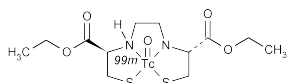


**Other requirements**—It meets the requirements for *Radionuclide identification* and *Radionuclidic purity* under *Sodium Pertechnetate Tc 99m Injection*. It meets also the requirements under *Injections* (1), except that it may be distributed or dispensed prior to completion of the test for *Sterility*, the latter test being started on the date of manufacture.

**Assay for radioactivity** (821)—Using a suitable counting assembly (see *Selection of a Counting Assembly*), determine the radioactivity, in MBq (or mCi) per mL, of Injection by use of a calibrated system.

## Technetium Tc 99m Bicisate Injection



» Technetium Tc 99m Bicisate Injection is a sterile, clear, colorless solution, suitable for intravenous administration, of bicisate dihydrochloride complexed to radioactive technetium ( $^{99m}\text{Tc}$ ). It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of  $^{99m}\text{Tc}$  as a complex with bicisate, expressed in megabecquerels (or in millicuries) per mL at the time indicated in the labeling. Other chemical forms of radioactivity do not exceed 10 percent of the total radioactivity.

**Packaging and storage**—Preserve in single-dose or multiple-dose containers, at controlled room temperature.

**Labeling**—Label it to include the following, in addition to the information specified for *Labeling* under *Injections* (1): the time and date of calibration; the amount of  $^{99m}\text{Tc}$  as labeled bicisate expressed as total megabecquerels (or millicuries) per mL 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  $^{99m}\text{Tc}$  is 6.0 hours.

**USP Reference standards** (11)—

USP Endotoxin RS

**Bacterial endotoxins** (85)—It contains not more than 175/ $V$  USP Endotoxin Units per mL, in which  $V$  is the maximum recommended total dose, in mL, at the expiration date or time.

**Radiochemical purity**—Prepare four vials of Injection and perform the test on each vial. Apply about 5  $\mu\text{L}$  of Injection 2 cm from the bottom of a 2.5-cm  $\times$  7.5-cm thin-layer chromatographic silica gel sheet. Allow the spot to dry for 5 to 10 minutes. Position the plate in a pre-equilibrated chromatographic chamber containing HPLC grade ethyl acetate, and develop the chromatogram until the solvent front has moved 5 cm from the origin (see *Chromatography* (621)). 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  $^{99m}\text{Tc}$  bicisate complex, and the activity on the lower section contains all radioimpurities. Calculate the percentage of radiochemical purity of the  $^{99m}\text{Tc}$  Bicisate Injection by the formula:

$$100P/(P + C)$$

in which  $P$  is the count from the top part of the plate, and  $C$  is the count from the bottom part of the plate: not less than 90% of the total radioactivity is found as  $\text{Tc}^{99m}$  bicisate. Calculate the mean percent radiochemical purity of the four test vials.

**Related radiochemical compounds**—[NOTE—This test is performed on the same test specimen used to perform the *Radiochemical purity* test. Perform the tests in parallel with a minimal delay in spotting of the chromatographic media following the 30-minute Injection incubation period.] Apply about 2  $\mu\text{L}$  of the Injection 1 cm from the bottom of a 2.5-cm  $\times$  7.5-cm reverse-phase thin-layer chromatographic plate (or equivalent), and allow the spot to air-dry thoroughly. Place the plate into a developing tank containing a mixture of acetone and 0.5 M ammonium acetate (60:40), develop to 7 cm, remove the plate, and air-dry (see *Chromatography* (621)). 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 as follows:

$^{99m}\text{Tc}$ bicisate	0.15-0.44
$^{99m}\text{Tc(IV)}$ bicisate	0.3-0.4
Tc $^{99m}$ Bicisate and Tc $^{99m(IV)}$ Bicisate	0.15-0.44
Hydrolyzed reduced Tc	0.00-0.14
Free pertechnetate and $^{99m}\text{Tc}$ ethylene cysteinate monomer	0.70-0.84
$^{99m}\text{Tc}$ EDTA	0.95-1.0

Calculate the quantity of  $^{99m}\text{Tc(IV)}$  ligand in the Injection by subtracting the Tc 99m Bicisate percentage obtained in the test for *Radiochemical purity* from the combined  $^{99m}\text{Tc}$  Bicisate and  $^{99m}\text{Tc(IV)}$  Bicisate Area percentage obtained in the *Related radiochemical compounds* test. The sum of the impurities is not greater than 10%.

**Other requirements**—It meets the requirements of the tests for *Radionuclide identification* and *Radionuclidic purity* under *Sodium Pertechnetate Tc 99m Injection*. It meets also the requirements for *Injections* (1), except that the Injection may be distributed or dispensed prior to the completion of the test for *Sterility*, the latter test being started on the day of manufacture.

**Assay for radioactivity** (821)—Using a suitable counting assembly (see *Selection of a Counting Assembly*), determine the radioactivity, in MBq (or in mCi) per mL, of the Injection by use of a calibrated system.

## Technetium Tc 99m Depreotide Injection

» Technetium Tc 99m Depreotide Injection is a sterile, aqueous solution suitable for intravenous injection that contains  $^{99m}\text{Tc}$  in the form of a depreotide complex. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of  $^{99m}\text{Tc}$  as the depreotide complex expressed in megabecquerels (or in millicuries) per mL at the time indicated in the labeling. It may contain reducing agents, stabilizing agents, and buffers. It contains no antimicrobial agents. Other chemical forms of radioactivity do not exceed 10.0 percent of the total radioactivity.

**Packaging and storage**—Preserve in single-dose containers, at controlled room temperature.

**Labeling**—Label it to include the following, in addition to the information specified for *Labeling* under *Injections* (1): the time and date of calibration; the amount of  $^{99m}\text{Tc}$  as labeled depreotide complex expressed as total MBq (or mCi) per mL at the time of calibration; the expiration date and time; the storage temperature; 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  $^{99m}\text{Tc}$  is 6.0 hours.

**USP Reference standards** (11)—  
USP Endotoxin RS

**Bacterial endotoxins** (85): not more than 175/V USP Endotoxin Unit per mL of the Injection, in which *V* is the maximum recommended total dose, in mL, at the expiration date or time.

**pH** (791): between 6.0 and 8.0.

**Radiochemical purity**—Separately apply equal volumes (about 10  $\mu\text{L}$ ) of Injection, accurately measured, about 1.0 cm from the bottom of each of two 1.5-cm  $\times$  10-cm instant chromatographic silica gel strips. Do not allow the plates to dry. Immediately develop the chromatograms by ascending chromatography (see *Chromatography* (621)), until the solvents reach the top of the strips, using saturated sodium chloride solution as the developing solvent for one strip (*Strip 1*), and a mixture of methanol and 1 M ammonium acetate (1:1) for the other strip (*Strip 2*). Remove the strips, and allow to air-dry. Cut *Strip 1* at an  $R_f$  value of about 0.75, and cut *Strip 2* at an  $R_f$  value of about 0.40. Separately record the counts for each portion in a dose calibrator. Calculate the percentage of nonmobile impurities in the portion of Injection taken by the formula:

$$100C_M / (C_M + P_M)$$

in which  $C_M$  is the count obtained from the bottom portion of *Strip 2*; and  $P_M$  is the count obtained from the top portion of *Strip 2*. Calculate the percentage of Tc 99m pertechnetate, Tc 99m glucoheptonate, and Tc 99m edetate in the portion of Injection taken by the formula:

$$100P_S / (C_S + P_S)$$

in which  $P_S$  is the count obtained from the top portion of *Strip 1*; and  $C_S$  is the count obtained from the bottom portion of *Strip 1*: not more than 10% of total impurities is found.

**Other requirements**—It meets the requirements for *Radionuclide identification* and *Radionuclidic purity* under *Sodium Pertechnetate Tc 99m Injection*. It also meets the requirements under *Injections* (1), except that the Injection is not subject to the recommendation on *Volume in Container*, and except that it may be distributed or dispensed prior to completion of the test for *Sterility*, the latter test being started on the date of manufacture.

**Assay for radioactivity** (821)—Using a suitable counting assembly, determine the radioactivity, in MBq (or mCi) per mL, of Injection by use of a calibrated system.

## Technetium Tc 99m Disofenin Injection

» Technetium Tc 99m Disofenin Injection is a sterile, aqueous solution, suitable for intravenous administration, of disofenin that is labeled with  $^{99m}\text{Tc}$ . It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of  $^{99m}\text{Tc}$  as a disofenin complex, expressed in megabecquerels (microcuries or millicuries) per mL at the time indicated on the labeling. It contains a suitable reducing agent.

**Packaging and storage**—Preserve in single-dose or in multiple-dose containers sealed under a suitable inert atmosphere.

**Labeling**—Label it to include the following, in addition to the information specified for *Labeling* under *Injections* (1): the time and date of preparation; the amount of  $^{99m}\text{Tc}$  as expressed as total megabecquerels (microcuries or millicuries) and concentration as megabecquerels (microcuries or millicuries) per mL at

the time of preparation; the expiration date and time; and a 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  $^{99m}\text{Tc}$  is 6.0 hours.

**pH** (791): between 4.0 and 5.0.

**Radiochemical purity**—The determination of radiochemical purity for this Injection requires the use of two separate chromatography systems.

**System A**—Apply a measured volume of Injection, appropriately diluted, such that it provides a count rate of about 20,000 counts per minute, about 13 mm from one end of a 10-  $\times$  51-mm thin-layer chromatographic strip impregnated with silica gel (see *Chromatography* (621)), and immediately develop the chromatogram over a suitable period by ascending chromatography, using methanol as the solvent. Allow the chromatogram to dry. Cut the chromatogram in two along a line about 13 mm from the top. Place the top and bottom strips into separate counting containers. Determine the radioactivity of each, using a suitable ionization chamber. Hydrolyzed Tc 99m and technetium-tin colloid are located at the origin of the bottom strip ( $R_f$  0 to 0.1).

**System B**—Pretreat a 1.3-  $\times$  51-mm strip of chromatographic paper by soaking it for 1 minute in a 0.3 M carbonate-bicarbonate buffer, pH 9.0, prepared by dissolving 0.3 g of anhydrous sodium carbonate and 1.9 g of anhydrous sodium bicarbonate in 100 mL of water. Remove the paper strip, blot lightly with absorbent paper, and dry in an oven for about 45 minutes at 85°. Proceed as directed for *System A* using the pretreated chromatographic paper and a developing solvent of methyl ethyl ketone. Free pertechnetate is located at the solvent front (top strip). The sum of the percentage of radioactivity at the origin in *System A* and the percentage of radioactivity at the solvent front in *System B* is not greater than 10.0%.

**Biological distribution**—Inject between 75 MBq and 111 MBq (2 mCi and 3 mCi) of Injection, in a volume not exceeding 0.1 mL, into the caudal vein of each of three 25- to 40-g male albino mice. One hour after the injection, anesthetize and then decapitate the animals. Drain the blood of each separately into pre-weighed counting containers. Dissect the animals, and place the kidneys, liver, stomach (exclusive of duodenum), and gallbladder, and intestines, of each mouse into separate counting containers. Using a suitable counting assembly, determine the radioactivity of each container. Correct all radioactivity measurements for decay. Determine the percentage of radioactivity in the kidneys, liver, stomach, and gallbladder and intestines taken by the formula:

$$100(A / B)$$

in which *A* is the radioactivity, in counts per minute, in the organ, and *B* is the total radioactivity, in counts per minute, injected. Determine the percentage of radioactivity in the blood taken by the formula:

$$[100(C / W_S)0.07(W_R)] / B$$

in which *C* is the radioactivity, in counts per minute, in the specimen of blood,  $W_S$  is the weight, in g, of the blood specimen, 0.07 is the assumption that the total blood weight of the mouse is 7% of the total body weight, and  $W_R$  is the weight, in g, of the mouse. Not less than 70% of the injected radioactivity is present in the gallbladder and intestines, not more than 10.0% of the injected radioactivity is present in the liver, not more than 10.0% of the injected radioactivity is present in the kidneys, not more than 3.0% of the injected radioactivity is present in the stomach, and not more than 3.0% of the injected radioactivity is present in the blood, in not less than two mice.

**Other requirements**—It meets the requirements of the tests for *Radionuclide identification*, *Radionuclidic purity*, and *Bacterial endotoxins* under *Sodium Pertechnetate Tc 99m Injection*. It also meets the requirements under *Injections* (1), except that it may be distributed or dispensed prior to completion of the test for