22700

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Carditan® H (Tablets)

Losartan Potassium
Hydrochlorothiazide
Angiotensin Receptor Blocker / Diuretic
Antihypertensive

CARDITAN® H TABLETS 50:12.5MG (FILM COATED)

PRESENTATION:
Carditan® H Tablets 50:12.5mg: Yellow, circular, biconvex film coated tablet embossed 'C' on one side and a breakline on the other side. Each film coated tablet contains: Losartan Potassium 50mg and Hydrochlorothiazide 12.5mg, Lactose and other excipients.

CLINICAL PHARMACOLOGY:
Angiotensin II (formed from angiotensin I in a reaction catalysed 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.
Hydrochlorothiazide is a thiazide diuretic. Thiazides affect the renal tubular mechanisms of electrolyte reabsorption, directly increasing excretion of sodium and chloride in approximately equivalent amounts. Indirectly, the diuretic action of hydrochlorothiazide reduces plasma volume, with consequent increases in plasma renin activity, increases in aldosterone secretion, increases in urinary potassium loss, and decreases in serum potassium. The renin-aldosterone link is mediated by angiotensin II, so coadministration of an angiotensin II receptor antagonist tends to reverse the potassium loss associated with these diuretics.

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.
Hydrochlorothiazide is fairly rapidly absorbed from the gastro-intestinal tract. It is estimated to have a plasma half-life of between 5 and 15 hours and appears to be preferentially bound to red blood cells. It is excreted mainly unchanged in the urine. Hydrochlorothiazide crosses the placental barrier and is distributed into breast milk.

USES:
Carditan®-H 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 initiating combination therapy in these patients.
Carditan®-H 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®-H is one tablet once daily.
Severe hypertension: The usual dose is one tablet once daily. For patients who do not respond adequately to Carditan®-H after 2 to 4 weeks of therapy, the dosage may be increased to 2 tablets once daily.

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CONTRA-INDICATIONS AND WARNINGS:
Carditan®-H is contra-indicated in patients who are hypersensitive to any component of this product. Because of the hydrochlorothiazide component, this product is contraindicated in patients with anuria or hypersensitivity to other sulfonamide-derived drugs. For pregnant and breast feeding women, a doctor should be consulted before use.

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.
Hydrochlorothiazide and other diuretics may provoke hyperglycaemia and glycosuria in diabetic and other susceptible patients. They may cause hyperuricaemia and precipitate attacks of gout. Hyponatraemia may occur in patients with severe heart failure who are very oedematous. Other adverse effects include anorexia, gastric irritation, nausea, vomiting, constipation, diarrhoea, headache, dizziness, photosensitivity reactions, postural hypotension, paraesthesia, impotence and yellow vision.

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.
Many of the interactions of hydrochlorothiazide and other thiazides are due to their effects on fluid and electrolyte balance. Diuretic-induced hypokalaemia may enhance the toxicity of digitalis glycosides and may also increase the risk of arrhythmias with drugs that prolong the QT interval.

Pregnancy and Lactation:
Pregnancy: Use of Losartan is not recommended during 1st trimester of pregnancy and is contra-indicated during 2nd and 3rd trimester of pregnancy. Hydrochlorothiazide should not be used for essential hypertension in pregnant women, except in rare situations where no other treatment could be used
Lactation: Because no information is available regarding the use of Losartan Potassium / Hydrochlorothiazide during breastfeeding, Losartan Potassium / Hydrochlorothiazide is not recommended and alternative treatments with better established safety profiles during breast-feeding are preferable, especially while nursing a new-born or preterm infant.

PHARMACEUTICAL PRECAUTIONS:
Store in a dry place below 30^{0}C. Protect from light. Keep all medicines out of the reach of children.

LEGAL CATEGORY:
Prescription Only Medicine (POM)

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