

**PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS'
REGULATIONS (PREPARATIONS) – 1986**

The medicine is dispensed with a doctor's prescription only

**Adizem CD® 120
Adizem CD® 180
Adizem CD® 240
Controlled release capsules**

Active ingredient:

Each capsule of **Adizem CD 120** contains 120 mg diltiazem hydrochloride.

Each capsule of **Adizem CD 180** contains 180 mg diltiazem hydrochloride.

Each capsule of **Adizem CD 240** contains 240 mg diltiazem hydrochloride.

For the list of the additional ingredients, see section 6.

Read the entire leaflet carefully before using the medicine.

This leaflet contains concise information about the medicine. If you have any further questions, please 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 it seems to you that their illness is similar to yours.

1. What is the medicine intended for?

The medicine is intended for treatment of high blood pressure and angina.

Therapeutic Group: calcium channel blocker.

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 the medicine contains (for the list of the additional ingredients, see section 6).
- You suffer from heart rhythm problems (such as: very slow [less than 40 beats per minute] or irregular heartbeat).
- You suffer from heart failure (which may cause shortness of breath or ankle swelling) and problems with blood flow to the lungs.
- You are pregnant, think you are pregnant, planning a pregnancy or are breastfeeding (see 'Pregnancy and breastfeeding' section).
- You are concomitantly treated with dantrolene infusions (a medicine serving as a muscle relaxant), see 'Drug interactions' section.
- You are taking lomitapide, a medicine used to reduce blood cholesterol levels (see 'Drug interactions' section).

Special warnings regarding the use of the medicine:

Before treatment with the medicine, tell the doctor if:

- You suffer or have suffered in the past from problems or impaired function of the: heart, blood vessels, liver, kidneys, or gastrointestinal tract (bowel problems).
- You suffer from porphyria (a rare blood disease).

- You suffer or have suffered in the past from heart failure, you experience new shortness of breath, slow heartbeat or low blood pressure. Since cases of damage to kidney function in patients suffering from these conditions have been reported, your doctor may need to monitor your kidney functions.

Additional warnings

- **Adizem CD** capsules have a controlled release mechanism, which enables the active ingredient to be gradually released over 24 hours. Do not break, chew, crush or dissolve the capsule or its contents, as this may cause rapid release of the active ingredient and its absorption in the body, which could be dangerous and cause serious problems, such as an overdose (see 'If you accidentally took a higher dosage' section').
- Do not take damaged capsules.
- You need to report that you are taking the medicine before any medical procedure that includes general anesthesia, since it may intensify some of the effects of the anesthesia.
- Elderly patients may be more sensitive to the effects of the medicine.
- If you are sensitive to any food or medicine, inform the doctor before taking the medicine.

Children and adolescents

This medicine is not intended for children.

Tests and follow-up

Before and during the treatment period with the medicine, the following tests need to be performed, according to the doctor's instructions:

- Blood pressure and heart function tests: ECG and heartbeat (pulse). In the elderly and in patients with kidney or liver insufficiency, especially at the beginning of the treatment, closer follow-up is recommended (mainly after the heartbeat).
- Kidney functions (see 'Special warnings regarding the use of the medicine' section).

Drug interactions

If you are taking or have recently taken any other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.

Especially if you are taking:

- Medicines containing lomitapide, which is used to reduce blood cholesterol levels. **Do not use concomitantly with Adizem CD.** Diltiazem could lead to a rise in the lomitapide concentration in the blood, which may lead to an increase in probability and severity of liver-related side effects (see 'Do not use the medicine if' section).
- Dantrolene - a muscle relaxant. Do not use concomitantly with **Adizem CD** when dantrolene is administered via infusion (see 'Do not use the medicine if' section).
- Other medicines for the treatment of high blood pressure, heart and blood vessel problems, such as: beta blockers (for instance atenolol), diuretics, ACE inhibitors (for instance captopril and enalapril); alpha blockers for the treatment of high blood pressure or prostate gland disorders (for instance prazosin); ivabradine, for the treatment of angina; anti-arrhythmic medicines for the treatment of irregular or rapid heartbeat (for instance amiodarone, digoxin or beta blockers); cilostazol to treat a condition causing leg pains because of a restriction in blood supply to the muscles, known as intermittent claudication; nitrate derivatives for the treatment of angina or high blood pressure (for instance glyceryl trinitrate [nitroglycerin] or isosorbide mononitrate).

- Medicines that may cause low blood pressure or slow the heartbeat (for instance antipsychotic medicines for the treatment of mental or behavioral problems, or aldesleukin for the treatment of kidney cancer).
- Carbamazepine or phenytoin (to treat epilepsy/seizures).
- Benzodiazepines, medicines for sleeping or to treat anxiety (for instance midazolam); barbiturates, for the treatment of convulsions or for sleep (for instance phenobarbital or primidone); tricyclic antidepressants (for instance amitriptyline or imipramine); lithium.
- Rifampicin (for the treatment of tuberculosis); protease inhibitors for the treatment of AIDS/HIV (for instance ritonavir or atazanavir).
- Ciclosporin, sirolimus, tacrolimus, to prevent organ transplant rejection or for the treatment of other immune system problems.
- Corticosteroids, for the treatment of infections or allergy (for instance methylprednisolone).
- Statins, to reduce blood cholesterol levels (such as: simvastatin or atorvastatin).
- H₂ antagonists, for the treatment of stomach ulcers, indigestion or heartburn, such as: cimetidine or ranitidine.
- Theophylline (for the treatment of breathing problems such as asthma).

Use of the medicine and food

The medicine can be taken independently of mealtimes.

Use of the medicine and alcohol consumption

Do not drink wines or other alcoholic beverages while taking the medicine.

Pregnancy and breastfeeding

- Do not use the medicine if you are pregnant, think you are pregnant, are planning a pregnancy or could become pregnant and you are not using an effective contraceptive.
- Do not breastfeed during treatment with the medicine, since the medicine passes into breast milk.

Driving and use of machinery

The use of the medicine can cause side effects which may affect your ability to drive or operate machinery, such as: dizziness and generally feeling unwell or tiredness (see section 4, for the full list of side effects). Usually, these effects are noticeable mainly at the beginning of the treatment or when the dosage is increased. If you experience effects that affect your ability to drive or operate machinery, do not perform these actions.

3. How to use the medicine?

Always use 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.

The dosage and manner of treatment will be determined by the doctor only.

This medicine is intended to be administered once daily (every 24 hours). Take the medicine at a set time.

Usually, the starting dose in adults is one 240 mg capsule every 24 hours. However, in elderly patients or with patients suffering from kidney or liver problems, the doctor will probably recommend a lower starting dose, a 120 mg capsule every 24 hours.

Do not exceed the recommended dose.

How to take the medicine

Swallow the capsule whole, with a glass of water. The medicine can be taken independently of mealtimes.

Do not chew or crush the capsule! Adizem CD capsules were designed to have the required effect for 24 hours, when the capsule is swallowed whole. See 'Special warnings regarding the use of the medicine' section.

If you accidentally took a higher dosage

If you have taken an overdose or if a child has accidentally swallowed the medicine, **refer immediately** to a doctor or a hospital emergency room, and bring the package of the medicine with you. Symptoms of an overdose may include: feeling unwell, feeling faint, slow pulse, decrease in kidney function, high levels of blood sugar and loss of consciousness.

If you forgot to take the medicine

- If you remembered within 4 hours from the time you were supposed to take the medicine, take the dose immediately. Take the next dose at the usual time.
- If you are more than 4 hours late for taking the medicine, consult with the doctor regarding the continuation of the treatment.
- Never take two doses together, to make up for the forgotten dose!

If you stop taking the medicine

Adhere to the treatment according to the doctor's recommendation. Even if your state of health improves, do not stop the treatment with the medicine without consulting the doctor.

Do not take medicines in the dark! Check the label and the dose each time you take a medicine.

Wear glasses if you need them.

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

4. Side Effects

As with any medicine, the use of **Adizem CD** may cause side effects in some users. Do not be alarmed while reading the list of side effects. You may not suffer from any of them.

Refer to a doctor immediately in cases of the following severe side effects, which have occurred in a small number of patients but their frequency is unknown:

Severe allergic (hypersensitivity) reaction. The symptoms can include: swelling of the face or throat; edema, shortness of breath.

Skin rash or itchiness, especially if covering the whole body, severe flaking, blistering or peeling of the skin, with or without fever (such as, Stevens-Johnson syndrome and toxic epidermal necrolysis).

Additional side effects

Very common side effects (appear in more than one user out of ten):

Swelling (edema) in the hands, ankles or feet.

Common side effects (appear in 1-10 users out of 100):

Nausea, abdominal pain, indigestion, constipation; dizziness, headache; flushing or redness of the skin, itchiness; rapid, slow or irregular heartbeat; generally feeling unwell; tiredness.

Uncommon side effects (appear in 1-10 users out of 1,000):

Diarrhea, vomiting; feeling faint, especially upon standing up; nervousness; sleeping difficulties; impaired liver functions (seen in blood tests), hypersensitivity (allergy).

Rare side effects (appear in 1-10 users out of 10,000):

Dry mouth; hives (a skin reaction with raised and itchy welts).

Side effects of unknown frequency (effects whose frequency has not yet been determined):

Heart failure which may cause shortness of breath or ankle swelling; sinoatrial block; inflammation of the liver; changes in muscle tone and/or movement disturbances (extrapyramidal effects); mood changes, including depression; skin problems, such as: allergic skin inflammation, increased sensitivity to sunlight; reduction in blood platelets which increases the risk of bleeding or bruising (blue marks); breast enlargement in men; gum problems, such as: bleeding, tenderness, enlargement; inflammation of blood vessels (frequently accompanied by skin rash); excessive sweating; low blood pressure; lupus-like syndrome - a condition in which the body's immune system attacks regular tissues and causes symptoms such as: swelling in the joints, tiredness and rash.

You may observe remnants of the capsule in your stool. This should not affect its action.

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

Side effects may be reported to the Ministry of Health by clicking on the link "Report on side effects following medicinal treatment" on the homepage of the Ministry of Health website (www.health.gov.il) which leads to an online form for reporting side effects, or by entering the link:

<https://sideeffects.health.gov.il/>

5. How to store the medicine?

- Avoid poisoning! This medicine and all other medicines must be stored in a safe place out of the reach and sight of children and/or babies, 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) stated on the package. The expiry date refers to the last day of that month.

Storage conditions:

- Store in the original package below 25°C.
 - Do not throw any medicines into the household waste bin or wastewater. Ask the pharmacist how to dispose of medicines no longer in use. These measures will help protect the environment.

6. Additional information

In addition to the active ingredient, the capsules also contain:

Adizem CD capsules-PIL-02-November-2023-01

Microcrystalline cellulose, ethylcellulose N10, colloidal anhydrous silica, polysorbate 80, dibutyl sebacate, magnesium stearate, erythrosine FD&C Red 3, indigo carmine FD&C Blue 2, gelatin.

Adizem CD 120 also contains quinoline yellow.

What does the medicine look like and what does the package contain

Capsules containing white-off white granules.

Capsule colors: **Adizem CD 120** - yellow/red; **Adizem CD 180** - blue/red; **Adizem CD 240** - purple/red.

Each package contains 30 or 100 capsules, packed in blisters.

Not all package sizes may be marketed.

7. Manufacturer and Registration Holder: Rafa Laboratories Ltd., P.O. Box 405, Jerusalem 9100301, Israel.

Medicine registration number in the Drug Registry of the Ministry of Health:

Adizem CD 120: 1029527680

Adizem CD 180: 1029627681

Adizem CD 240: 1029727682

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