OVERVIEW
The purpose of this document is to specifically identify the critical components involved in performing a pharmacologic stress test with regadenoson. This information serves as a standard for all nuclear cardiology laboratories. This document will cover dosage and side effects, indications, contraindications, testing procedure, and indications for reversal of infusion.

REGADENOSON
Regadenoson is an A2A adenosine receptor agonist that is a coronary vasodilator. Regadenoson is a low affinity agonist (Ki ≈ 1.3 µM) for the A2A adenosine receptor with at least 10-fold lower affinity for the A1 adenosine receptor (Ki>16.5 µM), and weak, if any, affinity for the A2B and A3 adenosine receptors.

Activation of the A2A adenosine receptor by regadenoson produces coronary vasodilation and increases coronary blood flow. The maximal plasma concentration of regadenoson is achieved within 1 to 4 minutes after injection and parallels the onset of the pharmacodynamic response. The half-life of this initial phase is approximately 2 to 4 minutes. An intermediate phase follows with an average half-life of 30 minutes coinciding with loss of the pharmacodynamic effect. The last phase consists of a decline in plasma concentration with a half-life of approximately 2 hours.

DOSAGE AND SIDE EFFECTS
The recommended intravenous dose of regadenoson is 5 mL (0.4 mg regadenoson) and should be given as a rapid (approximately 10 seconds) injection into a peripheral vein using a 22 gauge or larger catheter or needle.

As with any other parenteral drug, products should be inspected visually for particulate matter and discoloration prior to administration.

The most common reactions to administration of regadenoson are shortness of breath, headache, and flushing. Less common reactions are chest discomfort, angina pectoris or ST, dizziness, chest pain, nausea, abdominal discomfort, dysgeusia, and feeling hot.

Maximum hemodynamic effects of regadenoson:

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase in Heart Rate (&gt; 40 Beats/Minute)</td>
<td>5%</td>
</tr>
<tr>
<td>Decrease in Systolic Blood Pressure (&gt; 35 mm Hg)</td>
<td>7%</td>
</tr>
<tr>
<td>Decrease in Diastolic Blood Pressure (&gt; 25 mm Hg)</td>
<td>4%</td>
</tr>
</tbody>
</table>

In patients with a prior adenosine stress study, the following side effects have been noted:

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhythm or Conduction Abnormalities</td>
<td>26%</td>
</tr>
<tr>
<td>First Degree AV Block</td>
<td>3%</td>
</tr>
<tr>
<td>Second Degree AV Block</td>
<td>0.1%</td>
</tr>
<tr>
<td>Ventricular Conduction Abnormalities</td>
<td>6%</td>
</tr>
</tbody>
</table>

Many adverse reactions begin soon after dosing and generally resolve within 15 minutes, except for headache which resolves in most patients within 30 minutes.

Aminophylline may be administered in doses ranging from 50 mg to 250 mg by slow intravenous injection (50 mg to 100 mg over 30 to 60 seconds) to attenuate severe or persistent adverse reactions to regadenoson.
Pharmacologic Stress Test—Regadenoson continued

INDICATIONS
A regadenoson stress test is indicated in patients unable to undergo adequate exercise stress and in the presence of the following condition:
1) Inability to perform adequate exercise due to noncardiac physical limitations or lack of motivation

CONTRAINDICATIONS
Absolute contraindications for regadenoson stress testing include:
1) Patients with second- or third-degree AV block or sinus node dysfunction without a functioning pacemaker
2) Known hypersensitivity to adenosine or regadenoson
3) Systolic blood pressure less than 90mm Hg
4) Reactive airways disease. The safety of selective adenosine agonists is not definitively established in patients with bronchoconstrictive lung disease such as asthma or COPD. Regadenoson should be used with caution in these patients. Aminophylline, bronchodilators and resuscitative measures should be immediately available.
5) The risk of serious hypotension may be higher in patients with autonomic dysfunction, hypovolemia, left main coronary artery stenosis, stenotic valvular heart disease, pericarditis or pericardial effusions, or stenotic carotid artery disease with cerebrovascular insufficiency.

Relative contraindications for regadenoson stress testing include:
1) Profound sinus bradycardia (heart rate < 40 beats/minute)

TESTING PROCEDURE
Patients should avoid consumption of any products containing methylxanthines, including caffeinated coffee, tea, or other beverages, chocolate, caffeine-containing drug products and theophylline for at least 12 hours prior to testing. Dipyridamole should be withheld for at least 2 days prior to regadenoson administration.
1) Regadenoson (5 mL containing 0.4 mg of regadenoson) should be given as a rapid (approximately 10 seconds) injection into a peripheral vein using a 22-gauge or larger catheter or needle.
2) Monitor the ECG continuously during the procedure. 12 lead ECGs should be recorded every minute until the patient is stable.
3) Blood pressure should be monitored every minute during the procedure, and for at least 3 to 5 minutes into recovery.
4) Administer a 5 mL saline flush immediately after the injection of regadenoson.
5) Administer the radionuclide myocardial perfusion imaging agent 10 to 20 seconds after the saline flush. The radionuclide may be injected directly into the same catheter as regadenoson.

Note: Anti-ischemic cardiac medications can decrease the diagnostic accuracy of vasodilator stress testing.

INDICATIONS FOR REVERSAL OF REGADENOSON INFUSION
Aminophylline should be considered under any of the following circumstances:
1) Severe hypotension (systolic blood pressure <80mm Hg)
2) Development of symptomatic, persistent second-degree or complete heart block
3) Wheezing
4) Persistent chest pain or ST depression
5) Signs of poor perfusion (pallor, cyanosis, cold skin)
6) Technical problems with the monitoring equipment
7) Persistent symptoms thought to be due to regadenoson
Pharmacologic Stress Test—Regadenoson continued

SUGGESTED READING

ASNC thanks the following members for their contributions to this document: Fabio Esteves, MD; Christopher L. Hansen, MD; Sujith Kalathiveetl, MD; Maria Sciammarella, MD; and Aseem Vashist, MD.

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