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### **Daiichi Sankyo, Inc. Files Supplemental New Drug Application for AZOR<sup>®</sup> as Initial Therapy for High Blood Pressure**

Parsippany, NJ – September 17, 2008 – Daiichi Sankyo, Inc. today announced the filing of a supplemental New Drug Application (sNDA) with the United States Food and Drug Administration (FDA) for the combination treatment AZOR<sup>®</sup> (amlodipine and olmesartan medoxomil) as initial therapy in patients likely to need multiple antihypertensive agents to achieve their blood pressure goal. AZOR is indicated for the treatment of hypertension, alone or with other antihypertensive agents. Presently, AZOR is not indicated for the initial therapy of hypertension. AZOR may be substituted for its individually titrated components. AZOR may also be used to provide additional blood pressure lowering for patients not adequately controlled with any calcium channel blocker (CCB) or any angiotensin receptor blocker (ARB) alone.

The sNDA filing was based upon data from the pivotal registrational trial, which provided estimates of the probability of patients attaining blood pressure goals with AZOR compared to amlodipine or olmesartan medoxomil alone.

“Research suggests that more than two-thirds of patients often require multiple medications to help achieve blood pressure goals,” said Matthew R. Weir, MD, University of Maryland School of Medicine, Department of Nephrology. “If approved, this filing would support JNC-7 guideline recommendations to start patients likely to need multiple antihypertensive agents to reach their blood pressure goal on combination drugs as initial therapy.”

High blood pressure can cause permanent changes to blood vessels and the heart that may create serious problems elsewhere in the body.<sup>1</sup> Hypertension is one of the most prevalent conditions in the United States affecting approximately one in three American adults (about 73 million people age 20 and older) and approximately one billion people worldwide.<sup>2,3</sup> It is often difficult to control, and of those with high blood pressure, approximately 65 percent do not have the condition under control.<sup>4</sup> The number of people with high blood pressure is expected to reach about 1.6 billion worldwide by 2025.<sup>5</sup>

“Given the prevalence of patients with high blood pressure, the approval of AZOR as initial therapy would give physicians a valuable treatment option to help more patients reach their

blood pressure goal,” said William R. Sigmund II, MD, Daiichi Sankyo Vice President of Medical Affairs. “Research and innovation in cardiovascular care is a therapeutic focus for Daiichi Sankyo, and expansion of AZOR’s label is in line with our vision to contribute to the health of people in the United States.”

### **About AZOR**

AZOR is a convenient, once daily, single tablet combination of amlodipine, the most prescribed CCB on the market<sup>6</sup>, which inhibits the entrance of calcium into the blood vessel walls, with olmesartan medoxomil, the active ingredient in Benicar<sup>®</sup>, which blocks angiotensin II receptors. Angiotensin II is a hormone that causes blood vessels to tighten and narrow. Together the two medicines relax the blood vessels so that blood can flow more easily. Benicar (olmesartan medoxomil), Daiichi Sankyo’s flagship ARB product, is the fastest growing medication in the fastest growing class of blood pressure-lowering drugs.<sup>7</sup>

The U.S. Food and Drug Administration (FDA) granted marketing approval for AZOR in September 2007. AZOR is indicated for the treatment of hypertension, alone or with other antihypertensive agents. Presently, AZOR is not indicated for the initial therapy of hypertension. AZOR may be substituted for its individually titrated components. AZOR may also be used to provide additional blood pressure lowering for patients not adequately controlled with any calcium channel blocker or any angiotensin receptor blocker alone. In the pivotal registrational trial, AZOR demonstrated that eight weeks of double-blind treatment with combination therapy resulted in larger mean reductions in seated blood pressure and brought more patients to goal in comparison to the corresponding monotherapies.

### **IMPORTANT SAFETY INFORMATION ABOUT AZOR**

#### **USE IN PREGNANCY**

**When used in pregnancy during the second and third trimesters, drugs that act directly on the renin-angiotensin system can cause injury and even death to the developing fetus.**

When pregnancy is detected, AZOR should be discontinued as soon as possible. See

**WARNINGS AND PRECAUTIONS, Fetal/Neonatal Morbidity and Mortality.**

#### **Hypotension in Volume- or Salt-Depleted Patients**

In patients with an activated renin-angiotensin system, such as volume- and/or salt-depleted patients, symptomatic hypotension due particularly to the olmesartan component may occur after initiation of treatment with AZOR. Treatment should start under close medical supervision.

**Vasodilation**

Since the vasodilation attributable to amlodipine in AZOR is gradual in onset, acute hypotension has rarely been reported after oral administration. Nonetheless, caution, as with any other peripheral vasodilator, should be exercised when administering AZOR, particularly in patients with severe aortic stenosis.

**Severe Obstructive Coronary Artery Disease**

Patients, particularly those with severe obstructive coronary artery disease, may develop increased frequency, duration, or severity of angina or acute myocardial infarction on starting calcium channel blocker therapy or at the time of dosage increase.

**Congestive Heart Failure**

In general, calcium channel blockers should be used with caution in patients with heart failure.

**Impaired Renal Function**

In studies of ACE inhibitors in patients with unilateral or bilateral renal artery stenosis, increases in serum creatinine or blood urea nitrogen (BUN) have been reported. There has been no long-term use of olmesartan medoxomil in patients with unilateral or bilateral renal artery stenosis, but similar effects would be expected with AZOR because of the olmesartan medoxomil component.

**Hepatic Impairment**

Since amlodipine is extensively metabolized by the liver and the plasma elimination half-life ( $t_{1/2}$ ) is 56 hours in patients with severely impaired hepatic function, caution should be exercised when administering AZOR to patients with severe hepatic impairment.

**Laboratory Tests**

There was a greater decrease in hemoglobin and hematocrit in the combination product compared to either component alone.

**Adverse Reactions**

The only adverse reaction that occurred in greater than or equal to 3% of patients treated with AZOR and more frequently than placebo was edema. The placebo-subtracted incidence was 5.7% (5/20 mg), 6.2% (5/40 mg), 13.3% (10/20 mg), and 11.2% (10/40 mg). The edema incidence for placebo was 12.3%.

Adverse reactions seen at lower rates but at about the same or greater incidence as in patients receiving placebo included hypotension, orthostatic hypotension, rash, pruritus, palpitation, urinary frequency, and nocturia.

In individual clinical trials of amlodipine and olmesartan medoxomil, other commonly reported adverse reactions included headache, dizziness, and flushing.

For more information on AZOR, call 877-4-DSPROD (877-437-7763) or go to the web site [www.azor.com](http://www.azor.com).

#### **ABOUT DAIICHI SANKYO, INC.**

Daiichi Sankyo Inc., headquartered in Parsippany, New Jersey, is the U.S. subsidiary of Tokyo-based Daiichi Sankyo Co., Ltd. This global pharma innovator was established in 2005 through the merger of two leading Japanese pharmaceutical companies. The integration created a more robust organization that allows for continuous development of novel drugs that enrich the quality of life for patients around the world. A central focus of Daiichi Sankyo's research and development is cardiovascular disease, including therapies for dyslipidemia, hypertension, diabetes, and acute coronary syndrome. Equally important to the company is the discovery of new medicines in the areas of infectious diseases, cancer, bone and joint diseases, and immune disorders. For more information, visit [www.dsus.com](http://www.dsus.com).

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1 National Heart, Lung and Blood Institute, High Blood Pressure Key Points. [http://www.nhlbi.nih.gov/health/dci/Diseases/Hbp/HBP\\_Summary.html](http://www.nhlbi.nih.gov/health/dci/Diseases/Hbp/HBP_Summary.html). Accessed August 28, 2008

2 American Heart Association. 2004 High Blood Pressure Statistics. <http://www.americanheart.org/presenter.jhtml?identifier=4621>. Accessed August 27, 2008

3 Chobanian AV, Bakris GL, Black HR et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. JAMA. 2003;289:2560-2572

4 American Heart Association. 2004 High Blood Pressure Statistics <http://www.americanheart.org/presenter.jhtml?identifier=4621>. Site accessed August 28, 2008.

5 Kearney PM, et al. Global burden of hypertension: analysis of worldwide data. Lancet 2005, 365:217-23

6 <http://www.norvasc.com> -- Last accessed August 28, 2008.

7 Data are representing May 2002 - February 2006 from IMS Health. National Prescription Audit, February 2006.