2019 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 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.
2019 Medicare Reimbursement for Nuclear Medicine
Non-HEU Derived Tc-99m for Medicare Hospital Outpatients\textsuperscript{1,2}

For 2019, CMS will continue the $10 add-on payment for non-HEU derived Tc-99m for hospital outpatients.

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.

\textbf{HCPCS Descriptor}

\textbf{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\textsuperscript{2}.

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, 2013 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 2019, CMS continues to package the payment for diagnostic radiopharmaceuticals, the exercise stress test, CPT 93017, and all pharmacologic stress agents with the SPECT Myocardial Perfusion Imaging (MPI) procedure, CPT 78452, into one single packaged payment.

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 HOPPS SPECT Multiple Myocardial Perfusion CPT 78452

<table>
<thead>
<tr>
<th>Descriptor</th>
<th>2019(^3) payment</th>
<th>2018(^4) payment</th>
</tr>
</thead>
<tbody>
<tr>
<td>78452 SPECT MPI Multiple</td>
<td>$1229.38</td>
<td>$1202.60</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>Jxxxx 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 non-HEU source Tc-99m per dose</td>
<td>$10 paid separately</td>
<td>$10 paid separately</td>
</tr>
</tbody>
</table>

### Selected 2019 payment Medicare Hospital Outpatients and Physician Office

<table>
<thead>
<tr>
<th>CPT</th>
<th>Descriptor</th>
<th>APC</th>
<th>Payment HOPPS(^3)</th>
<th>Payment Non Hospital Office(^5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>78071</td>
<td>Parathyroid planar imaging (including subtraction, when performed); with tomographic (SPECT)</td>
<td>5591</td>
<td>$353.49</td>
<td>$370.12</td>
</tr>
<tr>
<td>78452</td>
<td>Myocardial Perfusion imaging multiple SPECT</td>
<td>5593</td>
<td>$1229.38</td>
<td>$490.13</td>
</tr>
<tr>
<td>78582</td>
<td>Pulmonary ventilation (e.g. aerosol or gas) and perfusion imaging</td>
<td>5592</td>
<td>$455.52</td>
<td>$347.42</td>
</tr>
<tr>
<td>78607</td>
<td>Brain imaging tomographic (SPECT)</td>
<td>5593</td>
<td>$1229.38</td>
<td>$360.03</td>
</tr>
<tr>
<td>78806</td>
<td>Radiopharmaceutical localization of inflammatory process; whole body</td>
<td>5593</td>
<td>$1229.38</td>
<td>$345.61</td>
</tr>
<tr>
<td>79101</td>
<td>Radiopharmaceutical therapy, by intravenous administration</td>
<td>5661</td>
<td>$230.89</td>
<td>$150.64</td>
</tr>
</tbody>
</table>

Physician Payment amounts as of January 1, 2019. National average payments based on Medicare Conversion factor of $36.0391 and January, 2019 Medicare Addendum B relative value units. Diagnostic and therapeutic radiopharmaceuticals are reimbursed separately in the non-hospital / office setting based on AWP or invoice. Check with your local Medicare contractor for local payment methodology.
Lantheus Medical Imaging 2019 HCPCS and NDC Information

QUADRAMET® HCPCS code A9604 - NDC 11994-016-01
Samarium 153 lexidronam therapeutic, per treatment dose, up to 150 millicuries.

Medicare Hospital Outpatients

- QUADRAMET®- Therapeutic radiopharmaceuticals reimbursed at 106% of ASP. Medicare Hospital Outpatient Payment® Q4 2018 - A9604, $14,658.43 per dose.
- Latest payment amount can be seen in Addendum B at: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/HospitalOutpatientPPS/Addendum-A-and-Addendum-B-Updates.html.

Medicare non hospital physician offices / IDTFs

- QUADRAMET®- Reimbursement based on AWP or invoice, check local Medicare contractor for local payment amount.

<table>
<thead>
<tr>
<th>Product</th>
<th>HCPCS</th>
<th>NDC codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiolite® Kit for the Preparation of Technetium Tc-99m Sestamibi for Injection</td>
<td>A9500</td>
<td>NDC 11994-001-20 (20 vials one box)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NDC 11994-001-52 (2 vials one box)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NDC 11994-001-55 (5 vials one box)</td>
</tr>
<tr>
<td>Kit for the Preparation of Technetium Tc-99m Sestamibi for Injection</td>
<td>A9500</td>
<td>NDC 11994-003-20 (20 vials one box)</td>
</tr>
<tr>
<td>Thallous Chloride Thallium 201 Injection</td>
<td>A9505</td>
<td>NDC 11994-427-11</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NDC 11994-427-15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NDC 11994-427-19</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NDC 11994-427-24</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NDC 11994-427-26</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NDC 11994-427-28</td>
</tr>
<tr>
<td>Gallium Citrate Ga-67 Injection</td>
<td>A9556</td>
<td>NDC 11994-121-06</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NDC 11994-121-08</td>
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<tr>
<td></td>
<td></td>
<td>NDC 11994-121-13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NDC 11994-121-19</td>
</tr>
<tr>
<td>NEUROLITE® Kit for the Preparation of Technetium Tc-99m Bicisate for Injection</td>
<td>A9557</td>
<td>NDC 11994-006-02 (2 kits one package)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NDC 11994-006-05 (5 kits one package)</td>
</tr>
<tr>
<td>Xenon Xe-133 Gas</td>
<td>A9558</td>
<td>NDC 11994-127-11</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NDC 11994-127-15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NDC 11994-127-21</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NDC 11994-127-25</td>
</tr>
<tr>
<td>Tc-99m from non-highly enriched uranium source, full cost recovery add-on, per study dose</td>
<td>Q9969</td>
<td>Paid $10 per dose for Tc-99m doses derived from ≥ 95% non-HEU for HOPPS in addition to APC payment for imaging procedure</td>
</tr>
</tbody>
</table>
Citations


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


NDC codes can be researched at http://www.accessdata.fda.gov/scripts/cder/ndc/
Waterproof gloves should be worn during the preparation procedure. With a sterile shielded syringe, aseptically obtain additive-free, sterile, non-pyrogenic Sodium Pertechnetate Tc99m Injection [925 - 5550 MBq, (25 - 150 mCi)] in approximately 1 to 3 mL. Remove the plastic disc from the vial and swab the top of the vial closure with an alcohol swab to the shield.

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

**INDICATIONS AND USAGE**

For Myocardial Imaging: CARDIOLITE® Kit for the Preparation of Technetium Tc99m Sestamibi for Injection, is a myocardial perfusion agent that is indicated for planar imaging as a second line diagnostic agent to assist in the evaluation of breast lesions in patients with an abnormal mammogram or a palpable breast mass. CARDIOLITE® is not indicated for breast cancer screening, to confirm the presence with an abnormal mammogram or a palpable breast mass.

For Myocardial Imaging: CARDIOLITE® is a myocardial perfusion agent indicated for:

1. CARDIOLITE® evaluation of myocardial ischaemia can be accomplished with rest and pharmacologic stress tests (e.g., exercise or pharmacologic stress in accordance with the pharmacologic stress agent's labeling).
2. It is usually not possible to determine the age of a myocardial infarction or to differentiate a recent myocardial infarction from ischaemia.
3. Breast Imaging: The suggested dose range for I.V. administration of CARDIOLITE® is a single dose to be employed in the average patient (70 Kg) is 370 - 1110 Mbq (10 - 30 mCi).
4. The potential for cracking and significant contamination exists whenever withdrawing the needle, remove an equal volume of headspace to maintain atmospheric pressure within the vial.
5. Shake vigorously, about 5 to 10 quick upward-downward motions.
6. The stereospecific α-channel for the thermal cyclers and the pattern that has been observed is S.
7. The radiation dosimetry calculations performed by Radiation Internal Dose Estimation of Radioactive Material (Recon-o-Stat (thermal cycler) Procedure:

The stereospecific α-channel for the thermal cyclers and the pattern that has been observed is S.
The TLC tank is prepared by pouring ethanol* to a depth of 3-4 mm. Cover 10

Calculate the % Tc99m Sestamibi as:

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

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-prep 10%
- Arthrymia 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 been reported (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>Breast or Cardiac Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women n = 673</td>
<td>Women n = 685 Men n = 2361 Total n = 3046</td>
</tr>
<tr>
<td>Body as a Whole</td>
<td>21 (3.1%)</td>
</tr>
<tr>
<td>Head</td>
<td>11 (1.6%)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>9 (1.3%)</td>
</tr>
<tr>
<td>Chest Pain/Angina</td>
<td>0%</td>
</tr>
<tr>
<td>ST segment changes</td>
<td>0%</td>
</tr>
<tr>
<td>Digestive System</td>
<td>8 (1.2%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>4 (0.6%)</td>
</tr>
<tr>
<td>Special Senses</td>
<td>132 (19.6%)</td>
</tr>
<tr>
<td>Taste Pervention</td>
<td>129 (19.2%)</td>
</tr>
<tr>
<td>Parosmia</td>
<td>8 (1.2%)</td>
</tr>
<tr>
<td>Excludes the 22 patients whose gender was not recorded</td>
<td></td>
</tr>
</tbody>
</table>

In the clinical studies for breast imaging, breast pain was reported in 12 (1.7%) of the patients. In 11 of these patients the pain appears to be associated with biopsy/surgical procedures.

The following adverse reactions have been reported in ≥0.5% of patients: signs and symptoms consistent with seizure occurring shortly after administration of the agent to patients with cardiomyopathy, angina pectoris, arrhythmia, dizziness, syncope, abdominal pain, vomiting, and severe hypersensitivity characterized by dyspnea, hypotension, bradycardia, asthenia, and vomitining within two hours after a second injection of Technetium Tc99m Sestamibi. A few cases of flushing, edema, injection site inflammation, dry mouth, fever, pruritis, rash, urticaria and fatique have also been attributed to administration of the agent.

7. DRUG INTERACTIONS

Specific drug-drug interactions have not been studied.

8. USE IN SPECIFIC PATIENTS

8.1 Pregnancy

Animal reproduction and teratogenicity studies have not been conducted with Technetium Tc99m Sestamibi. It is also not known whether Technetium Tc99m Sestamibi can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. There have been no studies in pregnant women. Technetium Tc99m Sestamibi should be given to a pregnant woman only if clearly needed.

8.3 Nursing Mothers

Technetium Tc99m Sestamibi is excreted in human milk during lactation. It is not known whether Technetium Tc99m Sestamibi is excreted in human milk. Therefore, formula feedings should be substituted for breast feedings.

8.4 Pediatric Use

Safety and effectiveness in the pediatric population have not been established.

No evidence of diagnostic efficacy or clinical utility of CARDOILITE® scan was found in clinical studies of children and adolescents with Kawasaki disease.

A prospective study of 445 pediatric patients with Kawasaki disease was designed to determine the predictive value of CARDOILITE® rest and stress myocardial perfusion imaging to define a pediatric population with Kawasaki disease that was at risk of developing cardiac events. Cardiac events were defined as cardiac death, MI, hospitalization due to cardiac etiology, heart failure, CABG or coronary angioplasty. The standard of truth was defined as cardiac events occurring 6 months following the administration of CARDOILITE®. Only three cardiac events were observed at six months in this study. In all three cases, the scan was normal. No clinically meaningful measurements of sensitivity, specificity or other diagnostic performance parameters could be demonstrated in this study.

In a clinical pharmacology study, 46 pediatric patients with Kawasaki disease received CARDIOILITE® 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 30 mCi), 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 CARDOILITE® in adults. Two of the 609 had a serious adverse event: one patient received a CARDIOILITE® overdose but remained asymptomatic, and one patient had an asthma exacerbation following administration.

8.5 Geriatric Use

Of 3068 patients in clinical studies of CARDOILITE®, 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 MIRALUMA®, 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 CARDIOILITE® are not known.

11. DESCRIPTION

Each 5 mL vial contains a sterile, non-pyrogenic, lyophilized mixture of:
- Tc-99m Sestamibi (2-mercaptoimidazole) isomer/ (I) tetrathiolonate - 1.0 mg
- Sodium Citrate Dihydrate - 2.6 mg
- L- Cysteine Monohydrate Monohydrate - 1.0 mg
- Mannitol – 20 mg
- Sodium Citrate Dihydrate - 2.6 mg
- Stannous Chloride, Dihydrate, minimum (SnCl2 + H2O) - 0.025 mg
- Stannous Chloride, Dihydrate, (SnCl2 + H2O) - 0.075 mg
- Stannous Chloride (stannic and stannous) Dihydrate, maximum (as SnCl2 + H2O) - 0.086 mg

Prior to lyophilization the pH is 3.5 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 Techinum Tc99m Injection. The pH of the reconstituted product is 9.5 (6.0 - 4.0). No bacteriostatic preservative is present.

The precise structure of the technetium complex is Tc99m(MMI)2, where MMI is 2-mercaptoimidazole isomirin.

11.1 Physical Characteristics

Technetium Tc99m decays by isomeric transition with a physical half-life of 6.02 hours. Photons that are useful for detection and imaging studies are listed below in Table 3.0.

<table>
<thead>
<tr>
<th>Energy (KeV)</th>
<th>Mean %/</th>
<th>Disintegration</th>
<th>Mean Energy (KeV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>140.4</td>
<td>36.6</td>
<td>0.0014</td>
<td>140.4</td>
</tr>
<tr>
<td>140.8</td>
<td>63.4</td>
<td>0.0016</td>
<td>140.8</td>
</tr>
</tbody>
</table>


11.2 External Radiation

The specific gamma ray constant for Tc99m is 5.4 microcuries/mg-Mbq-ke (0.7896/Me-Cr) 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 control of the radiation exposure from Megabequerel (microliter) amounts of this radionuclide, the use of a 0.25 mCi thickness of Pb will attenuate 90% of the radiation emitted by a factor of 1.003.

<table>
<thead>
<tr>
<th>Radiation</th>
<th>Mean %/ Disintegration</th>
<th>Mean Energy (KeV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.017</td>
<td>0.016</td>
<td>140.4</td>
</tr>
<tr>
<td>0.025</td>
<td>0.030</td>
<td>140.4</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.
12. CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Technetium Tc99m Sestamibi is a cationic Tc99m complex which has been found to accumulate in viable myocardial tissue in a manner analogous to that of thallious chloride Tl-201. Scintigraphic images obtained in humans after the intravenous administration of the drug have been comparable to those obtained with thallious chloride Tl-201 in normal and abnormal myocardial tissue.

Animal studies have shown that myocardial uptake is not blocked when the sodium pump mechanism is inhibited. Although studies of subcellular fractionation and electron micrographic analysis of heart cell aggregates suggest that Tc99m Sestamibi cellular retention occurs specifically within the mitochondria as a result of electrostatic interactions, the clinical relevance of these findings has not been determined.

The mechanism of Tc99m Sestamibi localization in various types of breast tissue (e.g., benign, inflammatory, malignant, fibrous) has not been established.

12.3 Pharmacokinetics

Pulmonary activity is negligible even immediately after injection. Blood clearance studies indicated that the fast component was constant with a t1/2 of 4.3 minutes at rest, and clears with a t1/2 of 1.6 minutes under exercise conditions. At five minutes post injection about 8% of the injected dose remains in circulation. There is less than 1% protein binding of Technetium Tc99m Sestamibi in plasma. The myocardial biological half-life is approximately six hours after a rest or exercise injection. The biological half-life for the liver is approximately 30 minutes after a rest or exercise injection. The effective half-life of clearance (which includes both the biological half-life and radiochemical decay) for the heart is approximately 8 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 6.0 illustrates the biological clearance as well as effective clearance (which includes biological clearance and radiochemical decay) of Tc99m Sestamibi from the heart and liver.

(Organ concentrations expressed as percentage of injected dose; data based on an average of 5 subjects at rest and 5 subjects during exercise).

Table 6.0 Biological and Effective Clearance

<table>
<thead>
<tr>
<th>Time</th>
<th>Biological</th>
<th>Effective</th>
<th>Biological</th>
<th>Effective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>Liver</td>
<td>Heart</td>
<td>Liver</td>
<td></td>
</tr>
<tr>
<td>5 min</td>
<td>1.2</td>
<td>1.2</td>
<td>9.6</td>
<td>19.4</td>
</tr>
<tr>
<td>30 min</td>
<td>1.1</td>
<td>1.0</td>
<td>12.2</td>
<td>11.5</td>
</tr>
<tr>
<td>1 hour</td>
<td>1.0</td>
<td>0.9</td>
<td>5.9</td>
<td>5.8</td>
</tr>
<tr>
<td>2 hours</td>
<td>1.0</td>
<td>0.8</td>
<td>2.2</td>
<td>1.7</td>
</tr>
<tr>
<td>4 hours</td>
<td>0.8</td>
<td>0.5</td>
<td>0.7</td>
<td>0.4</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 thallious 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.

12.3.1 Metabolism

The agent is excreted without any evidence of metabolism.

12.3.2 Elimination

The major pathway for clearance of Tc99m Sestamibi is the hepatobiliary route. In 48 hours. and approximately thirty-three percent of the injected dose is cleared through the feces in 48 hours.

The mechanism of Tc99m Sestamibi localization in various types of breast tissue (e.g., benign, inflammatory, malignant, fibrous) has not been established.

The major pathway for clearance of Tc99m Sestamibi is the hepatobiliary route. In 48 hours. and approximately thirty-three percent of the injected dose is cleared through the feces in 48 hours. The agent is excreted without any evidence of metabolism.

In earlier trials, using a template consisting of the anterior wall, inferior-posterior wall and isolated apex, localization in the anterior-inferior-posterior wall in patients with suspected angina or coronary artery disease was shown. Disease localization isolated to the apex has not been established. In adults, Tc99m Sestamibi has not been studied or evaluated in cardiac disorders other than coronary artery disease.

BREAST IMAGING: MIRALUMA® was evaluated in a multicenter, clinical trials of a total of 673 women patients. Overall the mean age was 52 (range 23 to 87 years). The racial and ethnic representation was 70% Caucasian, 15% African American, 14% Hispanic and 1% Asian.

Both clinical studies evaluated women who were referred for further evaluation for either: 1) a mammographically detected with varying degrees of malignant likelihood but not palpable breast lesion (study A, n=387, mean age = 54 years), or 2) a palpable breast lesion (study B, n=206, mean age = 50 years). In both studies all patients were scheduled for biopsy.

MIRALUMA® (20 - 30 mCi) was injected intravenously in a vein that was contralateral to the breast lesion to be imaged. Planar imaging was completed with a high resolution collimator with a 10% window centered at 140 KeV. and 128 x 128 matrix. An initial marker image, that was not used in the data analysis, was obtained using a cobalt Co57 source as a marker of a palpable mass. Images were obtained 5 minutes after injection as follows: lateral image of the affected breast for 10 minutes, lateral image of the contralateral breast for 10 minutes, and an anterior image of both breasts for 10 minutes. For the lateral image the patients were positioned in a prone position. For the anterior image, the patients were supine. The MIRALUMA® scintigraphic images were read in a randomized method by two groups of three blinded readers. MIRALUMA® uptake was scored as: normal (no uptake), mild, high uptake. The results of MIRALUMA® images and mammography were analyzed in comparison to histopathological findings of malignant or non-malignant disease. As shown in Table 8.0 for the 483 evaluable patients, the sensitivity and specificity of any degree of MIRALUMA® uptake appear to vary with the presence or absence of palpable mass.

Table 8.0 Overall MIRALUMA® Blinded Results of Target Lesions(a)

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Study A</th>
<th>Study B</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Palpable</td>
<td>52/127(79)</td>
<td>52/127(79)</td>
<td>1.0</td>
</tr>
<tr>
<td>Palpable</td>
<td>48/48(100)</td>
<td>11/11(100)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

(a) Excludes discordant lesions identified at entry and excludes 25% equivocal interpretations from Study A and 32 equivocal interpretations from Study B (See Tables 9.0 and 10.0).

In a separate retrospective subset analyses of 259 patients with dense (heterogeneously/extremely dense) and 275 patients with fatty (almost entirely fat/nuveauous/vague densities) breast tissue, the MIRALUMA® results were similar. Overall, the studies were not designed to compare the performance of MIRALUMA® with the performance of mammography in patients with breast densities or other conditions that may affect breast tissue density.

In general the histology seems to correlate with the degree of MIRALUMA® uptake. As shown in Tables 9.0 and 10.0, the majority of the normal MIRALUMA® images are associated with non-malignant tissue (78%) and the majority of low, moderate or high uptake MIRALUMA® images are associated with malignant disease (79%). In an individual patient, however, intensity of MIRALUMA® uptake can not be used to confirm the presence or absence of malignancy. Equivocal results do not have a correlation with histology.

An estimate of the likelihood of malignancy based on the MIRALUMA® uptake score in combination with the mammographic score has not been studied. In these two studies approximately 150 additional, non-biopsied lesions were found to be positive after MIRALUMA® imaging. These lesions were identified in sites that did not physically correlate with identified entry criteria mammographic lesions and these lesions were not palpable. These lesions were not biopsied. Whether these lesions were benign or malignant is not known. MIRALUMA® uptake can occur in both benign and malignant disease. THE CLINICAL USEFULNESS OF A POSSITIVE MIRALUMA® IMAGE IN THE ABSENCE OF AN ABNORMAL MAMMOGRAM OR ABALANCE LESION IS NOT KNOWN.

15. REFERENCES

Not applicable.

16. HOW SUPPLIED/STORAGE AND HANDLING

CARDOXIL® Kit for the Preparation of Technetium Tc99m Sestamibi for Injection is supplied as a 5 mL, in a kit of five (5) vials (NDC # 11994-001-05) and twenty (20) vials (NDC # 11994-001-20), sterile and non-pyrogenic.

The patient dose should be measured by a radioactivity calibration system immediately prior to patient administration. Radiochemical purity should be checked prior to patient administration.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. Prior to hylopliation the pH is between 5.3-5.9. The contents of the vial are lyophilized and stored under nitrogen. Store at 15-25°C (59-77°F) before and after reconstitution.

Technetium Tc99m Sestamibi contains no preservatives. Included in each five (5) vial kit is one (1) package insert, (six (6) vial shield labels and six (6) radiation warning labels. Included in each twenty (20) vial kit is one (1) package insert, twenty four (24) vial shield labels and twenty four (24) radiation warning labels. This reagent kit is approved for distribution to persons licensed pursuant to the Code of Massachusetts Regulations 105 CMR 120.500 for the users listed in 105 CMR 120.547 or 120.552, or under equivalent regulations of the U.S. Nuclear Regulatory Commission, Agreement States or Licensing States.

17. PATIENT COUNSELING INFORMATION

CARDOXIL® and MIRALUMA® are different names for the same drug. Patients should be advised to inform their health care provider if they had an allergic reaction to either drug or if they had an imaging study with either drug.