Olmesartan medoxomil, amlodipine and hydrochlorothiazide tablets may be taken with or without food.

The usual starting dose of olmesartan medoxomil, amlodipine and hydrochlorothiazide tablets is 40/10/25 mg.

This fixed combination drug is not indicated for the initial therapy of hypertension. Olmesartan medoxomil, amlodipine and hydrochlorothiazide tablets may be used to provide additional blood pressure lowering for patients not adequately controlled on amlodipine and/or hydrochlorothiazide therapy alone.

Some antihypertensive drugs have smaller blood pressure effects (as monotherapy) in black patients, and many antihypertensive drugs have additional approved indications based on findings from studies involving patients of other races.

This experience included about 900 patients treated for at least 6 months and more than 525 treated for at least 1 year. Treatment with olmesartan medoxomil, amlodipine and hydrochlorothiazide tablets for periods of up to 5 years has been associated with a sustained reduction in blood pressure in hypertensive patients.

The following adverse reactions occurred in <0.1% of patients: cardiac failure, pulse irregularity, extrasystoles, skin discoloration, urticaria, skin dryness, alopecia, dysuria, difficulty in urination, and perineal pain. Elevated transaminases and/or bilirubin were observed in about 0.5% of patients. The frequency of adverse reactions was similar in treated and placebo groups, except for dizziness, which was more frequent in the treated group. In general, the adverse events were of mild to moderate severity. The following reactions occurred in <0.1% of patients: heart failure, lability, palpitations, postural hypotension, palpitations, abnormal dreams, papilledema, epigastric or abdominal pain/discomfort, vomiting, dry mouth, increased serum creatinine, nasal infections, nasal congestion, rhinitis, sinusitis, urinary tract infections, cholecystitis, cholelithiasis, pancreatitis, jaundice (intrahepatic cholestatic jaundice), sialadenitis, cramping, gastric irritation, bradycardia, extrasystoles, palpitations, disorders of taste, abdominal pain, diarrhea, dyspepsia, enteritis, gastritis, gastrointestinal bleeding, hemorrhoids, stomatitis, vomiting, abnormal liver function tests, eosinophilia, and thrombocytopenia.

In clinical trials, the adverse reaction profile of olmesartan medoxomil, amlodipine and hydrochlorothiazide tablets was similar to that of olmesartan medoxomil with hydrochlorothiazide tablets. The adverse reaction profile of amlodipine was similar to that of hydrochlorothiazide tablets.

Limited data are available related to overdosage in humans. The most likely manifestations of overdosage would be hypotension and oliguria. In experimental animals, hypotension attributable to overdose has been reversed with vasopressors.

Increases in serum lithium concentrations and lithium toxicity have been reported with concomitant use of olmesartan or thiazide diuretics. Monitor lithium levels periodically in patients receiving olmesartan medoxomil and diuretic therapy.

Hemorrhage has been reported in patients treated with olmesartan and in patients treated with angiotensin receptor blockers. Most cases were reported in patients who were also receiving NSAIDs, aspirin, or other platelet aggregation inhibitors. In randomized, double-blind trials of patients with hypertension, the incidence of clinically significant bleeding events was 0.3% in patients treated with olmesartan medoxomil, amlodipine and hydrochlorothiazide tablets compared to 0.2% of patients receiving dual combination therapy. If progressive renal impairment becomes evident consider withholding or discontinuing the medications.
Olmesartan medoxomil.

Olmesartan medoxomil may be required.

Amlodipine.

The active ingredients of olmesartan medoxomil, amlodipine and hydrochlorothiazide tablets target three separate mechanisms involved in blood pressure regulation.

Olmesartan medoxomil.

Olmesartan medoxomil is a competitive and selective inhibitor of the Ang II AT1 receptor. Olmesartan medoxomil has no effect on the AT2 receptor.

Amlodipine is a peripheral arterial vasodilator that acts directly on vascular smooth muscle to cause a reduction in peripheral vascular resistance and reduction of blood pressure.

Hydrochlorothiazide is a diuretic that increases urine output, enhances excretion of sodium and water which leads to a reduction in volume and a lowering of blood pressure.

Olmesartan medoxomil.

Olmesartan is a benzenoid heterocyclic aromatic ring system with a quinazoline ring fused to the benzene ring. It has a single N-oxide impurity.

Amlodipine is an imidazoline-1,4-benzodiazepine with a chlorine atom in the 3 position.

Hydrochlorothiazide contains the thiazide ring system and the 2-chlorothiazole ring system.

Olmesartan medoxomil.

Olmesartan medoxomil is a prodrug that is rapidly converted to the active form olmesartan. Olmesartan is an orally active compound with a terminal elimination half-life of about 30 to 50 hours. Ten percent of the parent compound and 60% of the metabolites are excreted in the urine.

Amlodipine.

Amlodipine is extensively (about 90%) converted to inactive metabolites via hepatic metabolism. Elimination from the plasma is biphasic with a terminal elimination half-life of about 25 hours. Food does not affect the bioavailability of olmesartan medoxomil.

Hydrochlorothiazide.

After oral administration of hydrochlorothiazide, diuresis begins within 2 hours, peaks in about 4 hours, and lasts about 6 to 12 hours. Hydrochlorothiazide is not metabolized but is eliminated rapidly by the kidney. At least 61% of the oral dose is eliminated unchanged in the urine within 24 hours after oral administration of hydrochlorothiazide.

Olmesartan medoxomil.

The pharmacokinetics of olmesartan medoxomil were studied in the elderly (≥65 years). Overall, maximum plasma concentrations of olmesartan medoxomil were about 33% lower in the elderly compared to young adults. The volume of distribution of olmesartan is approximately 17 L. Olmesartan is highly bound to plasma proteins (99%) and does not accumulate in plasma with multiple daily doses.

Amlodipine.

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

Hydrochlorothiazide.

Hydrochlorothiazide inhibits the NaCl-co-transporter located in the thick ascending limb of the loop of Henle in the nephron. By this mechanism, hydrochlorothiazide reduces sodium and water reabsorption from the proximal tubules of the nephron, which leads to a decrease in blood volume and a lowering of blood pressure.

Olmesartan medoxomil.

Olmesartan medoxomil, amlodipine and hydrochlorothiazide tablets contain 3 different pharmacologically active ingredients.

1. Olmesartan is a competitive and selective inhibitor of the AT1 receptor.

2. Amlodipine is a peripheral arterial vasodilator that acts directly on vascular smooth muscle.

3. Hydrochlorothiazide is a diuretic that increases urine output and enhances excretion of sodium and water.

Olmesartan medoxomil.

The combined use of olmesartan medoxomil, amlodipine and hydrochlorothiazide tablets does not cause any additional changes in laboratory parameters compared to the individual components.

Amlodipine.

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 effects on cardiac muscle have been observed in vitro, but there is no evidence of clinically significant interactions with cardiac function in humans.

Hydrochlorothiazide.

Hydrochlorothiazide is a thiazide diuretic that increases urine output and enhances excretion of sodium and water. It decreases blood volume and blood pressure.

Olmesartan medoxomil.

Olmesartan medoxomil, amlodipine and hydrochlorothiazide tablets do not cause any additional changes in laboratory parameters compared to the individual components.

Amlodipine.

Amlodipine has no effect on renal function or acid-base status after oral administration of therapeutic doses.

Hydrochlorothiazide.

Hydrochlorothiazide has no effect on renal function or acid-base status after oral administration of therapeutic doses.

Olmesartan medoxomil.

Olmesartan medoxomil, amlodipine and hydrochlorothiazide tablets do not cause any additional changes in laboratory parameters compared to the individual components.

Amlodipine.

Amlodipine is well tolerated. The most common adverse reactions reported during clinical trials were headache, edema, and flushing.

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