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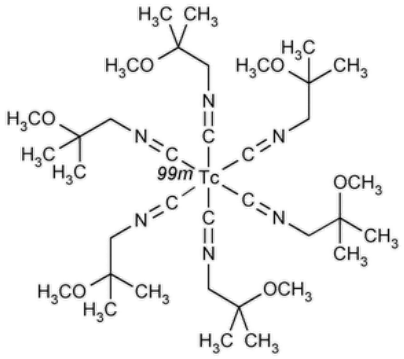
Technetium Tc 99m Sestamibi Injection



$C_{36}H_{66}N_6O_6{}^{99m}Tc$

Technetium(1+)-^{99m}Tc, hexakis(1-isocyano-2-methoxy-2-methylpropane)-, (*OC*-6-11)-;

Hexakis(2-methoxy-2-methylpropyl isocyanide)[^{99m}Tc]technetium(1+)

CAS RN®: 109581-73-9; UNII: 971Z4W1S09.

DEFINITION

Technetium Tc 99m Sestamibi Injection is a sterile, aqueous solution of tetrakis (2-methoxy-isobutyl isonitrile) copper (I) tetrafluoroborate that is labeled with radioactive technetium (^{99m}Tc) suitable for intravenous administration. It contains NLT 90% and NMT 110% of the labeled amount of ^{99m}Tc as a complex with sestamibi, expressed in megabecquerels (or in millicuries) per milliliter at the time indicated in the labeling. Other chemical forms of radioactivity are NMT 10% of the total radioactivity. It contains reducing agents, a buffer, and an inert filler.

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: Examine the radiochromatograms obtained in the test for *Radiochemical Purity, Procedure 2*.

Acceptance criteria: The distribution of the radioactivity contributes to the identification of the preparation.▲ (USP 1-Aug-2024)

ASSAY

• **Radioactive Concentration (Strength)**

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

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

Acceptance criteria: 90%–110% of the labeled amount of ^{99m}Tc at the 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 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

Sample solution: Constitute each of four vials with 1 mL (1875 ± 187.5 MBq, or 50 ± 5 mCi) of Sodium Pertechnetate Tc 99m Injection. Heat the vials in boiling water for 10 min. After heating, allow the vials to cool to room temperature for 15 min.

Chromatographic system

(See *Chromatography ⟨621⟩, General Procedures, Thin-Layer Chromatography*.)

Mode: TLC

Adsorbent: 25-mm × 7.75-cm reverse-phase chromatographic plate

Application volume: 1–2 µL of Injection

Developing solvent system: Acetonitrile, methanol, tetrahydrofuran, and 3.85% ammonium acetate (40:30:10:20). [NOTE—The *Developing solvent system* should be freshly prepared (NMT 4 h before use).]

Analysis: Apply the *Sample solution* about 1 cm from the bottom of the *Adsorbent*, and allow to dry. Position the plate in a chromatographic chamber and develop the chromatograms until the solvent front has moved 6 cm from the origin. Remove the plate and allow it to air-dry. Determine the radioactivity distribution by scanning the chromatogram with a suitable radiation detector.

Acceptance criteria: A mean of NLT 90% (area %) of the radioactivity is found at an R_F of 0.3–0.6. Free pertechnetate is located at an R_F of 0.8–1.0, and radio-colloid is located at an R_F of 0–0.1. The sum of the mean percentages of free pertechnetate and colloid is NMT 10%.

Procedure 2

Chromatographic system

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

Mode: LC

Mobile phase: Methanol, 0.05 M ammonium sulfate solution, and acetonitrile (45:35:20)

Detector: Gamma-ray detector

Column: 3.9-mm × 30-cm; 10-µm packing L1

Flow rate: 2 mL/min

Injection volume: About 5 µL (9.375 MBq or 250 µCi)

Retention times: ^{99m}Tc pentamibi dimethylvinyl isonitrile is 6–13 min; ^{99m}Tc sestamibi is 5–10 min

Analysis

[NOTE—If ^{99m}Tc pentamibi dimethylvinyl isonitrile is present, the relative retention between the ^{99m}Tc sestamibi peak and the ^{99m}Tc pentamibi dimethylvinyl isonitrile peak is 1.3 to 1.5.]

Inject Sodium Pertechnetate Tc 99m Injection into the chromatograph, and adjust the integrator/recording device so that the peak is 25%–100% of full scale. Separately inject equal volumes of the injection. Record the chromatograms, and measure the area percentage for all of the peaks present.

The retention time for ^{99m}Tc sestamibi is 5–10 min and the retention time for ^{99m}Tc pentamibi dimethylvinyl isonitrile is 6–13 min. Correct for the presence of colloid, which is not measured by this procedure, as follows:

$$C_f = [(100\%) - (A_c)]/100$$

C_f = correction factor

A_c = mean area percentage for the colloid obtained from the *Radiochemical Purity, Procedure 1* test

Obtain the corrected area percentage by multiplying the correction factor (C_f) by the area percentage of the peaks present in the chromatogram.

Acceptance criteria: A mean of NLT 90% (corrected area percentage) of the total radioactivity is represented by ^{99m}Tc sestamibi, and a mean of NMT 5% (corrected area percentage) of the total radioactivity is present as ^{99m}Tc pentamibi dimethylvinyl isonitrile.

SPECIFIC TESTS

Add the following:

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

Delete the following:

▲• **OTHER REQUIREMENTS**▲ (USP 1-AUG-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 constitution; the volume of constitution; the amount of ^{99m}Tc as labeled sestamibi expressed as total begabecquerels (or millicuries) per milliliter at the time of constitution; the expiration date and time; the lot number; 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 SESTAMIBI 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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