DESCRIPTION

Ultratag™ RBC (kit for the preparation of technetium Tc 99m-labeled red blood cells) is a sterile, nonpyrogenic, diagnostic kit for in vitro preparation of technetium Tc 99m-labeled red blood cells.

Each kit consists of three separate nonradioactive components:

1. A 10 milliliter reaction vial containing:
   - Stannous Chloride, Dihydrate (SnCl2•2H2O) – 50 ug minimum
   - Stannous Chloride, Dihydrate (SnCl2•2H2O) – 96 ug theoretical
   - Tin Chloride (Stannous and Stannic), Dihydrate (as SnCl2•2H2O) – 105 ug maximum
   - 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 – 120 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 followed for preparing technetium Tc 99m-labeled red blood cells using Ultratag™ RBC.

The specific gamma ray constant for technetium Tc 99m is 0.78 R/mCi-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 the relative 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 attenuate the radiation emitted by this radionuclide by 97% without lead and 5% with 0.017 cm lead.

The time of calibration are presented in Table 3.

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.

For in vitro preparation of technetium Tc 99m-labeled red blood cells, 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.

None known.

WARNINGS

Safety and efficacy in pediatric patients have not been established.

ADVERSE REACTIONS

None known.

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 ensure minimum radiation exposure to the patient, consistent with proper patient management, and to ensure minimum radiation exposure to occupational workers.

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

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Clinical trials were conducted with a variety of prescription and nonprescription medications and showed no significant effect on the in vitro 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.

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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 should be administered to a pregnant woman only if clearly needed. Ideally, examinations using radiopharmaceuticals, especially those elective 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.

DOSAGE AND ADMINISTRATION

The Instructions for Preparation must be carefully followed for preparing technetium Tc 99m-labeled red blood cells using Ultratag™ RBC.
The suggested dose range of technetium Tc 99m-labeled red blood cells in the average patient (70 kg) is 370 MBq (10 mCi) to 740 MBq (20 mCi).

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

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Aseptic procedures and a shielded syringe should be employed in preparing and withdrawing doses for administration to patients. The user should wear waterproof gloves during the administration procedure.

**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

<table>
<thead>
<tr>
<th>Organ</th>
<th>mg/740 MBq</th>
<th>rads/20 mCi</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>4.8</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>4.8</td>
<td>0.48</td>
</tr>
</tbody>
</table>

* Assumes non-resting 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 5.5%, 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 – 96 ug theoretical

   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.

**Storage**

The kit should be stored at controlled room temperature in the light-sensitive sodium hypochlorite.

Transfer 0.2 mL of the technetium Tc99m labeled red blood cell patient dose (as SnCl2•2H2O) 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-term technetium Tc 99 m-in-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. Aspiratically transfer the technetium Tc 99m-labeled red blood cells to a syringe for administration to the patient. Use largest bore 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 vacuumainer™ 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 reinjection.

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

Transfer 0.2 mL of the technetium Tc99m 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:

\[
\frac{\text{Activity Plasma}}{\text{Activity Plasma} + \text{Activity RBC}} \times 100
\]

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Ultratag™ RBC KIT FOR THE PREPARATION OF TECHNETIUM Tc 99m—LABELED RED BLOOD CELLS

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* Assumes non-resting 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 5.5%, spleen is 4.07%, and for remainder of body is 74.8%. Assumes patient voids at 2.0 hour intervals.

**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.**