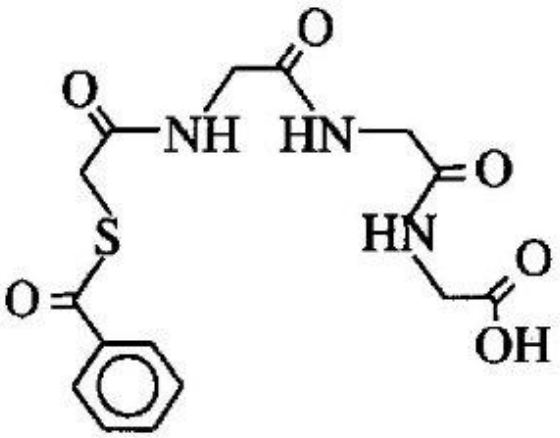
TECHNESCAN MAG3- technescan tc 99m mertiatide injection, powder, lyophilized, for solution
Curium US LLC

Technescan MAG3™
Kit for the Preparation of Technetium Tc 99m Mertiatide
Rx only
Diagnostic-For Intravenous Use

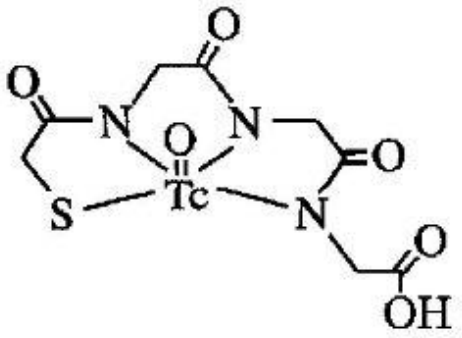
DESCRIPTION

Technescan MAG3™ is a kit for the preparation of technetium Tc 99m mertiatide, a diagnostic radiopharmaceutical. It is supplied as a sterile, nonpyrogenic, lyophilized powder. Each vial contains betiatide (N-[N-[N-[(benzoylthio) acetyl]glycyl]glycyl]-glycine). After reconstitution with sterile sodium pertechnetate Tc 99m injection, the technetium Tc 99m mertiatide (disodium[N-[N-[N-(mercaptoacetyl) glycyl]glycyl] glycinato (2-) - N,N′,N″,S′]oxotechnetate (2-)) which is formed is suitable for intravenous administration.

Each 10 milliliter vial contains 1 milligram betiatide, 0.05 milligram (minimum) stannous chloride dihydrate ($SnCl_2 \cdot 2H_2O$) and 0.2 milligram (maximum) total tin expressed as stannous chloride dihydrate ($SnCl_2 \cdot 2H_2O$), 40 milligrams sodium tartrate dihydrate ($Na_2C_4H_2O_6 \cdot 2H_2O$), and 20 milligrams lactose monohydrate. Prior to lyophilization, sodium hydroxide or hydrochloric acid may be added for pH adjustment. The pH of the reconstituted drug is between 5.0 and 6.0. No bacteriostatic preservative is present. The contents are sealed under argon. Betiatide is light sensitive and must be protected from light. Betiatide and technetium Tc 99m mertiatide have the following structural formulas:



betiatide



technetium Tc 99m mertiatide

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[1]

Radiation M	Mean % per Disintegration	Energy (keV)
Gamma-2	89.07	140.5

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

Shield Thickness (Pb) cm	Coefficient of Attenuation
0.017	0.5
0.08	10^{-1}
0.16	10^{-2}
0.25	10^{-3}
0.33	10^{-4}

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

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

Hours	Fraction	Hours	Fraction

Hours	Remaining	Hours	Remaining
0*	1.000	7	0.447
1	0.891	8	0.398
2	0.794	9	0.355
3	0.708	10	0.316
4	0.631	11	0.282
5	0.562	12	0.251
6	0.501		

* Calibration Time

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1 Kocher, David C., "Radioactive Decay Tables," DOE/TIC-11026, 108 (1981).

CLINICAL PHARMACOLOGY

Following intravenous injection of technetium Tc 99m mertiatide, the appearance, concentration, and excretion of the tracer in the kidney can be monitored to assess renal function. Although technetium Tc 99m mertiatide is highly plasma protein bound following intravenous injection, the protein binding is reversible and the tracer is rapidly excreted by the kidneys via active tubular secretion and glomerular filtration. Following intravenous injection of technetium Tc 99m mertiatide in normal volunteers, 89% of the tracer was plasma protein bound. In healthy subjects with normal renal function (mean serum creatinine 1.2 mg/dL) technetium Tc 99m mertiatide was rapidly cleared from the blood. The plasma clearance was approximately 0.3 liters/minute and the amount of technetium Tc 99m mertiatide excreted in the urine in three hours was nearly 90% of the dose. In a study performed in three patients with renal impairment (serum creatinine greater than 6.3 mg/dL), there was decreased blood clearance and a decrease in the amount excreted in the urine over three hours. In these patients, 78% of the tracer was plasma protein bound after intravenous injection. The mean plasma clearance of technetium Tc 99m mertiatide was 0.03 liters/minute and 21.3% was excreted in three hours on average. In both healthy subjects and patients with renal impairment, the plasma concentration-time profile showed a biexponential decline.

INDICATIONS AND USAGE

Technetium Tc 99m mertiatide is a renal imaging agent for use in the diagnosis of congenital and acquired abnormalities, renal failure, urinary tract obstruction, and calculi in adults and pediatric patients. (See Pediatric Use.) It is a diagnostic aid in providing renal function, split function, renal angiograms, and renogram curves for whole kidney and renal cortex.

CONTRAINDICATIONS

None known.

WARNINGS

None known.

PRECAUTIONS

General

1. The contents of this kit are not radioactive. However, after sodium pertechnetate Tc 99m is added, adequate shielding of the final preparation must be maintained.
2. Contents of the reaction vial are intended only for use in the preparation of technetium Tc 99m mertiatide and are NOT to be administered directly to the patient.
3. To help reduce the radiation dose to the bladder, as well as other target organs, the patient should increase his or her fluid intake (unless medically contraindicated) and void as often as possible after the injection of technetium Tc 99m mertiatide for six hours after the imaging procedure.
4. Technetium Tc 99m mertiatide should not be used more than six hours after preparation.
5. The components of the kit are sterile and nonpyrogenic. It is essential that the user follow the directions carefully and use aseptic procedures normally employed in making additions and withdrawals from sterile, nonpyrogenic containers during the addition of pertechnetate solution and the withdrawal of doses for patient administration.
6. The technetium Tc 99m labeling reactions involved in preparing Technescan MAG3 depend on maintaining the stannous ion in the reduced state. Any oxidant present in the sodium pertechnetate Tc 99m may adversely affect the quality of the radiopharmaceutical. Therefore, sodium pertechnetate Tc 99m containing oxidants should not be employed.
7. As in the use of any other radioactive material, care should be taken to ensure minimum radiation exposure to the patient and to occupational workers.
8. Radiopharmaceuticals should be used only by physicians who are qualified by specific training in the safe use and handling of radionuclides.

Carcinogenesis, Mutagenesis, Impairment of Fertility

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

Pregnancy

Pregnancy Category C.

Animal reproduction studies have not been conducted with technetium Tc 99m mertiatide. It is also not known whether this drug can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Technetium Tc 99m mertiatide should be given to a pregnant woman only if clearly needed.

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 effectiveness in pediatric patients under the age of 30 days have not been established.

ADVERSE REACTIONS

The following adverse reactions have been reported: nausea, vomiting, wheezing, dyspnea, itching, rash, tachycardia, hypertension, shaking chills, fever, and seizure.

DOSAGE AND ADMINISTRATION

The suggested dose range employed in the average adult patient (70 kg) for renal function and imaging studies is 185 MBq (5 mCi) to 370 MBq (10 mCi). In pediatric patients the recommended dose range is 2.6 MBq/kg (70 µCi/kg) to 5.2 MBq/kg (140 µCi/kg) with a minimum dose of 37 MBq (1 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.

Aseptic procedures and a shielded syringe should be employed in withdrawing doses for administration to patients. The user should wear waterproof gloves during the administration procedure.

RADIATION DOSIMETRY

The estimated absorbed radiation doses from an intravenous administration of technetium Tc 99m mertiatide are presented in Table 4.

HOW SUPPLIED

Catalog Number 096.

Technescan MAG3 is supplied as a lyophilized powder packaged in vials. Each reaction vial contains 1 mg betiatide, 0.05 mg (minimum) stannous chloride dihydrate ($SnCl_2 \cdot 2H_2O$), 0.2 mg (maximum) total tin expressed as stannous chloride dihydrate ($SnCl_2 \cdot 2H_2O$), 40 mg sodium tartrate dihydrate ($Na_2C_4H_2O_6 \cdot 2H_2O$), and 20 mg lactose monohydrate.

The pH of the reconstituted drug is between 5.0 and 6.0. No bacteriostatic preservative is present.

Packages containing 5 reaction vials (NDC 69945-096-20) are available.

STORAGE

Technescan MAG3 should be stored at controlled room temperature 20° to 25°C (68° to 77°F) and protected from light until use. The reconstituted vial should be stored at room temperature (15° to 30°C) and must be used within six hours of preparation.

Table 4. Radiation Dose Estimates for Tc 99m Mertiatide

	8-day Old	1-year Old**	5-year Old**	10-year Old**	15-year Old	Adult
Assumed Weight (kg)	3.4	9.8	19	32	57	70
Tc 99m Mertiatide	37 MBq	72.52 MBq	140.6 MBq	236.8 MBq	370 MBq	370 MBq

Mertiatide Dose	(1 mCi)		(1.96 mCi)		(3.8 mCi)		(6.4 mCi)		(10 mCi)		(10 mCi)	
Organ	mSv	rem	mSv	rem	mSv	rem	mSv	rem	mSv	rem	mSv	rem
Gallbladder Wall	2.701	0.27	2.466	0.235	1.547	0.160	1.658	0.166	1.961	0.200	1.628	0.160
Lower Large Intestine Wall	1.739	0.17	1.595	0.161	2.250	0.220	2.368	0.237	4.070	0.400	3.256	0.330
Small Intestine	0.518	0.052	0.5439	0.055	1.195	0.122	1.397	0.141	2.035	0.200	1.628	0.160
Upper Large Intestine Wall	0.962	0.096	0.943	0.096	1.828	0.186	2.0365	0.205	2.442	0.250	1.887	0.190
Kidneys	1.406	0.14	1.088	0.112	1.308	0.129	1.5155	0.154	1.739	0.180	1.443	0.140
Liver	0.3219	0.032	0.3046	0.031	0.394	0.038	0.4262	0.0435	0.481	0.048	0.3626	0.036
Ovaries	0.592	0.058	0.6164	0.061	1.322	0.133	1.5392	0.154	3.330	0.330	2.5900	0.260
Red Marrow	0.1628	0.016	0.1595	0.0161	0.281	0.0277	0.3552	0.0352	0.629	0.063	0.4810	0.050
Testes	0.518	0.051	0.5294	0.053	1.0826	0.110	1.1840	0.122	2.368	0.240	1.628	0.160
Urinary Bladder Wall	11.470	1.1	9.428	0.921	21.090	2.090	23.680	2.368	59.20	6.00	48.1000	4.80
Total Body	0.2405	0.024	0.2176	0.022	0.3656	0.0365	0.4026	0.0410	0.814	0.081	0.6660	0.065

*Calculated by Oak Ridge Associated Universities, based upon the pediatric phantom series of Christy and Eckerman of Oak Ridge National Laboratories. The adult radiation absorbed doses were calculated based on data from ten normal volunteers using the Medical Internal Radiation Dose Committee (MIRD) schema.

**Radioactive doses for 1-, 5-, and 10-year olds are based on a maximum dose of 7.4 MBq/kg (200 µCi/kg).

INSTRUCTIONS FOR THE PREPARATION OF TECHNETIUM Tc 99m MERTIATIDE

Note: Read complete directions thoroughly before starting preparation procedure.

Procedural Precautions and Notes

1. Solutions of sodium pertechnetate Tc 99m which contain oxidizing agents (i.e., sodium hypochlorite or hydrogen peroxide) should not be used.
   NOTE: Do not use Tc 99m eluate more than 6 hours after its elution from the generator.
2. All transfers and vial stopper entries must be done using aseptic technique.
3. The water bath used for heating the contents of the reaction vial must be at a continuous rolling boil during the heating step of the preparation procedure. The vial should be in direct contact with the rolling boil water of the bath, and the level of the bath must be at least even with the level of the contents of the vial.
4. The temperature of a lead incubation shield should be allowed to reach the temperature of the water bath before incubating the reaction vial. The shield should

be designed so that water flows through the interior of the shield.

Note 1: Wear waterproof gloves during the entire preparation procedure and during subsequent patient dose withdrawals from the reaction vial.

Note 2: Make all transfers of sodium pertechnetate Tc 99m solution during the preparation procedure with an adequately shielded syringe.

Note 3: Keep the radioactive preparation in the lead shield described below (with cap in place) during the useful life of the radioactive preparation. Maintain adequate shielding during the life of the product and use a shielded, sterile syringe for withdrawing and injecting the preparation.

Procedure for the Preparation of Technetium Tc 99m Mertiatide

1. Prepare a rolling boil water bath containing a vial shield with openings cut in it to allow the water to circulate through the shield. The openings should be oriented to prevent radiation leakage.
2. Place the reaction vial in a lead dispensing shield fitted with a lid and with a minimum wall thickness of 1/8 inch.
3. Swab the rubber stopper of the reaction vial with an appropriate antiseptic. Insert a filter-containing venting needle (provided) through the vial stopper. Inject 4 to 10 milliliters of sodium pertechnetate Tc 99m solution containing 740 megabecquerels (20 mCi) to 3.70 gigabecquerels (100 mCi) into the vial. If required, use nonbacteriostatic normal saline to dilute the sodium pertechnetate Tc 99m solution to the desired concentration prior to addition to the vial.
   NOTE: Make sure the water bath is at boiling temperature before adding sodium pertechnetate Tc 99m to the reaction vial.
4. Immediately following the addition of sodium pertechnetate Tc 99m solution to the reaction vial, withdraw the syringe plunger to a volume of 2 mL, thus removing 2 mL of argon gas and adding 2 mL of filtered air to the vial. The air is required to oxidize excess stannous ion. Remove both needles from the vial.
   NOTE: The addition of 2 mL air is required to prevent the progressive formation of technetium Tc 99m labeled impurities.
5. Invert the reaction vial several times to obtain complete mixing.
6. Immediately transfer the reaction vial to the water bath. Place it inside the lead shield which has been equilibrated to the temperature of the boiling water bath. Allow the reaction vial to incubate for 10 minutes.
   NOTE: The reaction vial **MUST** be placed in the boiling water bath within 5 minutes of the addition of sodium pertechnetate Tc 99m solution.
7. Remove the reaction vial from the boiling water bath and place in the lead dispensing shield. Allow the contents of the vial to cool for approximately 15 minutes to reach body temperature. Using proper shielding, the vial contents should be visually inspected.
   The solution should be clear and free of particulate matter. If not, the preparation should not be used.
8. Assay the reaction vial using a suitable radioactivity calibration system. Record the date, time, total technetium Tc 99m activity, volume, and technetium Tc 99m concentration on the radioassay information label and affix the label to the lead dispensing shield.
9. **The radiochemical purity of the reconstituted solution must be checked prior to administration to the patient. If the radiochemical purity is less than 90%, the product must not be used.**
10. Store the reaction vial containing the technetium Tc 99m mertiatide at room

temperature (15° to 30°C) until use. **The technetium Tc 99m mertiatide preparation must be used within six hours of preparation.**

RECOMMENDED METHOD FOR DETERMINATION OF RADIOCHEMICAL PURITY OF Technescan MAG3™

Required Materials:

Waters Sep-Pak™ C18 Cartridges, Part #51910,
200 proof ethanol
0.9% Sodium Chloride Injection, USP
0.001N hydrochloric acid*
1:1 ethanol/saline solution**
Disposable syringes:
- 10 mL, no needle required
- 1 mL, with needle

Disposable culture tubes or vials, minimum 15 mL capacity
Ion chamber for measurement of radioactive samples.

*May be prepared by diluting 1 mL of 0.10N hydrochloric acid to 100 mL with Water for Injection, USP, or by other appropriate dilution of more concentrated hydrochloric acid. For example, 0.1 mL of 36% (~11.6N) hydrochloric acid diluted to a total volume of 1,150 mL.

**Prepared by mixing equal volumes of the 200 proof ethanol and 0.9% Sodium Chloride Injection, USP.

Preparation of Sep-Pak Cartridge

1. Using a 10 mL syringe, push 10 mL of 200 proof ethanol through the Sep-Pak cartridge. Discard the eluate.
2. Similarly, flush the cartridge with 10 mL of the 0.001N hydrochloric acid. Discard the eluate.
3. Drain the cartridge by pushing 5 mL of air through the cartridge with the syringe. Discard the eluate.

Sample Analysis

1. Apply 0.1 mL of the technetium Tc 99m mertiatide preparation to the head of the cartridge through the longer end of the cartridge using a 1 mL syringe with needle. **Note:** The cartridge and all solutions eluted from it will be radioactive after this step.
2. With a disposable 10 mL syringe, slowly push 10 mL of 0.001N hydrochloric acid through the cartridge. Collect this fraction in a culture tube or vial for counting.
3. Similarly, elute the cartridge with 10 mL of the 1:1 ethanol/saline solution. Be sure that this solution is pushed through the cartridge slowly so that the elution occurs in a drop-wise manner. Collect this 10 mL fraction in a second culture tube or vial for counting.
4. Place the Sep-Pak cartridge in a third culture tube or vial for counting.

Counting

1. Assay the activity of the first sample elution in an ion chamber. This fraction contains the hydrophilic impurities (free pertechnetate, technetium tartrate, etc.) and a fraction of reduced-hydrolyzed technetium.
2. Assay the activity of the second elution. This fraction contains the technetium Tc 99m

mertiatide complex.
3. Assay the activity of the Sep-Pak cartridge in the third culture tube or vial. This component contains the remaining reduced-hydrolyzed technetium and non-elutable impurities.

Calculations

1. Percent technetium Tc 99m mertiatide =

$$\frac{\text{Activity of 2nd (ethanol/saline) fraction}}{\text{Total activity of all three fractions}} \times 100\%$$

2. Percent hydrophilic impurities =

$$\frac{\text{Activity of 1st (0.001N HCl acid) fraction}}{\text{Total activity of all three fractions}} \times 100\%$$

3. Percent non-elutable impurities =

$$\frac{\text{Activity remaining on Sep-Pak cartridge}}{\text{Total activity of all three fractions}} \times 100\%$$

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.

Manufactured by:
Curium US LLC
2703 Wagner Place
Maryland Heights, MO 63043

Made in USA

A096I0

R12/2018

CURIUM™

PRINCIPAL PANEL DISPLAY - A096V0

Technescan MAG3™

Kit for the Preparation of Technetium Tc 99m Mertiatide Diagnostic

Vial contains:

1 mg Betiatide
0.05 mg (minimum) Stannous Chloride Dihydrate ($SnCl_2 \bullet 2H_2O$)
40 mg Sodium Tartrate Dihydrate
0.2 mg (maximum) Total Tin as Stannous Chloride Dihydrate ($SnCl_2 \bullet 2H_2O$)
20 mg Lactose Monohydrate

Prior to lyophilization, sodium hydroxide or hydrochloric acid may be added for pH adjustment. The pH of the reconstituted drug is between 5.0 and 6.0. The contents are sealed under argon. Sterile, non-pyrogenic. For intravenous use after drug preparation. See package insert for directions for use. Store at 20˚ to 25˚C (68˚ to77˚F) and protect from light. Do not use sodium pertechnetate Tc 99m solutions containing an oxidizing agent.

Rx only

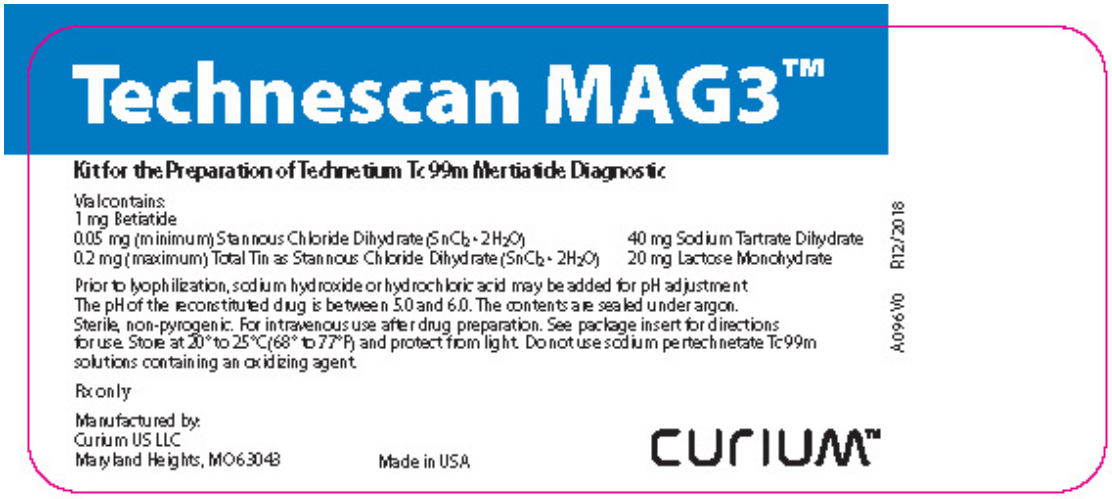
Manufactured by:
Curium US LLC
Maryland Heights, MO 63043

Made in USA

CURIUM™

A096V0

R12/2018



TECHNESCAN MAG3

technescan tc 99m mertiatide injection, powder, lyophilized, for solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:69945-096
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**

BETIATIDE (UNII: 9NV2SR34P8) (BETIATIDE - UNII:9NV2SR34P8)	BETIATIDE	1 mg

Inactive Ingredients

Ingredient Name	Strength
STANNOUS CHLORIDE (UNII: 1BQV3749L5)	0.05 mg
STANNOUS CHLORIDE ANHYDROUS (UNII: R30H55TN67)	0.2 mg
SODIUM TARTRATE (UNII: QTO9JB4MDD)	40 mg
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	20 mg
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:69945-096-20	5 in 1 CELLO PACK	06/15/1990	
1		1 in 1 VIAL; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA019882	06/15/1990	

Labeler - Curium US LLC (079875617)

Revised: 12/2022 Curium US LLC