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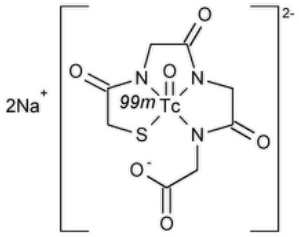
Technetium Tc 99m Mertiatide Injection



$C_8H_8N_3Na_2O_6S^{99m}Tc$

Technetate(2-)-^{99m}Tc,[*N*-[*N*-[*N*-(mercaptoacetyl)-glycyl]glycyl]glycinato(5-)-*N*,*N*′,*N*″,*S*]-oxo-, disodium, (*SP*-5-25)-;

Disodium [*N*-[*N*-[*N*-(mercaptoacetyl)glycyl]glycyl]glycinato (5-)-*N*,*N*′,*N*″,*S*]-oxo[^{99m}Tc]technetate(V)

CAS RN®: 125224-05-7.

DEFINITION

Technetium Tc 99m Mertiatide Injection is a sterile, aqueous solution, suitable for intravenous injection, that contains radioactive technetium (^{99m}Tc) in the form of a chelate of mertiatide. It contains NLT 90.0% and NMT 110.0% of the labeled amount of ^{99m}Tc as mertiatide complex expressed in megabecquerels (millicuries or microcuries) per milliliter at the date and time indicated in the labeling. It contains uncomplexed betiatide, a suitable ^{99m}Tc reducing agent, a transfer ligand, and stabilizers.

IDENTIFICATION

• **A. Radionuclidic Identity**

(See *Radioactivity ⟨821⟩, Identification of Radionuclides*.)

Acceptance criteria: Its gamma-ray spectrum is identical to that of a specimen of ^{99m}Tc that exhibits a major photopeak having an energy of 0.140 MeV.

Add the following:

▲• **B. Radiochemical Identity**

Analysis: After completing the *Analysis* for *Procedure 2 (Simultaneous determination of free pertechnetate and ^{99m}Tc mertiatide)* in the *Radiochemical Purity* test, examine the radiochromatograms obtained.

Acceptance criteria: The chromatogram shows the retention time of the major peak obtained with the *Sample solution* is between 10 and 14 min.▲ (USP 1-Dec-2024)

ASSAY

• **Radioactive Concentration (Strength)**

(See *Radioactivity ⟨821⟩, Assay of Radionuclides*.)

Analysis: Using a suitable counting assembly, determine the radioactivity, in megabecquerels (or millicuries) per milliliter, of the Injection by use of a calibrated system.

Acceptance criteria: 90.0%–110.0% of the labeled amount of ^{99m}Tc at the date and time indicated in the labeling

PURITY

• **Radionuclidic Purity**

(See *Radioactivity ⟨821⟩*.)

Analysis: Using a suitable counting assembly, determine the radioactivity of each radionuclidic impurity, in kilobecquerels per megabecquerel (microcuries per millicurie) of technetium 99m, in the Injection by use of a calibrated system.

Acceptance criteria

For Injection prepared from technetium 99m derived from parent molybdenum 99 formed as a result of neutron bombardment of stable molybdenum: See *Table 1*.

For Injection prepared from technetium 99m derived from parent molybdenum 99 formed as a result of uranium fission—gamma- and beta-emitting impurities: See *Table 2*.

Table 1

Radionuclidic Impurity	Most Prominent Photopeaks	Half-Life	Acceptance Criteria, NMT[a]
Molybdenum 99	0.181 MeV gamma 0.740 MeV gamma 0.780 MeV gamma	66.0 h	0.15 kBq/MBq (μCi/mCi)
Total of all other gamma-emitting radionuclidic impurities	—	—	0.5 kBq/MBq (μCi/mCi)[b]

[a] Radioactivity of radionuclidic impurity/radioactivity of Tc 99m per administered dose of the Injection at the time of administration.

[b] Does not exceed 92 kBq (2.5 μCi) per administered dose of the Injection at the time of administration.

Table 2

Radionuclidic Impurity	Most Prominent/Maximum Photopeaks	Half-Life	Acceptance Criteria, NMT[a]
Molybdenum 99	0.181 MeV gamma 0.740 MeV gamma 0.780 MeV gamma	66.0 h	0.15 kBq/MBq (μCi/mCi)
Iodine 131	0.364 MeV	8.08 d	0.05 kBq/MBq (μCi/mCi)
Ruthenium 103	0.497 MeV	39.5 d	0.05 kBq/MBq (μCi/mCi)
Strontium 89[b]	1.463 MeV beta	52.7 d	0.0006 kBq/MBq (μCi/mCi)
Strontium 90[b]	0.546 MeV beta	27.7 y	0.00006 kBq/MBq (μCi/mCi)
Gross alpha impurity	—	—	0.001 Bq/MBq (nCi/mCi)
All other beta- and gamma-emitting radionuclidic impurities	—	—	0.01%

[a] Radioactivity of radionuclidic impurity/radioactivity of Tc 99m present at the time of administration.

[b] Use a counting system appropriate for the detection of particulate radiations.

• **Radiochemical Purity**

Procedure 1 (Determination of hydrolyzed reduced technetium)

Chromatographic system

(See *Chromatography ⟨621⟩, General Procedures, Paper Chromatography*.)

Mode: Paper chromatography

Adsorbent: 25-mm × 20-cm strip of chromatographic paper

Application volume: About 5–10 μL (100–250 μCi)

Developing solvent system: Acetonitrile and water (60:40)

Analysis: Place the Injection 15 mm from the bottom of the *Adsorbent*. Immediately develop the chromatogram by ascending chromatography using the *Developing solvent system* until the solvent front has moved about 13 cm from the origin. Remove the strip, and allow to dry. Determine the radioactivity distribution by scanning the chromatogram using a suitable collimated radiation detector. Calculate the percentage of hydrolyzed reduced technetium:

$$\text{Result} = (A_{ht}/B_s) \times 100$$

A_{ht} = sum of all the peaks at or near the origin, where R_F is less than 0.25

B_s = sum of all of the peaks

Acceptance criteria: NMT 2.0%

Procedure 2 (Simultaneous determination of free pertechnetate and ^{99m}Tc mertiatide)

Solution A: 1.36 g/L of monobasic potassium phosphate in water. To each liter of this solution add 1.0 mL of triethylamine, and adjust with 1.0 N hydrochloric acid to a pH between 4.9 and 5.1.

Solution B: 1.36 g/L of monobasic potassium phosphate prepared as follows. Transfer a suitable amount of monobasic potassium phosphate to 900 mL of water, and add 100 mL of tetrahydrofuran to obtain a solution containing 1.36 g per L. To each liter of this solution, add 1.0 mL of triethylamine, and adjust with 1.0 N hydrochloric acid to a pH between 4.9 and 5.1.

Mobile phase: See *Table 3*. Before injection, equilibrate the system for 15 min with a *Mobile phase* consisting of a mixture of 90% *Solution A* and 10% *Solution B*.

Table 3

Time (min)	Solution A (%)	Solution B (%)
0	90	10
30	20	80
35	20	80
40	90	10

Sample solution: Immediately before testing, dilute a portion of the Injection with Water for Injection to obtain a concentration between 400 and 600 µCi. [NOTE—The extent to which the sample is diluted is determined by the sensitivity of the radiometric detector.]

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: Gamma-ray detector

Column: 3.9-mm × 15-cm; packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

Analysis

[NOTE—The retention times for ^{99m}Tc pertechnetate and ^{99m}Tc mertiatide are 1.8–2.2 min and 10–14 min respectively.]

Calculate the percentage of ^{99m}Tc pertechnetate:

$$\text{Result} = (r_{pt}/r_s) \times 100$$

r_{pt} = peak response of ^{99m}Tc pertechnetate

r_s = sum of all peak responses

Calculate the percentage of ^{99m}Tc mertiatide:

$$\text{Result} = (r_{mt}/r_s') \times 100$$

r_{mt} = peak response of ^{99m}Tc mertiatide

r_s' = sum of all peak responses

Acceptance criteria

^{99m}Tc pertechnetate: NMT 6.0%

^{99m}Tc mertiatide: NLT 90.0%

SPECIFIC TESTS

Add the following:

▲• **Appearance:** Clear, colorless solution, free from visible particulates▲ (USP 1-Dec-2024)

• **pH** ⟨791⟩**:** 5.0–6.0

Change to read:

• **Bacterial Endotoxins Test** ⟨85⟩**:** ▲Meets the requirements. The Injection may be distributed or dispensed prior to completion of the test.▲ (USP 1-Dec-2024)

Add the following:

▲• **Sterility Tests** ⟨71⟩**:** Meets the requirements. The Injection may be distributed or dispensed prior to completion of the test.▲ (USP 1-Dec-2024)

Delete the following:

▲• **Other Requirements**▲ (USP 1-Dec-2024)

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in single-dose or multiple-dose containers.

• **Labeling:** Label the Injection to include the following, in addition to the information specified under *Labeling* ⟨7⟩*, Labels and Labeling for Injectable Products*: the time and date of calibration; the amount of ^{99m}Tc as labeled mertiatide expressed as total megabecquerels (or millicuries) and the concentration as megabecquerels per milliliter (or as millicuries per milliliter) on the date and time of calibration; the expiration date and time; and the statement: [**Caution—**Radioactive Material]. The labeling indicates that, in making dosage calculations, correction is to be made for radioactive decay, and also indicates that the radioactive half-life of ^{99m}Tc is 6.0 h.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
TECHNETIUM TC 99M MERTIATIDE INJECTION	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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