2016 Medicare Nuclear Medicine

Reimbursement Information
If you have questions regarding reimbursement for Lantheus Medical Imaging products, call Randy VanCoughnett at 978-436-7995 or email randy.vancoughnett@lantheus.com.

**CPT® – Current Procedural Terminology**

- American Medical Association’s five digit numeric codes used to report medical procedures and services.

**HCPCS - Healthcare Common Procedure Coding System**

- Level II HCPCS codes alphanumeric five digit codes primarily to identify contrast agents, radiopharmaceuticals, supplies and devices.

**Q-codes**

- Temporary codes created by Medicare to identify items not assigned a CPT code. Many drugs, supplies and biologicals are assigned Q codes.

**NDC codes – National Drug Code**

- A unique numeric code to identify drugs. The first segment of numbers identifies the labeler or manufacturer, the second segment identifies the product, and the third identifies the package.

**HOPPS – Hospital Outpatient Prospective Payment System**

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**Three Basic Components of Reimbursement: Coding, Coverage and Payment.**

1. **Coding:** There must be a CPT® code or HCPCS code that accurately describes the service performed and/or the drugs provided.

2. **Coverage:** The existence of CPT and/or HCPCS codes used to report the services performed or items furnished does not guarantee coverage.

Medicare only covers a procedure, drug or supply when it is medically necessary. Providers should obtain and follow the policies and guidelines published by Medicare in the Local and National Coverage Determinations.

3. **Payment:** If the proper codes exist and there is coverage established, Medicare must set a payment amount for the drugs, supplies and/or procedures in order for providers to receive payment. Most payment amounts are determined by CMS nationally. There are differences in procedure payment amounts from region to region to reflect geographic differences in provider costs.

**Documentation:** When radiopharmaceuticals or contrast agents are reported, providers must document in the medical record the name of the drug and the amount administered.

Lantheus Medical Imaging, Inc. cannot guarantee coverage or payment for products or procedures. Payer policies can vary widely. For more specific information, contact the payer directly in order to obtain up to date coverage, coding and payment information.

**Medicare Hospital Inpatients**
- Hospital reimbursement is based on Diagnostically Related Group (DRG) payment.
- There is no additional payment for drugs or imaging procedures.

**Medicare Hospital Outpatients**
- Diagnostic radiopharmaceutical payments are packaged with the procedure payment and are not paid separately.
- Therapeutic radiopharmaceuticals are paid separately.

**Physician Offices and IDTFs**
- Radiopharmaceuticals are paid in addition to and separately from procedure.
- They are reimbursed based on the Average Wholesale Price (AWP) or invoice.
- Contact your local contractor for local reimbursement rules.
The United States government has established an agenda to eliminate domestic reliance on Tc-99m derived from nuclear reactors using Highly Enriched Uranium (HEU). CMS recognizes that Tc-99m derived from a non-HEU source may have a higher cost. In response, CMS will reimburse providers $10 per non-HEU derived Tc-99m dose in the hospital outpatient setting in addition to the payment for the imaging procedure.

Under this policy, hospitals report HCPCS code Q9969 (Tc-99m from non-highly enriched uranium source, full cost recovery add-on, per study dose) once per dose along with any diagnostic scan or scans furnished using Tc-99m as long as the Tc-99m doses used can be certified by the hospital to be at least 95 percent derived from non-HEU sources.

1. CMS created HCPCS code Q9969 to report non-HEU Tc-99m doses.

**HCPCS Descriptor**

**Q9969 Tc-99m from non-highly enriched uranium source, full cost recovery add-on, per study dose**

2. CMS will reimburse $10 per dose for Q9969 in addition to the imaging procedure.

3. Hospital reports token $1 charge per dose for Q9969.

Hospitals do not indicate a dose is from a non-HEU source on their claim form. They simply report HCPCS Q9969 for each non-HEU dose. If asked, a hospital has three options to document a dose was derived from a non-HEU source:

1. Produce invoices, patient dose labels or tracking sheets that indicate that a dose was produced from non-HEU sources.

2. Produce documentation that an entire batch of Tc-99m doses were derived from a non-HEU source for a specified period of time that a single non-HEU generator was in use or manufacturer attestation that a generator is non-HEU generator.

3. If the manufacturer has labeled a generator or a dose attesting to it being derived from a non-HEU source.

If a hospital has any questions about whether they are receiving Tc-99m derived from a non-HEU source, they should contact their radiopharmacy or the generator manufacturer.

For more information, please see Federal Register / Vol. 78, No. 237 / Tuesday, December 10, p.75002-75003 or Federal Register / Vol. 77, No. 221 / Thursday, November 15, 2012 / p. 68316-68317 or contact your local radiopharmacy or your Tc-99m generator manufacturer.
Medicare Hospital Outpatient

For 2016 CMS will package the payment for the exercise stress test (CPT 93017), all pharmacologic stress agents (Jxxxx) and the SPECT Myocardial Perfusion Imaging (MPI) procedure, CPT 78452, into a single payment. The exercise test, radiopharmaceutical and pharmacologic stress agent are not paid separately.

If a non-HEU derived Tc-99m dose is used, providers will receive a separate add on payment of $10 per dose by reporting HCPCS code Q9969.

Packaged components of SPECT Multiple Myocardial Perfusion CPT 78452

<table>
<thead>
<tr>
<th>Descriptor</th>
<th>2015</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>78452 SPECT MPI multiple</td>
<td>$1,140.54</td>
<td>$1,108.46</td>
</tr>
<tr>
<td>93017 Exercise test packaged with 78452</td>
<td>$0 packaged with 78452</td>
<td>$0 packaged with 78452</td>
</tr>
<tr>
<td>Jxxxxx Pharmacologic stress agent</td>
<td>$0 packaged with 78452</td>
<td>$0 packaged with 78452</td>
</tr>
<tr>
<td>A9500 Tc-99m sestamibi</td>
<td>$0 packaged with 78452</td>
<td>$0 packaged with 78452</td>
</tr>
<tr>
<td>Q9969 Tc-99m non-HEU source per dose</td>
<td>$10 paid separately</td>
<td>$10 paid separately</td>
</tr>
</tbody>
</table>

Selected 2016 payment* Medicare Hospital Outpatients and Physician Office

<table>
<thead>
<tr>
<th>CPT</th>
<th>Descriptor</th>
<th>Hospital APC</th>
<th>Hospital Outpatient Payment</th>
<th>Global Physician Office Payment</th>
</tr>
</thead>
<tbody>
<tr>
<td>78071</td>
<td>Parathyroid planar imaging (including subtraction, when performed); with tomographic (SPECT)</td>
<td>5591</td>
<td>$332.65</td>
<td>$372.61</td>
</tr>
<tr>
<td>78452</td>
<td>Myocardial Perfusion imaging multiple SPECT</td>
<td>5593</td>
<td>$1,108.46</td>
<td>$492.28*</td>
</tr>
<tr>
<td>78582</td>
<td>Pulmonary ventilation (e.g. aerosol or gas) and perfusion imaging</td>
<td>5592</td>
<td>$441.36</td>
<td>$348.96</td>
</tr>
<tr>
<td>78607</td>
<td>Brain imaging tomographic (SPECT)</td>
<td>5593</td>
<td>$1108.46</td>
<td>$365.44</td>
</tr>
<tr>
<td>78806</td>
<td>Radiopharmaceutical localization of inflammatory process; whole body</td>
<td>5593</td>
<td>$1108.46</td>
<td>$346.46</td>
</tr>
<tr>
<td>79101</td>
<td>Radiopharmaceutical therapy, by intravenous administration</td>
<td>5661</td>
<td>$249.98</td>
<td>$145.10</td>
</tr>
</tbody>
</table>

*Radiopharmaceutical, exercise test and pharmacologic stress agent all paid separately for physician office.
Diagnostic radiopharmaceuticals are not paid separately in the hospital outpatient setting; the payment is packaged in with the procedure payment. For the office setting radiopharmaceuticals are reimbursed based on AWP or invoice. Check your local Medicare contractor for payment methodology in your location.

NDC codes have been converted to a 5 – 4 – 2 format.

<table>
<thead>
<tr>
<th>Product</th>
<th>HCPCS</th>
<th>Units</th>
<th>Comments and NDC</th>
</tr>
</thead>
</table>
| Cardiolite® Kit for the Preparation of Technetium Tc99m Sestamibi for Injection | A9500  | Per Dose    | • NDC 11994-0001-00  
  • Packaged in HOPPS  
  • AWP or invoice for Part B                                               |
| Thallous Chloride Thallium 201 Injection                                 | A9505  | Per mCi     | • NDC codes vary by size  
  • Payment is packaged in HOPPS  
  • AWP or invoice for Part B                                                 |
| QUADRAMET®, Samarium Sm-153 lexidronam, therapeutic, per treatment dose, up to 150 millicuries | A9604  | Per treatment dose up to 150 mCi. | • NDC 11994-0016-01  
  • Payment in HOPPS ASP + 6%  
  • Updated quarterly by CMS  
  • 3 ml per vial, 50 mCi / ml                                                 |
| Gallium Citrate Ga 67 Injection                                          | A9556  | Per mCi     | • NDC Varies by size  
  • Payment is packaged in HOPPS  
  • AWP or invoice for Part B                                                 |
| NEUROLITE®, Kit for the Preparation of Technetium Tc99m Bicisate for Injection | A9557  | Per Dose    | • NDC 11994-0006-00  
  • Payment is packaged in HOPPS  
  • AWP or invoice for Part B                                                 |
| Xenon Xe 133 Gas                                                        | A9558  | Per 10mCi   | • NDC Varies by size                                                            |
| Tc-99m from non-highly enriched uranium source, full cost recovery add-on, per study dose | Q9969  | Per study dose | • Paid $10 per dose for HOPPS in addition to APC payment for imaging procedure  
  • $10 add on payment not paid in office setting                             |

*NDC codes can be researched at http://www.accessdata.fda.gov/scripts/cder/ndc/
Citations


2. Federal Register / Vol. 77, No. 221 / Thursday, November 15, 2012 68316


CARDIOLITE® Kit for the Preparation of Technetium Tc99m Sestamibi for Injection

FOR DIAGNOSTIC USE

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use CARDIOLITE® safely and effectively. See full prescribing information for CARDIOLITE®.

CARDIOLITE®, kit for the preparation of Technetium Tc99m Sestamibi for Injection. Initial U.S. Approval: December, 1990

RECENT MAJOR CHANGES
Use in specific populations (8.3)

INDICATIONS AND USAGE
CARDIOLITE® is a myocardial perfusion agent indicated for:

- Detecting coronary artery disease by localizing myocardial ischemia (reversible defects) and infarction (non-reversible defects)
- Evaluating myocardial function and developing information for use in patient management decisions

DOSE AND ADMINISTRATION

For Myocardial Imaging: The suggested dose range for IV administration of CARDIOLITE® in a single dose to be employed in the average patient (70 Kg) is 370 - 1110 MBq (10 - 30 mCi).

For Breast Imaging: The recommended dose range for IV administration of MIRALUMA® is a single dose of 740 - 1110 MBq (20 - 30 mCi).

DOSE FORMS AND STRENGTHS

CARDIOLITE®, the Kit for the Preparation of Technetium Tc99m Sestamibi for Injection is supplied as a lyophilized mixture in a 5 ml vial.

CONTRAINDICATIONS

None known

WARNINGs AND PRECAUTIONS

- Pharmacologic induction of cardiovascular stress may be associated with serious adverse events such as myocardial infarction, arrhythmia, hypotension, stroke, myocardial necrosis and cerebrovascular events.
- CARDIOLITE® has been rarely associated with severe allergic anaphylactic events of angioneurodema and generalized urticaria. In some patients the allergic symptoms developed on the second injection during CARDIOLITE® imaging.
- Caution should be exercised and emergency equipment should be available when administering CARDIOLITE®.
- Before administering CARDIOLITE®, patients should be asked about the possibility of allergic reactions to either drug.
- The contents of the vials are intended only for use in the preparation of Technetium Tc99m Sestamibi and are not to be administered directly to the patient without first undergoing the preparatory procedure.

ADVERSE REACTIONS

- The following adverse reactions have been reported in < 0.5% of patients: signs and symptoms consistent with those occurring shortly after administration of the agent; transient arthritis, angioneurodema, erythema, dizziness, syncope, abdominal pain, vomiting, and severe hypersensitivity characterized by dyspnea, hypotension, hypoxia, bradycardia, asthma, and vomiting within two hours after a second injection of Technetium Tc99m Sestamibi. A few cases of flushing, edema, injection site inflammation, dry mouth, fever, pruritus, rash, urticaria and fatigue have also been attributed to administration of the agent.

To report SUSPECTED ADVERSE REACTIONS, contact Lantheus Medical Imaging, Inc. at 1-800-362-0668 or FDA at 1-800-FDA-1088 or report it to MedWatch: 1-800-FDA-1088 or visit MedWatch: Site.

DRUG INTERACTIONS

Specific drug-drug interactions have not been studied.

USE IN SPECIFIC POPULATIONS

In one study of 46 subjects who received CARDIOLITE® administration, the radioactivity in both children and adolescents exhibited blood PK profiles similar to those previously reported in adults.

See 17 FOR PATIENT COUNSELING INFORMATION

Revised: May 2014

FULL PRESCRIBING INFORMATION: CONTENTS:

1. INDICATIONS AND USE
2. DOSAGE AND ADMINISTRATION
2.1 Image Acquisition
2.2 Radiation Dosimetry
2.3 Instructions For Preparation
2.4 Determination of Radiolabeled Purine in Technetium Tc99m Sestamibi
3. DOSAGE FORMS AND STRENGTHS
4. CONTRAINDICATIONS
5. WARNINGS AND PRECAUTIONS
5.1 Warnings
5.2 General Precautions
6. ADVERSE REACTIONS
7. DRUG INTERACTIONS
8. USE IN SPECIFIC PATIENTS
8.1 Pregnancy
8.3 Nursing Mothers
Radiopharmaceuticals should be used only by physicians who are qualified by training and experience in the safe use and handling of radionuclides and whose training and experience have been approved by the appropriate government agency authorized to license the use of radionuclides.

Stress testing should be performed only under the supervision of a qualified physician and in a laboratory equipped with appropriate resuscitation and support equipment.

The most frequent exercise stress test endpoints sufficient to stop the test reported during controlled studies (two-thirds were cardiac patients) were:

- Fatigue 35%
- Dyspnea 17%
- Chest Pain 16%
- T-depression 14%
- Arthrixy 1%

### 6. ADVERSE REACTIONS

Adverse events were evaluated in 3741 adults who were evaluated in clinical studies. Of these patients, 3068 (77% men, 22% women, and 0.7% of the patient’s genders were not recorded) were in cardiac clinical trials and 673 (100% women) in breast imaging trials. Cases of angina, chest pain, and death have occurred (see Section 5). Adverse events reported at a rate of 0.5% or greater after receiving Technetium Tc99m Sestamibi administration are shown in the following table:

<table>
<thead>
<tr>
<th>Body System</th>
<th>Adverse Reaction</th>
<th>Occurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>Angina</td>
<td>0.1%</td>
</tr>
<tr>
<td></td>
<td>Bronchospasm</td>
<td>0.1%</td>
</tr>
<tr>
<td></td>
<td>Chest pain</td>
<td>0.2%</td>
</tr>
<tr>
<td></td>
<td>Dyspnea</td>
<td>0.3%</td>
</tr>
</tbody>
</table>

### 7. Cut the TLC plate 4 cm from the bottom and measure the Tc99m activity in each piece by appropriate radiation detector.

### 8. Calculate the % Tc99m Sestamibi as:

\[
\% \text{Tc99m Sestamibi} = \frac{\mu Ci \text{Top Piece}}{\mu Ci \text{Both Pieces}} \times 100
\]

*The ethanol used in this procedure should be 95% or greater. Absolute ethanol (99%) should remain at ≥ 95% content each week for one week after opening if stored tightly capped, in a cool dry place.

### 3. DOSAGE FORMS AND STRENGTHS

CARDIOLITE®, Kit for the Preparation of Technetium Tc99m Sestamibi for Injection is supplied as a lyophilized mixture in a 5 mL vial.

### 4. CONTRAINdications

None known.

### 5. WARNINGS AND PRECAUTIONS

#### 5.1 Warnings

In studying patients in whom cardiac disease is known or suspected, care should be taken to assure continuous monitoring and treatment in accordance with accepted clinical protocol. Infrrequently, death has occurred 4 to 24 hours after Tc99m Sestamibi use and is usually associated with exercise stress testing (see Section 5.2).

Pharmacologic induction of cardiovascular stress may be associated with serious adverse events such as myocardial infarction, arrhythmia, hypotension, bronchoconstriction and cerebrovascular events. Caution should be used when pharmacologic stress is selected as an alternative to exercise; it should be used when indicated and in accordance with the pharmacologic stress agent’s labeling.

Technetium Tc99m Sestamibi has been rarely associated with acute severe allergic and anaphylactic events of angioedema and generalized urticaria. In some patients the allergic symptoms developed on the second injection during CARDIOLITE® imaging. Patients who receive CARDIOLITE® or MARILUMA® imaging are receiving the same drug. Caution should be exercised and emergency equipment should be available when administering Technetium Tc99m Sestamibi. Also, before administering either CARDIOLITE® or MARILUMA®, patients should be asked about the possibility of allergic reactions to either drug.

#### 5.2 General Precautions

The contents of the vial are intended only for use in the preparation of Technetium Tc99m Sestamibi and are not to be administered directly to the patient without first undergoing the preparative procedure. Radioactive drugs must be handled with care and appropriate safety measures should be used to minimize radiation exposure to clinical personnel. Also, care should be taken to minimize radiation exposure to the patients consistent with proper patient management.

Contents of the kit before preparation are not radioactive. However, after the Sodium Perchlorate Tc99m Injection is added, adequate shielding of the final preparation must be maintained. The contents of the kit are sterile and non-pyrogenic. It is essential to follow directions carefully and to adhere to strict aseptic procedures during preparation. Technetium Tc99m labeling reactions depend on maintaining the stannous ion in the reduced state. Hence, Sodium Perchlorate Tc99m Injection containing oxidants should not be used.

Technetium Tc99m Sestamibi should not be used more than 6 hours after preparation.

In a clinical pharmacology study, 46 pediatric patients with Kawasaki disease received CARDIOLITE® administration at the following doses: 0.1 - 0.2 mCi/kg for rest, 0.3 mCi/kg for stress in one day studies; 0.2 mCi/kg for rest and 0.2 mCi/kg for stress in two day studies.

The radioactivity both in younger children and in adolescents exhibited PK profiles similar to those previously reported in adults (See Section 12).

The radiation absorbed doses in adolescents, both at rest and stress, were similar to those observed in adults (see Section 2). When comparing weight-adjusted radioactivity (up to 0.3 mCi/kg) dosed administered to adolescents and younger children to the recommended dose administered to adults (up to 0.3 mCi/kg), the radiation absorbed doses in both adolescents and younger children were similar to those in adults.

Adverse events were evaluated in 609 pediatric patients from the three clinical studies described above. The frequency and the type of the adverse events were similar to the ones observed in the studies of CARDIOLITE® in adults. Two of the 609 had a serious adverse event: one patient received a CARDIOLITE® overdose, but remained asymptomatic, and one patient had an asthma exacerbation following administration.

### 8.5 Geriatric Use

Of 3068 patients in clinical studies of CARDIOLITE®, Kit for the Preparation of Technetium Tc99m Sestamibi for Injection, 693 patients were 65 or older and 121 were 75 or older.

Of 673 patients in clinical studies of MARILUMA®, Kit for the Preparation of Technetium Tc99m Sestamibi for Injection, 138 patients were 65 or older and 30 were 75 or older.

Based on the evaluation of the frequency of adverse events and review of vital signs data, no overall differences in safety were observed between these subjects and younger subjects. Although reported clinical experience has not identified differences in response between elderly and younger patients, greater sensitivity of some older individuals cannot be ruled out.

### 9. DRUG ABUSE AND DEPENDENCE

#### 9.1 Controlled Substance

Not applicable.

#### 9.2 Abuse

Not applicable.

#### 9.3 Dependence

Not applicable.

#### 10. OVERDOSAGE

The clinical consequences of overdosing with CARDIOLITE® are not known.

### 11. DESCRIPTION

Each 5 mL vial contains a sterile, non-pyrogenic, lyophilized mixture of:

- Tetrakis (2-methoxy isobutyl isonitrile) Copper (I) tetrafluoroborate - 1.0 mg
- Sodium Citrate Dihydrate - 2.6 mg
- L-Cysteine Hydrchloride Monohydrate - 1.0 mg
- Mannitol - 20 mg
- Stannous Chloride, Dihydrate, minimum (SnCl2+2H2O) - 0.025 mg
- Stannous Chloride, Dihydrate, (SnCl2+2H2O) - 0.075 mg
- Stannous chloride (stannic) Dihydrate, maximum (as SnCl2+2H2O) - 0.086 mg

Prior to lyophilization the pH is 5.3 to 5.9. The contents of the vial are lyophilized and stored under nitrogen.

This drug is administered by intravenous injection for diagnostic use after reconstitution with sterile, non-pyrogenic, oxygen-free Sodium Perchlorate Tc99m Injection. The pli of the reconstituted product is 9.5 (5.0 - 4.0). No bacteriostatic preservative is present.

The precise structure of the technetium complex is Tc99m(MIBI)2, where MIBI is 2-methoxy isobutyl isonitrile.

### 11.1 Physical Characteristics

Technetium Tc99m decays by isomeric transition with a physical half-life of 60.2 hours2. Photons that are useful for detection and imaging studies are listed below in Table 3.0.

<p>| Table 3.0. Principal Radiation Emission Data | | |</p>
<table>
<thead>
<tr>
<th>Radiation</th>
<th>Mean %</th>
<th>Disintegration</th>
<th>Energy (KeV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gamma</td>
<td>90.0%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


### 11.2 External Radiation

The specific gamma ray constant for Tc99m is 5.4 microlicorns/kg-Mbq-hr (0.739m-Hr/Mc) at 1 cm. The first half value layer is 0.017 cm of Pb. A range of values for the relative attenuation of the radiation emitted by this radionuclide that results from interposition of various thicknesses of Pb is shown in Table 4.0. To facilitate the control of radiation exposure from Megabecquerel (micrlicore) amounts of this radionuclide, the use of a 0.25 cm thickness of Pb will attenuate these photon emissions by at least a factor of 10.

### 4.0 Table 4.0. Radiation attenuation by Lead Shielding

<table>
<thead>
<tr>
<th>Shield Thickness (Pb)</th>
<th>Coefficient of Attenuation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.017 cm</td>
<td>0.017</td>
</tr>
<tr>
<td>0.08 cm</td>
<td>0.017</td>
</tr>
<tr>
<td>0.16 cm</td>
<td>0.017</td>
</tr>
<tr>
<td>0.25 cm</td>
<td>0.017</td>
</tr>
<tr>
<td>0.33 cm</td>
<td>0.017</td>
</tr>
</tbody>
</table>

To correct for physical decay of this radionuclide, the fractions that remain at selected intervals after the time of calibration are shown in Table 5.0.
MYOCARDIAL IMAGING: In a trial of rest and stress CARDIOLITE® microinjection test at a dose which caused systemic and bone marrow toxicity (9 mg/kg), an increase in cells with chromosome aberrations was observed in the in vitro human lymphocyte studies. In comparison with most other diagnostic technetium labeled myocardial perfusion agents, approximately thirty-three percent of the injected dose is cleared through biological clearance as well as effective clearance (which includes biological clearance and radionuclide decay) of Tc99m Sestamibi from the heart and liver. The effective half-life of clearance (which includes both the biological half-life and radionuclide decay) for the heart is approximately 3 hours, and for the liver is approximately 30 minutes, after a rest or exercise injection. The ideal imaging time reflects the best compromise between heart count rate and surrounding organ uptake.

Myocardial uptake which is coronary flow dependent is 1.2% of the injected dose at rest and 1.5% of the injected dose at exercise. Table 2.0 illustrates the biological clearance as well as effective clearance (which includes biological clearance and radionuclide decay) of Tc99m Sestamibi from the heart and liver. (Organ concentrations expressed as percentage of injected dose; data based on clearance and radionuclide decay) of Tc99m Sestamibi from the heart and liver. (Concentrations expressed as percentage of injected dose; data based on average of 5 subjects at rest and 5 subjects during exercise).

<table>
<thead>
<tr>
<th>Time</th>
<th>Biological Clearance</th>
<th>Effective Clearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 min</td>
<td>1.2</td>
<td>19.6</td>
</tr>
<tr>
<td>30 min</td>
<td>1.0</td>
<td>12.2</td>
</tr>
<tr>
<td>2 hours</td>
<td>0.8</td>
<td>2.2</td>
</tr>
<tr>
<td>4 hours</td>
<td>0.5</td>
<td>0.7</td>
</tr>
</tbody>
</table>

A study in a dog myocardial ischemia model reported that Technetium Tc99m Sestamibi undergoes myocardial distribution (redistribution), although more slowly and less completely than thallous chloride Tl-201. A study in a dog myocardial infarction model reported that the drug showed no redistribution of any consequence. Definitive human studies to demonstrate possible redistribution have not been reported. In patients with documented myocardial infarction, imaging revealed the infarct up to four hours post dose.

12.1 Metabolism
The agent is excreted without any evidence of metabolism.

12.2 Elimination
The major pathway for clearance of Tc99m Sestamibi is the hepatobiliary system. Activity from the gall bladder appears in the intestines within one hour of injection. Twenty-seven percent of the injected dose is excreted in the urine, and approximately thirty-three percent of the injected dose is cleared through the feces in 48 hours.

13. NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
In comparison with most other diagnostic technetium labeled radiopharmaceuticals, the radiation dose to the ovaries (1.5 rads/30 mCi at rest, 1.2 rads/30 mCi at exercise) is high. Minimal exposure (ALARA) is necessary in women of childbearing capability. (See Section 2.)

The active intermediate, CuMBO2BF4, was genotoxic for potential sensitivity in a battery of five tests. No genotoxic activity was observed in the Ames, CHO/HHT and in vitro chromosomal exchange test (V-79 Chinese hamster fibroblasts). An increase in cells with chromosome aberrations was observed in the in vivo human lymphocyte assays. CuMBO2BF4 did not show genotoxic effects in the in vivo mouse micronuclei test at a dose which caused systemic and bone marrow toxicity (9 mg/kg, > 600 X maximal human dose).

14. CLINICAL STUDIES: CLINICAL TRIALS:
MYOCARDIAL IMAGING: In a trial of rest and stress CARDIOLITE® imaging, the relationship of normal or abnormal perfusion scans and long term cardiac events was evaluated in 521 patients (511 men, 10 women) with stable chest pain. There were