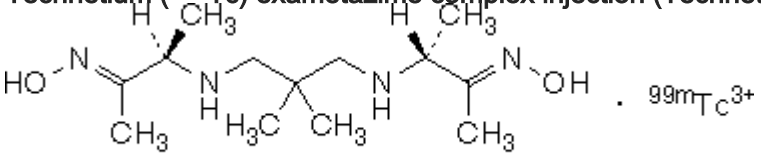
Technetium (^{99m}Tc) exametazime complex injection (Technetii (^{99m}Tc) exametazimi multiplex injectio)



and enantiomer

$C_{13}H_{28}N_4O_2.^{99m}Tc$

Chemical name. *rac-N,N'*-bis[(1*R*,2*E*)-2-(Hydroxyimino)-1-methylpropyl]-2,2-dimethylpropane-1,3-diamine complex with [^{99m}Tc]technetium(III).

Other names. (^{99m}Tc)-D,L-Hexamethylpropyleneamine oxime complex injection; (^{99m}Tc)-D,L-HMPAO injection.

Description. Technetium (^{99m}Tc) exametazime complex injection is a clear, colourless aqueous solution.

Technetium-99m has a half-life of 6.02 hours.

Category. Diagnostic.

Storage. Technetium (^{99m}Tc) exametazime complex injection should be kept at a temperature between 2°C to 8°C.

Technetium (^{99m}Tc) exametazime complex injection should be used within 30 minutes of reconstitution of the unlabelled kit with Technetium-99m, unless the preparation has been stabilized with either cobalt chloride solution or methylene blue solution.

Additional information. Wherever V is used within the tests of this monograph, V is the maximum recommended dose in millilitres.

Requirements

Complies with the monograph for "Parenteral Preparations" and with that for "Radiopharmaceuticals".

Definition. Technetium (^{99m}Tc) exametazime injection is a sterile solution of *rac-N,N'*-bis[(1*R*,2*E*)-2-(hydroxyimino)-1-methylpropyl]-2,2-dimethylpropane-1,3-diamine (exametazime) complexed with technetium-99m. The injection is suitable for intravenous administration and contains sufficient sodium chloride to make the solution isotonic with blood. The content of technetium-99m is not less than 90% and not more than 110% of the content of technetium-99m stated on the label at the reference date and time stated on the label. Not less than 80% of the total technetium-99m radioactivity is present as lipophilic (^{99m}Tc) exametazime complex. The injection contains a variable quantity of tin (Sn) not more than 0.6 µg/mL.

Manufacture

Radionuclide production. Technetium-99m is a radioactive nuclide formed by the radioactive decay of molybdenum-99. Molybdenum-99 is a radioactive isotope of molybdenum and may be produced by neutron irradiation of natural molybdenum or of molybdenum enriched in molybdenum-98 or it may be produced by uranium fission.

Production of radiopharmaceutical preparation. Technetium (^{99m}Tc) exametazime injection is prepared aseptically from sterile starting materials such as a sterile kit containing a mixture of *rac-N,N'*-bis[(1*R*,2*E*)-2-(hydroxyimino)-1-methylpropyl]-2,2-dimethylpropane-1,3-diamine and stannous salt with sodium pertechnetate (^{99m}Tc) injection (fission or non-fission). The injection may have the pH adjusted and may contain stabilizing agents. The injection may also be prepared under aseptic processing combined with sterilization by Filtration (see 5.8 Methods of sterilization).

Identity tests

• Either tests A and C or tests B and C may be applied.

A. Record the gamma-ray spectrum using a suitable instrument with a sample of technetium-99m, suitably diluted if needed. The spectrum is concordant with the *reference spectrum* of a specimen of technetium-99m in that it exhibits a major peak of 140 keV.

Standardized technetium-99m solutions are available from laboratories recognized by the relevant national or regional authority.

B. The half-life determined using a suitable detector system is between 5.72 and 6.32 hours.

C. Examine the radiochromatograms obtained in the test for Radiochemical purity. The distribution of the radioactivity contributes to the identification of the preparation.

pH value. Carry out the test as described under the monograph for "Radiopharmaceuticals". pH of the injection, Between 5.0 to 10.0.

Sterility. The injection complies with 3.2 Test for sterility, modified as described in the monograph for “Radiopharmaceuticals”. Test for sterility will be initiated on the day of manufacture. The injection may be released for use before completion of the test.

Bacterial endotoxins. Carry out the test as described under 3.4 Test for bacterial endotoxins, modified as described in the monograph for “Radiopharmaceuticals”. The injection contains not more than 175/V I.U of endotoxins per millilitre. The injection may be released for use before completion of the test.

Radionuclidic purity. Record the gamma-ray spectrum using a suitable instrument and measure the half-life using a suitable method. Determine the relative amounts of technetium-99m and radionuclidic impurities that may be present.

Radiochemical purity. Carry out three separate tests as described under 1.14.2 Paper chromatography and ascending conditions. Use suitable cellulose paper strips and methyl ethyl ketone R (system A) or sodium chloride (9 g/l) TS (system B) as the mobile phases. Use suitable silica gel impregnated glass fiber paper strips and a mixture of equal volumes of acetonitrile R and water R as the mobile phase (system C). Apply to the paper about 5 µl of the injection to be examined, suitably diluted to give an optimum count rate and develop for a distance of about 15 cm. Allow the paper to dry in air and determine the radioactivity distribution by a suitable method. In system (A), the secondary exametazime complex and reduced hydrolysed technetium-99m have an Rf value of 0, and the lipophilic exametazime complex and the pertechnetate ion have an Rf value of 0.8 to 1.0. In system (B), reduced hydrolysed technetium-99m has an Rf value of 0, and the lipophilic exametazime complex, the secondary exametazime complex and the pertechnetate ion have an Rf value of 0.8 to 1.0. In system (C), the pertechnetate ion has an Rf value of 0.8 to 1.0, and the lipophilic exametazime complex, the secondary exametazime complex and reduced hydrolysed technetium-99m have an Rf value of 0. The sum of the percentages of radioactivity corresponding to the pertechnetate ion in system (C) and reduced hydrolysed technetium-99m in system (B) is less than 10%. Not less than 80% of the total technetium-99m radioactivity is present as lipophilic exametazine complex.

Chemical purity

> **Tin.** Carry out the test as described under R2.1.4 Tin estimation by UV absorption, using 1.0 mL of a test solution prepared by diluting 1.5 mL of the injection to be examined to 25.0 mL with hydrochloric acid (1 mol/l) VS and mixing thoroughly. Prepare the reference solution by dissolving 0.115 g of stannous chloride R in hydrochloric acid (1 mol/l) VS, diluting to 1000 mL with the same solvent and mixing thoroughly. The absorbance of the test solution is not greater than that of the reference solution; not more than 0.6 µg of Sn per mL.

Radioactivity. Measure the radioactivity as described under R.1.1 Detection and measurement of radioactivity in a suitable calibrated counting equipment by comparison with a standardized technetium-99m solution or by measurement in an instrument calibrated with the aid of such a solution (a good approximation may be obtained using an ionization chamber and employing a standardized solution of cobalt-57 provided that correction for the differences in the radiations emitted are made).

Standardized technetium-99m and cobalt-57 solutions are available from laboratories recognized by the relevant national or regional authority.

Biodistribution. Carry out the test as described under R3.1 Biological distribution using a set of three mice. At 5 to10 minutes post injection not less than 1.5% of the injected radioactivity should be found in the brain and not more than 20% of the injected radioactivity should be found in the intestine. Not more than 15% of the injected radioactivity should be found in the liver.