

PATIENT LEAFLET 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 further 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.

1. What is the medicine intended for?

The medicine is intended for treatment of hypertension 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 additional ingredients, see section 6).
- You suffer from heart rhythm problems (such as very slow [less than 40 beats per minute] or irregular heart beat).
- You suffer from heart failure (which may cause shortness of breath or swelling of the ankles) and problems with blood flow to the lungs.
- You are pregnant, think you are pregnant, are planning a pregnancy or are breastfeeding (see section "Pregnancy and breastfeeding").
- You are concomitantly treated with dantrolene infusion (a medicine used for relaxing muscles), see section "Drug interactions".
- You are taking lomitapide, a medicine used for lowering blood cholesterol levels (see section "Drug interactions").

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, the blood vessels, the liver, the kidneys or the digestive system (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 heart beat 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 function.

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 content, as this may cause the active ingredient to be rapidly released and absorbed in the body, which may be dangerous and cause serious problems, such as an overdose (see section "If you accidentally took a higher dosage").
- Do not take damaged capsules.
- You should report that you are taking this medicine before any medical procedure that involves general anesthesia, since it may intensify some of the effects of the anesthetic medicine.
- 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 this medicine.

Children and adolescents

This medicine is not intended for children.

Tests and follow-up

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

- Blood pressure and heart function tests: ECG and heart rate (pulse). In the elderly and in patients with kidney or liver failure, closer monitoring (mainly of the heart rate) is recommended, especially at the beginning of treatment.
- Kidney function (see section "Special warnings regarding the use of the medicine").

Drug interactions

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

- Medicines containing lomitapide, used for lowering blood cholesterol levels. **Do not use concomitantly with Adizem CD.** Diltiazem could lead to an increase in the concentration of lomitapide in the blood, which may increase the probability and severity of liver-related side effects (see section "Do not use the medicine if").
- Dantrolene – a muscle relaxant. Do not use concomitantly with **Adizem CD** when

dantrolene is administered via infusion (see section "Do not use the medicine if").

- Other medicines for treatment of high blood pressure, cardiovascular problems, such as: beta blockers (e.g., atenolol), diuretics, ACE inhibitors (e.g., captopril and enalapril); alpha blockers for treatment of hypertension or prostate gland disorders (e.g., prazosin); ivabradine, for treatment of angina; anti-arrhythmic medicines for treatment of irregular or rapid heart beat (e.g., amiodarone, digoxin or beta blockers); cilostazol, for treatment of a condition that causes leg pain due to a restriction in blood supply to the muscles, known as intermittent claudication; nitrate derivatives, for treatment of angina or hypertension (e.g., glyceryl trinitrate [nitroglycerin] or isosorbide mononitrate).
- Medicines that may cause low blood pressure or slow down the heart beat (e.g., anti-psychotic medicines for treatment of mental or behavioral problems, or aldesleukin for treatment of renal cancer).
- Carbamazepine or phenytoin (for treatment of epilepsy/seizures).
- Benzodiazepines, medicines for sleep or for treatment of anxiety (e.g., midazolam); barbiturates, for treatment of convulsions or for sleep (e.g., phenobarbital or primidone); tricyclic antidepressants (e.g., amitriptyline or imipramine); lithium.
- Rifampicin (for treatment of tuberculosis); protease inhibitors for treatment of AIDS/HIV (e.g., ritonavir or atazanavir).
- Cyclosporine, sirolimus, tacrolimus, for prevention of transplant rejection or for treatment of other immune system problems.
- Corticosteroids, for treatment of infections or allergy (e.g., methylprednisolone).
- Statins, for lowering blood cholesterol levels (such as: simvastatin or atorvastatin).
- H₂ antagonists, for treatment of stomach ulcers, indigestion or heartburn, such as: cimetidine or ranitidine.
- Theophylline (for treatment of breathing problems, such as asthma).
- Diltiazem may lead to an increased risk of bleeding if taken together with blood thinners of the direct oral anticoagulant type (such as apixaban, rivaroxaban, dabigatran).

Use of the medicine and food

The medicine may be taken with no regard to meal times.

Use of the medicine and alcohol consumption

Do not drink wine or 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 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

Using the medicine may cause side effects that may affect your ability to drive or operate machinery, such as dizziness and general malaise or tiredness (for the full list of side effects see section 4). Usually, these effects are mainly noticed at the beginning of treatment or when increasing the dosage. If you feel effects that affect your ability to drive or operate machinery, do not perform these activities.

3. How to use the medicine?

Always use according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and manner of treatment.

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

This medicine is intended for administration once daily (every 24 hours). Take the medicine at a fixed time.

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

Do not exceed the recommended dose.

Method of use

Swallow the capsule whole with a glass of water. The medicine may be taken with no regard to meal times.

Do not chew or crush the capsule!

Adizem CD capsules are designed to have the required effect over 24 hours, when the capsule is swallowed whole. See section "Special warnings regarding the use of the medicine".

If you accidentally took a higher dosage

If you took an overdose or if a child accidentally swallowed the medicine, **refer immediately** to a doctor or a hospital emergency room and bring the medicine package with you. Overdose symptoms can include: feeling unwell, feeling faint, slow heartbeat, decreased kidney function, high levels of blood sugar and loss of consciousness.

If you forgot to take the medicine

- If you remember 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, consult with the doctor regarding the continuation of the treatment.
- Never take two doses together to compensate for the forgotten dose!

If you stop taking the medicine

Adhere to the treatment as recommended by the doctor. Even if there is an improvement in your state of health, do not stop treatment with the medicine without consulting the

doctor.

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 further questions regarding the use of the medicine, consult the doctor or the pharmacist.

4. Side effects

As with any medicine, using **Adizem CD** 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.

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

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

Skin rash or itching, especially if they are spread over the entire body, severe flaking, blisters or skin peeling, with or without fever (such as Stevens-Johnson syndrome and toxic epidermal necrolysis).

Additional side effects

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

Swelling (edema) in the hands, ankles or feet. *Common side effects (occur in 1-10 users out of 100):*

Nausea, abdominal pain, indigestion, constipation; dizziness, headache; flushing or redness of the skin, itching; rapid, slow or irregular heartbeat; general malaise; tiredness.

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

Diarrhea, vomiting; a feeling of faintness, particularly when standing up; nervousness; sleeping difficulties; liver function impairments (seen in blood tests), hypersensitivity (allergy).

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

Dry mouth; urticaria (skin rash with raised and itchy lesions).

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

Heart failure which may cause shortness of breath or swollen ankles; sinoatrial block; liver inflammation; changes in muscle tone and/or movement impairments (extrapyramidal effects); mood swings, including depression; skin problems, such as: allergic skin inflammation, increased sensitivity to sunlight; decrease in 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 (often accompanied by skin rash); excessive sweating; low blood pressure; lupus-like syndrome – a condition in which the body's defense system attacks normal tissues, causing symptoms such as: joint swelling, tiredness and rash. You may notice the remains of the capsule in your stool. This should not affect its action.

If a side effect occurs, 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 side effects due to medicinal treatment" found on the Ministry of Health website homepage (www.health.gov.il), which leads to the online form for reporting side effects, or by clicking on the 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) 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 discard medicines via wastewater or household waste. Ask the pharmacist how to dispose of medicines that are no longer in use. These measures will help protect the environment.

6. Additional information

In addition to the active ingredient the capsules also contain:

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 the medicine looks like and what the package contains

Capsules containing white to cream 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.

Manufacturer and registration holder: Rafa Laboratories Ltd., P.O. Box 405, Jerusalem 9100301, Israel.

Medicine registration numbers in the national medicines registry of the Ministry of Health:

Adizem CD 120: 102-95-27680

Adizem CD 180: 102-96-27681

Adizem CD 240: 102-97-27682

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