Indication
Lexiscan® (regadenoson) injection is a prescription drug given through an IV line that increases blood flow through the arteries of the heart during a cardiac nuclear stress test. Lexiscan is given to patients when they are unable to exercise adequately for a stress test.

Important Safety Information
Lexiscan should not be given to patients who have certain abnormal heart rhythms unless they have a pacemaker. Lexiscan can cause serious or fatal cardiac arrest, abnormal heart rhythms or heart attack.

GETTING A LEXISCAN STRESS TEST? SKIP THE CAFFEINE.

- DON’T CONSUME caffeine-containing foods, drinks, or medications for 12 HOURS before your test

Look inside for a list of specific foods, drinks, and medications to avoid.

PLEASE SEE ADDITIONAL IMPORTANT SAFETY INFORMATION ON PAGES 2-4.
PLEASE SEE FULL PRESCRIBING INFORMATION AT THE END OF THE DOCUMENT.
HELP PREVENT A RESCHEDULED TEST

Methylxanthines (pronounced meth-ill-zan-theenz) are a type of substance found in many common foods, drinks, and medications. Some examples of methylxanthines include caffeine, aminophylline, and theophylline.

DO NOT consume any foods, drinks, or medications containing methylxanthines for at least 12 hours before your scheduled stress test. In addition, do not take any medications containing dipyridamole for at least 48 hours before your stress test.

12 HOURS OR LESS, NO STRESS TEST

Important Safety Information (Continued)
Allergic reactions can occur after Lexiscan® (regadenoson) injection.

Drugs such as Lexiscan may cause an increase or decrease in blood pressure, especially in patients with certain heart and blood vessel disorders.
The tables below list examples of foods, drinks, and medications to avoid before your stress test. This is only a partial list. Your doctor and pharmacist will know about other products, foods, drinks, and medications you shouldn’t have before your test. Be sure to tell your doctor which over-the-counter (OTC) and prescription drugs you’re currently taking. Your doctor will then give you instructions about those medications.

### FOODS TO AVOID
- chocolate candies
- chocolate cakes
- brownies
- chocolate pudding
- energy bars
- foods containing guarana

### DRINKS TO AVOID
- chocolate milk/chocolate protein shake
- hot cocoa
- coffee (brewed, instant, iced, decaf)
- tea (brewed, instant, iced, decaf)
- soda pop (including “caffeine-free”)
- energy drinks
- drinks containing guarana

### MEDICATIONS TO AVOID

<table>
<thead>
<tr>
<th>OTC drugs containing caffeine</th>
<th>Prescription drugs containing caffeine</th>
<th>Prescription drugs containing dipyridamole (withhold for 48 hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anacin® (aspirin, caffeine)</td>
<td>Cafergot® (ergotamine tartrate, caffeine)</td>
<td>Persantine® (dipyridamole)</td>
</tr>
<tr>
<td>Excedrin® (acetaminophen, aspirin, caffeine)</td>
<td>Esgic® (butalbital, acetaminophen, caffeine)</td>
<td>Aggrenox® (aspirin, dipyridamole)</td>
</tr>
<tr>
<td>Vivarin® (caffeine)</td>
<td>Fioricet® (butalbital, acetaminophen, caffeine)</td>
<td>Elixophyllin® (theophylline)</td>
</tr>
<tr>
<td>NoDoz® (caffeine)</td>
<td>Fiorinal® (butalbital, aspirin, caffeine)</td>
<td>Theo-24® (theophylline)</td>
</tr>
</tbody>
</table>

**Important Safety Information (Continued)**
Lexiscan can cause breathing difficulties. Before receiving Lexiscan, tell your doctor if you have respiratory diseases, such as COPD (chronic obstructive pulmonary disease) or asthma. Tell your doctor about all medications you use to manage these conditions.

**PLEASE SEE ADDITIONAL IMPORTANT SAFETY INFORMATION ON PAGES 2-4. PLEASE SEE FULL PRESCRIBING INFORMATION AT THE END OF THE DOCUMENT.**
GETTING READY FOR YOUR TEST

CAFFEINE REMINDER! 12 HOURS OR LESS, NO PHARM STRESS

DO NOT APPLY CREAMS, LOTIONS, OR POWDERS TO YOUR CHEST AREA ON THE DAY OF THE TEST

WEAR COMFORTABLE CLOTHING AND SHOES

Important Safety Information (Continued)

Lexiscan® (regadenoson) injection can increase the risk of seizures. Before receiving Lexiscan, tell your doctor if you have a history of seizures. Lexiscan can cause stroke, which may be a result of an increase or decrease in blood pressure.

The most common side effects that occurred in clinical trials of Lexiscan were shortness of breath, headache, flushing, chest discomfort or chest pain, dizziness, nausea, abdominal discomfort, a metallic taste in the mouth, and feeling hot. Most common side effects began soon after receiving Lexiscan and went away within 15 minutes except for headache, which resolved in most patients within 30 minutes.

Avoid consuming any caffeine-containing foods and beverages or medicines containing caffeine, aminophylline or theophylline in the 12 hours before your scheduled heart scan.

Ask your doctor if you should stop taking any medications you usually take before the day of the test.

For women who are nursing, pump and discard breast milk for 10 hours after receiving Lexiscan.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

PLEASE SEE FULL PRESCRIBING INFORMATION AT THE END OF THE DOCUMENT.
LEXISCAN® (regadenoson) injection is a pharmacologic stress agent indicated for radionuclide myocardial perfusion imaging (MPI) in patients unable to undergo adequate exercise stress (1).

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**INDICATIONS AND USAGE**

LEXISCAN® is a pharmacologic stress agent indicated for radionuclide myocardial perfusion imaging (MPI) in patients unable to undergo adequate exercise stress (1).

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**DOSE AND ADMINISTRATION**

- The recommended dose of LEXISCAN is 5 mL (0.4 mg regadenoson) administered as an intravenous injection within 10 seconds; followed immediately by saline flush and radiopharmaceutical (2).

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**WARNINGs AND PRECAUTIONS**

1. Myocardial Ischemia

   Fatal cardiac events have occurred. Avoid use in patients with symptoms or signs of acute myocardial ischemia, for example unstable angina or cardiovascular instability, or patients at greater risk. Cardiac resuscitation equipment and trained staff should be available before administration (5.1).

   2. Sinotrial (SA) and Atrialventricular (AV) Nodal Block

      Adenosine receptor agonists, including LEXISCAN, can depress AV nodes and may cause first-, second- or third-degree AV block, or sinus bradycardia (5.2).

   3. Atrial Fibrillation/Atrial Flutter

      New-onset or recurrent atrial fibrillation with rapid ventricular response and atrial flutter have been reported (5.3).

   4. Hypersensitivity, Including Anaphylaxis

      Hypersensitivity reactions were reported in fewer than 1 percent of patients (5.4).
5.6 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 Clinical Pharmacology (12.2)]. 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 Adverse Reactions (6.2)].

5.7 Bronchoconstriction
Adenosine receptor agonists, including LEXISCAN, may cause dyspnea, bronchoconstriction, and respiratory compromise. Appropriate bronchodilator therapy and resuscitative measures should be available prior to and following LEXISCAN administration [see Adverse Reactions (6.1), Clinical Pharmacology (12.2), Overdosage (10) and Patient Counseling Information (17)].

5.8 Seizure
LEXISCAN may lower the seizure threshold; obtain a seizure history. New-onset or recurrence of convulsive seizures has occurred following LEXISCAN injection. Some seizures are prolonged and require emergent anti-convulsant management. Aminophylline may increase the risk of seizures associated with LEXISCAN injection. Methylxanthine use is not recommended in patients who experience a seizure in association with LEXISCAN administration.

5.9 Cerebrovascular Accident (Stroke)
Hemorrhagic and ischemic cerebrovascular accidents have occurred. Hemodynamic effects of LEXISCAN including hypotension or hypertension may be associated with these adverse reactions [see Warnings and Precautions (5.5) and (5.6)].

6 ADVERSE REACTIONS
The following adverse reactions are discussed in more detail in other sections of the labeling.
- Myocardial Ischemia [see Warnings and Precautions (5.1)]
- Sinoatrial and Atrioventricular Nodal Block [see Warnings and Precautions (5.2)]
- Atrial Fibrillation/Atrial Flutter [see Warnings and Precautions (5.3)]
- Hypersensitivity, Including Anaphylaxis [see Warnings and Precautions (5.4)]
- Hypotension [see Warnings and Precautions (5.5)]
- Hypertension [see Warnings and Precautions (5.6)]
- Bronchoconstriction [see Warnings and Precautions (5.7)]
- Seizure [see Warnings and Precautions (5.8)]
- Cerebrovascular Accident (Stroke) [see Warnings and Precautions (5.9)]

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

During clinical development, 1,601 patients were exposed to LEXISCAN, with most receiving 0.4 mg as a rapid (<10 seconds) intravenous injection. Most of these patients received LEXISCAN in two clinical studies that enrolled patients who had no history of bronchospastic lung disease as well as no history of a cardiac conduction block of greater than first-degree AV block, except for patients with functioning artificial pacemakers. In these studies (Studies 1 and 2), 2,015 patients underwent myocardial perfusion imaging after administration of LEXISCAN (N = 1,327) or ADENOSCAN (N = 687). The population was 26–93 years of age (median 68 years), 76% male and primarily Caucasian (76% Caucasian, 7% African American, 9% Hispanic, 5% Asian). Table 1 shows the most frequently reported adverse reactions.

Overall, any adverse reaction occurred at similar rates between the study groups (80% for the LEXISCAN group and 83% for the ADENOSCAN group). Aminophylline was used to treat the reactions in 3% of patients in the LEXISCAN group and 2% of patients in the ADENOSCAN group. Most adverse reactions began soon after dosing, and generally resolved within approximately 15 minutes, except for reactions which resolved in most patients within 30 minutes.

Table 1 Adverse Reactions in Studies 1 and 2 Pooled (Frequency ≥ 5%)

<table>
<thead>
<tr>
<th>Reaction</th>
<th>LEXISCAN N = 1,337</th>
<th>ADENOSCAN N = 678</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea</td>
<td>28%</td>
<td>26%</td>
</tr>
<tr>
<td>Headache</td>
<td>26%</td>
<td>17%</td>
</tr>
<tr>
<td>flushing</td>
<td>16%</td>
<td>25%</td>
</tr>
<tr>
<td>chest discomfort</td>
<td>13%</td>
<td>18%</td>
</tr>
<tr>
<td>angina pectoris or ST segment depression</td>
<td>12%</td>
<td>18%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>8%</td>
<td>7%</td>
</tr>
<tr>
<td>chest pain</td>
<td>7%</td>
<td>10%</td>
</tr>
<tr>
<td>nausea</td>
<td>6%</td>
<td>6%</td>
</tr>
<tr>
<td>Abdominal discomfort</td>
<td>5%</td>
<td>2%</td>
</tr>
<tr>
<td>dysuria</td>
<td>5%</td>
<td>7%</td>
</tr>
<tr>
<td>feeling hot</td>
<td>5%</td>
<td>8%</td>
</tr>
</tbody>
</table>

EGG Abnormalities
The frequency of rhythm or conduction abnormalities following LEXISCAN or ADENOSCAN is shown in Table 2 [see Warnings and Precautions (5.2)].

Table 2 Rhythm or Conduction Abnormalities in Studies 1 and 2

<table>
<thead>
<tr>
<th>Reaction</th>
<th>LEXISCAN N = 1,337</th>
<th>ADENOSCAN N = 678</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhythm or conduction abnormalities†</td>
<td>332/1275 (26%)</td>
<td>192/645 (30%)</td>
</tr>
<tr>
<td>rhythm abnormalities</td>
<td>260/1275 (20%)</td>
<td>131/645 (20%)</td>
</tr>
<tr>
<td>PACs</td>
<td>86/1274 (7%)</td>
<td>57/645 (9%)</td>
</tr>
<tr>
<td>PVCs</td>
<td>175/1274 (14%)</td>
<td>122/645 (19%)</td>
</tr>
<tr>
<td>first-degree AV block (PR prolongation &gt; 220 msec)</td>
<td>34/1209 (3%)</td>
<td>43/618 (7%)</td>
</tr>
<tr>
<td>Second-degree AV block</td>
<td>1/1209 (0.1%)</td>
<td>9/618 (1.5%)</td>
</tr>
<tr>
<td>AV conduction abnormalities (other than AV blocks)</td>
<td>1/1209 (0.1%)</td>
<td>0/618 (0%)</td>
</tr>
<tr>
<td>Ventricular conduction abnormalities</td>
<td>64/1152 (5.6%)</td>
<td>31/581 (5.1%)</td>
</tr>
</tbody>
</table>

* 12-lead ECGs were recorded before and for up to 2 hours after dosing.
† includes rhythm abnormalities (PACs, PVCs, atrial fibrillation/flutter, wandering atrial pacemaker, supraventricular or ventricular arrhythmia) or conduction abnormalities, including AV block.

Respiratory Abnormalities
In a randomized, placebo-controlled trial of 999 patients with asthma (n = 532) or stable chronic obstructive pulmonary disease (n = 467), the overall incidence of pre-specified respiratory adverse reactions was greater in the LEXISCAN group compared to the placebo group (p < 0.001). Most respiratory adverse reactions resolved without therapy, a few patients received aminophylline or a short-acting bronchodilator. No differences were observed between treatment arms in the reduction of >15% from baseline at two-hours in FEV1 (Table 3).

Table 3 Respiratory Adverse Effects

<table>
<thead>
<tr>
<th>Reaction</th>
<th>LEXISCAN (N=356)</th>
<th>Placebo (N=176)</th>
<th>LEXISCAN (N=316)</th>
<th>Placebo (N=151)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall prevalence of respiratory adverse reactions</td>
<td>12.9%</td>
<td>2.3%</td>
<td>19.0%</td>
<td>4.0%</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>10.7%</td>
<td>1.1%</td>
<td>18.0%</td>
<td>2.6%</td>
</tr>
<tr>
<td>Wheezing</td>
<td>3.1%</td>
<td>1.1%</td>
<td>0.9%</td>
<td>0.7%</td>
</tr>
<tr>
<td>FEV1 reduction &gt;15%†</td>
<td>1.1%</td>
<td>2.9%</td>
<td>4.2%</td>
<td>5.4%</td>
</tr>
</tbody>
</table>

* All patients continued the use of their respiratory medications as prescribed prior to administration of LEXISCAN.
† Patients may have reported more than one type of adverse reaction. Adverse reactions were collected up to 24 hours following drug administration. Pre-specified respiratory adverse reactions included dyspnea, wheezing, obstructive airway disorder, dyspnea exertional, and tachypnea.

6.2 Post-Marketing Experience
The following adverse reactions have been reported from worldwide marketing experience with regadenoson administration. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Cardiovascular
Myocardial infarction, cardiac arrest, ventricular arrhythmias, supraventricular tachyarrhythmias including atrial fibrillation with rapid ventricular response (new-onset or recurrent), atrial flutter, heart block (including third-degree block), asystole, marked hypotension, symptomatic hypotension in association with transient ischemic attack, acute coronary syndrome (ACS), seizures and syncope [see Warnings and Precautions (5.1), (5.2), (5.3), (5.5), (5.6) and (5.8)] have been reported. Some events required intervention with fluids and/or aminophylline [see Overdosage (10)]. QTc prolongation shortly after LEXISCAN administration has been reported.

Central Nervous System
Tremor, seizure, transient ischemic attack, and cerebrovascular accident including intracranial hemorrhage [see Warnings and Precautions (5.8) and (5.9)].

Gastrointestinal
Abdominal pain, occasionally severe, has been reported a few minutes after LEXISCAN administration, in association with nausea, vomiting, or myalgias; administration of aminophylline, an adenosine antagonist, appeared to lessen the pain. Diarrhea and fecal incontinence have also been reported following LEXISCAN administration.

Hypersensitivity
Anaphylaxis, angioedema, cardiac or respiratory arrest, respiratory distress, decreased oxygen saturation, hypotension, throat tightness, urticaria, rashes have occurred and have required treatment including resuscitation [see Warnings and Precautions (5.4)].
Musculoskeletal pain has occurred, typically 10-20 minutes after LEXISCAN administration; the pain was occasionally severe, localized in the arms and lower back and extended to the buttocks and lower legs bilaterally. Administration of aminophylline appeared to lessen the pain.

Respiratory arrest, dyspnea and wheezing have been reported following LEXISCAN administration. Musculoskeletal pain has occurred, typically 10-20 minutes after LEXISCAN administration; the administration of aminophylline has been used to alleviate severe or persistent adverse reactions to LEXISCAN (see [Clinical Pharmacology (12.2) and Patient Counseling Information (17)]. Patients should avoid concurrent use of any products containing methylxanthines as well as any drugs containing methylxanthine or aminophylline for at least 12 hours before LEXISCAN administration. Aminophylline may be used to attenuate severe or persistent adverse reactions to LEXISCAN (see [Overdosage (10)]).

In clinical studies, LEXISCAN was administered to patients taking other cardioactive drugs (i.e., β-blockers, calcium channel blockers, ACE inhibitors, nitrates, cardiac glycosides, and angiotensin receptor blockers) without reported adverse reactions or apparent effects on efficacy. Dipryramine may cause additive effects of LEXISCAN. With possible, withhold dipryramine for at least two days prior to LEXISCAN administration.

7.2 Effect of LEXISCAN on Other Drugs
Regadenoson does not inhibit the metabolism of substrates for CYP1A2, CYP2C8, CYP2D6, or CYP34A in human liver microsomes, indicating that it is unlikely to alter the pharmacokinetics of drugs metabolized by these cytochrome P450 enzymes. Therefore, no formal drug interaction studies have been conducted with LEXISCAN.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Risk Summary
There are no available data on LEXISCAN use in pregnant women to inform a drug-associated risk. In animal reproduction studies, adverse developmental outcomes were observed with the administration of regadenoson to pregnant rats and rabbits during organogenesis only at doses that produced maternal toxicity (see Data). In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively. Data
Animal Data
Reproductive studies in rats showed that regadenoson doses 10 and 20 times the maximum recommended human dose (MRHD) based on body surface area caused reduced fetal body weights and delays in fore- and hind limb phalanges and metatarsals; maternal toxicity also occurred at these doses. Skeletal variations were increased in all treated groups. In rabbits, maternal toxicity occurred at regadenoson doses administered during organogenesis 4 times the MRHD; however, there were no teratogenic effects in offspring at this dose. At higher doses, 12 and 20 times the MRHD, maternal toxicity occurred along with increased embryo-fetal loss and fetal malformations.

8.2 Lactation
Risk Summary
There is no information on the presence of regadenoson in human milk, the effects on the breastfed infant, or the effects on milk production. Because of the potential risk of serious cardiac reactions in the breastfed infant, advise the nursing mother to pump and discard breast milk for 10 hours after administration of LEXISCAN.

8.4 Pediatric Use
Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use
Of the 1,337 patients receiving LEXISCAN in Studies 1 and 2, 56% were 65 years of age and over and 24% were ≥75 years of age and over. Older patients (≥75 years of age) had a similar adverse event profile compared to younger patients (<65 years of age), but had a higher incidence of hypotension (2% vs. ≤1%).

8.6 Renal Impairment
No dose adjustment is needed in patients with renal impairment including patients with end stage renal disease and/or dependent on dialysis [see Pharmacokinetics (12.3)].

10 OVERDOSAGE
LEXISCAN overdose may result in serious reactions [see Warnings and Precautions (5)]. In a study of healthy volunteers, symptoms of flushing, dizziness and increased heart rate were assessed as intolerable at LEXISCAN doses greater than 0.02 mg/kg. Aminophylline to Reverse Effects
Methylxanthines, such as caffeine, aminophylline, and theophylline, are competitive receptor antagonists that interfere with the vasodilation activity of LEXISCAN [see [Clinical Pharmacology (12.2) and Patient Counseling Information (17)]. Patients should avoid concurrent use of any products containing methylxanthines as well as any drugs containing methylxanthine or aminophylline for at least 12 hours before LEXISCAN administration. Aminophylline may be used to attenuate severe or persistent adverse reactions to LEXISCAN (see [Overdosage (10)]).

9 CLINICAL PHARMACOLOGY
9.1 Mechanism of Action
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 A3 adenosine receptors. Activation of the A2A adenosine receptor by regadenoson produces coronary vasodilatation and increases coronary blood flow (CBF).

9.2 Pharmacodynamics
Coronary Blood Flow
LEXISCAN causes a rapid increase in CBF which is sustained for a short duration. In patients undergoing coronary catheterization, pulsed-wave Doppler ultrasonography was used to measure the average peak velocity (APV) of coronary blood flow before and up to 30 minutes after LEXISCAN administration (200 or 400 mg). Mean APV increased to greater than twice baseline by 30 seconds and decreased to less than twice the baseline level within 10 minutes [see Clinical Pharmacology (12.3)].

9.3 Adverse Effects of the Radiopharmaceutical
The radiopharmaceutical is proportional to CBF. Because LEXISCAN increases blood flow in normal coronary arteries with little or no increase in stenotic arteries, LEXISCAN causes relatively less uptake of the radiopharmaceutical in vascular territories supplied by stenotic arteries. MPI intensity after LEXISCAN administration is therefore greater in areas perfused by normal relative to stenosed arteries.

Effect of duration of injection
A study in dogs compared the effects of intravenous injection of 2.5 µg/kg regadenoson (in 10 mL) over 10 seconds and 30 seconds on CBF. The duration of a two-fold increase in CBF was 97±14 seconds (n=6) and 221±20 seconds (n=4), respectively, for the 10 second and 30 second injections. The peak effects (i.e., maximal increase) on CBF after the 10 second and 30 second injections were 217±15% and 297±33% above baseline, respectively. The times to peak effect on CBF were 17±2 seconds and 27±6 seconds, respectively.

Effect of Aminophylline
Aminophylline (100 mg, administered by slow intravenous injection over 60 seconds) injected 1 minute after a 0.4 mg LEXISCAN in patients undergoing cardiac catheterization, was shown to shorten the duration of the coronary blood flow response to LEXISCAN as measured by pulsed-wave Doppler ultrasonography [see Overdosage (10)].

Effect of Caffeine
Ingestion of caffeine decreases the ability to detect reversible ischemic defects. In a placebo-controlled, parallel group clinical study, patients with known or suspected myocardial ischemia received a baseline rest/stress MPI followed by a second stress MPI. Patients received caffeine or placebo 90 minutes before the second LEXISCAN stress MPI. Following caffeine administration (200 or 400 mg), the mean number of reversible defects identified was reduced by approximately 60%. This decrease was statistically significant [see Drug Interactions (7.1) and Patient Counseling Information (17)].

9.4 Hemodynamic Effects
In clinical studies, the majority of patients had an increase in heart rate and a decrease in blood pressure within 45 minutes after administration of LEXISCAN and ADENOSCAN in Studies 1 and 2 are summarized in Table 5.

Table 5 Hemodynamic Effects in Studies 1 and 2

<table>
<thead>
<tr>
<th>Vital Sign Parameter</th>
<th>LEXISCAN N = 1,337</th>
<th>ADENOSCAN N = 678</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate</td>
<td>Increase &gt; 10 bpm</td>
<td>22%</td>
</tr>
<tr>
<td></td>
<td>Increase &gt; 40 bpm</td>
<td>5%</td>
</tr>
<tr>
<td>Systolic Blood Pressure</td>
<td>&lt; 90 mm Hg</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td>Decrease &gt; 35 mm Hg</td>
<td>7%</td>
</tr>
<tr>
<td></td>
<td>≥ 200 mm Hg</td>
<td>1.9%</td>
</tr>
<tr>
<td></td>
<td>Increase &gt; 50 mm Hg</td>
<td>0.7%</td>
</tr>
<tr>
<td></td>
<td>≥ 180 mm Hg and increase of ≥ 20 mm Hg from baseline</td>
<td>4.6%</td>
</tr>
<tr>
<td>Diastolic Blood Pressure</td>
<td>&lt; 50 mm Hg</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td>Decrease &gt; 25 mm Hg</td>
<td>4%</td>
</tr>
<tr>
<td></td>
<td>≥ 115 mm Hg</td>
<td>0.9%</td>
</tr>
<tr>
<td></td>
<td>Increase &gt; 30 mm Hg</td>
<td>0.5%</td>
</tr>
</tbody>
</table>

Hermodynamic Effects Following Inadequate Exercise Stress
In a clinical study, LEXISCAN was administered for MPI following inadequate exercise stress. More patients with LEXISCAN administration three minutes following inadequate exercise stress had an increase in heart rate and a decrease in systolic blood pressure compared with LEXISCAN administered at rest. The changes were not associated with any clinically significant adverse reactions. Maximum hemodynamic changes are presented in Table 6.

Table 6 Hemodynamic Effects in Inadequate Exercise Stress Study

<table>
<thead>
<tr>
<th>Vital Sign Parameter</th>
<th>LEXISCAN 3 minutes following exercise</th>
<th>LEXISCAN 1 hour following exercise (N=367)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate</td>
<td>Increase &gt; 10 bpm</td>
<td>44%</td>
</tr>
<tr>
<td></td>
<td>Increase &gt; 40 bpm</td>
<td>5%</td>
</tr>
<tr>
<td>Systolic Blood Pressure</td>
<td>&lt; 90 mm Hg</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td>Decrease &gt; 35 mm Hg</td>
<td>29%</td>
</tr>
<tr>
<td></td>
<td>≥ 200 mm Hg</td>
<td>0.9%</td>
</tr>
<tr>
<td></td>
<td>Increase &gt; 50 mm Hg</td>
<td>2%</td>
</tr>
<tr>
<td></td>
<td>≥ 180 mm Hg and increase of ≥ 20 mm Hg from baseline</td>
<td>5%</td>
</tr>
</tbody>
</table>
Table 6 continued

<table>
<thead>
<tr>
<th>Diastolic Blood Pressure</th>
<th>Study 1</th>
<th>Study 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 56 mm Hg</td>
<td>6%</td>
<td>6%</td>
</tr>
<tr>
<td>&gt; 56 mm Hg</td>
<td>3%</td>
<td>3%</td>
</tr>
</tbody>
</table>

Each patient received an initial stress scan using ADENOSCAN (6-minute infusion using a dose of 0.14 mg/kg/min, without exercise) with a radionuclide gated SPECT imaging protocol. After the initial scan, patients were randomized to either LEXISCAN or ADENOSCAN, and received a second stress scan with the same radionuclide imaging protocol that was used for the initial scan. The median time between scans was 7 days (range of 1–104 days).

The most common cardiovascular histories included hypertension (81%), CABC, PTCA or stenting (51%), angina (63%), and history of myocardial infarction (41%) or arrhythmia (33%); or other history included diabetes (32%) and COPD (5%). Patients with a recent history of serious uncontrolled ventricular arrhythmia, myocardial infarction, or unstable angina, a history of greater than first-degree AV block, or with symptomatic bradycardia, sick sinus syndrome, or a heart rate below 45 beats per minute were excluded. A number of patients took cardiovascular medications on the day of the scan, including β-blockers (18%), calcium channel blockers (9%), and nitrates (6%). In the pooled study population, 68% of patients had 0–1 segments showing reversible defects on the initial scan, 24% had 2–4 segments, and 9% had >5 segments.

Comparison of the images obtained with LEXISCAN to those obtained with ADENOSCAN was performed as follows. Using the 17-segment model, the number of segments showing a reversible perfusion defect was calculated for the initial ADENOSCAN study and for the randomized study obtained using LEXISCAN or ADENOSCAN. The agreement rate for the image obtained with LEXISCAN or ADENOSCAN relative to the initial ADENOSCAN image was calculated by determining how frequently each of the 32 patients were placed in the same category with the randomized scan. The agreement rates for LEXISCAN and ADENOSCAN were calculated as the average of the agreement rates across the three categories determined by the initial scan. Studies 1 and 2 each demonstrated that LEXISCAN is similar to ADENOSCAN in assessing the extent of reversible perfusion abnormalities (Table 7). Table 7 Agreement Rates in Studies 1 and 2

<table>
<thead>
<tr>
<th>Study 1</th>
<th>Study 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEXISCAN – ADENOSCAN Agreement Rate (≤ SE)</td>
<td>61 ± 3%</td>
</tr>
<tr>
<td>LEXISCAN – LEXISCAN Agreement Rate (≤ SE)</td>
<td>62 ± 2%</td>
</tr>
<tr>
<td>Rate Difference (LEXISCAN – ADENOSCAN) (≤ SE)</td>
<td>1 ± 4%</td>
</tr>
<tr>
<td>95% Confidence Interval</td>
<td>-7.5, 9.2%</td>
</tr>
</tbody>
</table>

Use of LEXISCAN in Patients with Inadequate Exercise Stress

The efficacy and safety of LEXISCAN administered 3 minutes (Group 1) or 1 hour (Group 2) following static exercise stress was evaluated in an open-label randomized, multi-center, non-inferiority study. Adequate exercise was defined as ≥ 85% maximum predicted heart rate and ≥ 5 METS. SPECT MPI was performed 60-90 minutes after LEXISCAN administration in Group 1 and 90-120 minutes in Group 2. Patients received 1-14 days later to undergo a second stress MPI with LEXISCAN without exercise (MPI 2).

All patients were referred for evaluation of coronary artery disease. Of the 1,147 patients randomized, a total of 1,073 patients received LEXISCAN and had interpretable SPECT scans at all visits; 538 in Group 1 and 535 in Group 2. The median age of the patients was 62 years (range 28 to 90 years) and included 633 (59%) men and 440 (41%) women. Images from MPI 1 and MPI 2 for the two groups were compared for presence or absence of perfusion defects. The level of agreement between the MPI 1 and the MPI 2 reads in Group 1 was similar to the level of agreement between MPI 1 and MPI 2 reads in Group 2. However, two patients receiving LEXISCAN 3 minutes following inadequate exercise experienced a serious cardiac adverse reaction. No serious cardiac adverse reactions occurred in patients receiving LEXISCAN 1 hour following inadequate exercise stress [see Adverse Reactions (6.1), Clinical Pharmacology (12.2)].

16 HOW SUPPLIED/STORAGE AND HANDLING

LEXISCAN is supplied as a sterile, preservative-free solution containing 0.08 mg/mL LEXISCAN in the following package:

- Single-dose 5 mL pre-filled plastic Amyst® syringes with luer-lock fitting

Store at controlled room temperature, 25°C (77°F); excursions permitted to 15° to 30°C (59°– 86°F).

17 PATIENT COUNSELING INFORMATION

Drug Interactions

Patients should be instructed to avoid consumption of any products containing methylxanthines, including caffeinated coffee, tea, or other caffeinated beverages, caffeine-containing drug products, amphetamine and theophylline for at least 12 hours before a scheduled radionuclide MPI [see Warnings and Precautions (5.8) and Clinical Pharmacology (12.2)].

Respiratory

Advising patients that they may be at increased risk of fatal and nonfatal heart attacks, abnormal heart rhythms, cardiac arrest, significant increase or decrease in blood pressure, or cerebrovascular accidents (stroke) with the use of LEXISCAN [see Warnings and Precautions (5.1), (5.3), (5.5), (5.6) and (5.9)].

Hypersensitivity

Inform patients that allergic reactions have been reported with LEXISCAN. Advise patients how to recognize such a reaction and when to seek medical attention [see Warnings and Precautions (5.4)].

Pregnancy

Advise patients with COPD or asthma about the need for administration of pre- and post-study bronchodilator therapy and to call their clinician if they experience any shortness of breath or exacerbation of respiratory disease following an MPI study with LEXISCAN [see Warnings and Precautions (5.7)].

Seizures

Advising patients that they may be at increased risk of seizures. Question patients about a history of seizures [see Warnings and Precautions (5.8)].

Lactation

Advise a woman to pump and discard breast milk for 10 hours after LEXISCAN administration [see Use in Specific Populations (8.2)].

Marketing by:

Astellas Pharma US, Inc.
Northbrook, IL 60062 USA

Syringes Manufactured by:
Hospira, Inc.
Lake Forest, IL 60045 USA.

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