

Cardual®

Amlodipine & Atorvastatin

Description

Cardual® is a combination preparation of Amlodipine & Atorvastatin. Amlodipine is a calcium channel blocker of dihydropyridine group having long duration of action. The contractile processes of cardiac muscle and vascular smooth muscle are dependent upon the movement of extracellular calcium ions into these cells through specific ion channels. Amlodipine inhibits calcium ion influx across cell membranes selectively, with a greater effect on vascular smooth muscle cells than on cardiac muscle cells. Thus, Amlodipine acts as a peripheral arterial vasodilator that causes a reduction in peripheral vascular resistance and reduction in blood pressure. In angina, Amlodipine reduces the total peripheral resistance (afterload) against which the heart works and reduces the rate pressure product, and thus myocardial oxygen demand, at any given level of exercise.

Atorvastatin is a synthetic lipid-lowering agent. Atorvastatin inhibits 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase & stops cholesterol synthesis in the liver and by increasing the number of hepatic LDL receptors on the cell-surface to enhance uptake and catabolism of LDL. Atorvastatin reduces total-C, LDL-C, VLDL-C, apo B, TG, and non-HDL-C, and increases HDL-C.

Indications and usage

Cardual® may be used to initiate treatment in patients, with hyperlipidemia and either hypertension or angina, whom treatment with Amlodipine and Atorvastatin is appropriate at the dose presented.

Amlodipine is indicated for

- Hypertension
- Coronary Artery Disease (CAD)
 - Chronic stable angina
 - Angiographically Documented CAD

Atorvastatin is indicated for

- Heterozygous familial and non familial Hypercholesterolemia
- Prevention of cardio vascular diseases
 - Reduce the risk of non-fatal myocardial infarction
 - Reduce the risk of fetal & non fetal stroke
 - Reduce the risk for revascularization procedures
 - Reduce the risk of hospitalization for CHF
 - Reduce the risk of angina
- Homozygous familial Hypercholesterolemia
- Elevated serum TG levels
- Primary dysbetalipoproteinemia

Dosage and administration

The recommended starting dose of Cardual® should be based on the appropriate combination of recommendations for the monotherapies.

For adult

Dosage of Cardual® must be individualized on the basis of both effectiveness and tolerance for each individual component in the treatment of hypertension/angina and hyperlipidemia.

Amlodipine: The recommended initial dose of amlodipine for patient with hypertension, chronic stable or vasospastic angina, coronary artery disease is 5mg once daily with a maximum dose of 10 mg once daily. Elderly individuals, or patients with hepatic insufficiency may be started on 2.5 mg once daily and this dose may be used when adding Amlodipine to other antihypertensive therapy.

Atorvastatin: Adults: The patient should be placed on a standard cholesterol-lowering diet before receiving Atorvastatin and should continue on this diet during treatment with Atorvastatin Hypercholesterolemia (Heterozygous Familial and Nonfamilial) and Mixed Dyslipidemia (Fredrickson Types IIa and IIb): The recommended starting dose of Atorvastatin is 10 mg daily. The dosage range is 10 to 80 mg once daily. Atorvastatin can be administered as a single dose at any time of the day with or without food. Homozygous Familial Hypercholesterolemia: The dosage of Atorvastatin in patients with homozygous FH is 10 to 80 mg daily. Patients with renal insufficiency: Renal disease has no influence on the plasma concentrations or lipid effects of Atorvastatin; thus no adjustment of dose is required.

Use in pregnancy and lactation

There is no clinical experience with Amlodipine and Atorvastatin in pregnancy or lactation. Therefore, it should not be administered during pregnancy or lactation.

Precautions

Caution should be exercised when administering Amlodipine and Atorvastatin as with any other peripheral vasodilator particularly in patients with severe aortic stenosis. Although there is no evidence of worsened heart failure Amlodipine and Atorvastatin should be used with caution in patients with heart failure. Caution should be exercised if an HMG-CoA reductase inhibitor is administered concomitantly with drugs that may decrease the levels or activity of endogenous steroid hormones, such as ketoconazole, spironolactone, and cimetidine.

Side effects

Amlodipine is well tolerated, the most commonly observed side effects were headache, edema, fatigue, skin erythema, nausea, flushing and dizziness. Atorvastatin is generally well tolerated. The most frequent adverse events related to atorvastatin calcium were constipation, flatulence, dyspepsia, and abdominal pain.

Drug interactions

Amlodipine: Co-administration of amlodipine with cimetidine, Antacid, Sildenafil, Digoxin, Ethanol did not alter the pharmacokinetics of amlodipine. Amlodipine has been safely administered with thiazide diuretics, beta-blockers, angiotensin-

converting enzyme inhibitors, long-acting nitrates, sublingual nitroglycerin, digoxin, warfarin, non-steroidal anti-inflammatory drugs, antibiotics, and oral hypoglycemic drugs.

Atorvastatin: Concomitant administration of atorvastatin with inhibitors of cytochrome P450 3A4 (e.g. Clarithromycin, erythromycin), ritonavir plus saquinavir, lopinavir plus ritonavir, itraconazole, Diltiazem hydrochloride, Cyclosporine can lead to increases in atorvastatin AUC. Concomitant administration of atorvastatin with inducers of cytochrome P450 3A4 (eg efavirenz, rifampin), Antacid, Colestipol can lead to reduction in plasma concentrations of atorvastatin. Coadministration of multiple doses of atorvastatin and digoxin increases steady-state plasma digoxin concentration. Atorvastatin plasma concentrations and LDL-C reduction were not altered by co-administration of cimetidine. Atorvastatin had no clinically significant effect on prothrombin time when administered to patients receiving chronic warfarin treatment.

Contraindications

This combination contains atorvastatin and is therefore contraindicated in patients with active liver disease or unexplained persistent elevations of serum transaminases.

It is also contraindicated in patients with known hypersensitivity to any component of this medication.

Overdose

There is no well-documented experience with Amlodipine overdose. Since Amlodipine absorption is slow, gastric lavage may be worthwhile in some cases. Gross overdose could result in excessive peripheral vasodilatation with subsequent marked and probably prolonged systemic hypotension. There is no specific treatment for atorvastatin overdose

Pharmaceutical precautions

Store in a cool, dry place. Protect from light.

Presentation

Cardual® 10 tablet: Each coated tablet contains Amlodipine 5mg as Besilate BP and Atorvastatin 10mg as Calcium INN.

Package quantities

Cardual® 10 tablet: Carton of 30 tablets in blister pack.

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