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Technetium Tc 99m Mebrofenin Injection

» Technetium Tc 99m Mebrofenin Injection is a sterile aqueous solution of Stannous Fluoride and Mebrofenin labeled with radioactive technetium Tc 99m suitable for intravenous administration. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of ^{99m}Tc, as the complex with mebrofenin, expressed in megabecquerels (or in millicuries) per mL at the time indicated in the labeling. It may contain antimicrobial agents and buffers. Other chemical forms of radioactivity do not exceed 10.0 percent of the total radioactivity.

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

Labeling—Label it to include the following, in addition to the information specified for *Labeling ⟨7⟩, Labels and Labeling for Injectable Products*: the time and date of calibration; the amount of ^{99m}Tc as labeled mebrofenin expressed as total megabecquerels (or millicuries) and the concentration as megabecquerels per mL (or as millicuries per mL) 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 hours.

pH ⟨791⟩**:** between 4.2 and 5.7.

Radiochemical purity—[Note—The determination of radiochemical purity for this product requires the use of two separate chromatographic methods.]

Method 1—

pH 6.8 phosphate buffer—Mix 64 mL of 0.2 M monobasic sodium phosphate and 61 mL of 0.1 M dibasic sodium phosphate in a 1-liter volumetric flask, dilute with water to volume, and mix.

Mobile phase—Prepare a filtered and degassed mixture of methanol and *pH 6.8 phosphate buffer* (625:375). Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 3.9-mm × 30-cm column that contains 10-µm packing L1. It is also equipped with a flow-through gamma ray detector having a cell volume of about 10 µL. A constant flow rate of about 1 mL per minute is maintained, and counts are recorded and charted at about 5-second intervals.

Procedure—Constitute the Injection, and allow to stand for 15 minutes. Chromatograph a volume of Injection, with activity of 0.6 to 15 MBq (16 to 400 µCi), and record the chromatogram. The resolution between the secondary characteristic peak, eluting at about 3.5 minutes, and the principal peak, eluting at about 6 minutes, is not less than 1.5. The time interval between the elution of the Tc 99m pertechnetate peak, at about 2 minutes, and the principal peak is not less than 3.0 minutes. If the foregoing criteria are met, record the counts for the pertechnetate Tc 99m peak, the two complex peaks, a representative baseline segment, and the total counts for the chromatogram. Calculate the percentage of complexed radioactivity in the two characteristic peaks taken by the formula:

$$100C/(T - P)$$

in which C is the count of the complex peak of interest, T is the total count, and P is the pertechnetate peak count, each being corrected for the corresponding baseline count. The complexed radioactivity is not less than 90.0% in the principal peak and between 1% and 6% in the second characteristic peak. Calculate the percentage of all other complexed radioactivity (this excludes the main, secondary, and free pertechnetate peaks) taken by the formula:

$$100K/(T - P)$$

in which K is the sum of all other peaks, and T and P are as defined above. Record the result for use in the calculation as directed under *Method 2*.

Method 2—

Chromatographic system A (see *Chromatography ⟨621⟩*)—Prepare a 1.0- × 12.5-cm silicic acid-impregnated glass microfiber strip by dipping it in a 10% sodium chloride solution and removing the excess liquid by blotting. Dry the strip by heating in an oven at about 80°. Apply about 5 µL of the Injection with activity of about 3.7 MBq (100 µCi) about 1.5 cm from one end of the strip, and immediately develop the chromatogram in a chromatographic chamber containing saturated sodium chloride solution until the solvent front reaches a level about 1 cm from the top of the strip. Remove the strip from the chamber, and allow to air-dry. Separate the top and bottom portions of the

chromatogram by cutting the strip in half, and record the counts separately for each portion. Calculate the percentage of unreduced pertechnetate taken by the formula:

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

in which P is the count from the top half of the strip, and C is the count from the bottom half of the strip.

CHROMATOGRAPHIC SYSTEM B—Proceed as directed under *Chromatographic system A* except to use a 1.0- × 12.5-cm silica gel-impregnated glass microfiber strip, without preliminary treatment, and a mixture of acetonitrile and water (3:1) as the developing solvent. Calculate the percentage of reduced hydrolyzed Tc 99m taken by the formula:

$$100R/(R + D)$$

in which R is the count from the bottom half of the strip, and D is the count from the top half of the strip. The sum of the percentage of unreduced pertechnetate from *System A*, the percentage of reduced hydrolyzed Tc 99m from *System B*, and the percentage of other complexed radioactivity determined from *Method 1* is not greater than 10.0%.

Biological distribution—Inject 0.25 mL of Injection containing between 15 and 19 MBq (0.4 and 0.5 mCi) into the external jugular vein of each of three anesthetized male rats weighing between 150 and 350 g, and from which food has been withheld for 15 to 24 hours prior to the test. Thirty minutes after the injection, sacrifice the animals and carefully remove the liver, kidneys, and gastrointestinal tract of each rat. Place the organs in separate counting containers. Using a suitable counting assembly, determine the radioactivity in each container. Correct radioactivity measurements for decay. Determine the percentages of radioactivity in the liver, kidneys, and gastrointestinal tract taken by the formula:

$$100(A/B)$$

in which A is the radioactivity, in counts per minute, in the organ, and B is the average injected radioactivity, in counts per minute, in the corresponding standards. Not less than 75% of the injected radioactivity is found in the gastrointestinal tract, not more than 10% in the liver, and not more than 5% in the kidneys in not less than 2 of the rats.

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 for *Injections and Implanted Drug Products* ⟨1⟩, except that it may be distributed and dispensed prior to the completion of the test for *Sterility*, the latter being started on the day of manufacture, and except that it is not subject to the recommendation on *Container Content*.

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

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

Topic/Question	Contact	Expert Committee
TECHNETIUM TC 99M MEBROFENIN 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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