Carditan® AM (Tablets)

1314
Ref.No.:INS314/04.18

Losartan Potassium

Amlodipine Besylate

Antihypertensive

CARDITAN® AM TABLETS 50:5MG (FILM COATED)

PRESENTATION:

Carditan® AM Tablets 50:5mg: Blue, circular, biconvex film coated tablet embossed 'C' on one side and a breakline on the other side. Each tablet contains: Losartan Potassium 50mg and Amlodipine Besylate equivalent to Amlodipine 5mg, lactose and other excipients.

CLINICAL PHARMACOLOGY:

Angiotensin II (formed from angiotensin I in a reaction catalyzed by angiotensin converting enzyme (ACE, kininase II), is a potent vasoconstrictor, the primary vasoactive hormone of the renin-angiotensin system and an important component in the pathophysiology of hypertension. It also stimulates aldosterone secretion by the adrenal cortex. Losartan and its principal active metabolite block the vasoconstrictor and aldosterone-secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT_1 receptor found in many tissues (e.g vascular smooth muscle, adrenal gland) There is also an AT_2 receptor found in many tissues but it is not known to be associated with cardiovascular homeostasis. Both losartan and its principal active metabolite do not exhibit any partial agonist activity at the AT_1 receptor and have much greater affinity (about 1000-fold) for the AT_1 receptor than for the AT_2 receptor. *In vitro* binding studies indicate that losartan is a reversible, competitive inhibitor of the AT_1 receptor. The active metabolite is 10 to 40 times more potent by weight than losartan and appears to be a reversible, non-competitive inhibitor of the AT_1 receptor.

Neither losartan nor its active metabolite inhibits ACE (kininase II, the enzyme that converts angiotensin I to angiotensin II and degrades bradykinin) nor do they bind to or block other hormone receptors or ion channels known to be important in cardiovascular regulation.

Amlodipine is a dihydropyridine calcium - channel blocker. It is a peripheral and coronary vasodilator, but, unlike the calcium - channel blockers verapamil or diltiazem, has little or no effect on cardiac conduction and negative inotropic activity is rarely seen at therapeutic doses. Administration of Amlodipine results primarily in vasodilatation, with reduced peripheral resistance, blood pressure, and afterload, increased coronary blood flow, and a reflex increase in heart rate. This in turn results in an increase in myocardial oxygen supply and cardiac output.

Pharmacokinetics:

Losartan is readily absorbed from the gastrointestinal tract after oral doses, but undergoes substantial first-pass metabolism resulting in a systemic bioavailability of about 33%. It is metabolised to an active carboxylic acid metabolite E-3174 (EXP-3174), which has greater pharmacological activity than losartan; some inactive metabolites are also formed. Metabolism is primarily by cytochrome P450 isoenzymes CYP2C9 and CYP3A4. Peak plasma concentrations of losartan and E-3174 occur about 1 hour and 3 to 4 hours, respectively, after an oral dose. Both Losartan and E-3174 are more than 98% bound to plasma proteins. Losartan is excreted in the urine, and in the faeces via bile, as unchanged drug and metabolites. About 4% of an oral dose is excreted unchanged in urine and about 6% is excreted in urine as the active metabolite. The terminal elimination half-lives of losartan and E-3174 are about 1.5 to 2.5 hours and 3 to 9 hours, respectively.

Amlodipine is well absorbed after oral doses with peak blood concentrations occurring after 6 to 12 hours. The bioavailability varies but is usually about 60 to 65%. Amlodipine is reported to be about 97.5% bound to plasma proteins. It has a prolonged terminal elimination half-life of 35 to 50 hours and steady-state plasma concentrations are not achieved until after 7 to 8 days of use. Amlodipine is extensively metabolised in the liver; metabolites are mostly excreted in urine together with less than 10% of a dose as unchanged drug. Amlodipine is not removed by dialysis

USES:

Carditan® AM is indicated for the treatment of hypertension. This fixed dose combination is not indicated for initial therapy of hypertension, except when the hypertension is severe enough that the value of achieving prompt blood pressure control exceeds the risk of

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initiating combination therapy in these patients.
Carditan® AM is also indicated to reduce the risk of stroke in patients with hypertension and left ventricular hypertrophy.

DOSAGE AND ADMINISTRATION:
The usual dose of Carditan® AM is one tablet once daily.
Severe hypertension: The usual dose is one tablet once daily. For patients who do not respond adequately to Carditan® AM after 2 to 4 weeks of therapy, the dosage may be increased to 2 tablets once daily.

CONTRA-INDICATIONS AND WARNINGS:
Carditan® AM is contra-indicated in patients who are hypersensitive to any of the component of this product.

Adverse Effects:
Adverse effects of losartan have been reported to be usually mild and transient , and include dizziness, headache, and dose-related orthostatic hypotension. Hypotension may occur particularly in patients with volume depletion. Impaired renal function and, rarely, rash, urticaria, pruritus, angioedema, and raised liver enzyme values may occur. Hyperkalaemia, myalgia, and arthralgia have been reported. Losartan appears less likely than ACE inhibitors to cause cough. Other adverse effects that have been reported with angiotensin II receptor antagonists include respiratory-tract disorders, back pain, gastrointestinal disturbances, fatigue, and neutropenia.
The most common adverse effects of amlodipine are associated with its vasodilator action and often diminish on continued therapy. They include dizziness, flushing, headache, hypotension, peripheral oedema, tachycardia, and palpitations. Nausea and other gastrointestinal disturbances, increased micturition frequency, lethargy, eye pain, visual disturbances, and mental depression have also occurred. A paradoxical increase in ischaemic chest pain may occur at the start of treatment and in a few patients excessive fall in blood pressure has led to cerebral or myocardial ischaemia or transient blindness.

Interactions:
The antihypertensive effects of losartan may be potentiated by drugs or other agents that lower blood pressure. An additive hyperkalaemic effect is possible with potassium supplements, potassium-sparing diuretics, or other drugs that can cause hyperkalaemia; losartan and potassium-sparing diuretics should not generally be given together. Losartan and some other angiotensin II receptor antagonists are metabolised by cytochrome P450 isoenzymes and interactions may occur with drugs that affect these enzymes.
Amlodipine may enhance the antihypertensive effects of other antihypertensive drugs such as beta blockers although the combination is generally well tolerated. Enhanced antihypertensive effects may also be seen if used with drugs such as aldesleukin and antipsychotics that cause hypotension. As with other dihydropyridine calcium channel blockers amlodipine may modify insulin and glucose responses and therefore diabetic patients may need to adjust their antidiabetic treatment when receiving amlodipine.

PHARMACEUTICAL PRECAUTIONS:
Store in a dry place below 30ºC. Protect from light. Keep all medicines out of the reach of children.

LEGAL CATEGORY:
Prescription Only Medicine (POM)

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COSMOS

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