Hartan 50mg film-coated tablets

COMPOSITION

Active ingredient: One tablet contains 50 mg losartan potassium.

PHARMACODYNAMICS

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 AT1 receptor found in many tissues, (e.g., vascular smooth muscle, adrenal gland).

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 AT1 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.

PHARMACOKINETICS

Losartan is readily absorbed from the gastrointestinal tract following oral administration, 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. Following oral dosing about 4% of the 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.

INDICATIONS

- *Hypertension:*
  Hartan 50mg film-coated tablets is indicated for the treatment of hypertension.
- *Hypertensive patients with left ventricular hypertrophy:*
  Hartan 50mg film-coated tablets is indicated to reduce the risk of stroke in patients with hypertention and left ventricular hypertrophy.
- *Nephropathy in type 2 diabetic patients:*
  Indicated for the treatment of diabetic nephropathy with an elevated serum creatinine and proteinuria (urinary albumin to creatinine ratio is not less than 300mg/g) in patients with type 2 diabetes and a history of hypertension. In this population, **Hartan 50mg film-coated tablets** reduces the rate of progression of nephropathy as measured by the occurrence of doubling the serum creatinine or end stage renal disease (need for dialysis or renal transplantation) or death.

DOSAGE & ADMINISTRATION

Administration

Hartan 50mg film-coated tablets may be administered with or without food, or with other antihypertensive agents.

Posology

- *Hypertension:*
  Adult: The usual dose is 50 mg once daily. The dose may be increased, if necessary, to 100 mg daily as a single dose or in two divided doses. The maximum hypotensive effect is achieved in about 3 to 6 weeks after initiating treatment.
  For patients with intravascular volume-depletion (e.g., those treated with high-dose diuretics), a starting dose of 25 mg once daily should be considered.
  No initial dosage adjustment is necessary for elderly patients or for patients with renal impairment, including patients on dialysis.
  A lower dose should be considered for patients with a history of hepatic impairment.
- *Hypertensive patients with left ventricular hypertrophy:*
  The usual starting dose is 50 mg of **Hartan 50mg film-coated tablets** once daily. A low dose of hydrochlorothiazide should be added and/or the dose of **Hartan 50mg film-coated tablets** should be increased to 100 mg once daily based on blood pressure response.
- *Renal protection in type 2 diabetic patients with proteinuria and hypertension:*
  The usual starting dose is 50 mg once daily. The dose may be increased to 100 mg once daily based on blood pressure response. **Hartan 50mg film-coated tablets** may be administered with other antihypertensive agents (e.g. diuretics, calcium-channel blockers, alpha- or beta-blockers and centrally acting agents) as well as with insulin and other commonly used hypoglycemic agents (e.g. sulfonylureas, glitazones and glucosidase inhibitors).
  For further information, do not hesitate to ask your physicians.

CONTRAINDICATIONS

Losartan is contraindicated in patients who are hypersensitive to losartan potassium or to any of its excipients.

PRECAUTIONS

- Losartan should be used with caution in patients with renal artery stenosis.
- Losartan is excreted in urine and in bile and reduced doses may therefore be required in patients with renal impairment and should be considered in patients with hepatic impairment.
- Patients with volume depletion (for example those who have received high-dose diuretic therapy) may experience hypotension; volume depletion should be corrected before starting therapy, or a low initial dose should be used.
- Since hyperkalaemia may occur, serum-potassium concentrations should be monitored, especially in the elderly and patients with renal impairment, and the concomitant use of potassium-sparing diuretics should generally be avoid.

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 (for example those who have received high-dose diuretics).
- 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.
- Rhabdomyolysis has been reported rarely.

Notify your physicians if you should experience any of adverse effects.

DRUG INTERACTIONS

- No significant drug-drug pharmacokinetic interactions have been found in interaction studies with hydrochlorothiazide, digoxin, warfarin, cimetidine and phenobarbital.
- Rifampin, an inducer of drug metabolism, decreased the concentrations of losartan and its active metabolite.
- Fluconazole, an inhibitor of P450 2C9, decreased active metabolite concentration and increased losartan concentration.
- As with other drugs that block angiotensin II or its effects, concomitant use of potassium-sparing diuretics (e.g., spironolactone, triamterene, amiloride), potassium supplements, or salt substitutes containing potassium may lead to increases in serum potassium.
- As with other antihypertensive agents, the antihypertensive effect of losartan may be blunted by the non-steroidal anti-inflammatory drug indomethacin.

PREGNANCY AND LACTATION

Pregnancy

When used in pregnancy during the second and third trimesters, drugs that act directly on the renin-angiotensin system can cause injury and even death to the developing fetus. When pregnancy is detected, losartan should be discontinued as soon as possible.

Breast-feeding

Because of the potential for adverse effects on the nursing infant, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

OVERDOSAGE

- Limited data are available in regard to overdosage in humans. The most likely manifestation of over dosage would be hypotension and tachycardia; bradycardia could occur from parasympathetic (vagal) stimulation.
- If symptomatic hypotension should occur, supportive treatment should be instituted. Neither losartan nor its active metabolite can be removed by hemodialysis.

SHELF-LIFE AND STORAGE INSTRUCTIONS:

The expiry date of this pack is printed on the box. Do not use this pack after this date.

Protect from light. Do not store above 30^{o}C.

Keep all medicines out of reach of children.

PREPARATION AND PACK SIZE

Hartan 50mg film-coated tablets appears as a white, round-shaped, film-coated tablet, biconvex, quadrisected on both sides, blister packed in PVC-PVDC/Aluminium foil and packed in cardbox (packs of 30's).

USE ONLY AS DIRECTED BY THE PHYSICIAN
DO NOT EXCEED THE PRESCRIBED DOSES

Manufactured by:
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