FDA Approves EDARBI (azilsartan medoxomil) for the Treatment of Hypertension

Deerfield, Ill., February 25, 2011, and Osaka, Japan, February 26, 2011 – Takeda Pharmaceutical Company Limited (Takeda) and its wholly-owned subsidiary, Takeda Pharmaceuticals North America, Inc., today announced that the U.S. Food and Drug Administration (FDA) approved EDARBI (azilsartan medoxomil) for the treatment of hypertension, or high blood pressure, in adults. EDARBI is an angiotensin II receptor blocker (ARB) that lowers blood pressure by blocking the action of angiotensin II, a vasopressor hormone that constricts blood vessels. When the angiotensin II receptor is blocked, blood vessels stay relaxed and open and blood pressure can be reduced. EDARBI is approved as a once-daily oral therapy for use alone and for use in combination with other antihypertensive medications.

Takeda Global Research & Development Center, Inc. U.S. submitted a new drug application (NDA) for EDARBI in April 2010. The NDA was supported by seven controlled phase 3 clinical trials involving more than 5,900 patients with hypertension. Pivotal phase 3 studies showed EDARBI (80 mg/day) was statistically superior to placebo and the highest approved doses of two commonly prescribed ARBs, olmesartan medoxomil (40 mg/day) and valsartan (320 mg/day), in lowering both clinic and 24-hour mean blood pressure measurements.

“We are pleased to be able to build upon our global expertise in the cardiovascular therapeutic area with the approval of EDARBI in the U.S.,” said Shinji Honda, president and CEO, Takeda Pharmaceuticals North America. “Through the discovery, development and commercialization of new medicines, Takeda is committed to bringing therapies like EDARBI to market. EDARBI is an important new treatment option for patients with hypertension and the health care professionals who treat them.”

The safety and efficacy of EDARBI were studied as a once-daily oral therapy, as well as in combination with chlorthalidone and amlodipine. Results from the phase 3 clinical trials showed EDARBI successfully met the primary endpoint, change in 24-hour mean systolic blood pressure (SBP) as measured by Ambulatory Blood Pressure Monitoring, with statistical significance of lowering blood
pressure compared to placebo and head-to-head active comparators. Specifically, results from one study showed EDARBI at doses of 80 mg/day and 40 mg/day lowered 24-hour mean SBP by 14.3 mm Hg and 13.2 mm Hg from baseline, respectively. The blood pressure reductions of EDARBI (80 mg/day) were statistically superior to those of the active comparators valsartan 320 mg/day (-10.0 mm Hg) and olmesartan medoxomil 40 mg/day (-11.7 mm Hg). Similar results were observed in all three comparator studies. The most common adverse reaction in adults was diarrhea (2%).

About Hypertension

Hypertension, or high blood pressure, is a chronic medical condition in which blood pressure is elevated at levels of 140 mm Hg or greater systolic or 90 mm Hg or greater diastolic. Hypertension impacts approximately 75 million Americans, or nearly one in three adults. It is estimated that nearly one billion people are affected by hypertension worldwide, and this figure is predicted to increase to 1.5 billion by 2025. Hypertension typically has no symptoms. Adults of all ages and backgrounds can develop hypertension; however, the risk of developing the condition increases with age, with more than half of people over age 60 affected. Hypertension is also costly to the nation’s health care system. The American Heart Association recently estimated that direct and indirect expenses associated with hypertension cost the nation more than $73 billion in 2009.

About EDARBI (azilsartan medoxomil)

EDARBI (azilsartan medoxomil) is an angiotensin II receptor blocker (ARB) developed by Takeda for the treatment of high blood pressure, or hypertension, in adults. EDARBI lowers blood pressure by blocking the action of angiotensin II, a vasopressor hormone, which naturally exists within the body. When EDARBI blocks the angiotensin II receptor, blood vessels can stay relaxed and open and blood pressure can be reduced. EDARBI is indicated for the treatment of hypertension in adults, either alone or in combination with other antihypertensive agents. The recommended dose of EDARBI in adults is 80 mg taken once daily. A starting dose of 40 mg may be appropriate for patients on high doses of diuretics.

Important Safety Information

Boxed Warning

When pregnancy is detected, discontinue EDARBI as soon as possible. Drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus.

Avoid fetal or neonatal exposure. Drugs that act directly on the renin-angiotensin system can cause fetal and neonatal morbidity and death when administered to pregnant women during the second and third trimester.

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 treatment with EDARBI. Correct volume or salt depletion prior to administration of EDARBI, or start treatment at 40 mg.
Monitor for worsening renal function in patients with renal impairment. In patients whose renal function may depend on the activity of the renin-angiotensin system, treatment with ACE inhibitors and ARBs has been associated with oliguria or progressive azotemia and rarely with acute renal failure and death. Similar results may be anticipated in patients treated with EDARBI. In studies of ACE inhibitors in patients with unilateral or bilateral renal artery stenosis, increases in serum creatinine or blood urea nitrogen have been reported. There has been no long-term use of EDARBI in these patients but similar results may be expected.

Monitor renal function periodically in patients receiving EDARBI and NSAIDs who are also elderly, volume-depleted (including those on diuretics), or who have compromised renal function due to potential reversible deterioration of renal function.

Small reversible increases in serum creatinine are seen in patients receiving 80 mg of EDARBI. The increase may be larger when coadministered with chlorthalidone or hydrochlorothiazide. In addition, patients taking EDARBI who had moderate to severe renal impairment at baseline or those older than 75 years of age were more likely to report serum creatinine increases.

The most common adverse reaction that occurred more frequently with EDARBI than placebo in adults was diarrhea (two percent versus 0.5 percent).

Please click here for complete Prescribing Information, including boxed warning for pregnancy.

**Takeda Pharmaceuticals North America, Inc. and Takeda Global Research & Development Center, Inc.**

Based in Deerfield, Ill., Takeda Pharmaceuticals North America, Inc. and Takeda Global Research & Development Center, Inc. are subsidiaries of Takeda Pharmaceutical Company Limited, the largest pharmaceutical company in Japan. The respective companies currently market oral diabetes, insomnia, rheumatology and gastroenterology treatments and seek to bring innovative products to patients through a pipeline that includes compounds in development for diabetes, cardiovascular disease, gastroenterology, neurology and other conditions. To learn more about these Takeda companies, visit [www.tpna.com](http://www.tpna.com).

**About Takeda Pharmaceutical Company Limited**

Located in Osaka, Japan, Takeda is a research-based global company with its main focus on pharmaceuticals. As the largest pharmaceutical company in Japan and one of the global leaders of the industry, Takeda is committed to strive towards better health for patients worldwide through leading innovation in medicine. Additional information about Takeda is available through its corporate website, [www.takeda.com](http://www.takeda.com).

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