TECHNESCAN® MAA KIT FOR THE PREPARATION OF TECHNETIUM Tc 99m ALBUMIN AGGREGATED

For Intravenous Use

**DESCRIPTION**

The kit consists of five or thirty multidose reaction vials which contain the sterile, non-pyrogenic, non-radioactive ingredients necessary to produce Technetium Tc99m Albumin Aggregated Injection for diagnostic use by intravenous injection.

Each 10-milliliter reaction vial contains 2 milligrams of succinic acid and 1.1 milligrams of sodium acid as sodium pertechnetate Tc 99m solution. Approximately 90 percent are 10 to 40 microns in size. Typically, approximately 90 percent are within the 10 to 40 micron range. There are no aggregated albumin particles greater than 150 microns in size.

Technetium Tc 99m Albumin Aggregated Injection for intravenous use is in its final dosage form when sterile isotonic sodium pertechnetate Tc 99m solution is added to each vial. No less than 90% of the pertechnetate Tc 99m added to the reaction vials is bound to the aggregates at preparation time and remains bound throughout the 8-hour lifetime of the preparation.

The precise structure of the stannous-technetium-albumin complex is unknown at this time.

**PHYSICAL CHARACTERISTICS**

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

### Table 1. Principal Radiation Emission Data

| Gamma-2 | 89.07 | 140.5 |

**EXTERNAL RADIATION**

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 that results from interposition of various thicknesses of Pb is shown in Table 2. For example, the use of 0.25 cm of Pb will decrease the external radiation exposure by a factor of about 1000.

### Table 2. Radiation Attenuation by Lead Shielding

<table>
<thead>
<tr>
<th>Shield Thickness (Pb) cm</th>
<th>Coefficient of Attenuation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.07</td>
<td>0.5</td>
</tr>
<tr>
<td>0.09</td>
<td>10^4</td>
</tr>
<tr>
<td>0.16</td>
<td>10^4</td>
</tr>
<tr>
<td>0.25</td>
<td>10^4</td>
</tr>
<tr>
<td>0.33</td>
<td>10^4</td>
</tr>
</tbody>
</table>

**CLINICAL PHARMACOLOGY**

Within 1 to 5 minutes of intravenous injection, over 90 percent of the technetium Tc 99m albumin aggregated particles are trapped in the arterioles and capillaries of the lung.

Organ selectivity is a direct result of particle size. Below 10 microns, the albumin aggregates are taken up by the reticuloendothelial system. Above 10 to 15 microns, the aggregates become lodged in the lung capillaries by a purely mechanical process. Distribution of aggregated albumin in the lungs is a function of regional pulmonary blood flow.

The albumin aggregated is sufficiently fragile for the capillary microocclusion to be temporary. Erosion and fragmentation reduce the particle size, allowing passage of the aggregates through the pulmonary alveolar capillary bed. The fragments are then accumulated by the reticuloendothelial system.

In animal tissue distribution studies, measurements of radioactivity activity showed a lung to liver ratio of about 70:1 within the first thirty minutes. Elimination of the technetium Tc 99m albumin aggregated from the lungs occurs with a biological half-life of about 6.2 hours. Cumulative urinary excretion studies show an average of about 75% elimination of the injected technetium Tc99m dose 24 hours post administration.

Elimination of the technetium Tc 99m albumin aggregates from the normal and abnormal human lungs occurs with a biological half-life of 10.8 hours. The effective half-life was estimated to be 3.8 hours for the lung.

Following administration of technetium Tc 99m albumin aggregated by intraparenchymal injection, the radiopharmaceutical mixes with the peritoneal fluid. Clearance from the peritoneal cavity varies from insignificant, which may occur with complete shunt blockage, to very rapid clearance with subsequent transfer into the systemic circulation when the shunt is patent.

Serial images should be obtained of both the shunt and lung (target organ). However, an adequate evaluation of the difference between total blockage of the shunt and partial blockage may not be feasible in all cases.

**INDICATIONS AND USAGE**

Technetium MAA Tc 99m is indicated for scintigraphic imaging of the lungs as an adjunct to other diagnostic procedures when information about pulmonary circulation is desired.

The use of Technetium MAA Tc 99m is contraindicated in patients with severe pulmonary hypertension.

The use of Technetium MAA Tc 99m is contraindicated in children with a history of hypersensitivity reactions to products containing human serum albumin.

**WARNINGS**

The possibility of allergic reactions should be considered in patients who receive multiple doses of Technetium MAA Tc 99m.

**CONTRAINDICATIONS**

Technetium MAA Tc 99m should not be administered to patients with severe pulmonary hypertension.

The use of Technetium MAA Tc 99m is contraindicated in children with a history of hypersensitivity reactions to products containing human serum albumin.

**ADVERSE REACTIONS**

The literature contains reports of deaths occurring after the administration of aggregated technetium Tc 99m albumin aggregated injection to patients with pre-existing severe pulmonary hypertension. Instances of hemodynamic or disoxicotic reactions to preparations of technetium Tc 99m albumin aggregated injection have been reported.

**Pediatric Use**

Safety and effectiveness in pediatric patients has not been established.

**Nursing Mothers**

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

**ADVERSE REACTIONS**

The literature contains reports of deaths occurring after the administration of aggregated technetium Tc 99m albumin aggregated injection to patients with pre-existing severe pulmonary hypertension. Instances of hemodynamic or disoxicotic reactions to preparations of technetium Tc 99m albumin aggregated injection have been reported.
Hypersensitivity reactions are possible whenever protein-containing materials such as technetium Tc 99m albumin aggregated injection are used in man. Epinephrine, antihistamines and corticosteroid agents should be available for use.

**DOSEAGE AND ADMINISTRATION**

**Lung Imaging**
The recommended intravenous dosage range for the average patient (70 kg) is 37 to 148 megabecquerels (1 to 4 millicuries). The volume of the dose may vary from 0.4 to 1.0 milliliter.

The recommended number of aggregated albumin particles to be administered per dose is 200,000 to 1,200,000 with the suggested number being approximately 600,000.

While the number of particles available per millicurie dose of Technescan® MAA Tc 99m will vary corresponding to the physical decay of technetium Tc 99m which has occurred, the particles available in any specific dose may be estimated from Table 4.

In cases of right-to-left cardiac shunt the number of aggregated albumin particles administered per dose should be reduced to the minimum feasible.

The patient dose should be measured by a suitable radioactivity calibration system for total radioactivity immediately prior to administration. Resuspend particiles by repeated inversion of the syringe immediately prior to injection. Technescan MAA Tc99m is injected intravenously, without aspirating, over a 20- to 30-second interval with the patient in the supine position. If blood is drawn into the syringe, any unnecessary delay prior to injection may lead to clot formation in the syringe. Do not back flush the syringe. For optional results, lung imaging should begin as soon as possible. It is recommended the Technescan MAA Tc 99m not be injected through intravenous tubing because of the occasional observation of “hot spots” in the lung.

LeVeen Shunt Patency

The suggested intraperitoneal dosage range used in the average patient (70 kg) from an intravenous (LeVeen) shunt patency evaluation is 37 to 111 megabecquerels (1 to 3 millicuries). Adequate radioactivity calibration system for total radioactivity is immediately prior to administration. Resuspend particles by repeated inversion of the syringe immediately prior to injection. Technescan MAA Tc99m is injected intravenously, without aspirating, over a 20- to 30-second interval with the patient in the supine position. If blood is drawn into the syringe, any unnecessary delay prior to injection may lead to clot formation in the syringe. Do not back flush the syringe. For optional results, lung imaging should begin as soon as possible. It is recommended the Technescan MAA Tc 99m not be injected through intravenous tubing because of the occasional observation of “hot spots” in the lung.

LeVeen Shunt Patency

The suggested intraperitoneal dosage range used in the average patient (70 kg) from an intravenous (LeVeen) shunt patency evaluation is 37 to 111 megabecquerels (1 to 3 millicuries). Adequate measures should be taken to assure uniform mixing with peritoneal fluid. Serial images of both the shunt and target organ should be obtained and correlated with other clinical findings. Alternatively, the drug may be administered by percutaneous transabdominal injection. The suggested percutaneous transluminal (effenter limb) dosage range for the average patient (70 kg) is 12 to 37 megabecquerels (0.3 to 1.0 milliliter) in a volume not to exceed 0.5-ml.

**RADIATION DOSEIMTRY**
The estimated absorbed radiation doses to an average ADULT patient (70 kg) from an intravenous injection of 4 millicuries of Technetium Tc 99m Albumin Aggregated Injection are shown in Table 5.

Table 6 represents the absorbed radiation dose resulting from the intraperitoneal administration of 111 megabecquerels (3 millicuries) of technetium Tc 99m albumin aggregated.

**HOW SUPPLIED**

Catalog Number 093.

Technescan MAA is supplied as a lyophilized powder packaged in vials. Each vial contains:

- 2 mg Aggregated Albumin Human
- 0.5 mg Albumin Human
- 130 µg Maximum Tin (as SnCl₂·2H₂O)
- 80 mg Lactose
- 24 mg Sucinic Acid
- 1.1 mg Sodium Acetate
- Hydrochloric Acid or Sodium Hydroxide is added for pH adjustment. The vial is sealed under an atmosphere of nitrogen. Each vial contains 8±4 x 10⁶ aggregated albumin particles.

*Method of calculation: “S”; Absorbed Dose per Unit Cumulated Activity for Selected Radiocolloids and Organs, MIRED Pamphlet No. 11 (1975).

**POINTS TO REMEMBER**

Kits containing 5 vials (NDC 1909-0939-BO) or 30 vials (NDC 1909-0939-DO) are available.

**STORAGE**

Technescan MAA Kit should be stored refrigerated at 2°C to 8°C before reconstitution. Technescan MAA contains no preservatives; after reconstitution, the shielded vial should be stored refrigerated at 2-8°C (36-46°F).

**DIRECTIONS FOR USE**

**Procedural Precautions**

**SOLUTIONS OF SODIUM PERTECHNETATE Tc 99m WHICH CONTAIN OXIDIZING AGENTS (I.e., sodium hypochlorite or hydrogen peroxide) SHOULD NOT BE USED.**

Reagents obtained from the following technetium-99m generators were tested and found to be acceptable for use with Technescan MAA: Mallinkrodt Inc.’s Ultra-Technescan® FM Generators, Du Pont-Merck’s Nuclear’s Technetium Tc 99m Generator and Squibb’s Minitec® Generator. Other sources of technetium Tc 99m can be used if the user has demonstrated that they are compatible with Technescan MAA.

All transfers and vial stopper entries must be done using aseptic techniques.

**Procedure**

For the preparation of Technetium Tc 99m Albumin Aggregated.

1. Wear waterproof gloves during the entire procedure.

2. Attach radioassay information label with radiation warning symbol to the Reaction Vial.

3. Keep the Radioactive Preparation in the lead shield described (with cap in place) during the useful life of the Radioactive Preparation. Make all withdrawals and injections of the Radioactive Preparation with an adequately shielded syringe.

4. Attach radioassay information label with radiation warning symbol to the Reaction Vial.

5. Make all transfers of sodium pertechnetate Tc 99m solution during the preparation procedure with an adequately shielded syringe.

6. Prior to withdrawing a dose, the contents of the Reaction Vial should be gently agitated sufficiently to effect homogeneous suspension of the aggregated albumin. Withdrawals for administration must be made aseptically using a sterile needle (18-21 gauge) and syringe. Since the vials contain nitrogen to prevent oxidation of the complex, the vials should not be vented. If repeated withdrawals are made from the vial, the contents should not be replaced with air.

7. Store the Reaction Vial in the Dispensing Shield at 2°C to 8°C when not in use and discard after 8 hours from the time of preparation.

This reagent kit is approved for distribution to persons licensed by the U.S. Nuclear Regulatory Commission to use byproduct material identified in Section 35.200 or under an equivalent license of an Agreement State.

Table 4. Example Calculation for Particles/Dose

<table>
<thead>
<tr>
<th>Tc 99m added to vial</th>
<th>37 MBq (1 mCi) Dose</th>
<th>74 MBq (2 mCi) Dose</th>
<th>111 MBq (3 mCi) Dose</th>
<th>148 MBq (4 mCi) Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.74 (20)</td>
<td>0.40</td>
<td>0.80</td>
<td>1.20</td>
<td>1.60</td>
</tr>
<tr>
<td>1.11 (30)</td>
<td>0.27</td>
<td>0.54</td>
<td>0.81</td>
<td>1.03</td>
</tr>
<tr>
<td>1.49 (40)</td>
<td>0.20</td>
<td>0.40</td>
<td>0.60</td>
<td>0.80</td>
</tr>
<tr>
<td>1.85 (50)</td>
<td>0.16</td>
<td>0.32</td>
<td>0.48</td>
<td>0.64</td>
</tr>
<tr>
<td>2.22 (60)</td>
<td>0.13</td>
<td>0.26</td>
<td>0.39</td>
<td>0.50</td>
</tr>
</tbody>
</table>

*The particles per millicurie dose will increase in relation to the physical decay of technetium-99m such that at six hours (one half-life) after preparation, the values in the table will increase by a factor of two.

Table 5. Absorbed Radiation Doses

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Technetium Tc99m Albumin Aggregated</th>
<th>mGy/148 MBq</th>
<th>rad/148 mCi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Body</td>
<td>0.60</td>
<td>0.060</td>
<td></td>
</tr>
<tr>
<td>Lungs</td>
<td>8.6</td>
<td>0.88</td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>0.72</td>
<td>0.072</td>
<td></td>
</tr>
<tr>
<td>Spleen</td>
<td>0.68</td>
<td>0.068</td>
<td></td>
</tr>
<tr>
<td>Kidneys</td>
<td>0.44</td>
<td>0.044</td>
<td></td>
</tr>
<tr>
<td>Bladder Wall</td>
<td>1.2</td>
<td>0.12</td>
<td></td>
</tr>
<tr>
<td>2-hr. void</td>
<td>2.2</td>
<td>0.22</td>
<td></td>
</tr>
<tr>
<td>4.8-hr. void</td>
<td>0.24</td>
<td>0.024</td>
<td></td>
</tr>
<tr>
<td>Testes</td>
<td>0.28</td>
<td>0.026</td>
<td></td>
</tr>
<tr>
<td>Ovaries</td>
<td>0.30</td>
<td>0.030</td>
<td></td>
</tr>
<tr>
<td>4.8-hr. void</td>
<td>0.34</td>
<td>0.034</td>
<td></td>
</tr>
</tbody>
</table>

Table 6. Absorbed Radiation Doses

<table>
<thead>
<tr>
<th>Organ</th>
<th>Shunt Patency (Open)</th>
<th>Shunt Patency (Closed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>6.9</td>
<td>0.69</td>
</tr>
<tr>
<td>1.88</td>
<td>0.168</td>
<td></td>
</tr>
<tr>
<td>Ovaries &amp; Testes</td>
<td>0.18</td>
<td>0.018</td>
</tr>
<tr>
<td>0.30</td>
<td>0.030</td>
<td></td>
</tr>
<tr>
<td>Organs in the Peritoneal Cavity</td>
<td>1.68</td>
<td>0.168</td>
</tr>
<tr>
<td>Total Body</td>
<td>0.96</td>
<td>0.006</td>
</tr>
<tr>
<td>0.57</td>
<td>0.057</td>
<td></td>
</tr>
</tbody>
</table>

ASSUMPTIONS:
Calculations for the absorbed radiation dose are based upon an effective half-time of 3 hours for the open shunt and 6.02 hours for the closed shunt and an even distribution of the radiochromepatic activity in the peritoneal cavity with no biological clearance.

Revised 8/2000

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