Sodium pertechnetate (^{99m}Tc) injection (fission) (Natrii pertechnetatis (^{99m}Tc) fissione formati injectio)

This monograph applies to sodium pertechnetate (^{99m}Tc) injection obtained from generators containing molybdenum-99 (99Mo) extracted from fission products of uranium.

$Na^{99m}TcO_4$

Description. Sodium pertechnetate (^{99m}Tc) injection (fission) is a clear, colourless solution.

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

Category. Diagnostic.

Labelling. Label must state that the injection has been prepared from molybdenum-99 produced from uranium fission. Level of molybdenum-99 per vial may be required.

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. Sodium pertechnetate (^{99m}Tc) injection (fission) is a sterile solution of technetium-99m in the form of pertechnetate ion, suitable for intravenous administration and that contains sufficient sodium chloride to make the solution isotonic with blood. The injection contains 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 95% of the total technetium-99m radioactivity is present as pertechnetate ion.

The radioactivity due to radionuclides other than technetium-99m, apart from that due to technetium-99 resulting from the decay of technetium-99m, is not greater than that shown below, expressed as a percentage of the total radioactivity:

molybdenum-99	10^{-1}
iodine-131	$5x10^{-3}$
ruthenium-103	$5x10^{-3}$
strontium-89	$6x10^{-5}$
strontium-90	$6x10^{-6}$
alpha-emitting impurities	$1x10^{-7}$
other impurities	$1x10^{-2}$

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 produced by uranium fission.

Production of radiopharmaceutical preparation. Molybdenum-99 is normally loaded into an ion-exchange column which allows separation of technetium-99m from parent molybdenum-99 using a suitable generator system. The columns of molybdenum-99 may be sterilized by "Heating in an autoclave" (see 5.8 Methods of sterilization) and a sterile solution may be used to elute under aseptic conditions. 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, molybdenum-99, iodine-131, ruthenium-103, strontium-89 and strontium-90 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 radiochromatogram 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 in the monograph for "Radiopharmaceuticals". pH of the injection, 4.5 to 7.5.

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.

Molybdenum-99. Record the gamma-ray spectrum using a suitable instrument and measure the half-life using a suitable method. Molybdenum-99 exhibits major peaks of 181, 740 and 778 keV and a half-life of 66.2 hours. Determine the relative amount of molybdenum-99. As molybdenum-99 has been produced by uranium fission, iodine-132 may be present. Iodine-132 has a high abundance of gamma photons in the 700 to 800 keV region and its presence may cause the failure, in this test, of a product that meets the formal requirements for radionuclidic purity. Iodine-132 has a short half-life of 2.29 hours.

Take a volume of the injection to be examined equivalent to 37 MBq (1 mCi) and determine the gamma-ray spectrum using a sodium iodide detector with a shield of lead, of thickness of 6 mm, interposed between the sample and the detector. The response in the region corresponding to the 740 keV photon of molybdenum-99 does not exceed that obtained using 37 kBq (1 µCi) of a standardized solution of molybdenum-99 measured under the same conditions. Not more than 0.1% of the total radioactivity is due to molybdenum-99.

Iodine-131. Record the gamma-ray spectrum using a suitable instrument and measure the half-life using a suitable method. Iodine-131 exhibits major peaks of 284, 364 and 637 keV and a half-life of 8.06 days. Determine the relative amount of iodine-131. As molybdenum-99 has been produced by uranium fission, the content of iodine-131 is not greater than 18.5kBq in 37 MBq (0.5 µCi per 1 mCi) of technetium-99m. Not more than $5x10^{-3}$% of the total radioactivity is due to iodine-131.

Ruthenium-103. Record the gamma-ray spectrum using a suitable instrument and measure the half-life using a suitable method. Ruthenium-103 exhibits major peaks of 497 keV and a half-life of 39.3 days. Not more than $5x10^{-3}$% of the total radioactivity is due to ruthenium-103.

Stronium-89. Record the beta-ray spectrum using a suitable instrument and measure the half-life using a suitable method. An initial chemical separation may be required. Strontium-89 exhibits a major peak of maximum 1.492 MeV and a half-life of 50.6 days. Not more than $6x10^{-5}$% of the total radioactivity is due to strontium-89.

Strontium-90. Record the gamma- and beta-ray spectra using a suitable instrument and measure the half-life using a suitable method. Determine the relative amounts of yttrium-90, strontium-89 and strontium-90. Distinguish strontium-90 from strontium-89, comparing strontium-90 to its daughter nuclide yttrium-90. Strontium-90 exhibits a major peak of maximum 546 keV and a half-life of 29.1 years. Yttrium-90 exhibits a major peak of maximum 2280 keV and a half-life of 64.0 hours. Not more than $6x10^{-6}$% of the total radioactivity is due to strontium-90.

Other radionuclidic impurities. Record the gamma-ray spectrum using a suitable instrument and measure the half-life using a suitable method. Determine the relative amounts of other radionuclidic impurities. Not more than $1x10^{-2}$% of the total radioactivity is due to other radionuclidic impurities.

Alpha-emitting impurities. When the injection has been prepared from molybdenum-99 produced by uranium fission, record the alpha-ray spectrum using a suitable instrument, measure the half-life using a suitable method and determine the relative amount of alpha-emitting impurities. Not more than $1x10^{-7}$% of the total radioactivity is due to alpha-emitting impurities.

Radiochemical purity. Carry out the test as described under 1.14.2 Paper chromatography and ascending conditions, using paper for chromatography R. Apply to the paper about 5 µl of the injection to be examined, suitably diluted to give an optimum count rate and develop for 2 hours with a mixture of 80 volumes of methanol R and 20 volumes of water R. Allow the paper to dry in air and determine the radioactivity distribution by a suitable method. In this system, technetium-99m has an Rf value of about 0.6. Not less than 95% of the total radioactivity is in the spot corresponding to the pertechnetate ion.

Chemical purity

Aluminium. Dilute 1 mL of the injection to be examined to 2.5 mL with water R. Mix 2 mL of the resulting solution and 1 mL of acetate buffer, pH 4.6, TS in a test tube of about 12 mm in internal diameter. Add 0.05 mL of a 10 g/l solution of chromazurol S R. Allow to stand for 3 minutes. The colour of the solution is not more intense than that of an aluminium standard (2 ppm Al) TS prepared in the same manner; not more than 5 ppm of Al.

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.