



NATIONAL PBM BULLETIN

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DEPARTMENT OF VETERANS AFFAIRS VETERANS HEALTH ADMINISTRATION (VHA)
PHARMACY BENEFITS MANAGEMENT SERVICES (PBM), MEDICAL ADVISORY PANEL (MAP),
AND CENTER FOR MEDICATION SAFETY (VA MEDSAFE)

REGADENOSON (LEXISCAN) AND ADENOSINE (ADENOSCAN): RISK OF HEART ATTACK AND DEATH

I. ISSUE

Previous product labeling for regadenoson (Lexiscan) and adenosine (Adenoscan) already documents the known risk of heart attack and death with use of these drugs. However, accounts of myocardial infarction (MI) and death associated with regadenoson (Lexiscan) and adenosine (Adenoscan) continue to be reported in the FDA Adverse Event Reporting System (FAERS) database as well as in the medical literature. As such, FDA approved changes to the drug labels of these agents to reflect these serious events and updated recommendations for use.

II. BACKGROUND

Regadenoson (Lexiscan) and adenosine (Adenoscan) are intravenous (IV) cardiac nuclear stress tests agents that produce coronary vasodilation and increase coronary blood flow in an effort to elucidate coronary artery obstructions. These agents may direct blood circulation to unblocked arteries, detouring blood flow away from obstructed vessels. The reduction in blood flow in an obstructed artery can lead to a heart attack and death in at-risk patients, especially those with ongoing cardiac ischemia. Health care professionals should thus avoid using regadenoson (Lexiscan) and adenosine (Adenoscan) in patients displaying signs or symptoms of unstable angina or cardiovascular instability, since they may harbor a greater risk for serious cardiovascular adverse reactions.

III. DISCUSSION

- Data from FAERS shows:
 - 26 MI cases and 29 cases of death associated with the use of regadenoson (Lexiscan) from June 24, 2008, to April 10, 2013.
 - 6 cases of MI and 27 cases of death associated with the use of adenosine (Adenoscan) from May 18, 1995, to April 10, 2013.
 - Onset of these adverse events occurred within 6 hours after administration of regadenoson (Lexiscan) and adenosine (Adenoscan).
 - A few deaths occurred when regadenoson (Lexiscan) and adenosine (Adenoscan) was administered with exercise stress testing (not an FDA approved use of these drugs).
- Data from the medical literature reports 2 cases of MI associated with regadenoson (Lexiscan); however, published studies do not suggest an increased incidence of cardiovascular adverse events with regadenoson (Lexiscan) and adenosine (Adenoscan).
- The difference in risk of heart attack or death between regadenoson (Lexiscan) and adenosine (Adenoscan) cannot be assessed at this time due to limitations in data.
- In response to these reports, the manufacturer has updated the Warnings and Precautions sections of labeling material with the following information:
 - 5.1 *Myocardial Ischemia*
Fatal and nonfatal myocardial infarction, ventricular arrhythmias and cardiac arrest have occurred following Lexiscan injection. Avoid use in patients with symptoms or signs of acute myocardial ischemia, for example unstable angina or cardiovascular instability; these patients may be at greater risk of serious cardiovascular reactions to Lexiscan. Cardiac resuscitation equipment and trained staff should be available before administering Lexiscan. If serious reactions to

Lexiscan occur, consider the use of aminophylline, an adenosine antagonist, to shorten the duration of increased coronary blood flow induced by Lexiscan.

IV. PROVIDER RECOMMENDATIONS

As cases of myocardial infarction and death have occurred in patients with pre-existing unstable angina or cardiovascular instability, FDA recommends:

- *"Screen all nuclear stress test candidates for their suitability to receive regadenoson (Lexiscan) and adenosine (Adenoscan).*
- *Avoid using these drugs in patients with symptoms or signs of acute myocardial ischemia such as unstable angina or cardiovascular instability; these patients may be at greater risk of serious cardiovascular reactions to regadenoson (Lexiscan) and adenosine (Adenoscan).*
- *Cardiac resuscitation equipment and trained staff should be readily available before administering regadenoson (Lexiscan) and adenosine (Adenoscan)."*

V. REFERENCES

1. FDA Drug Safety Communication: FDA warns of rare but serious risk of heart attack and death with cardiac nuclear stress test drugs Lexiscan (regadenoson) and Adenoscan (adenosine).
<http://www.fda.gov/Drugs/DrugSafety/ucm375654.htm>. Accessed 11/20/2013.
2. Lexiscan (Regadenoson) product package insert. Northbrook, IL: Astellas; October 2013.

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., **primary care providers, 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).