

CARDIPINE® HIKMA PHARMACEUTICALS

Isosorbide Dinitrate

ACTION

The principal pharmacological action of Cardipine is relaxation of vascular smooth muscles via stimulation of intracellular cyclic guanosine monophosphate (cGMP) production. Cardipine produces a vasodilatory effect on both peripheral arteries and veins with predominant effect on the latter. Cardipine promotes peripheral pooling of blood and decreases venous return to the heart, thereby reducing left ventricular end-diastolic pressure (pre-load). Arteriolar relaxation reduces systemic vascular resistance and arterial pressure (after load), thus reducing cardiac load and implicitly myocardial oxygen demand.

Effective coronary perfusion pressure is usually maintained and more efficient redistribution of blood flow within the myocardium is achieved. Thus, Cardipine improves perfusion to the ischemic myocardium.

INDICATIONS

Long-term therapy of disturbances of coronary blood flow (coronary heart disease).

Prophylaxis of anginal attacks (chest pain).

Follow-up therapy of myocardial infarction in the presence of anginal complaints.

Therapy of severe myocardial insufficiency (chronic heart failure), in combination with cardiac glycosides and/or diuretics.

DOSAGE AND ADMINISTRATION

Cardipine tablets are administered in the following manner:

Sublingual tablets: For the treatment of angina pectoris, the usual starting dose of sublingual Isosorbide dinitrate is 2.5 to 5mg. Isosorbide dinitrate should be titrated upward until angina is relieved or side effects limit the dose.

The initial dosage of sublingual Isosorbide dinitrate for acute prophylactic therapy in angina pectoris patients is generally 5 or 10 mg every 2 to 3 hours.

Oral tablets: For the treatment of chronic stable angina pectoris, the usual starting dose are 5 to 20 mg. For maintenance therapy, oral doses of 10 - 40 mg given every 6 hours are generally recommended.

CONTRAINDICATIONS

- allergy to nitrate-type drugs
- acute myocardial infarction with low filling pressures
- acute circulatory failure (shock, circulatory collapse)
- very low blood pressure (marked hypotension: systolic blood pressure <90 mm Hg)
- cardiogenic shock, unless a sufficiently high left ventricular end-diastolic pressure is ensured by intra-aortic counter-pulsation or positive inotropic drugs

During a therapy with Cardipine, no phosphodiesterase type 5 inhibitors such as Viagra must be taken because this may result in a severe blood pressure lowering effect.

In which cases do you have to consult your doctor before taking Cardipine?

The following section describes the cases in which Cardipine may be used only on certain conditions and observing particular caution. Please ask your doctor in such cases. This section is also relevant when the factors mentioned below applied to you in the past.

Medical monitoring must be particularly careful in cases of:

- aortic and/or mitral stenosis (narrowing of the aortic and/or mitral valve)
- tendency towards orthostatic circulatory dysregulation (circulatory dysregulation in the presence of too low blood pressure)
- hypertrophic obstructive cardiomyopathy (myocardial disease with reduction of the cardiac cavities)
- constrictive pericarditis (constrictive inflammation of the pericardium)
- cardiac tamponade

- diseases associated with elevated intracranial pressure (further increases in pressure have so far been seen only after the i.v. administration of high doses of glyceryl trinitrate)

Cardipine is not intended for the treatment of an acute anginal attack.

What do you have to observe during pregnancy and lactation?

For reasons of particular caution, isosorbide dinitrate should be used only at a physician's special order during pregnancy and lactation. Animal experiments have not yielded any indication of fetal damage.

What has to be considered in children?

There are no reports so far concerning the treatment of children.

PRECAUTIONS AND WARNINGS

Which precautions have to be observed?

What do you have to observe when driving a motor-vehicle or operating machinery or working in unsafe places?

Even when used in accordance with the instructions, this drug can alter the reactivity such as to impair the ability required to drive a motor-vehicle, to operate machinery or to work in unsafe places. This is particularly true when the therapy is started, the dose is raised, the drug is changed or the drug interacts with alcohol.

SIDE EFFECTS

What side effects can appear during the use of Cardipine?

Headache (nitrate headache) commonly occurs when the treatment begins; experience has shown it to subside in most cases after several days of regular use.

On the first use, but also when the dose is raised, a decrease in blood pressure and/or circulatory dysregulation on changes of position (orthostatic hypotension) are occasionally observed; these symptoms can be accompanied by a reflex increase in heart rate, dizziness, and feelings of vertigo and weakness.

Nausea, vomiting, temporary skin reddening (flushing), and allergic skin reactions are rare.

Frequently a marked general decrease in blood pressure results in so great a reduction of coronary blood flow that an exacerbation of the anginal symptoms can be induced.

States of collapse, sometimes associated with low heart rate (bradycardia) and short-term loss of consciousness (synope), are seldom seen.

Exfoliative dermatitis (inflammatory skin disease) may occur in rare cases.

Loss of drug effect (development of tolerance) as well as a loss of drug effect after therapies with other nitrate drugs (cross-tolerance towards other nitrate-type drugs) was described. A loss of drug effect decrease in hemodynamic effects) was already observed within 24 hours of continuous use.

INTERACTIONS

Which other drugs affect the effect of Cardipine?

The concomitant use of antihypertensives, calcium antagonists, neuroleptics, other vasodilators, beta blockers or tricyclic anti-depressants, and alcohol can enhance the blood pressure lowering effect of Cardipine.

This is true in particular for the concomitant use of phosphodiesterase type 5 inhibitors such as Viagra.

How are the effects of other drugs affected by Cardipine?

When used together with dihydroergotamine, Cardipine may lead to an increase in the dihydroergotamine level and thus enhance the effect of the latter.

Please note that this information may also apply to drugs you took a short time ago.

OVERDOSAGE

Remarks referring to overdosage, forgotten use, or notes concerning the risk of adverse consequences of discontinuation.

Please inform your doctor immediately in such cases.

STORAGE CONDITIONS

Store in a dry place between 15-25°C, away from light

PRESENTATIONS

Cardipine 2.5 Isosorbide dinitrate USP 2.5 mg/tablet
Cardipine 2.5 sublingual Isosorbide dinitrate USP 2.5 mg/tablet

Cardipine 5 Isosorbide dinitrate USP 5 mg/tablet
Cardipine 5 sublingual Isosorbide dinitrate USP
5 mg/tablet

Excipients: Magnesium stearate, ammonium phosphate dibasic, starch, lactose, microcrystalline cellulose, colloidal silicon dioxide.

Cardipine 10: Isosorbide dinitrate USP 10 mg/tablet

Excipients: Magnesium stearate, ammonium phosphate dibasic, sodium starch glycolate, lactose, microcrystalline cellulose.

Cardipine 20: Isosorbide dinitrate USP 20 mg/tablet

Excipients: Magnesium stearate, ammonium phosphate dibasic, sodium starch glycolate, lactose, microcrystalline cellulose, D & C Yellow No.10, FD & C Blue No.1, FD & C Yellow No.6.