



## News Release

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### **FOR IMMEDIATE RELEASE**

#### **New Analysis Supports Tolerability of Lexiscan<sup>®</sup> (regadenoson) Injection for Pharmacologic Myocardial Perfusion Imaging Studies**

*– Study finds aminophylline needs comparable to current standard –*

Minneapolis – October 2, 2009 – A new analysis reaffirms that Lexiscan<sup>®</sup> (regadenoson) Injection, the first selective A<sub>2A</sub> adenosine receptor agonist approved for use as a pharmacologic stress agent in radionuclide myocardial perfusion imaging (MPI) in patients unable to undergo adequate exercise stress, requires infrequent use of the drug aminophylline to reverse its effect in the case of adverse events. The low use of aminophylline demonstrates that Lexiscan is similar to the current standard, Adenoscan (adenosine injection). Results were presented today at the 14th Annual Scientific Sessions of the American Society of Nuclear Cardiology (ASNC) in Minneapolis, Minnesota.

“This data further underscores that Lexiscan is not only as effective as Adenoscan in detection of perfusion defects by myocardial perfusion imaging, but it also demonstrates that it is well-tolerated and has a side effect profile comparable to Adenoscan,” said Manuel Cerqueira, M.D., Chairman of Nuclear Medicine in the Imaging Institute and Staff Cardiologist in the Heart and Vascular Institute at the Cleveland Clinic. “Based on the expanding body of evidence, Lexiscan proves to be an excellent choice for patients who cannot undergo adequate exercise stress.”

Aminophylline is a nonspecific, competitive adenosine receptor antagonist used to reverse the effects of pharmacologic stress agents like Lexiscan and Adenoscan. It is administered to ease symptoms in patients who experience adverse events after receiving a pharmacologic stress agent during an MPI test.

Using data from pivotal ADVANCE 1 and ADVANCE 2 double-blind, Phase III trials of Lexiscan, researchers compared patient characteristics, side effects, and aminophylline treatment timing and dosage for 2,015 patients randomized to Lexiscan (n = 1337) or Adenoscan (n = 678). Results showed that aminophylline was administered to 46 Lexiscan patients and 12 Adenoscan patients (3.4 and 1.8 percent respectively, p = 0.035).

Although the use of aminophylline was slightly higher for patients randomized to Lexiscan than Adenoscan, no specific adverse event occurred significantly more often in Lexiscan than Adenoscan. The most common adverse events for which aminophylline was administered were angina pectoris, headache, electrocardiography (ECG) changes/ST segment depression, chest pain, and dyspnea (shortness of breath). Patients randomized to Lexiscan who received aminophylline were treated on average 4.5 minutes later than patients randomized to Adenoscan (p = 0.026). Total aminophylline doses ranged from 72 to 300 milligrams (mg) for Lexiscan and from 25 to 240 mg for Adenoscan.

For Lexiscan stress MPI, there were no significant differences in age, body mass index, race, chronic obstructive pulmonary disease (COPD) history, diabetes history, serum creatinine levels, or creatinine clearance between those receiving aminophylline and those not receiving aminophylline. Patients receiving aminophylline were more likely to have a history of unstable angina (P<0.001), be of female gender (P<0.05), and have enrolled in a clinical trial conducted outside the United States (P<0.001).

### **About Myocardial Perfusion Imaging**

MPI tests, commonly called cardiac stress tests, identify areas of poor blood flow in the heart to determine the extent of coronary artery disease (CAD)<sup>3</sup>, a condition that affects 16 million Americans and is responsible for more than 445,000 deaths annually in the United States. Many patients exercise on a treadmill to generate the increase in coronary blood flow necessary to perform an MPI study. However, almost half of patients undergoing cardiac stress tests each year are unable to exercise adequately because of medical conditions. For these patients, a pharmacologic stress agent that temporarily increases blood flow through the coronary arteries is used to mimic the increase in coronary blood flow caused by exercise. Approximately 7.5 million MPI studies were performed in 2007 in the U.S.

### **About Lexiscan**

Lexiscan is an A<sub>2A</sub> adenosine receptor agonist approved for use as a pharmacologic stress agent in radionuclide MPI in patients unable to undergo adequate exercise stress. Lexiscan was designed to produce coronary vasodilation and increase coronary blood flow by activation of the A<sub>2A</sub> adenosine receptor. Lexiscan is administered as an intravenous injection (approximately 10 seconds) with no dose adjustment required for body weight. Lexiscan should not be administered to patients with second- or third-degree AV block or sinus node dysfunction unless these patients have a functioning artificial

pacemaker. Adenosine receptor agonists, including Lexiscan, induce arterial vasodilation and hypotension. The risk of serious hypotension may be higher in patients with cardiac or cerebrovascular insufficiency. In post-marketing experience, syncope, symptomatic hypotension, and transient ischemic attacks have been observed. Decreased systolic blood pressure (>35 mm Hg) was observed in 7% of patients and decreased diastolic blood pressure (>25 mm Hg) was observed in 4% of patients within 45 minutes of Lexiscan administration. Adenosine receptor agonists, including Lexiscan, may cause bronchoconstriction and respiratory compromise. For patients with known or suspected bronchoconstrictive disease, chronic obstructive pulmonary disease (COPD), or asthma, appropriate bronchodilator therapy and resuscitative measures should be available prior to Lexiscan administration. Complete prescribing information for Lexiscan is available at <http://www.astellas.us/docs/lexiscan.pdf>. For more information on Lexiscan, visit the Web site at <http://www.Lexiscan.com>.

### **About Astellas Pharma US, Inc.**

Astellas Pharma US, Inc., located in Deerfield, Illinois, is a U.S. affiliate of Tokyo-based Astellas Pharma Inc. Astellas is a pharmaceutical company dedicated to improving the health of people around the world through the provision of innovative and reliable pharmaceutical products. The organization is committed to becoming a global category leader in focused areas by combining outstanding R&D and marketing capabilities. In the U.S., Astellas markets products in the areas of immunology, urology, anti-infectives, cardiovascular and dermatology. For more information about Astellas Pharma US, Inc., please visit our Web site at <http://www.us.astellas.com>.

Astellas currently markets Adenoscan<sup>®</sup> (adenosine injection), the leading pharmacologic stress agent for MPI studies in the United States. Adenoscan is indicated as an adjunct to thallium-201 myocardial perfusion scintigraphy in patients unable to exercise adequately. Adenoscan is contraindicated in patients with second- or third-degree AV block, unless these patients have a functioning artificial pacemaker, sinus node disease, and known or suspected bronchoconstrictive or bronchospastic lung disease. Fatal cardiac arrest, sustained ventricular tachycardia (requiring resuscitation), and nonfatal myocardial infarction have been reported coincident with Adenoscan infusion. Patients with unstable angina may be at greater risk. Appropriate resuscitative measures should be available. Adenoscan is a potent peripheral vasodilator and can cause significant hypotension. The risk of hypotension may be higher in patients with cardiac or cerebrovascular insufficiency. Adenoscan exerts a direct depressant effect on the SA and AV nodes and has the potential to cause first-, second- or third-degree AV block, or sinus bradycardia. Increases in systolic and diastolic pressure have been observed. Adenosine receptor agonists, including Adenoscan, may cause bronchoconstriction and respiratory compromise. Atrial fibrillation has been reported in patients with Adenoscan infusion and may last from a few seconds to hours, however, patients spontaneously converted to normal sinus rhythm. Most common adverse reactions (≥5%) to Adenoscan are flushing, chest discomfort, dyspnea, headache, discomfort of the throat, neck, or jaw,

gastrointestinal discomfort, and lightheadedness/dizziness. Side effects with Adenoscan usually resolve quickly when the infusion is discontinued, although delayed or persistent effects have been observed. For full prescribing information, please visit <http://www.adenoscan.com>.

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