Bosch

For Medical Professional only

Caloc Tablets

(Amlodipine Besylate)

(Product Specs.: U.S.P.)

کیلوک ٹیبلیٹس

(ایملوڈِپین بیسِلیٹ)

Description:
CALOC is the besylate salt of amlodipine, a long-acting calcium channel blocker. Amlodipine besylate is chemically described as 3-Ethyl-5-methyl (±)-2-[(2-aminoethoxy)methyl]-4- (2-chlorophenyl)-1, 4-dihydro-6-methyl-3,5-pyridinedicarboxylate, monobenzenesulphonate. Its empirical formula is $C_{20}H_{25}ClN_2O_5 \cdot C_6H_6O_3S$. Amlodipine besylate is a white crystalline powder with a molecular weight of 567.1. It is slightly soluble in water and sparingly soluble in ethanol.

Composition:
Each Caloc tablet 5mg contains:
Amlodipine Besylate U.S.P.
eq. to Amlodipine....5mg
(Product Specs.: U.S.P.)

Each Caloc tablet 10mg contains:
Amlodipine Besylate U.S.P.
eq. to Amlodipine....10mg
(Product Specs.: U.S.P.)

Clinical Pharmacology:
Pharmacodynamic Properties:
Pharmacotherapeutic group: calcium channel blockers – Dihydropyridine derivatives. ATC code: C08CA01.

Mechanism of Action:
Amlodipine is a dihydropyridine calcium antagonist that inhibits the transmembrane influx of calcium ions into vascular smooth muscle and cardiac muscle. 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. Amlodipine is a peripheral arterial vasodilator that acts directly on vascular smooth muscle to cause a reduction in peripheral vascular resistance and reduction in blood pressure. The precise mechanisms by which amlodipine relieves angina have not been fully delineated. This inhibition of coronary spasm is responsible for the effectiveness of CALOC in vasospastic angina.

Pharmacokinetic Properties
Absorption & Distribution:
After oral administration of therapeutic doses of CALOC, absorption produces peak plasma concentrations between 6 and 12 hours. Absolute bioavailability has been estimated to be between 64 and 90%. The bioavailability of CALOC is not altered by the presence of food.

Metabolism & Elimination:
Amlodipine is extensively (about 90%) converted to inactive metabolites via hepatic metabolism with 10% of the parent compound and 60% of the metabolites excreted in the urine. Elimination from the plasma is biphasic with a terminal elimination half-life of about 30–50 hours. Steady-state plasma levels of amlodipine are reached after 7 to 8 days of consecutive daily dosing.

Specific Populations
Renal Impairment:
The pharmacokinetics of amlodipine are not significantly influenced by renal impairment. Patients with renal failure may therefore receive the usual initial dose.

Hepatic impairment:
Very limited clinical data are available regarding amlodipine administration in patients with hepatic impairment. Patients with hepatic insufficiency have decreased clearance of Amlodipine resulting in a longer half-life and an increase in AUC of approximately 40-60%.

Elderly:
Elderly patients and patients with hepatic insufficiency have decreased clearance of amlodipine with a resulting increase in AUC of approximately 40–60%, and a lower initial dose may be required. A similar increase in AUC was observed in patients with moderate to severe heart failure.

Therapeutic Indications:
- Hypertension
- Coronary Artery Disease (CAD)
- Chronic Stable Angina
- Vasospastic Angina (Prinzmetal's or Variant Angina)
- Angiographically Documented CAD

Dosage And Administration:
Adults:
The usual initial antihypertensive oral dose of CALOC is 5 mg once daily, and the maximum dose is 10 mg once daily.

Angina: The recommended dose for chronic stable or vasospastic angina is 5–10 mg, with the lower dose suggested in the elderly and in patients with hepatic insufficiency. Most patients will require 10 mg for adequate effect.

Coronary artery disease: The recommended dose range for patients with coronary artery disease is 5–10 mg once daily.
Small, fragile, or elderly patients, or patients with hepatic insufficiency may be started on 2.5 mg once daily and this dose may be used when adding CALOC to other antihypertensive therapy.

Pediatric:
The effective antihypertensive oral dose in pediatric patients ages 6–17 years is 2.5 mg to 5 mg once daily. Doses in excess of 5 mg daily have not been studied in pediatric patients

Contraindications:
CALOC is contraindicated in patients with known sensitivity to amlodipine.

Warnings And Precautions:
Hypotension
Symptomatic hypotension is possible, particularly in patients with severe aortic stenosis. Because of the gradual onset of action, acute hypotension is unlikely.

Increased Angina or Myocardial Infarction
Worsening angina and acute myocardial infarction can develop after starting or increasing the dose of CALOC, particularly in patients with severe obstructive coronary artery disease.

Patients with Hepatic Failure
Because CALOC is extensively metabolized by the liver and the plasma elimination half-life (t 1/2) is 56 hours in patients with impaired hepatic function, titrate slowly when administering CALOC to patients with severe hepatic impairment.

Drug Interactions:
CYP3A Inhibitors
Co-administration with CYP3A inhibitors (moderate and strong) results in increased systemic exposure to amlodipine and may require dose reduction. Monitor for symptoms of hypotension and edema when amlodipine is co-administered with CYP3A inhibitors to determine the need for dose adjustment.

CYP3A Inducers
No information is available on the quantitative effects of CYP3A inducers on amlodipine. Blood pressure should be closely monitored when amlodipine is co-administered with CYP3A inducers.

Grapefruit juice
Administration of amlodipine with grapefruit or grapefruit juice is not recommended as bioavailability may be increased in some patients resulting in increased blood pressure lowering effects.

Sildenafil
Monitor for hypotension when sildenafil is co-administered with amlodipine. Each agent independently exerted its own blood pressure lowering effect.

Simvastatin
Co-administration of simvastatin with amlodipine increases the systemic exposure of simvastatin. Limit the dose of simvastatin in patients on amlodipine to 20 mg daily

Immunosuppressant
Amlodipine may increase the systemic exposure of cyclosporine or tacrolimus when co-administered. Frequent monitoring of trough blood levels of cyclosporine and tacrolimus is recommended and adjust the dose when appropriate.

Adverse Effects:
Very Common: Oedema

Common: Somnolence, dizziness, headache, Visual disturbance (including diplopia), Palpitations, Flushing, Dyspnoea, Abdominal pain, nausea, dyspepsia, altered bowel habits (including diarrhoea and constipation), Ankle swelling, muscle cramps, Fatigue, asthenia.

Uncommon: Depression, mood changes (including anxiety), insomnia, Tremor, dysgeusia, syncope, hypoesthesia, paraesthesia, Tinnitus, Arrhythmia (including bradycardia, ventricular tachycardia and atrial fibrillation), Hypotension, Cough, rhinitis, Vomiting, dry mouth, Alopecia, purpura, skin discolouration, hyperhidrosis, pruritus, rash, exanthema, urticarial, Arthralgia, myalgia, back pain, Micturition disorder, nocturia, increased urinary frequency, Impotence, gynaecomastia, Chest pain, pain, malaise, Weight increased, weight decreased.

Rare: Confusion

Very rare: Leukopenia , thrombocytopenia, Allergic reactions, Hyperglycaemia, Hypertonia, peripheral neuropathy, Myocardial infarction, Vasculitis, Pancreatitis, gastritis, gingival hyperplasia, Hepatitis, jaundice, hepatic enzymes increased, Angioedema, erythema multiforme, exfoliative dermatitis, Stevens-Johnson syndrome, Quincke oedema, photosensitivity,

Not Known: Toxic Epidermal Necrolysis

Use In Pregnancy And Lactation:
Pregnancy:
The safety of amlodipine in human pregnancy has not been established. Use in pregnancy is only recommended when there is no safer alternative and when the disease itself carries greater risk for the mother and foetus.

Lactation:
Amlodipine is excreted in human milk. The effect of amlodipine on infants is unknown. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with amlodipine should be made taking into account the benefit of breast-feeding to the child and the benefit of amlodipine therapy to the mother.

Overdose:
Over dosage might be expected to cause excessive peripheral vasodilation with marked hypotension and possibly a reflex tachycardia. If massive overdose should occur, initiate active cardiac and respiratory monitoring. Frequent blood pressure measurements are essential. Should hypotension occur, provide cardiovascular support including elevation of the extremities and the judicious administration of fluids. If hypotension remains unresponsive to these conservative measures, consider administration of vasopressors (such as phenylephrine) with attention to circulating volume and urine output. As CALOC is highly protein bound, hemodialysis is not likely to be of benefit.

Shelf Life
3 years

Storage and Instruction:
Protect from heat, sunlight & moisture, store below 30°C.
The expiration date refer to the product correctly stored at the required condition. Keep out of the reach of children.
Patients and healthcare professionals can also report suspected adverse drug reaction at ade@bosch-pharma.com.
To be sold on prescription of a registered medical practitioner only.

Presentation:
Caloc (Amlodipine Besylate) 5mg in blister pack of 2 x 10's
Caloc (Amlodipine Besylate) 10mg in blister pack of 2 x 10's

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
دھوپ، گرمی اور نمی سے محفوظ ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
بچوں کی پہنچ سے دُور رکھیں۔
صرف مستند ڈاکٹر کے نسخے پر فروخت کے لئے۔

Manufactured by:
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ISO 9001:2015 Certified Company