Radiopharmaceuticals are eligible for separate reimbursement under the Medicare program in the physician office/freestanding imaging setting. Check with the local Medicare contractor for additional information.

In the hospital outpatient setting, under the Medicare program, generally, the cost of a contrast agent or diagnostic radiopharmaceutical is considered and then included into the payment rate for the procedure under the Medicare Hospital Outpatient APC program. Per CMS transmittal 2386\(^1\) (item #5a page 5, 1/13/2012):

“Hospitals are strongly encouraged to report charges for all drugs, biologicals, and radiopharmaceuticals, regardless of whether the items are paid separately or packaged, using the correct HCPCS codes for the items used. It is also of great importance that hospitals billing for these products make certain that the reported units of service of the reported HCPCS codes are consistent with the quantity of a drug, biological, or radiopharmaceutical that was used in the care of the patient. More complete data from hospitals on the drugs and biologicals provided during an encounter would help improve payment accuracy for separately payable drugs and biologicals in the future. CMS strongly encourages hospitals to report HCPCS codes for all drugs and biologicals furnished, if specific codes are available. CMS realizes that this may require hospitals to change longstanding reporting practices. Precise billing of drug and biological HCPCS codes and units, especially in the case of packaged drugs and biologicals for which the hospital receives no separate payment, is critical to the accuracy of the OPPS payment rates for drugs and biologicals each year.”

Non-Medicare and Private Payer policies regarding radiopharmaceutical reimbursement vary. Check with the local insurer for more information.

\(^1\) http://www.cms.gov/transmittals/downloads/R2386CP.pdf

The material referenced and provided is based upon research of current Medicare reference sources. The final decision of billing for any product or procedure must be made by the provider of care considering the medical necessity of the services and supplies provided, the regulations of insurance carriers and any local, state or federal laws that apply to the supplies and services rendered. We are providing you this information in an educational capacity with the understanding that we are not engaged in rendering legal, accounting or other professional services.
<table>
<thead>
<tr>
<th>Code*</th>
<th>Description</th>
<th>Professional</th>
<th>Technical</th>
<th>Medicare Hospital Outpatient Payment as of 1/13/2012 Unadjusted for Geography**</th>
</tr>
</thead>
<tbody>
<tr>
<td>78451</td>
<td>Myocardial perfusion imaging: tomographic (SPECT) (including attenuation correction, qualitative or quantitative wall motion, ejection fraction by first pass or gated technique, additional quantification, when performed); single study at rest or stress (exercise or pharmacologic) (Not all imaging agents are approved for all these uses, please check indication statements on page 4 and consult the attached package insert for approved indications.)</td>
<td>$65</td>
<td>$295</td>
<td>Assigned to APC 377 with a payment rate of $672</td>
</tr>
<tr>
<td>78452</td>
<td>Myocardial perfusion imaging: tomographic (SPECT) (including attenuation correction, qualitative or quantitative wall motion, ejection fraction by first pass or gated technique, additional quantification, when performed); multiple studies at rest and/or stress (exercise or pharmacologic) and/or redistribution and/or rest reinjection (Not all imaging agents are approved for all these uses, please check indication statements on page 4 and consult the attached package insert for approved indications.)</td>
<td>$76</td>
<td>$426</td>
<td>Assigned to APC 377 with a payment rate of $672</td>
</tr>
<tr>
<td>78453</td>
<td>Myocardial perfusion imaging planar (including qualitative or quantitative wall motion, ejection fraction by first pass or gated technique, additional quantification, when performed); single study at rest and/or stress (exercise or pharmacologic) (Not all imaging agents are approved for all these uses, please check indication statements on page 4 and consult the attached package insert for approved indications.)</td>
<td>$47</td>
<td>$263</td>
<td>Assigned to APC 377 with a payment rate of $672</td>
</tr>
<tr>
<td>78454</td>
<td>Myocardial perfusion imaging planar (including qualitative or quantitative wall motion, ejection fraction by first pass or gated technique, additional quantification, when performed); multiple studies at rest or stress (exercise or pharmacologic) and/or redistribution and/or rest reinjection (Not all imaging agents are approved for all these uses, please check indication statements on page 4 and consult the enclosed package insert for approved indications.)</td>
<td>$62</td>
<td>$381</td>
<td>Assigned to APC 377 with a payment rate of $672</td>
</tr>
<tr>
<td>78472</td>
<td>Cardiac blood pool imaging, gated equilibrium; planar, single study at rest or stress (exercise and/or pharmacologic), wall motion study plus ejection fraction, with or without additional quantitative processing (Not all imaging agents are approved for all these uses, please check indication statement on page 4 and consult the attached package insert for approved indications)</td>
<td>$47</td>
<td>$200</td>
<td>Assigned to APC 398 with a payment rate of $297</td>
</tr>
<tr>
<td>78473</td>
<td>Cardiac blood pool imaging, gated equilibrium; planar, multiple studies, wall motion study plus ejection fraction, at rest and stress (exercise and/or pharmacologic) with or without additional quantification (Not all imaging agents are approved for all these uses, please check indication statement on page 4 and consult the attached package insert for approved indications)</td>
<td>$71</td>
<td>$248</td>
<td>Assigned to APC 398 with a payment rate of $297</td>
</tr>
</tbody>
</table>

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**Actual Medicare allowables vary by region of the country.

See page 4 for indications and Important Risk Information.

The material referenced and provided is based upon research of current Medicare reference sources. The final decision of billing for any product or procedure must be made by the provider of care considering the medical necessity of the services and supplies provided, the regulations of insurance carriers and any local, state or federal laws that apply to the supplies and services rendered. We are providing you this information in an educational capacity with the understanding that we are not engaged in rendering legal, accounting or other professional services.
## Coding and Medicare Reimbursement Information

<table>
<thead>
<tr>
<th>Code*</th>
<th>Description</th>
<th>Professional</th>
<th>Technical</th>
<th>Medicare Outpatient Payment as of 1/13/2012 Unadjusted for Geography**</th>
</tr>
</thead>
<tbody>
<tr>
<td>78481</td>
<td>Cardiac blood pool imaging (planar), first pass technique; single study, at rest or with stress (exercise and/or pharmacologic), wall motion study plus ejection fraction, with or without quantification (Not all imaging agents are approved for all these uses, please check indication statement on page 4 and consult the attached package insert for approved indications)</td>
<td>$48</td>
<td>$153</td>
<td>Assigned to APC 398 with a payment rate of $297</td>
</tr>
<tr>
<td>78483</td>
<td>Cardiac blood pool imaging (planar), multiple studies, at rest and with stress (exercise and/or pharmacologic), wall motion study plus ejection fraction, with or without quantification (Not all imaging agents are approved for all these uses, please check indication statement on page 4 and consult the attached package insert for approved indications)</td>
<td>$72</td>
<td>$202</td>
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</tr>
<tr>
<td>78494</td>
<td>Cardiac blood pool imaging (SPECT), at rest, wall motion study plus ejection fraction, with or without quantitative processing (Not all imaging agents are approved for all these uses, please check indication statement on page 4 and consult the attached package insert for approved indications)</td>
<td>$57</td>
<td>$193</td>
<td>Assigned to APC 398 with a payment rate of $297</td>
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</tbody>
</table>

### CV Stress

<table>
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<th>Code</th>
<th>Description</th>
<th>Global Payment</th>
</tr>
</thead>
<tbody>
<tr>
<td>93015</td>
<td>Cardiovascular stress test; with physician supervision, with interpretation and report</td>
<td>$88</td>
</tr>
<tr>
<td>93016</td>
<td>Cardiovascular stress test; physician supervision only, without interpretation and report</td>
<td>$22</td>
</tr>
<tr>
<td>93017</td>
<td>Cardiovascular stress test; tracing only</td>
<td>$51</td>
</tr>
<tr>
<td>93018</td>
<td>Cardiovascular stress test; interpretation and report only</td>
<td>$14</td>
</tr>
</tbody>
</table>

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** Actual Medicare allowables vary by region of the country.

See page 4 for indications and Important Risk Information.

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Radiopharmaceuticals

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<thead>
<tr>
<th>RP</th>
<th>2012 Code and Description Published Verbatim from Medicare's Internet Site</th>
<th>2012 Medicare Part B Payment</th>
<th>2012 Medicare Hospital Outpatient Payment</th>
</tr>
</thead>
<tbody>
<tr>
<td>99m Tc Sestamibi</td>
<td>A9500-Technetium Tc99m Sestamibi, diagnostic per study dose</td>
<td>Invoice or Allowable</td>
<td>Assigned status of “N” payment packaged into procedure</td>
</tr>
<tr>
<td>Tl201</td>
<td>A9505-Thallium Tl 201 Thallous Chloride, diagnostic per millicurie (mCi)</td>
<td>Invoice or Allowable</td>
<td>Assigned status of “N” payment packaged into procedure</td>
</tr>
</tbody>
</table>

Cardiac Blood Pool Imaging Agents

| Ultratag™ RBC | A9560-Technetium Tc99m, labeled red blood cells, diagnostic, per study dose, up to 30 millicurie | Invoice or Allowable | Assigned status of “N” payment packaged into procedure |

INDICATIONS

Thallous Chloride TI 201 Injection may be useful in myocardial perfusion imaging using either planar or SPECT (Single Photon Emission Computed Tomography) techniques for the diagnosis and localization of myocardial infarction. It may also have prognostic value regarding survival, when used in the clinically stable patient following the onset of symptoms of an acute myocardial infarction, to assess the size and site of the perfusion defect. Thallous Chloride TI 201 may also be useful in conjunction with exercise stress testing as an adjunct to the diagnosis of ischemic heart disease (atherosclerotic coronary artery disease). Thallous Chloride TI 201 is also indicated for scintigraphic imaging of the myocardium to identify changes in perfusion induced by pharmacologic stress in patients with known or suspected coronary artery disease and who cannot exercise adequately. It is usually not possible to differentiate recent from old myocardial infarction, or to differentiate exactly between recent myocardial infarction and ischemia.

IMPORTANT RISK INFORMATION

In studying patients with known or suspected coronary artery disease, care should be taken to ensure continuous cardiac monitoring and the availability of emergency cardiac treatment. Stress testing should be performed only under the supervision of a qualified physician. Caution should be used when pharmacologic stress is selected. It should be used when indicated and in accordance with the agent's labeling, and may be associated with serious adverse events such as myocardial infarction, arrhythmia, hypotension, bronchoconstriction, and cerebrovascular events. Following the administration of Thallous Chloride TI 201 Injection, adverse reactions reported are: hypotension, pruritus, flushing, diffuse rash, itching, nausea/vomiting, mild diarrhea, tremor, shortness of breath, chills, fever, conjunctivitis, sweating and blurred vision. For Full Prescribing Information, see attached package insert.

INDICATIONS

Kit for the Preparation of Technetium Tc 99m Sestamibi Injection (Tc 99m Sestamibi) is a myocardial perfusion agent that is indicated for detecting coronary artery disease by localizing myocardial ischemia (reversible defects) and infarction (non-reversible defects) in evaluating myocardial function and developing information for use in patient management decisions. Kit for the Preparation of Technetium Tc 99m Sestamibi Injection (Tc 99m Sestamibi) evaluation of myocardial ischemia can be accomplished with rest and cardiovascular stress techniques (e.g., exercise or pharmacologic stress in accordance with the pharmacologic stress agent's labeling). It is usually not possible to determine the age of a myocardial infarction or to differentiate a recent myocardial infarction from ischemia.

IMPORTANT RISK INFORMATION

Exercise and pharmacologic stress testing should be performed only under the supervision of a qualified physician. Kit for the Preparation of Technetium Tc 99m Sestamibi Injection (Tc 99m Sestamibi) has been rarely associated with acute severe allergic events of angioedema and urticaria. The most frequently reported adverse events include headache, chest pain/angina, ST segment changes on ECG, nausea, and abnormal taste and smell. In clinical studies for breast imaging, breast pain was reported in 1.7% of patients. For Full Prescribing Information, see attached package insert.

INDICATIONS

Kit for the Preparation of Technetium Tc 99m-Labeled Red Blood Cells are used for blood pool imaging including cardiac first pass and gated equilibrium imaging and for detection of gastrointestinal bleeding.

IMPORTANT RISK INFORMATION

Nuclear medicine procedures involving withdrawal and reinjection of blood have the potential for transmission of blood borne pathogens. Procedures should be implemented to avoid administration errors and viral contamination of personnel during drug product labeling. For Full Prescribing Information, see attached package insert.

For more information, contact:
- Local Covidien Representative: 800-634-1515
- Customer Service: 888-744-1414
- http://imaging.covidien.com

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Mallinckrodt

The material referenced and provided is based upon research of current Medicare reference sources. The final decision of billing for any product or procedure must be made by the provider of care considering the medical necessity of the services and supplies provided, the regulations of insurance carriers and any local, state or federal laws that apply to the supplies and services rendered. We are providing you this information in an educational capacity with the understanding that we are not engaged in rendering legal, accounting or other professional services.
Full prescribing information: Contents*  

1 INDICATIONS AND USES  
2 DOSAGE AND ADMINISTRATION  
3 CLINICAL PHARMACOLOGY  
4 CONTRAINDICATIONS  
5 WARNINGS AND PRECAUTIONS  
6 ADVERSE REACTIONS  
7 DRUG INTERACTIONS  
8 USE IN SPECIFIC POPULATIONS  
9 DRUG ABUSE AND DEPENDENCE  
10 OVERDOSAGE  
11 DESCRIPTION  
12 CLINICAL PHARMACOLOGY  
13 NONCLINICAL TOXICOLOGY  
14 REFERENCES  
15 HOW SUPPLIED/STORAGE AND HANDLING  
17 PATIENT COUNSELING INFORMATION  
18 FAQs  

For complete study, see the full prescribing information and use in the following sections.

The radiation doses and tissues of an average patient (170 cm tall and 70 kg) are shown in Table 1.

Radiation absorbed doses to from the Kit for the Preparation of Technetium Tc 99m Sestamibi Injection are shown in Table 2.

Dosage and drug interactions of Technetium Tc 99m Sestamibi are shown in Table 3.

Solvents or substances entitled from the full prescribing information are not listed.

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Solvents or substances entitled from the full prescribing information are not listed.
The most frequent exercise stress test endpoints were exercise-induced angina (3.5%), transient ischemic phenomenon (3.2%), chest pain (2.8%), and palpable breast lesion (2.2%). The medical center used standardized controls (two-thirds were cancer patients). Fatigue 17% (251 patients), 12% (158 patients), and 17% (157 patients) for the 60-year-olds, 75-year-olds, and women. All patients were not randomized in 154 patients. There was no statistical difference from the three clinical studies described above. The mechanism of the clinical consequences of overdosing with Technetium Tc 99m Sestamibi uptake appear to vary with the presence or absence and extent of fibrosis. To facilitate control of the histology of the technetium complex is 220 (8.6% total) and 2.7 (0.1% total).

6 ADVERSE REACTIONS

Adverse events were evaluated in 3174 adults who were evaluable in clinical studies. Of those patients, 3206 (20.3%), 2019 (12.4%), and 1076 (6.7%) were 65 years or older, 75 years or older, and 1000 (6.7%) were women in all clinical trials. Causes of angina, chest pain, and syncope are not known. 121 were 75 or older. The clinical consequences of overdosing with Technetium Tc 99m Sestamibi are not known. The aorta in a dog myocardiectomy ischemia model reported that Technetium Tc 99m Sestamibi unstable myocardial ischemia scintigraphy is superior to thallous chloride Tl-201. A study in a dog model in which myocardial ischemia was induced by femoral artery ligation and reperfusion of the ischemic limb caused an increased clearance through the brain in 40 hours. 12.3 Metabolism

The agent is excreted without any evidence of metabolites.

12.4 Elimination

The major pathway for clearance of Technetium Tc 99m Sestamibi is through the kidneys. The finding was not evaluated for defect location, diagnosis of disease, or disease management. The findings were not evaluated for defect location, diagnosis of disease, or disease management. In this trial as summarized in Table 5, the Technetium Tc 99m Sestamibi study in 3741 adults who were evaluable in clinical studies. Of those patients, 3206 (20.3%), 2019 (12.4%), and 1076 (6.7%) were 65 years or older, 75 years or older, and 1000 (6.7%) were women. Women (54% of the patients) in breast imaging trials. Cases of angina, chest pain, and syncope are not known. 121 were 75 or older. The clinical consequences of overdosing with Technetium Tc 99m Sestamibi are not known. The aorta in a dog myocardiectomy ischemia model reported that Technetium Tc 99m Sestamibi unstable myocardial ischemia scintigraphy is superior to thallous chloride Tl-201. A study in a dog model in which myocardial ischemia was induced by femoral artery ligation and reperfusion of the ischemic limb caused an increased clearance through the brain in 40 hours.
Thallous Chloride Tl-201 Injection
Rx Only

DESCRIPTION
Thallous Chloride Tl-201 Injection is supplied in an isotonic solution as a sterile, non-pyrogenic diagnostic radiopharmaceutical for intravenous administration.

Each milliliter contains 37 megabecquerels (1 milli-Ci) Thallium Tl-201 at calibration time, made isotonic with 9 milligrams sodium chloride and preserved with 0.95% (v/v) benzyl alcohol. The pH is adjusted between 4.5 to 7.0 with hydrochloric acid and/or sodium hydroxide. Thallium Tl-201 is cyclotron produced. At the time of calibration it contains no more than 1.0% Thallium-200, no more than 1.0% Thallium-202, no more than 0.25% Lead Pb-203, and no less than 98% Thallium Tl-201 as a percentage of total activity. No carrier has been added.

It is recommended that Thallous Chloride Tl-201 be administered close to calibration time to minimize the effect of higher levels of radionuclidic contaminants present at pre- and post-calibration dates. The concentration of each radionuclidic contaminant as a percentage of total activity. No carrier has been added.

To correct for physical decay of the radionuclide, the fractions that remain at selected intervals after calibration time are shown in Table 3.

Clinical Pharmacology
Thallous Chloride Tl-201 is indicated for myocardial imaging, because of its physical properties. Thallous Chloride Tl-201 is recommended for myocardial imaging, because of its physical properties. Thallous Chloride Tl-201 is recommended for myocardial imaging, because of its physical properties.

In clinical studies, Thallous Chloride Tl-201 images have been found to visualize areas of infarction as “cold” or nonlabeled regions which are confirmed by electrocardiographic and enzyme changes. When the “cold” or nonlabeled regions comprise a substantial portion of the left ventricle, the prognosis for survival is unfavorable. Regions of transient myocardial ischemia corresponding to areas perfused by coronary arteries with partial stenoses have been visualized when Thallous Chloride Tl-201 was administered in conjunction with an exercise stress test. Anatomic configurations may interfere with visualization of the right coronary artery.

After intravenous administration, Thallous Chloride Tl-201 clears rapidly from the blood with maximal concentration by normal myocardium occurring at about 10 minutes. It will, in addition, localize in parathyroid adenomas; it is not specific since it will localize to a lesser extent in sites of parathyroid hyperplasia and other abnormal tissues such as thyroid adenomas, neoplasia (e.g., parathyroid carcinoma) and sarcoid. Biodistribution is generally proportional to organ blood flow at the time of injection. Blood clearance of Thallous Chloride Tl-201 is primarily by the myocardium, thyroid, liver, kidneys and stomach with the remainder distributing fairly uniformly throughout the body. The dosimetry data in Table 3 reflect this distribution pattern and are based on a biological half-life of 2.4 days. Thallous Chloride Tl-201 is excreted slowly and to an equal extent in both feces and urine.

Five minutes after intravenous administration only 5 to 8 percent of injected activity remained in the blood. A biexponential disappearance curve was obtained, with 91.6 percent of the blood radioactivity disappearing with a half-time of about 5 minutes. The remainder had a half-time of about 40 hours.

Approximately 4 to 8 percent of the injected dose was excreted in the urine in the first 24 hours. The whole-body disappearance half-time was 9.8 ± 2.5 days. Kidney concentration was found to be about 3 percent of the injected activity and the testicular content was 0.15 percent. Net thyroid activity was determined to be only 0.2 percent of the injected dose, and the activity disappeared in 24 hours. From anterior and posterior whole-body scans, it was determined that about 45 percent of the injected dose was in the large intestines and contiguous structures (liver, kidneys, abdominal musculature).

INDICATIONS AND USAGE
Thallous Chloride Tl-201 may be useful in myocardial perfusion imaging using either planar or SPECT (Single Photon Emission Computed Tomography) techniques for the diagnosis and localization of myocardial infarction. It may also have prognostic value regarding survival, when used in the clinically stable patient following the onset of symptoms of an acute myocardial infarction, to assess the site and size of the perfusion defect.

Thallous Chloride Tl-201 may also be useful in conjunction with exercise stress testing as an adjunct to the diagnosis of ischemic heart disease (atherosclerotic coronary artery disease).

Thallous Chloride Tl-201 is also indicated for scintigraphic imaging of the myocardium to identify changes in perfusion induced by pharmacologic stress in patients with known or suspected coronary artery disease and who cannot exercise adequately.

It is usually not possible to differentiate recent from old myocardial infarction, or to differentiate exactly between recent myocardial infarction and ischemia.

Thallous Chloride Tl-201 is not known to affect reproduction capacity. Thallous Chloride Tl-201 may likewise be affected. As in the use of any radioactive material, care should be taken to assure continuous clinical monitoring and treatment in accordance with safe, accepted procedures. Exercise stress testing should be performed only under the supervision of a qualified physician and in a laboratory equipped with appropriate resuscitation and support apparatus.

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.

PRECAUTIONS
Data are not available concerning the effect on the quality of Thallous Chloride Tl-201 images of marked alterations in blood glucose, insulin or pH (such as is found in diabetes mellitus). Attention is directed to the fact that thallium is a potassium analog, and since the transport of potassium is affected by these factors, the possibility exists that the Thallous Chloride Tl-201 may likewise be affected.

General
This drug should not be used after six (6) days from the calibration date, or nine (9) days from date of manufacture, whichever comes first.

As in the use of any radioactive material, care should be taken to minimize radiation exposure to the patient consistent with proper management and to insure minimum radiation exposure to occupational workers.

Radiopharmaceuticals should be used only by those who are qualified by training and experience in the safe use and handling of radionuclides.

Carcinogenesis, Mutagenesis, Impairment of Fertility
No long-term animal studies have been performed to evaluate carcinogenic potential, mutagenic potential or whether this drug affects fertility in males or females.

Pregnancy Category C
Animal reproductive studies have not been conducted with Thallous Chloride Tl-201. It is also not known whether Thallous Chloride Tl-201 can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Thallous Chloride Tl-201 should be given to a pregnant woman only if clearly needed.
ADVERSE REACTIONS

Following the administration of Thallous Chloride Tl-201, adverse anaphylactoid reactions have been reported (characterized by cardiovascular, respiratory and cutaneous symptoms), some severe enough to require treatment. Hypotension, pruriitus, flushing, and diffuse rash which responds to antihistamines have been reported. Other reported events include itching, nausea/vomiting, mild diarrhea, tremor, shortness of breath, chills, fever, conjunctivitis, sweating, and blurred vision.

Adverse events, some of which were serious, have also been reported in patients who have undergone thallium pharmacologic testing (see WARNINGS). Please refer to the package inserts of approved pharmacologic stress agents for more detailed information on those adverse reactions.

DOSE AND ADMINISTRATION

The recommended adult dose of intravenous Thallous Chloride Tl-201 for planar myocardial imaging is 37 to 74 MBq (1 to 2 mCi). The recommended intravenous doses for SPECT myocardial imaging are 74 to 111 MBq (2 to 3 mCi). The efficacy of a 1.0 mCi dose for SPECT imaging has not been well established.

For the localization of parathyroid hyperactivity, Thallous Chloride Tl-201 may be administered before, with or after a minimal dose of a thyroid imaging agent such as sodium pertechnetate Tc-99m or sodium iodide I-123 to enable thyroid subtraction imaging.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use if contents are turbid.

Waterproof gloves should be worn during the handling procedures.

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

With a shielded sterile syringe, aseptically withdraw the material for use.

For rest and Thallous Chloride Tl-201 studies, imaging should begin 10 to 20 minutes after injection. Myocardial-to-background ratios are improved when the patient is injected upright and in the fasting state; the upright position reduces the hepatic and gastric Thallium Tl-201 concentration.

When utilized in conjunction with exercise stress testing, Thallous Chloride Tl-201 should be administered at the inception of a period of maximum stress which is sustained for approximately 30 seconds after injection. Imaging should begin within ten minutes after administration to obtain maximum target-to-background ratios. Several investigators have reported that within four hours after the completion of stress testing, the target-to-background ratios may decrease significantly in lesions that are attributable to transient ischemia.

Radiation Dosimetry

The estimated absorbed radiation dosesa at calibration time to an average patient (70 kg) from an intravenous injection of Thallous Chloride Tl-201 are shown in Table 4.

Table 4. Radiation Dose Estimates for Tl-201 Chloride (plus contaminants)

<table>
<thead>
<tr>
<th>Organ</th>
<th>Estimated Radiation Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mGy/MBq</td>
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<tr>
<td>Adrenals</td>
<td>6.2E-02</td>
</tr>
<tr>
<td>Brain</td>
<td>5.9E-02</td>
</tr>
<tr>
<td>Breasts</td>
<td>3.6E-02</td>
</tr>
<tr>
<td>GB Wall</td>
<td>8.3E-02</td>
</tr>
<tr>
<td>LLJ Wall</td>
<td>3.4E-01</td>
</tr>
<tr>
<td>Small Intestine</td>
<td>4.5E-01</td>
</tr>
<tr>
<td>Stomach</td>
<td>1.9E-01</td>
</tr>
<tr>
<td>ULI Wall</td>
<td>3.3E-01</td>
</tr>
<tr>
<td>Heart Wall</td>
<td>2.8E-01</td>
</tr>
<tr>
<td>Kidneys</td>
<td>4.6E-01</td>
</tr>
<tr>
<td>Liver</td>
<td>9.9E-02</td>
</tr>
<tr>
<td>Lungs</td>
<td>4.7E-02</td>
</tr>
<tr>
<td>Muscle</td>
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<tr>
<td>Ovaries</td>
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<td>Pancreas</td>
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<td>Red Marrow</td>
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<tr>
<td>Bone Surfaces</td>
<td>8.8E-02</td>
</tr>
<tr>
<td>Skin</td>
<td>3.3E-01</td>
</tr>
<tr>
<td>Spleen</td>
<td>1.8E-01</td>
</tr>
<tr>
<td>Testes</td>
<td>8.2E-01</td>
</tr>
<tr>
<td>Thymus</td>
<td>4.6E-02</td>
</tr>
<tr>
<td>Thyroid</td>
<td>6.2E-01</td>
</tr>
<tr>
<td>Urinary Bladder Wall</td>
<td>5.2E-02</td>
</tr>
<tr>
<td>Uterus</td>
<td>8.5E-02</td>
</tr>
<tr>
<td>Effective Dose</td>
<td></td>
</tr>
<tr>
<td></td>
<td>mSv/MBq</td>
</tr>
<tr>
<td>Liver Wall</td>
<td>2.8E-01</td>
</tr>
</tbody>
</table>


HOW SUPPLIED

Catalog Number 120, NDC No. 0019-N120-28, NDC No. 0019-N120-56, NDC No. 0019-N120-63, NDC No. 0019-N120-99.

Thallous Chloride Tl-201 is supplied in a sterile, non-pyrogenic solution for intravenous administration. Each mL contains 37 MBq (1 mCi) Thallous Chloride Tl-201 at calibration time, 9 mg sodium chloride and 0.8 percent (v/v) benzyl alcohol. The pH is adjusted to between 4.5 to 7.0 with hydrochloric acid and/or sodium hydroxide solution. Vials are available in the following quantities of radioactivity: 103.6, 207.2, 233.1, 366.3 megabecquerels (2.8, 5.6, 6.3 and 9.9 millicuries) of thallium Tl-201.

The contents of the vial are radioactive. Adequate shielding and handling precautions must be maintained.

Storage Conditions

Store this drug at controlled room temperature, 20° to 25°C (68° to 77°F) [see USP].

Storage and disposal of Thallous Chloride Tl-201 Injection should be controlled in a manner that is in compliance with the appropriate regulations of the government agency authorized to license the use of this radionuclide.

a Values listed include an average maximum correction of 6 percent to the radiation doses from Thallium Tl-201 due to the radionuclides Thallium Tl-200 and Thallium Tl-202 on calibration date.
UltraTag® RBC
Kit for the preparation of Technetium Tc 99m—Labeled Red Blood Cells
Rx Only.

Diagnostic—For Intravenous Use

DESCRIPTION

UltraTag® RBC (kit for the preparation of technetium Tc 99m-labeled red blood cells) is a sterile, nonpyrogenic, diagnostic kit for the intravenous preparation of technetium Tc 99m-labeled red blood cells.

Each kit consists of three separate nonradioactive components:
1. A 10 ml injection vial containing:
   - Stannous Chloride, Dihydrate (SnCl₂·2H₂O) – 50 μg minimum
   - Stannous Chloride, Dihydrate (SnCl₂·2H₂O) – 96 μg theoretical
   - Tim Chloride (Tannic and Stannic), Dihydrate (as SnCl₂·2H₂O) – 105 μg maximum
   - Sodium Citrate, Dihydrate – 3.67 mg
   - Dextrose, Anhydrous – 5.50 mg

Prior to lyophilization, the pH is adjusted to 7.1 to 7.2 with sodium hydroxide. The contents of the vial are lyophilized and stored under argon.

2. Syringe I contains:
   - Sodium Hypochlorite – 0.6 mg in Sterile Water for Injection

The total volume of this syringe is 0.6 mL. Sodium hydroxide may have been added for pH adjustment. The pH of this solution is 11 to 13. The syringe must be protected from light to prevent degradation of the light-sensitive sodium hypochlorite.

3. Syringe II contains:
   - Citric Acid, Monohydrate – 8.7 mg
   - Sodium Citrate, Dihydrate – 32.5 mg
   - Dextrose, Anhydrous – 12.0 mg in Sterile Water for Injection

The total volume of this syringe is 1.0 mL. The pH range of this solution is adjusted to 4.5 to 5.5 with sodium citrate or citric acid.

PHYSICAL CHARACTERISTICS

Technetium Tc 99m decays by isomeric transition with a physical half-life of 6.02 hours.¹ The principal photon that is useful for detection and imaging is listed in Table 1.

Table 1. Principal Radiation Emission Data

<table>
<thead>
<tr>
<th>Radiation</th>
<th>Mean % Disintegration</th>
<th>Energy (keV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gamma-2</td>
<td>89.07</td>
<td>140.5</td>
</tr>
</tbody>
</table>

The specific gamma ray constant for technetium Tc99m is 0.78 R/min·hr·at 1 cm. The first half-value thickness of lead (Pb) for technetium Tc 99m is 0.017 cm. A range of values for therelative attenuation of the radiation emitted by this radionuclide resulting from the interposition of various thicknesses of lead (Pb) is presented in Table 2. For example, the use of 0.25 cm of lead will decrease the external radiation exposure by a factor of about 1000.

Table 2. Radiation Attenuation by Lead Shielding

<table>
<thead>
<tr>
<th>Thickness (Pb) cm</th>
<th>Coefficient of Attenuation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.017</td>
<td>0.5</td>
</tr>
<tr>
<td>0.06</td>
<td>10¹</td>
</tr>
<tr>
<td>0.16</td>
<td>10¹</td>
</tr>
<tr>
<td>0.25</td>
<td>10¹</td>
</tr>
<tr>
<td>0.33</td>
<td>10¹</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 presented in Table 3.


Table 3. Physical Decay Chart: Technetium Tc 99m, Half-Life: 6.02 Hours

<table>
<thead>
<tr>
<th>Hours</th>
<th>Fraction Remaining</th>
<th>Hours</th>
<th>Fraction Remaining</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.000</td>
<td>7</td>
<td>0.447</td>
</tr>
<tr>
<td>1</td>
<td>0.891</td>
<td>8</td>
<td>0.398</td>
</tr>
<tr>
<td>2</td>
<td>0.794</td>
<td>9</td>
<td>0.355</td>
</tr>
<tr>
<td>3</td>
<td>0.708</td>
<td>10</td>
<td>0.316</td>
</tr>
<tr>
<td>4</td>
<td>0.631</td>
<td>11</td>
<td>0.282</td>
</tr>
<tr>
<td>5</td>
<td>0.562</td>
<td>12</td>
<td>0.251</td>
</tr>
</tbody>
</table>

*Calibration Time

CLINICAL PHARMACOLOGY

In vivo Tc 99m red blood cell labeling is accomplished by adding 1.0 to 3.0 milliliters of autologous whole blood, anticoagulated with heparin or Anticoagulant Citrate Dextrose Solution (ACD), to the reaction vial. A portion of the stannous ion in the reaction vial diffuses across the red blood cell membrane and accumulates intracellularly. The in vitro Tc 99m red blood cell labeling efficiency can decrease in the presence of excess ACD. Excess ACD apparently impairs the diffusion of stannous ion across the red blood cell membrane. Therefore, the ACD concentration used for blood collection should not exceed 0.15 mL ACD per mL of blood. Sodium hypochlorite is then added to the reaction vial to oxidize the extracellular stannous ion. Since the hypochlorite does not cross the red blood cell membrane, the oxidation of stannous ion is selective for the extracellular fluid. A citric acid, sodium citrate and dextrose solution is then added to the reaction vial to sequester any residual extracellular stannous ion, rendering it more readily available for oxidation by sodium hypochlorite.

Radioactive labeling of the red blood cells is completed by addition of sodium pertechnetate Tc 99m to the oxidized reaction vial. The pertechnetate Tc 99m diffuses across the red blood cell membrane and is reduced by the intracellular stannous ion. The reduced technetium Tc 99m cannot diffuse out of the red blood cells. The red blood cell labeling is essentially complete within 20 minutes of sodium pertechnetate Tc 99m addition to the reaction vial. Red blood cell labeling efficiency of 95% is typically obtained using this in vitro labeling procedure. In vivo Tc 99m red blood cell labeling efficiency can decrease when excessive amounts of Tc 99m are allowed to accumulate in the sodium pertechnetate Tc 99m generator eluate, in this situation, efficiency decreases even further if excess (i.e. >0.15 mL per mL of blood) ACD buffer is used. Therefore, long Tc 99m in-growth times are to be avoided, the use of fresh (24 hour in-growth time) sodium pertechnetate Tc 99m generator eluate is recommended. After the labeling procedure is completed, the technetium Tc 99m-labeled red blood cells are then reinfused intravenously into the patient for gamma scintigraphic imaging.

Following intravenous injection, the technetium Tc 99m-labeled red blood cells distribute within the blood pool with an estimated distribution of approximately 5.6% of bodyweight. The technetium Tc 99m is well retained in the blood pool with an estimated half-life of approximately 24 hours. Of the total technetium Tc 99m retained in the whole blood pool 24 hours after administration, 95% remains bound to the red blood cells. Approximately 25% of the injected dose is excreted in the urine in the first 24 hours.

INDICATIONS AND USAGE

Technetium Tc 99m-labeled red blood cells are used for blood pool imaging, including cardiac first pass and gated equilibrium imaging and for detection of sites of gastrointestinal bleeding.

CONTRAINDICATIONS

None known.

WARNINGS

None known.

PRECAUTIONS

General

The components of the kit are sterile and nonpyrogenic. It is essential that the user follow the directions carefully and adhere to strict aseptic procedures during preparation.

The contents of the kit are intended only for use in the preparation of technetium Tc 99m-labeled red blood cells and are NOT to be administered directly to the patient.

The contents of this kit are not radioactive. After sodium pertechnetate Tc 99m is added, however, adequate shielding of the final preparation must be maintained.

Technetium Tc 99m-labeled red blood cells must be handled with care to insure minimum radiation exposure to the patient, consistent with proper patient management, and to insure minimum radiation exposure to occupational workers.

The labeled red blood cells must be rejected only into the patient from whom the blood was drawn.

Nuclear medicine procedures involving withdrawal and reinjection of blood have the potential for transmission of blood borne pathogens. Procedures should be implemented to avoid administration errors and a contamination of personnel during blood product labeling. A system of checks similar to the ones used for administering blood transfusions should be routine.

Clinical trials were conducted with a variety of prescription and nonprescription medications and showed no significant effect on the in vivo labeling efficiency of UltraTag® RBC. Unlike stannous pyrophosphate red blood cell kits, heparinized patients (11) showed minimal interference with UltraTag® RBC labeling efficiency (95%) with heparin, 97% without heparin.

It is recommended that the labeled red blood cells be administered within 30 minutes of preparation or as soon as possible thereafter. A small study showed that technetium Tc 99m-labeled red blood cells prepared with UltraTag® RBC have equivalent in vivo labeling efficiency when administered both immediately after preparation (5 patients studied) and at 6 hours after preparation (6 patients studied) with a 24-hour labeling efficiency averaging 97% for both groups.

Radiopharmaceuticals should be used only by physicians who are qualified by specific training in the safe use and handling of radionuclides and whose experience and training have been approved by the appropriate government agency authorized to license the use of radionuclides.

Carcinogenesis, Mutagenesis, Impairment of Fertility

No long-term animal studies have been performed to evaluate carcinogenic or mutagenic potential or to determine the effects on male or female fertility.

Pregnancy Category C

Animal reproduction studies have not been conducted with technetium Tc 99m labeled red blood cells. It is also not known whether this drug can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Technetium 99m-labeled red blood cells are not to be administered to a pregnant woman only if clearly needed. Ideally, examinations using radiopharmaceuticals, especially those that are excreted in nature, of a woman of childbearing capability should be performed during the first few (approximately 10) days following the onset of menses.

Nursing Mothers

Technetium Tc 99m is excreted in human milk during lactation. Therefore, formula feedings should be substituted for breast feeding.

Pediatric Use

Safety and efficacy in pediatric patients have not been established.

ADVERSE REACTIONS

None known.

DOSAGE AND ADMINISTRATION

The instructions for Preparation must be carefully followed for preparing technetium Tc 99m-labeled red blood cells using UltraTag® RBC.
The kit should be stored at controlled room temperature 20-25°C (68-77°F). Syringe I should be protected from light if not stored in the kit tray.

**RADIATION DOSIMETRY**

The estimated radiation doses to an average adult (70 Kg) from an intravenous injection of a maximum dose of 740 MBq (20 mCi) of technetium Tc 99m-labeled red blood cells are shown in Table 4.

These radiation absorbed dose values were calculated using the Medical Internal Radiation Dose (MIRD) Committee Schema.

**Table 4. Absorbed Radiation Dose Estimates For UltraTag® RBC Technetium Tc 99m Labeled Red Blood Cells**

<table>
<thead>
<tr>
<th>Organ</th>
<th>mGy/740MBq</th>
<th>rads/20mCi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Body</td>
<td>3.0</td>
<td>0.30</td>
</tr>
<tr>
<td>Spleen</td>
<td>22</td>
<td>2.2</td>
</tr>
<tr>
<td>Bladder Wall</td>
<td>4.6</td>
<td>0.48</td>
</tr>
<tr>
<td>Testes</td>
<td>2.2</td>
<td>0.22</td>
</tr>
<tr>
<td>Ovaries</td>
<td>3.2</td>
<td>0.32</td>
</tr>
<tr>
<td>Blood</td>
<td>8.0</td>
<td>0.80</td>
</tr>
<tr>
<td>Red Marrow</td>
<td>3.0</td>
<td>0.30</td>
</tr>
<tr>
<td>Heart Wall</td>
<td>20</td>
<td>2.0</td>
</tr>
<tr>
<td>Liver</td>
<td>5.8</td>
<td>0.58</td>
</tr>
<tr>
<td>Bone Surfaces</td>
<td>4.6</td>
<td>0.48</td>
</tr>
</tbody>
</table>

* Assumes non-feeding state and biological half-life for all organs and whole body of 63.7 hours. The peak percent dose for heart chambers is 15.5%, for liver is 5.57%, spleen is 4.07% and for remainder of body is 74.8%. Assumes patient voids at 2.0 hour intervals.

**HOW SUPPLIED**

Catalog Number 068.

UltraTag® RBC consists of three separate nonradioactive components:

1. A 10 milliliter reaction vial containing:
   - Stannous Chloride, Dihydrate (SnCl2·2H2O) – 50 μg minimum
   - Stannous Chloride, Dihydrate (SnCl2·2H2O) – 96 μg theoretical
   - Tin Chloride (Stannous and Stannic), Dihydrate (as SnCl2·2H2O) – 105 μg maximum
   - Sodium Citrate, Dihydrate – 3.67 mg
   - Dextrose, Anhydrous – 5.00 mg

   Prior to lyophilization, the pH is adjusted to 7.1 to 7.2 with sodium hydroxide. The contents of the vial are lyophilized and stored under argon.

2. Syringe I contains:
   - Sodium Hypochlorite – 0.6 mg in Sterile Water for Injection
   - The total volume of this syringe is 0.6 mL. Sodium hydroxide may have been added for pH adjustment. The pH of this solution is 11 to 13. The syringe must be protected from light to prevent degradation of the light-sensitive sodium hypochlorite.

   - Dose estimates based on Phase I human biodistribution data generated at Brookhaven National Laboratories. Dose estimates were calculated at Oak Ridge Associated Universities, Oak Ridge, Tennessee.

   - 3. Syringe II contains:
     - Citric Acid, Monohydrate - 8.7 mg
     - Sodium Citrate, Dihydrate - 32.5 mg
     - Dextrose, Anhydrous - 12.0 mg in Sterile Water for Injection

   - The total volume of this syringe is 1.0 mL. The pH range of this solution is adjusted to 4.5 to 5.5 with sodium citrate or citric acid.

   **STORAGE**

   The kit should be stored at controlled room temperature 20-25°C (68-77°F). Syringe I should be protected from light if not stored in the kit tray.

   **Instructions for the Preparation of Technetium Tc 99m-Labeled Red Blood Cells Using UltraTag® RBC**

   1. Collect patient's blood sample (1.0 to 3.0 mL) using heparin or ACD as an anticoagulant. The amount of ACD should not exceed 0.15 mL of ACD per mL of blood. The recommended amount of heparin is 10-15 units per mL of blood. DO NOT USE EDTA OR OXALATE AS AN ANTICOAGULANT.

   2. Using a large-bore (19 to 21 gauge) needle, transfer 1.0 to 3.0 mL of anticoagulated whole blood to the reaction vial and gently mix to dissolve the lyophilized material. Allow to react for five minutes.

   3. Add contents of Syringe I, mix by gently inverting four to five times.

   4. Add the contents of Syringe II to the reaction vial. Mix by gently inverting four to five times.

   5. Place the vial in a lead shield fitted with a lead cap and having a minimum wall thickness of 1/8 inch. Add 370 to 3700 MBq (10 to 100 mCi) sodium pertechnetate Tc 99m (in a volume of up to 3 mL) to the reaction vial. The avoidance of long technetium Tc 99m-growth times and the use of fresh sodium pertechnetate Tc 99m generator eluate is recommended.

   6. Mix by gently inverting reaction vial four to five times. Allow to react for 20 minutes with occasional mixing.

   7. Technetium Tc 99m-labeled red blood cells should be injected within 30 minutes of preparation or as soon as possible thereafter.

   8. If desired, assay labeling efficiency immediately prior to injection. Typical labeling efficiency is greater than 95%.

   9. Mix gently prior to withdrawal of patient dose. Aseptically transfer the technetium Tc 99m-labeled red blood cells to a syringe for administration to the patient. Use largest bone needle compatible with patient administration to prevent hemolysis.

   10. Assay the Tc 99m-labeled red blood cell patient dose in a suitable calibrator and complete the radioassay information label. Affix the radioassay information label to the shield.

   **NOTES**

   1. The kit does not contain an anticoagulant. Therefore, a syringe or vacuum™ tube treated with ACD or heparin must be used for drawing the patient's blood. The amount of ACD should not exceed 0.15 mL of ACD per mL of blood. The recommended amount of heparin is 10-15 units per mL of blood. Improperly anticoagulated blood will be unsuitable for reinfusion.

   2. If desired, the labeling yield determination can be carried out as follows:

   - Transfer 0.2 mL of the technetium Tc 99m-labeled red blood cells to a centrifuge tube containing 2 mL of 0.9% NaCl. Centrifuge for five minutes and carefully pipet off the diluted plasma. Measure the radioactivity in the plasma and red blood cells separately in a suitable counter. Calculate labeling efficiency as follows:

   - % RBC Labeling = Activity RBC 
   Activity RBC + Activity Plasma 

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   A06850