

NEW DRUG UPDATE

Drug Name:	azilsartan medoxomil
Trade Name (Manufacturer):	Edarbi™ (Takeda)
Form:	Oral tablets
Strength:	40 mg, 80 mg
FDA Approval:	February 25, 2011
Market Availability:	Currently available
FDA Approval Classification:	Standard review
Classification:	Specific Therapeutic Class (HIC3): Antihypertensives, Angiotensin Receptor Antagonists (A4F)

Indication:¹ Azilsartan medoxomil (Edarbi) is an angiotensin receptor blocker (ARB) indicated for the treatment of hypertension, either alone or in combination with other antihypertensives.

Contraindications/Warnings: Pregnant women should not use azilsartan. Drugs that affect the renin-angiotensin system have been noted to cause fetal morbidity and death when used during the second and third trimester.

Volume or salt depletion should be corrected prior to initiation of therapy with azilsartan to minimize the risk of hypotension.

ARBs may result in oliguria, progressive azotemia, or acute renal failure in patients who require renin-angiotensin activation to maintain adequate renal function. Thus, azilsartan should be used with caution in patients with severe congestive heart failure, renal artery stenosis, or volume depletion.

Drug Interactions: No clinically significant drug interactions involving azilsartan have been noted.

Caution should be used in patients receiving non-steroidal anti-inflammatory drugs (NSAIDs) in combination with azilsartan, especially in elderly, volume-depleted patients or patients with compromised renal function. This combination may result in a reduction in renal functions.

Common Adverse Effects: Adverse reactions reported with an incidence of 0.3 percent or higher and more often than with placebo include: asthenia, diarrhea, dizziness, fatigue, muscle spasms, and nausea.

Special Populations:

Pediatrics: The safety and efficacy of azilsartan patients less than 18 years of age have not been established.

Pregnancy Category: C (first trimester), D (second and third trimesters)

Geriatrics: Other than increased serum creatinine values in patients age 75 or over, no differences have been noted between elderly and younger patients. No dose adjustment is required for use in geriatric patients.

Renal Impairment: No dose adjustment is required for patients with renal disease. However, patients with moderate to severe renal impairment are more likely to experience abnormally high serum creatinine levels.

Hepatic Impairment: Azilsartan can be used in patients with mild to moderate hepatic impairment without dose adjustment. Azilsartan has not been studied in patients with severe hepatic impairment.

Dosages: The target dose for azilsartan is 80 mg once daily. Providers should consider starting patients treated with high dose diuretics at 40 mg daily. Additional antihypertensives may be added if sufficient blood pressure reduction is not achieved with azilsartan alone.

Clinical Trials: A literature search was performed using "azilsartan". Placebo-controlled trials were included in the absence of comparative trials.

One randomized, double blind study compared 2 doses of azilsartan (40 mg and 80 mg) with valsartan 320 mg, olmesartan 40 mg, and placebo². The primary endpoint was change in from baseline in 24 hours mean systolic blood pressure. This study included 1,291 patients with baseline 24 hour mean systolic BP of 145 mm Hg. Azilsartan 80 mg demonstrated superior efficacy to both valsartan at 320 mg (-10 mmHg, $p < 0.001$) and olmesartan at 40 mg (-11.7 mm Hg; $p = 0.009$). Safety and tolerability among placebo and the four active treatment groups were similar.

In another randomized, double-blind, placebo controlled trial of 1,275 patients, azilsartan was compared to olmesartan, again using change from baseline in mean 24-hour ambulatory systolic blood pressure after six weeks of treatment as the primary endpoint³. Patients had an initial systolic blood pressure of 130 mmHg to 170 mmHg. Treatment arms included: placebo, azilsartan 20, 40, and 80 mg, and olmesartan 40 mg. Reduction in 24-hour mean systolic blood pressure was greater with azilsartan 80 mg than olmesartan 40 mg (-2.1 mmHg, $p = .038$), while azilsartan 40 mg was found to be non-inferior to olmesartan 40 mg.

Other Drugs Used for Condition: A number of therapeutic classes are used for the treatment of hypertension, including: diuretics, beta-blockers, calcium channel blockers, ACE inhibitors, angiotensin receptor blockers, and direct renin inhibitors. Other angiotensin receptor blockers include: candesartan (Atacand[®]), eprosartan (Teveten[®]), irbesartan (Avapro[®]), losartan (Cozaar[®]), olmesartan (Benicar[®]), telmisartan (Micardis[®]), and valsartan (Diovan[®]),

Place in Therapy:

ARBs generally lower blood pressure to a similar degree, with limited data historically suggesting that candesartan, valsartan, and irbesartan offer more benefit than losartan. ARBs are generally well tolerated. Initial trials indicate that azilsartan may produce a greater systolic blood pressure lowering effect than some other agents, but the clinical significance and impact on long-term blood pressure control are yet to be determined.

References

¹ Edarbi [package insert]. Deerfield, IL; Takeda Pharmaceuticals; February 2011.

² White WB, Weber MA, Sica D, et al. Effects of the Angiotensin receptor blocker azilsartan medoxomil versus olmesartan and valsartan on ambulatory and clinic blood pressure in patients with stages 1 and 2 hypertension. *Hypertension*. 2011; 57 (3):413-420.

³ Bakris GL, Sica D, Weber M, et al. The comparative effects of azilsartan medoxomil and olmesartan on ambulatory and clinic blood pressure. *J Clin Hypertens*. 2011; 12(2): 81-88.