

## BRIEF SUMMARY

## For Intravenous Infusion Only

## DESCRIPTION

Adenosine is an endogenous nucleoside occurring in all cells of the body. It is chemically 6-amino-9-beta-D-ribofuranosyl-9-H-purine. Adenosine is a white crystalline powder. It is soluble in water and practically insoluble in alcohol. Solubility increases by warming and lowering the pH of the solution.

Each Adenoscan vial contains a sterile, non-pyrogenic solution of adenosine 3 mg/mL and sodium chloride 9 mg/mL in Water for Injection, q.s. The pH of the solution is between 4.5 and 7.5.

## INDICATIONS AND USAGE:

Intravenous Adenoscan is indicated as an adjunct to thallium-201 myocardial perfusion scintigraphy in patients unable to exercise adequately. (See **WARNINGS**).

## CONTRAINDICATIONS:

Intravenous Adenoscan should not be administered to individuals with:

1. Second- or third-degree AV block (except in patients with a functioning artificial pacemaker).
2. Sinus node disease, such as sick sinus syndrome or symptomatic bradycardia (except in patients with a functioning artificial pacemaker).
3. Known or suspected bronchoconstrictive or bronchospastic lung disease (e.g., asthma).
4. Known hypersensitivity to adenosine.

## WARNINGS:

**Fatal Cardiac Arrest, Life Threatening Ventricular Arrhythmias, and Myocardial Infarction.**

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.

**Sinoatrial and Atrioventricular Nodal Block**

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. Approximately 6.3% of patients develop AV block with Adenoscan, including first-degree (2.9%), second-degree (2.6%) and third-degree (0.8%) heart block. All episodes of AV block have been asymptomatic, transient, and did not require intervention. Adenoscan can cause sinus bradycardia. Adenoscan should be used with caution in patients with pre-existing first-degree AV block or bundle branch block and should be avoided in patients with high-grade AV block or sinus node dysfunction (except in patients with a functioning artificial pacemaker). Adenoscan should be discontinued in any patient who develops persistent or symptomatic high-grade AV block. Sinus pause has been rarely observed with adenosine infusions.

**Hypotension**

Adenoscan is a potent peripheral vasodilator and can cause significant hypotension. Patients with an intact baroreceptor reflex mechanism are able to maintain blood pressure and tissue perfusion in response to Adenoscan by increasing heart rate and cardiac output. However, Adenoscan should be used with caution in patients with autonomic dysfunction, stenotic valvular heart disease, pericarditis or pericardial effusions, stenotic carotid artery disease with cerebrovascular insufficiency, or uncorrected hypovolemia, due to the risk of hypotensive complications in these patients. Adenoscan should be discontinued in any patient who develops persistent or symptomatic hypotension.

**Hypertension**

Increases in systolic and diastolic pressure have been observed (as great as 140 mm Hg systolic in one case) concomitant with Adenoscan infusion; most increases resolved spontaneously within several minutes, but in some cases, hypertension lasted for several hours.

**Bronchoconstriction**

Adenoscan is a respiratory stimulant (probably through activation of carotid body chemoreceptors) and intravenous administration in man has been shown to increase minute ventilation (V<sub>e</sub>) and reduce arterial PCO<sub>2</sub>, causing respiratory alkalosis. Approximately 28% of patients experience breathlessness (dyspnea) or an urge to breathe deeply with Adenoscan. These respiratory complaints are transient and only rarely require intervention.

Adenoscan administered by inhalation has been reported to cause bronchoconstriction in asthmatic patients, presumably due to mast cell degranulation and histamine release. These effects have not been observed in normal subjects. Adenoscan has been administered to a limited number of patients with asthma and mild to moderate exacerbation of their symptoms has been reported. Respiratory compromise has occurred during adenosine infusion in patients with obstructive pulmonary disease. Adenoscan should be used with caution in patients with obstructive lung disease not associated with bronchoconstriction (e.g., emphysema, bronchitis, etc.) and should be avoided in patients with bronchoconstriction or bronchospasm (e.g., asthma). Adenoscan should be discontinued in any patient who develops severe respiratory difficulties.

## PRECAUTIONS:

**Drug Interactions**

Intravenous Adenoscan has been given with other cardioactive drugs (such as beta adrenergic blocking agents, cardiac glycosides, and calcium channel blockers) without apparent adverse interactions, but its effectiveness with these agents has not been systematically evaluated. Because of the potential for additive or synergistic depressant effects on the SA and AV nodes, however, Adenoscan should be used with caution in the presence of these agents. The vasoactive effects of Adenoscan are inhibited by adenosine receptor antagonists, such as methylxanthines (e.g., caffeine and theophylline). The safety and efficacy of Adenoscan in the presence of these agents has not been systematically evaluated. The vasoactive effects of Adenoscan are potentiated by nucleoside transport inhibitors, such as dipyridamole. The safety and efficacy of Adenoscan in the presence of dipyridamole has not been systematically evaluated. Whenever possible, drugs that might inhibit or augment the effects of adenosine should be withheld for at least five half-lives prior to the use of Adenoscan.

**Carcinogenesis, Mutagenesis, Impairment of Fertility**

Studies in animals have not been performed to evaluate the carcinogenic potential of Adenoscan. Adenosine was negative for genotoxic potential in the Salmonella (Ames Test) and Mammalian Microsome Assay.

Adenosine, however, like other nucleosides at millimolar concentrations present for several doubling times of cells in culture, is known to produce a variety of chromosomal alterations. Fertility studies in animals have not been conducted with adenosine.

**Pregnancy Category C**

Animal reproduction studies have not been conducted with adenosine; nor have studies been performed in pregnant women. Because it is not known whether Adenoscan can cause fetal harm when administered to pregnant women, Adenoscan should be used during pregnancy only if clearly needed.

**Pediatric Use**

The safety and effectiveness of Adenoscan in patients less than 18 years of age have not been established.

**Geriatric Use**

Clinical studies of Adenoscan did not include sufficient numbers of subjects aged younger than 65 years to determine whether they respond differently. Other reported experience has not revealed clinically relevant differences of the response of elderly in comparison to younger patients. Greater sensitivity of some older individuals, however, cannot be ruled out.

## ADVERSE REACTIONS:

The following reactions with an incidence of at least 1% were reported with intravenous Adenoscan among 1421 patients enrolled in controlled and uncontrolled U.S. clinical trials. Despite the short half-life of adenosine, 10.6% of the side effects occurred not with the infusion of Adenoscan but several hours after the infusion terminated. Also, 8.4% of the side effects that began coincident with the infusion persisted for up to 24 hours after the infusion was complete. In many cases, it is not possible to know whether these late adverse events are the result of Adenoscan infusion.

Flushing	44%	Lightheadedness/dizziness	12%	Hypotension	2%
Chest discomfort	40%	Upper extremity discomfort	4%	Nervousness	2%
Dyspnea or urge to breathe deeply	28%	ST segment depression	3%	Arrhythmias	1%
Headache	18%	First-degree AV block	3%		
Throat, neck or jaw discomfort	15%	Second-degree AV block	3%		
Gastrointestinal discomfort	13%	Paresthesia	2%		

Adverse experiences of any severity reported in less than 1% of patients include:

**Body as a Whole:** back discomfort; lower extremity discomfort; weakness.

**Cardiovascular System:** nonfatal myocardial infarction; life-threatening ventricular arrhythmia; third-degree AV block; bradycardia; palpitation; sinus exit block; sinus pause; sweating; T-wave changes, hypertension (systolic blood pressure > 200 mm Hg).

**Central Nervous System:** drowsiness; emotional instability; tremors.

**Genital/Urinary System:** vaginal pressure; urgency.

**Respiratory System:** cough.

**Special Senses:** blurred vision; dry mouth; ear discomfort; metallic taste; nasal congestion; scotomas; tongue discomfort.

## OVERDOSAGE:

The half-life of adenosine is less than 10 seconds and side effects of Adenoscan (when they occur) usually resolve quickly when the infusion is discontinued, although delayed or persistent effects have been observed. Methylxanthines, such as caffeine and theophylline, are competitive adenosine receptor antagonists and theophylline has been used to effectively terminate persistent side effects. In controlled U.S. clinical trials, theophylline (50-125 mg slow intravenous injection) was needed to abort Adenoscan side effects in less than 2% of patients.

## DOSAGE AND ADMINISTRATION:

For intravenous infusion only.

Adenoscan should be given as a continuous peripheral intravenous infusion.

The recommended intravenous dose for adults is 140 mcg/kg/min infused for six minutes (total dose of 0.84 mg/kg).

The required dose of thallium-201 should be injected at the midpoint of the Adenoscan infusion (i.e., after the first three minutes of Adenoscan).

Thallium-201 is physically compatible with Adenoscan and may be injected directly into the Adenoscan infusion set.

The injection should be as close to the venous access as possible to prevent an inadvertent increase in the dose of Adenoscan (the contents of the IV tubing) being administered. There are no data on the safety or efficacy of alternative Adenoscan infusion protocols.

The safety and efficacy of Adenoscan administered by the intracoronary route have not been established.

**Note:** Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration.

Rx only

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# Electronic Records Can Improve Quality of Care

BY MARY ELLEN SCHNEIDER

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Successful implementation of an electronic medical record system to improve quality requires attention and effort from physicians at the start of the process, according to experts.

The more time physicians spend up front customizing the system to fit their needs, the less they will struggle later on, said Dr. Barry Bershaw, director of quality and informatics at Fairview Health Services in Minnesota.

Dr. Bershaw has seen first hand how effective electronic medical record tools can improve quality. At Fairview Health Services, which includes hospital and clinics across Minnesota, there has been significant improvement in quality measures in recent years. For example, screening for chlamydia has nearly doubled from 2004 to 2005, and there have been major improvements in asthma management and obesity screening.

Electronic medical records also can improve quality within small practices, he said. Before coming to work for the Fairview system 2 years ago, Dr. Bershaw spent about 28 years working in a small family medicine practice affiliated with the Fairview system. In 1999, the practice became a pilot site to test Fairview's electronic medical record. The implementation proved successful, and the practice continues to use the system today.

Implementation of the EMR system led to reduction of staff by approximately four full-time employees and to improvements in quality, particularly in coronary artery disease and diabetes care, he said.

"It wasn't just because we were really good doctors," he said. In fact, the performance improvements they saw were in areas where the EMR included clinical decision support and other prompts.

But Dr. Bershaw doesn't downplay the tough transition to the system. It took 3 months before the physicians in the practice could start to go home at the same time they did before implementation. But at 6 months, half of the physicians were going home earlier than before, he said.

In the first couple of months, physician and staff satisfaction dropped, according to satisfaction surveys. At that point the excitement was gone, and they had yet to realize the benefits. But at 4-6 months, patients started coming in for return visits, and staff began to see efficiency in the system. At 6 months, all the results had improved including patient satisfaction, Dr. Bershaw said.

One common mistake that physicians make is not building in the shortcuts at the beginning, he said.

Implementation of an electronic health record is not a guarantee of improved quality. In fact, a qualitative look at one suburban family medicine practice shows that a lack of communication about the goals of the EMR has actually led to a drop in quality improvement activities.

Jesse C. Crosson, Ph.D., of the New Jer-

sey Medical School, Newark, and his colleagues, analyzed the EMR use of a family medicine practice in an upper middle-class suburban community in 2002 with follow-up in 2003 (Ann. Fam. Med. 2005;3:307-11).

Dr. Crosson and his team found that before the implementation of the EMR, the practice had used reminder stickers on their paper charts for screening, prevention, and disease management. But when the practice switched to an electronic system, the EMR's built-in reminders were disabled because they were too cumbersome, leaving the practice without any formal reminder system.

The lack of communication was a real obstacle in this practice, Dr. Crosson said in an interview. He recommended that physicians planning to implement an EMR meet early on with a broad group of people within the practice to figure out how to maintain existing quality of care system once the electronic system is in place. This could mean using duplicate systems during the transition period, he said.

One barrier to realizing the full potential of EMR systems is that physicians are trained to take care of one person at a time, Dr. Crosson said, and many of the innovative EMR functions help in caring for groups of patients. There needs to be a shift in the mind set of physicians in order to truly take advantage of the advances in technology, he said.

When shopping for an EMR that can aid in the collection and reporting of quality improvement measures, look for a system that can export the data in an electronic format, advised Dr. David C. Kibbe, director of the American Academy of Family Physicians' Center for Health Information Technology. ■

## Health IT Lessons

Officials at the Agency for Healthcare Research and Quality are putting out some of the lessons learned from their health information technology projects. The information is available on the ARHQ Web site—[www.healthit.ahrq.gov](http://www.healthit.ahrq.gov).

The Web site includes some of the early lessons from AHRQ-funded projects in a range of settings including health plans, hospitals, and small practices. The site also features links to more than 5,000 health IT resources, an evaluation tool kit to help implement health IT projects, and funding information.

"Adoption of health IT will be too slow if providers have to reinvent the wheel one by one," AHRQ Director Dr. Carolyn Clancy said in a statement. "This shared learning tool brings the lessons of experience together in one place, so we can help providers avoid problems and achieve greater benefits when they make their move to health IT."