

NATIONAL PBM COMMUNICATION · September 22, 2010

Regadenoson (Lexiscan®) and Updated Labeling Changes

- In December 2009, the Food and Drug Administration (FDA) Center for Drug Evaluation and Research (CDER) approved safety labeling changes for Regadenoson (Lexiscan®) to include adverse events reported post-marketing as well as in the warnings and precautions section. The following communication outlines these changes.
- Regadenoson (Lexiscan®) is an intravenous (IV) pharmacologic stress agent that received FDA approval in April 2008 for use in radionuclide myocardial perfusion imaging (MPI).
- Regadenoson (Lexiscan®) works as an A(2A) adenosine receptor agonist that produces coronary vasodilation and increases coronary blood flow.
- Changes to the WARNINGS AND PRECAUTIONS section as well as to the POST-MARKETING EXPERIENCE section of the package insert include¹⁻²:
 - **WARNINGS AND PRECAUTIONS**
 - **Hypotension**
In postmarketing experience, ...seizures have been observed [see 6.2 Post-Marketing Experience].
 - **Hypertension**
Administration of adenosine receptor agonists, including Lexiscan, may result in clinically significant increases in blood pressure in some patients. Among patients who experienced an increase in blood pressure in clinical trials, the increase was observed within minutes of Lexiscan administration. Most increases resolved within 10 to 15 minutes, but in some cases, increases were observed at 45 minutes following administration [see 12.2 Pharmacodynamics]. In post-marketing experience, cases of potentially clinically significant hypertension have been reported, particularly with underlying hypertension and when low-level exercise was included in the MPI [see 6.2 Post-Marketing Experience].
 - **ADVERSE REACTIONS (Post-Marketing Experience)**
 - Cardiovascular
...marked hypertension, symptomatic hypotension in association with transient ischemic attack, seizures and syncope [see Warnings and Precautions (5)], requiring intervention with fluids and/or aminophylline have occurred.
 - Central Nervous System
Tremor, seizure (particularly with a history of seizure).
- Aminophylline does reverse the effects of adenosine and regadenoson, but it is unknown whether or not aminophylline would specifically reverse hypertension or attenuate seizure due to regadenoson.
- Within the VA system, a total of 17 adverse drug events associated with regadenoson have been reported to the VA Adverse Drug Event Reporting System (VA ADERS) since its approval.
 - 6/17 were classified as severe.
 - Severe reactions included cardiac arrest, asystole, convulsions, tremor, dyspnea, and respiratory depression.
 - From the information available on those cases with full reports, most cases of cardiac arrest/asystole resolved spontaneously or following intervention with atropine, aminophylline.
 - 5/17 were classified as moderate.
 - There were 2 reports of tremor and 2 reports of syncope.
- Providers should continue to report any adverse events with regadenoson by entering the information into CPRS¹ Allergies/Adverse Reactions field and/or via local reporting mechanisms. Facilities should continue to report adverse events into VA ADERS and to the FDA (as appropriate).

REFERENCES

1. FDA. <http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm197103.htm> . (Accessed 09/09/10).
2. Lexiscan (Regadenoson) product package insert. Deerfield, IL: Astellas; December 2009.

ACTIONS:

- **Facility Director** (or physician designee): Forward this document to the Facility Chief of Staff (COS).
- **Facility COS and Chief Nurse Executives**: Forward this document to all appropriate providers who prescribe these medications (e.g., cardiologists and nuclear medicine clinicians as well as nurses and technicians who work in imaging settings, including contract providers, etc.). In addition, forward to the Associate Chief of Staff (ACOS) for Research and Development (R&D). Forward to other VA employees as deemed appropriate.
- **ACOS for R&D**: Forward this document to Principal Investigators (PIs) who have authority to practice at the facility and to your respective Institutional Review Board (IRB).