Size : 3.997 x 10.731 Inch

Telmisartan with Amlodipine Tablets

AMTEL

POM

COMPOSITION

Each film coated tablet contains:

Telmisartan B.P.	40mg.
Amlodipine Besilate B.P. eq. to Amlodipine	5mg.
Excipients	Q.S.

Colour : Erythrosine

DESCRIPTION

Telmisartan is a nonpeptide angiotensin II receptor (type AT1) antagonist. Amlodipine is a dihydropyridine calcium antagonist that inhibits the trans-membrane influx of calcium ions into vascular smooth muscle and cardiac muscle. The combination provides additive reduction in blood pressure.

PHARMACOLOGY

Pharmacodynamics

Telmisartan : Angiotensin II is formed from angiotensin I in a reaction catalyzed by ACE, kininase II. Angiotensin II is the principal pressor agent of the renin-angiotensin system, with effects that include vasoconstriction, stimulation of synthesis and release of aldosterone, cardiac stimulation, and renal reabsorption of sodium. Telmisartan blocks the vasoconstrictor and aldosterone secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT1 receptor in many tissues, such as vascular smooth muscle and the adrenal gland.

Telmisartan does not inhibit ACE (kininase II), it does not affect the response to bradykinin. Telmisartan does not bind to or block other hormone receptors or ion channels known to be important in cardiovascular regulation.

In normal volunteers, a dose of telmisartan 80 mg inhibited the pressor response to an intravenous infusion of angiotensin II by about 90% at peak plasma concentrations with approximately 40% inhibition persisting for 24 hours. Plasma concentration of angiotensin II and plasma renin activity (PRA) increased in a dose-dependent manner. The once-daily administration of up to 80 mg telmisartan to healthy subjects did not influence plasma aldosterone concentrations. In multiple dose studies with hypertensive patients, there were no clinically significant changes in electrolytes (serum potassium or sodium), or in metabolic function (including serum levels of cholesterol, triglycerides, HDL, LDL, glucose, or uric acid).

Amlodipine: Amlodipine is a dihydropyridine calcium ion antagonist or slow-channel blocker that inhibits the trans-membrane influx of calcium ions into vascular smooth muscle and cardiac muscle. Amlodipine binds to both dihydropyridine and nondihydropyridine binding sites. Amlodipine inhibits calcium ion influx across cell membranes selectively, with a greater effect on vascular smooth muscle cells than on cardiac muscle cells. Negative inotropic have not been seen in intact animals at therapeutic doses. Serum calcium concentration is not affected by amlodipine. Within the physiologic pH range, amlodipine is an ionized compound (pKa=8.6), and its kinetic interaction with the calcium channel receptor is characterized by a gradual rate of association and dissociation with the receptor binding site, resulting in a gradual onset of effect.

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. Following administration of therapeutic doses to patients with hypertension, amlodipine produces vasodilation resulting in a reduction of supine and standing blood pressures.

With once daily oral administration, antihypertensive effectiveness is maintained for at least 24 hours. Plasma concentrations correlate with effect in both young and elderly patients. In hypertensive patients with normal renal function, therapeutic doses of amlodipine resulted in a decrease in renal vascular resistance and an increase in glomerular filtration rate and effective renal plasma flow without change in filtration fraction or proteinuria.

Pharmacokinetics

Telmisartan: Following oral administration, peak concentrations (Cmax) of telmisartan are reached in 0.5-1 hour after dosing. Food slightly reduces the bioavailability of telmisartan, The absolute bioavailability of telmisartan is dose dependent. The terminal elimination half-life is of approximately 24 hours.

Telmisartan is highly bound to plasma proteins (more than 99.5%). Plasma protein binding is constant over the concentration range achieved with recommended doses. The volume of distribution for telmisartan is approximately 500 liters indicating additional tissue binding.

Following either intravenous or oral administration, most of the administered dose (more than 97%) was eliminated unchanged in faeces via biliary excretion; only minute amounts were found in the urine (0.91% and 0.49% of total radioactivity, respectively).

Telmisartan is metabolized by conjugation to form a pharmacologically inactive acylglucuronide. After a single dose, the glucuronide represents approximately 11% of the measured radioactivity in plasma. The cytochrome P450 isoenzymes are not involved in the metabolism of telmisartan. Total plasma clearance of telmisartan is more than 800 mL/min. Terminal half-life and total clearance appear to be independent of dose.

Amlodipine: After oral administration of therapeutic doses of amlodipine, absorption produces peak plasma concentrations between 6 and 12 hours. The bioavailability of amlodipine is not altered by the presence of food. 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. Ex vivo studies have shown that approximately 93% of the circulating drug is bound to plasma proteins in hypertensive patients. 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. The pharmacokinetics of amlodipine is not significantly influenced by renal impairment. Patients with renal failure may therefore receive the usual initial dose.

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.

INDICATION

AMTEL is indicated In Hypertension. In patient whose blood pressure is not adequately controlled with telmisartan or amlodipine monotherapy may be switched to the combination therapy. As Replacement Therapy: For convenience, patients receiving telmisartan and amlodipine from separate tablets may instead wish to receive combination tablets containing the same component doses.

DOSAGE AND ADMINISTRATION

Dosage should be individualized. The recommended dose is one tablet of AMTEL once daily. If necessary, the dose may be increased to two tablets of AMTEL once daily. In small, fragile or elderly patients or patients with hepatic insufficiency initiate on separate tablet of telmisartan 40 mg & amlodipine 2.5 mg. When the patient is able to tolerate up to 5 mg of amlodipine, shift to one tablet of AMTEL.

CONTRAINDICATION

AMTEL is contraindicated in patients with known hypersensitivity to telmisartan or amlodipine

WARNINGS AND PRECAUTIONS

Drug Interactions: Digoxin: Coadministration of telmisartan and digoxin increases the plasma levels of digoxin.

Warfarin: Telmisartan slightly decreased the mean warfarin trough plasma concentration; this decrease did not result in a change in International Normalized Ratio.

Other drugs: Coadministration of telmisartan did not result in a clinically significant interaction with acetaminophen, amlodipine, glibenclamide, simvastatin, hydrochlorothiazide or ibuprofen. Telmisartan is not metabolized by the cytochrome P450 system, Telmisartan is not expected to interact with drugs that inhibit cytochrome P450 enzymes; it is also not expected to interact with drugs metabolized by cytochrome P450 enzymes, except for possible inhibition of the metabolism of drugs metabolized by CYP2C19.

In clinical trials, 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.

Hypotension in volume-depleted patients: In patients with an activated renin-angiotensin system, such as volume- and/or salt-depleted patients (e.g., those being treated with high doses of diuretics), symptomatic hypotension may occur after initiation of therapy with AMTEL . This condition should be corrected prior to administration of AMTEL, or treatment should start under close medical supervision with a reduced dose.

Increased Angina and/or Myocardial Infarction: Rarely, patients, particularly those with severe obstructive coronary artery disease, have developed documented increased frequency, duration and/or severity of angina or acute myocardial infarction on starting calcium channel blocker therapy or at the time of dosage increase. The mechanism of this effect has not been elucidated.

General: Since the vasodilation induced by amlodipine is gradual in onset, acute hypotension has rarely been reported. Nonetheless, caution, as with any other peripheral vasodilator, should be exercised when administering AMTEL, particularly in patients with severe aortic stenosis.

Use in Patients with Congestive Heart Failure: In general, calcium channel blockers should be used with caution in patients with heart failure. In studies with amlodipine, there is no evidence of worsened heart failure based on measures of exercise tolerance, NYHA classification, symptoms, or LVEF.

Hepatic Impairment: As the majority of telmisartan is eliminated by biliary excretion, patients with biliary obstructive disorders or hepatic insufficiency can be expected to have reduced clearance. In patients with hepatic insufficiency, plasma concentrations of telmisartan are increased, and absolute bioavailability approaches 100%. Amlodipine is extensively metabolized by the liver and the plasma elimination half-life is prolonged in patients with impaired hepatic function. AMTEL should be used with caution in these patients.

Renal impairment: In studies of ACE inhibitors in patients with unilateral or bilateral renal artery stenosis, increases in serum creatinine or blood urea nitrogen were observed. There has been no long-term use of telmisartan in patients with unilateral or bilateral renal artery stenosis but an effect similar to that seen with ACE inhibitors should be anticipated.

Pregnancy: Pregnancy Categories C (first trimester) and D (second and third trimesters) Drugs that act directly on the renin-angiotensin system can cause foetal and neonatal morbidity and death when administered to pregnant women. Oligohydramnios has also been reported, presumably resulting from decreased foetal renal function. When pregnancy is detected, AMTEL should be discontinued as soon as possible.

Lactation; It is not known whether telmisartan or amlodipine is excreted in human milk. In the absence of this information, it is recommended that nursing be discontinued while AMTEL is administered.

Pediatric Use: Safety and effectiveness in pediatric patients have not been established.

UNDESIRABLE EFFECTS

The combination of telmisartan and amlodipine is generally well tolerated. A combination of telmisartan and amlodipine is associated with few adverse effects, which are mild to moderate in intensity and transient, and the safety of this combination is comparable to that of amlodipine monotherapy. The most frequent clinical adverse effects in patients treated with this combination are dizziness, headache, nausea, diarrhoea, fatigue, edema, flushing and palpitations.

OVERDOSAGE

Telmisartan: Limited data are available with regard to overdosage in humans. The most likely manifestation of overdosage with telmisartan would be hypotension, dizziness and tachycardia; bradycardia could occur from parasympathetic (vagal) stimulation. If symptomatic hypotension should occur, supportive treatment should be instituted. Telmisartan is not removed by hemodialysis.

Amlodipine: If massive overdose should occur, active cardiac and respiratory monitoring should be instituted. Frequent blood pressure measurements are essential. Should hypotension occur, cardiovascular support including elevation of the extremities and the judicious administration of fluids should be initiated. If hypotension remains unresponsive to these conservative measures, administration of vasopressors (such as phenylephrine) should be considered with attention to circulating volume and urine output. Intravenous calcium gluconate may help to reverse the effects of calcium entry blockade. As amlodipine is highly protein-bound, hemodialysis is not likely to be of benefit.

Storage: Store below 30 °C. Protect from light and moisture.

KEEP THE MEDICINE OUT OF REACH OF CHILDREN

PACKAGING INFORMATION: 3 x 10 tablets strip pack in a carton

Manufactured in India by :
CORONA Remedies Pvt. Ltd.
Village. Jatoli, Post Office - Oachghat,
Tehsil Solan, Dist. Solan (H.P)-173 223.INDIA
www.coronaremedies.com

Manufactured for & Distributed by:
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