometimes with presence of blood in urine leading to inability of the kidneys to work properly (anticoagulant-related nephropathy).

Side effects characteristic of Eliquis administration to prevent stroke and systemic 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.
- Anemia, which may cause tiredness or paleness.
- Low blood pressure, which may cause a feeling of faintness or a quicker heartbeat.
- Nausea (feeling sick).
- 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 hemorrhoids, 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 (their frequency cannot be estimated from the existing data):
- Blood vessel inflammation (vasculitis) which may result in skin rash or pointed, flat, red, round spots under the skin's surface or bruising.
- Bleeding in the kidney sometimes with presence of blood in urine leading to inability of the kidneys to work properly (anticoagulant-related nephropathy).

The following side effects are known if you take Eliquis 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.
- Anemia, which may cause tiredness or paleness.
- Reduced number of platelets in your blood (may affect clotting).
- Nausea (feeling sick).
- 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 urine, bleeding occurring after a surgery, including bruising and swelling, blood or liquid leaking from the incision or injection site, bleeding from hemorrhoids, 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 (the frequency cannot be estimated from the existing 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 (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.
- Bleeding in the kidney sometimes with presence of blood in urine leading to inability of the kidneys to work properly (anticoagulant-related nephropathy).

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects or by using the link: https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE?
- Prevent poisoning! This and any other medicine should be kept in a closed 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) which is stated on the package. The expiry date refers to the last day of that month.
- **Storage conditions:** Store below 30°C.

6. FURTHER INFORMATION
In addition to the active ingredient, this medicine also contains:
Tablet core: anhydrous lactose, microcrystalline cellulose, croscarmellose sodium, sodium lauryl sulfate, magnesium stearate.
Film coat: hypromellose, lactose monohydrate, titanium dioxide, triacetin, 2.5 mg - iron oxide yellow, 5 mg - iron oxide red.

Each film-coated 2.5 mg tablet contains:
51.4 mg lactose and 0.08 mg sodium.
Each film-coated 5 mg tablet contains:
102.9 mg lactose and 0.16 mg sodium.

2.5 mg - A round (5.95 mm in diameter), film-coated yellow tablet. "893" is debossed on one side and "2½" on the other side.
5 mg - An oval (9.73 mm * 5.16 mm), film-coated pink tablet. "894" is debossed on one side and "5" on the other side.

Registration holder and address: Pfizer Pharmaceuticals Israel Ltd., 9 Shenkar St., Herzliya Pituach 46725.

Registration numbers of the medicine in the Ministry of Health's National Drug Registry:
Eliquis 2.5 mg: 148.31.33496
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