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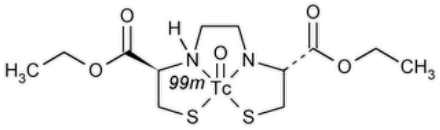
Technetium Tc 99m Bicisate Injection



DEFINITION

Technetium Tc 99m Bicisate Injection is a sterile, clear, colorless solution, suitable for intravenous administration, of bicisate dihydrochloride complexed to radioactive technetium (^{99m}Tc). It contains NLT 90.0% and NMT 110.0% of the labeled amount of ^{99m}Tc as a complex with bicisate, 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.

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**

Acceptance criteria: The retardation factors of the spots for Tc 99m bicisate and/or Tc(IV) 99m bicisate in the chromatogram of the *Sample* correspond with the ranges stated in the test for *Radiochemical Impurities*.▲ (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 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.

Change to read:

• **Radiochemical Purity**

Sample solution: Prepare four vials of Injection and perform the test on each vial.

Chromatographic system

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

Mode: TLC

Adsorbent: 2.5-cm × 7.5-cm chromatographic silica gel sheet

Application volume: About 5 µL

Developing solvent system: Ethyl acetate

Analysis

Sample: ▲The *Sample solution* used to perform this test is also used to perform the test for *Radiochemical Impurities*. Perform the tests in parallel with a minimal delay in spotting of the chromatographic media following the 30-min Injection incubation period.▲ (USP 1-Dec-2024)

Place the *Sample solution* about 2 cm from the bottom of the *Adsorbent* and allow to dry for 5–10 min. Position the plate in a pre-equilibrated chromatographic chamber containing the *Developing solvent system*, and develop the chromatogram until the solvent front has moved 5 cm from the origin. Remove the plate from the chamber, and allow to dry. Cut the chromatographic sheet 4.5 cm from the

bottom. Separately count the activity on each piece in a dose calibrator or a gamma counter. The activity on the upper portion contains the ^{99m}Tc bicisate complex, and the activity on the lower section contains all radioimpurities.

Calculate the percentage of radiochemical purity of the Injection taken:

$$\text{Result} = 100P/(P + C)$$

P = count from the top part of the sheet

C = count from the bottom part of the sheet

Acceptance criteria: NLT 90% of the total radioactivity is found as Tc^{99m} bicisate. Calculate the mean percentage of radiochemical purity of the four test vials.

IMPURITIES

Change to read:

• **Radiochemical Impurities**

▲▲ (USP 1-Dec-2024)

Chromatographic system

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

Mode: TLC

Adsorbent: 2.5-cm × 7.5-cm reverse-phase thin-layer chromatographic plate (or equivalent)

Developing solvent system: Acetone and 0.5 M ammonium acetate (60:40)

Application volume: About 2 µL

Analysis

Sample: *Sample solution* used to perform the test for *Radiochemical Purity*. Perform the tests in parallel with a minimal delay in spotting of the chromatographic media following the 30-min Injection incubation period.

Apply the *Sample* 1 cm from the bottom of the *Adsorbent*, and allow the spot to air-dry thoroughly. Develop the chromatogram until the solvent front has moved 7 cm from the origin. Remove the plate from the chamber and air-dry. Using a suitable calibrated scanner, determine the compounds present by calculating the retention factors for all peaks present. Compounds and approximate R_F values are shown in *Table 3*.

Table 3

Compound	Approximate R_F Value
^{99m}Tc bicisate	0.15–0.44
^{99m}Tc(IV) bicisate	0.3–0.4
^{99m}Tc bicisate and ^{99m}Tc(IV) bicisate	0.15–0.44
Hydrolyzed reduced Tc	0.00–0.14
Free pertechnetate and ^{99m}Tc ethylene cisteinate monomer	0.70–0.84
^{99m}Tc EDTA	0.95–1.0

Calculate the quantity of ^{99m}Tc(IV) ligand in the Injection by subtracting the ^{99m}Tc bicisate percentage obtained in the test for *Radiochemical Purity* from the combined ^{99m}Tc bicisate and ^{99m}Tc(IV) bicisate area percentage obtained in the test for *Radiochemical Impurities*.

Acceptance criteria: The sum of the impurities is NMT 10%.

SPECIFIC TESTS

Add the following:

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

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, at controlled room temperature.

• **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 bicisate expressed as total megabecquerels (or millicuries) per milliliter at the time of calibration; 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 BICISATE INJECTION	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

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