Patient package insert according to Pharmacists' Regulations (Preparations) – 1986
This medicine can be sold with a physician's prescription only

RIVAROXABAN DEXCEL® 2.5 MG, Film-coated tablets

Each tablet contains Rivaroxaban 2.5 mg.

Inactive ingredients and allergens in the medicine – see section 6 "Additional information" and in section 2 "Important information about some of the ingredients of the medicine"

Read this entire leaflet carefully before using the medicine. This leaflet contains concise information about the medicine. If you have any further questions, refer to the 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 you think that their illness is similar to yours.

In addition to the leaflet, the medicine **Rivaroxaban Dexcel 2.5 mg** has a patient safety information card. This card contains important safety information that you must know and follow before starting treatment and during treatment with **Rivaroxaban Dexcel 2.5 mg**. Carefully read the patient safety information card and the patient leaflet before starting to use the medicine. Keep the card for further review if needed.

1. What is the medicine intended for?

Rivaroxaban Dexcel 2.5 mg, in combination with acetylsalicylic acid (known as aspirin), or in combination with acetylsalicylic acid plus clopidogrel, is indicated for the prevention of atherothrombotic events (coagulation events) in adult patients after an acute coronary syndrome (a group of conditions including heart attack and unstable angina, which is a severe type of chest pain), and who have an increase in certain cardiac biomarkers in blood tests.

Rivaroxaban Dexcel 2.5 mg, in combination with acetylsalicylic acid (known as aspirin), is indicated for the prevention of atherothrombotic events (coagulation events) in adult patients with coronary artery disease or symptomatic peripheral artery disease who are at high risk of ischaemic events.

Therapeutic group: Rivaroxaban Dexcel 2.5 mg belongs to a group of medicines called anticoagulants, and acts by reducing the tendency to form blood clots by blocking a factor involved in the clotting process (Factor 10a).

2. Before using the medicine

Do not use the medicine if:

- You are hypersensitive (allergic) to the active ingredient (Rivaroxaban), or to any of the other ingredients this medicine contains (see section 6).
- You are suffering from excessive bleeding.
- You have a disease or a condition in an organ of the body that increases the risk of serious bleeding (e.g., stomach ulcer, injury or bleeding in the brain, recent surgery of the brain or eyes).
- You are taking medicines to prevent blood clots (e.g., warfarin, dabigatran, apixaban or heparin), except in cases of switching from one anticoagulant to another, or when you are receiving heparin through a venous or arterial catheter to keep it open.
- You are suffering from an acute coronary syndrome and have previously experienced bleeding or a blood clot in the brain (stroke).
- You are suffering from an coronary artery disease or peripheral artery disease and previously had bleeding in your brain (stroke) or there was a blockage of the small arteries providing blood to the brain's deep tissues (lacunar stroke) or if you had a blood clot in your brain (ischemic, non-lacunar stroke) in the previous month.
- You are suffering from a liver disease, which leads to an increased risk of bleeding.
- You are pregnant or breastfeeding.

Do not take Rivaroxaban Dexcel 2.5 mg and tell your doctor if any of the conditions described above apply to you.

Special warnings regarding the use of the medicine
Talk to the doctor or pharmacist before taking **Rivaroxaban Dexcel 2.5 mg**.
Do not use **Rivaroxaban Dexcel 2.5 mg** in combination with certain medicines which reduce blood clotting, such as prasugrel or ticagrelor, with the exception of acetylsalicylic acid (aspirin) and clopidogrel.

Special caution is required when using Rivaroxaban Dexcel 2.5 mg. Before the treatment with Rivaroxaban Dexcel 2.5 mg, tell the doctor if:
- you are at high risk of bleeding, as could be the case in any of the following situations:
    - severe kidney disease, since your kidney function may affect the amount of medicine acting in your body.
    - you are taking other medicines to prevent blood clots (e.g., warfarin, dabigatran, apixaban or heparin), when you are switching from one anticoagulant to another or when you are receiving heparin through a venous or arterial catheter to keep it open (see “Drug interactions” in section 2).
    - bleeding disorders.
    - very high blood pressure, which is not controlled by medicinal treatment.
    - disease of the stomach or bowel that may cause bleeding, e.g., inflammation of the bowel or stomach, or inflammation of the esophagus e.g., due to gastroesophageal reflux disease (a disease where stomach acid goes upwards into the esophagus) or tumors located in the stomach or bowels or genital tract or urinary tract.
    - problems with the blood vessels of the retina (retinopathy).
    - a lung disease in which the bronchi are widened and filled with pus (bronchiectasis), or previous bleeding from the lung.
    - you are over the age of 75 years.
    - you weigh less than 60 kg.
    - you have a coronary artery disease with severe symptomatic heart failure.
- you have a prosthetic heart valve.
- you know that you are suffering from 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 any of the above mentioned conditions apply to you, tell the doctor before taking the medicine. The doctor will decide if you should be treated with **Rivaroxaban Dexcel 2.5 mg** and if you need close monitoring.
- If the doctor will think that you are at increased risk of developing a stomach or intestinal ulcer, he may also give a treatment to prevent it.

If you need to undergo surgery or an invasive procedure
- it is very important to take **Rivaroxaban Dexcel 2.5 mg** before and after the surgery or the invasive procedure at the exact times that the doctor determined for you.
- if your operation involves a catheter or injection into the spinal column (e.g., for epidural or spinal anesthesia or for pain relief):
    - it is very important to take **Rivaroxaban Dexcel 2.5 mg** before and after the injection or removal of the catheter exactly at the times determined for you by the doctor.
    - refer to the attending doctor immediately if you suffer from numbness or weakness of the legs or from problems with the bowel or bladder after the anesthesia has worn off, because urgent medical intervention is necessary.

Children and adolescents
The medicine is not intended for children and adolescents under 18 years of age. There is not enough information about the use in children and adolescents.

Drug interactions
If you are taking or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. Especially if you are taking:
- certain medicines for fungal infections (e.g., fluconazole, itraconazole, voriconazole, posaconazole), with the exception of those intended for application to the skin only.
- tablets containing ketoconazole to treat Cushing's syndrome – a condition in which the body produces an excess of cortisol.
- certain medicines to treat bacterial infections (e.g., clarithromycin, erythromycin).
- certain antiviral medicines to treat AIDS (HIV) virus infection (e.g., ritonavir).
- other anticoagulants (e.g., enoxaparin, clopidogrel or vitamin K antagonists such as warfarin and acenocoumarol, prasugrel and ticagrelor [see "Special warnings regarding use of the medicine" in section 2]).
- anti-inflammatory and pain relieving medicines (e.g., naproxen or acetylsalicylic acid [aspirin]).
- dronedarone, a medicine to treat irregular heartbeat.
- certain medicines to treat depression (selective serotonin reuptake inhibitors [SSRIs] or serotonin norepinephrine reuptake inhibitors [SNRIs]).

If any of the above mentioned conditions apply to you, tell the doctor before taking the medicine, because these medicines may cause to increased activity of **Rivaroxaban Dexcel 2.5 mg**. Your doctor will decide if you should be treated with **Rivaroxaban Dexcel 2.5 mg** and if a close medical observation is necessary.

Likewise, inform the doctor or pharmacist if you are taking:
- certain medicines for treatment of epilepsy (e.g., phenytoin, carbamazepine, phenobarbital).
- St. John's Wort (Hypericum)- an herbal preparation for treatment of depression.
- rifampicin (an antibiotic).

If any of the above mentioned conditions apply to you, tell the doctor before taking the medicine, because these medicines may cause to decreased activity of **Rivaroxaban Dexcel 2.5 mg**. Your doctor will decide if you should be treated with **Rivaroxaban Dexcel 2.5 mg** and if a close medical observation is necessary.

Use of the medicine and food
Rivaroxaban Dexcel 2.5 mg can be taken with or without food.

Pregnancy, breastfeeding and fertility
Do not take **Rivaroxaban Dexcel 2.5 mg** if you are pregnant or breastfeeding.
If there is a chance that you will become pregnant, use a reliable contraceptive while taking **Rivaroxaban Dexcel 2.5 mg**.
If you become pregnant while taking the medicine, refer immediately to the doctor, who will decide upon the continuation of the treatment.

Driving and using machines
Rivaroxaban Dexcel 2.5 mg may cause dizziness (a common side effect) or fainting (an uncommon side effect) (see section 4 "Side Effects"). Do not drive, ride a bicycle, use tools or operate machines while using **Rivaroxaban Dexcel 2.5 mg** if you are affected by these symptoms.

Important information about some of the ingredients of the medicine
Rivaroxaban Dexcel 2.5 mg contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially "sodium-free".

3. How to use the medicine?

Always use the medicine according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure about the dosage and the manner of treatment with the medicine.

The dosage and manner of treatment will be determined by the doctor only. The usual recommended dosage is:

- One tablet of **Rivaroxaban Dexcel 2.5 mg**, twice a day. Take **Rivaroxaban Dexcel 2.5 mg** at approximately the same times every day (for example, one tablet in the morning and one tablet in the evening).
- **Rivaroxaban Dexcel 2.5 mg** will not be given to you as a single medicine on its own. The doctor will instruct you to also take one of the following medicines:
  - acetylsalicylic acid, known as aspirin, or
  - acetylsalicylic acid together with clopidogrel.

The doctor will instruct you what dosage of the additional medicines you should take (the recommended dosage is usually between 75 mg to100 mg acetylsalicylic acid once a day, or a daily dose of 75 mg to 100 mg acetylsalicylic acid with a daily dose of 75 mg clopidogrel).

Do not exceed the recommended dose.

Treatment with **Rivaroxaban Dexcel 2.5 mg** after acute coronary syndrome should be started as soon as possible after stabilization of the acute coronary syndrome is achieved, at the earliest 24 hours after admission to hospital and at the time when anticoagulation therapy given by injection is normally stopped.
Your doctor will instruct you when to start treatment with **Rivaroxaban Dexcel 2.5 mg** if you have been diagnosed with coronary artery disease or peripheral artery disease.

Your doctor will decide on the duration of treatment.

Method of Administration
If it is hard for you to swallow the tablet whole, talk to your doctor about other ways of taking **Rivaroxaban Dexcel 2.5 mg**.
The tablet can be crushed and mixed with water or apple puree immediately before administration.
If necessary, your doctor will give you crushed **Rivaroxaban Dexcel 2.5 mg** through a stomach feeding tube.
Do not halve the tablet as there is no score line. There is no information regarding chewing the tablet.
Taking the medicine at the same time every day will help you remember to take it.

If you have accidentally taken a higher dosage
You should refer to the attending doctor immediately. Taking too much **Rivaroxaban Dexcel 2.5 mg** increases the risk of bleeding.
If you have taken an overdose or if a child has accidentally swallowed the medicine, proceed immediately to a doctor or a hospital emergency room and bring the package of the medicine with you.

If you forgot to take the medicine
If you forgot to take this medicine at the designated time, do not take a double dose to make up for a forgotten dose. Take the next dose at the regular time and consult a doctor.

Continue with the treatment as recommended by the doctor.

Even if there is an improvement in your health, do not stop taking this medicine without consulting the doctor.

If you stop taking the medicine
This may increase the risk of having another stroke or heart attack or dying from a disease related to your heart or blood vessels.

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

If you have further questions on the use of this medicine, consult the doctor or pharmacist.

4. <u>Side effects</u>
Like any medicine, the use of **Rivaroxaban Dexcel 2.5 mg** 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.
Like other similar medicines to reduce the formation of blood clots, **Rivaroxaban Dexcel 2.5 mg** can cause bleeding, which may be life threatening. Excessive bleeding may lead to a sudden drop in blood pressure (shock). In some cases, the bleeding may not be obvious.

Refer to the doctor immediately if you suffer from any of the following side effects:
Signs of bleeding:
- bleeding into the brain or inside the skull (symptoms can include: headache, one-sided weakness, vomiting, seizure, decreased level of consciousness, and neck stiffness). This is a serious medical emergency; seek medical attention immediately!
- prolonged or excessive bleeding.
- exceptional weakness, tiredness, paleness, dizziness, headache, unexplained swelling, breathlessness, chest pain or angina pectoris.

Your doctor will decide whether close monitoring or a change in the treatment is necessary.

Signs of a severe skin reaction:
- spreading intense skin rash, blisters or mucosal lesions, e.g., in the mouth or eyes (Stevens-Johnson syndrome/Toxic epidermal necrolysis).
- a drug reaction that causes rash, fever, inflammation of internal organs, blood abnormalities and systemic illness (DRESS syndrome).

The frequency of these side effects is very rare (effects that occur in less than 1 in 10,000 users).

Signs of a severe allergic reaction:
- swelling of the face, lips, mouth, tongue or throat; difficulty swallowing; hives and breathing difficulties; sudden drop in blood pressure.

The frequencies of severe allergic reactions are very rare (anaphylactic reactions, including anaphylactic shock; effects that occur in less than 1 in 10,000 users) and uncommon (angioedema and allergic edema; effects that occur in 1-10 out of 1,000 users).

Additional side effects
Common side effects (effects that occur in 1-10 out of 100 users):
- reduction in red blood cells which can cause pallor, weakness or breathlessness

- bleeding in the stomach or bowel, urogenital bleeding (including blood in the urine and heavy menstrual bleeding), nose bleed, bleeding in the gums
- bleeding into the eye (including bleeding from the white of the eye)
- bleeding into tissue or a cavity of the body (localized hematoma, bruising)
- coughing up blood
- bleeding from the skin or under the skin
- bleeding following an operation
- oozing of blood or fluid from a surgical wound
- swelling of the limbs
- pain in the limbs
- impaired function of the kidneys (can be detected in tests performed by the doctor)
- fever
- abdominal pain, indigestion, nausea or vomiting, constipation, diarrhea
- low blood pressure (symptoms of this may be dizziness or fainting when standing up)
- decreased general strength and energy (weakness, tiredness), headache, dizziness
- rash, itchy skin
- blood tests can indicate an increase in some liver enzymes

Uncommon side effects (effects that occur in 1-10 out of 1,000 users):
- bleeding into the brain or inside the skull (see above, signs of bleeding)
- bleeding into a joint causing pain and swelling
- thrombocytopenia (a low number of platelets, which are cells that help blood to clot)
- allergic reactions, including allergic skin reactions
- impaired function of the liver (can be detected in tests performed by the doctor)
- blood tests may indicate an increase in bilirubin, some pancreatic or liver enzymes or in the number of platelets
- fainting
- general unwell feeling
- faster heartbeat
- dry mouth
- hives (urticaria)

Rare side effects (effects that occur in 1-10 out of 10,000 users):
- bleeding into a muscle
- cholestasis (decreased bile flow), hepatitis including hepatocellular injury (inflamed liver including liver injury)
- yellowing of the skin and eyes (jaundice)
- localized swelling
- localized collection of blood (hematoma) in the groin resulting from a complication of a cardiac procedure where a catheter is inserted into the leg artery

Very rare side effects (effects that occur in less than 1 in 10,000 users):
- accumulation of eosinophils, a type of white granulocytic blood cells that cause inflammation in the lungs (eosinophilic pneumonia)

Side effects with unknown frequency (effects for which a frequency has not yet been determined):
- kidney failure after a severe bleeding
- bleeding in the kidney, sometimes with presence of blood in urine leading to inability of the kidneys to work properly (anticoagulant-related nephropathy)
- increased pressure within muscles of the legs or arms after a bleeding, which leads to pain, swelling, altered sensation, numbness or paralysis (compartment syndrome after a bleeding)

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

Side effects can be reported to the Ministry of Health by clicking the link "דיווח על תופעות לוואי עקב טיפול תרופתי" found on the homepage of the Ministry of Health website (www.health.gov.il) directing to the online form for reporting side effects or via the link: https://sideeffects.health.gov.il

5. How to store the medicine?

- Avoid poisoning! This medicine and any other medicine must be stored 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) stated on the package. The expiry date refers to the last day of that month.
- **Storage conditions**:
  - No special storage conditions. It is recommended to store at room temperature.
  - Crushed tablets: crushed tablets are stable in water or apple puree for up to 4 hours.
- Do not throw away any medicines via wastewater or household waste. Ask the pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Additional information

In addition to the active ingredient, the medicine also contains:
Microcrystalline cellulose, lactose monohydrate, hypromellose, croscarmellose sodium, magnesium stearate, sodium lauryl sulfate, macrogol 3350, titanium dioxide (E171), iron oxide yellow (E172).

What the medicine looks like and what the package contains:
Light yellow, round biconvex, film-coated tablets marked with “III” on one side.

Approved package size: 56 tablets.

Manufacturer name and address: Medichem S.A., Barcelona, Spain.

Revised in September 2023 according to MOH guidelines.

Drug registration number at the national drug registry of the Ministry of Health:
172-92-36481-99

Registration holder:
Dexcel Ltd., 1 Dexcel Street, Or Akiva 3060000, Israel