## HIGHLIGHTS OF PRESCRIBING INFORMATION

- **DRUG CLASS:** Antihypertensive
- **INDICATIONS:** Hypertension

### CONTRAINDICATIONS
- Anuria; Hypersensitivity to sulfonamide-derived drugs
- Pregnancy Category D

### DOSAGE FORMS AND STRENGTHS
- Olmesartan Medoxomil, Amlodipine and Hydrochlorothiazide Tablets

### PRECAUTIONS
- **Dose Reductions:**
  - Consider decreases in dosage in patients with hepatic impairment.
  - Consider increases in dosage in patients with impaired renal function.
- **Drug Interactions:**
  - Use with caution in patients receiving other medications that enhance the hypotensive effect of antihypertensives.

### ADVERSE REACTIONS
- **Most Common Adverse Reactions:** Edema peripheral

### CLINICAL STUDIES
- Amlodipine (5 to 10 mg per day) has been studied in a placebo-controlled trial of 1153 patients with New York Heart Association (NYHA) Class III or IV heart failure.

### CLINICAL PHARMACOLOGY
- Olmesartan Medoxomil, Amlodipine and Hydrochlorothiazide Tablets are chemically described as 6-chloro-3,4-dihydro-2-propyl-1-[4-(1-hydroxy-1-methylethyl)-2-propyl-1-[2-(4-dimethylaminophenyl)]imidazole-5-carboxylate, cyclic 2,3-carbonate. Its empirical formula is C29 H30 N6O6.

### CLINICAL TRIALS EXPERIENCE
- Amlodipine (5 to 10 mg per day) has been studied in a placebo-controlled trial of 1153 patients with New York Heart Association (NYHA) Class III or IV heart failure.

### OVERDOSAGE
- Overdosage might be expected to cause excessive peripheral vasodilation with marked hypotension and possibly a reflex tachycardia.
The seated blood pressure reductions attributable to the addition of a single high-dose drug to each high-dose dual drug combination are shown in Amlodipine.

Azide were administered to pregnant mice at oral doses up to 1625 mg/kg/day (122 times the MRHD on a mg/m^2 basis) or pregnant rats up to 1625 mg/kg/day (243 red blood cells. The protein binding is constant at plasma olmesartan concentrations well above the range achieved with recommended doses.

Amlodipine.

Olmesartan medoxomil. In plasma occurs with once-daily dosing.

Following single oral doses of up to 320 mg and multiple oral doses of up to 80 mg. Steady-state levels of olmesartan are achieved within 3 to 5 days and no accumulation of olmesartan. Total plasma clearance of olmesartan is 1.3 L/h, with a renal clearance of 0.6 L/h. Approximately 35% to 50% of the absorbed dose is recovered in urine.

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

Olmesartan medoxomil is rapidly and completely bioactivated by ester hydrolysis to olmesartan during absorption from the gastrointestinal tract.

Hydrochlorothiazide. There was no effect on the fertility of rats treated orally with amlodipine maleate (males for 64 days and females for 14 days prior to mating) at doses of amlodipine up to 24 times the MRHD for man on a mg/m^2 basis. Amlodipine maleate caused a dose-related decrease in fertility in a cross-breeding study in mice, lowering the number of sperm per dose level by 50% at the highest dose level tested (120 mg/kg/day). Amlodipine maleate caused a dose-related decrease in fertility in a cross-breeding study in mice, lowering the number of sperm per dose level by 50% at the highest dose level tested (120 mg/kg/day). Amlodipine maleate caused a dose-related decrease in fertility in a cross-breeding study in mice, lowering the number of sperm per dose level by 50% at the highest dose level tested (120 mg/kg/day).

Mutagenicity studies conducted with amlodipine maleate revealed no drug related effects at either the gene or chromosome level. In vitro and in vivo mouse lymphoma assay. Olmesartan medoxomil tested negative in the Ames (bacterial mutagenicity) test. However, both were shown to induce chromosomal aberrations in cultured cells. Both olmesartan medoxomil and olmesartan tested negative in the Syrian hamster embryo cell transformation assay and showed no evidence of genetic toxicity in

Population pharmacokinetic analysis indicated that gender had no effect on the clearance of olmesartan and amlodipine. Female patients had approximately 20% smaller area under the curve and Cmax compared to high doses of dual combination drugs.

Caution patients that inadequate fluid intake, excessive perspiration, diarrhea, or vomiting can lead to an excessive fall in blood pressure, with the same consequences of syncope. Notify your physician if you experience any of these side effects.

See FDA-Approved Patient Labeling.