Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-May-2018
Document Type: USP Monographs
DocId: GUID-00B6E976-0B68-4FC1-8430-70004DA94A3E_3_en-US
DOI: https://doi.org/10.31003/USPNF_M80625_03_01
DOI Ref: m8289

Technetium Tc 99m Exametazime Injection

2-Butanone, 3,3'-[(2,2-dimethyl-1,3-propanediyl)diimino]bis-dioxime-^{99m}Tc.

d,1-Hexamethylpropylene amine oxime-^{99m}Tc

CAS RN®: 105613-48-7.

» Technetium Tc 99m Exametazime Injection is a sterile, aqueous solution, suitable for intravenous administration, composed of the primary lipophilic complex of exametazime that is labeled with radioactive ^{99m}Tc. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of ^{99m}Tc as primary lipophilic exametazime complex expressed in megabecquerels (or in microcuries or millicuries) per mL at the date and time indicated in the labeling. It may contain antioxidants, reducing agents, and buffers. A stabilizing solution containing methylene blue and phosphate buffer may be added to the final radio labeled product to extend the expiration time. Other chemical forms of radioactivity (^{99m}Tc pertechnetate, ^{99m}Tc hydrolyzed reduced species, and ^{99m}Tc secondary exametazime complex) do not exceed 20.0 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 ⟨7⟩, Labels and Labeling for Injectable Products*: the time and date of calibration; the amount of ^{99m}Tc as labeled exametazime expressed as total megabecquerels (or as total microcuries or millicuries) and concentration as megabecquerels (or as microcuries or millicuries) per mL at the time of calibration; 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}Tc is 6.0 hours. [Note—The label states that, upon constitution with Sodium Pertechnetate Tc 99m Injection, the beyond-use time is 30 minutes for the unstabilized Injection and between 4 hours and 6 hours for the stabilized Injection.]

pH ⟨791⟩: between 9.0 and 9.8 for unstabilized Injection, and between 6.5 and 7.5 for stabilized Injection.

Radiochemical purity—Prepare three 12- × 75-mm chromatographic tubes by packing with about 0.3 mL of fresh methyl ethyl ketone, 0.9% nonbacteriostatic sodium chloride solution, and a 50% acetonitrile solution, prepared with nonbacteriostatic water, respectively. To each of two 6- × 0.7-cm instant thin-layer chromatographic strips[1] and one 6- × 0.7-cm strip of chromatographic paper,[2] apply 5 µL of freshly prepared (within 2 minutes of reconstitution) Injection about 1 cm from the bottom of the strip. Do not allow to dry. Place one instant thin-layer chromatographic strip into the tube containing methyl ethyl ketone, the second instant thin-layer chromatographic strip into the tube containing the 0.9% sodium chloride solution, and the paper strip into the tube containing the 50% acetonitrile solution. The strips must not adhere to the sides of the tubes. Allow the chromatograms to develop until the solvent front has moved to the top of the strips. Remove the strips from the tubes, and allow the solvents to evaporate. Determine the radioactive distribution by scanning the strip sections, using a suitable collimated radiation detector. The difference between the radioactivity detected at the origin of the 0.9% sodium chloride strip and at the origin of the methyl ethyl ketone strip represents the primary lipophilic ^{99m}Tc exametazime complex. The radioactivity at the solvent front of the 0.9% sodium chloride strip represents the ^{99m}Tc pertechnetate radiochemical impurity. The radioactivity at the origin of the 50% acetonitrile strip represents the ^{99m}Tc hydrolyzed, reduced radiochemical impurity. The difference between the radioactivity detected at the origin of the methyl ethyl ketone strip and the origin of the 50% acetonitrile strip represents the secondary ^{99m}Tc exametazime complex radiochemical impurity. Not less than 80% of the total radioactivity is found as primary lipophilic ^{99m}Tc exametazime complex. [Note—Complete the measurement within 30 minutes after constitution of the unstabilized Injection and between 4 hours and 6 hours after constitution of the stabilized Injection.]

Biological distribution—Inject between 18.5 MBq and 37 MBq (between 0.5 mCi and 1 mCi) of Injection in a volume not exceeding 0.1 mL into the caudal vein of each of three 130- to 190-g Sprague-Dawley rats. Five to ten minutes after the injection, sacrifice the animals and carefully remove the brain, liver, and intestines (including gall bladder). Place each organ and the remaining carcass in separate, suitable counting containers, and determine the radioactivity, in counts per minute, in each container with an appropriate detector, using the same counting geometry. Determine the percentage of radioactivity in the brain, liver, intestines, and remaining carcass by the formula:

$$100(A/B)$$

in which *A* is the net radioactivity, in counts per minute, in the organ, and *B* is the total radioactivity, in counts per minute in the brain, liver, intestines, and carcass. Not less than 1.5% of the radioactivity is found in the brain. Not more than 20% of the radioactivity is found in the intestines, and not more than 15% of the radioactivity is found in the liver, in not less than two of the animals.

Other requirements—It meets the requirements of the tests for *Radionuclidic identification* and *Radionuclide purity* and *Bacterial endotoxins* under *Sodium Pertechnetate Tc 99m Injection*. It meets also the requirements under *Injections and Implanted Drug Products* ⟨1⟩, except that it may be distributed or dispensed prior to completion of the test for *Sterility*, the latter test 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 µCi) per mL, of Injection by use of a calibrated system.

[1] ITLC/SG, 6- × 0.7-cm strip available from Biodex Medical Systems, Shirley, NY.

[2] Whatman Grade 31ET Chr, available from Whatman LabSales, Hillsboro, OR.

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

Topic/Question	Contact	Expert Committee
TECHNETIUM TC 99M EXAMETAZIME 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

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 49(1)

Current DocID: GUID-00B6E976-0B68-4FC1-8430-70004DA94A3E_3_en-US
Previous DocID: GUID-00B6E976-0B68-4FC1-8430-70004DA94A3E_1_en-US
DOI: https://doi.org/10.31003/USPNF_M80625_03_01
DOI ref: m8289