World Health Organization

Monograph for Sodium pertechnetate (^{99m}Tc) injection (non-fission)

(Natrii pertechnetatis (^{99m}Tc) sine fissione formati injectio)

(September 2017)

DRAFT FOR COMMENT

Please send any comments on the revision of this draft document to Dr Sabine Kopp Group Lead, Medicines Quality Assurance, Technologies Standards and Norms (kopps@who.int) with a copy to Ms Xenia Finnerty (finnertyk@who.int) by **1 November 2017.**

Our working documents will be sent out electronically only and will also be placed on the Medicines website for comment under "Current projects". If you do not already receive our draft working documents please let us have your email address (to bonnyw@who.int) and we will add it to our electronic mailing list.

SCHEDULE FOR THE ADOPTION PROCESS OF DOCUMENT QAS/17.734

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	Date
IAEA consultation	3–7 December 2012
IAEA consultation	6–10 May 2013
Draft monograph received from IAEA in track-change mode according to format/template described in QAS/13.544	June 2013
Discussion at informal consultation on new medicines, quality control and laboratory standards	12–14 June 2013
Feedback to IAEA by WHO Secretariat	June 2013
Circulation for comments to IAEA and WHO Panel of Experts	June 2013
Feedback to IAEA, as appropriate	August–September 2013
Discussion during WHO Expert Committee on Specifications for Pharmaceutical Preparations	October 2013
Follow up by IAEA, including review of comments received	October 2013–February 2014
Discussion of revised version at IAEA consultation, Vienna, Austria	February 2014
Finalization by IAEA	February 2014
Circulation of revision to WHO and IAEA mailing list of experts for comments	March 2014
Compilation of feedback	April 2014
Discussion at informal consultation on Specifications for The International Pharmacopoeia and laboratory standards in Geneva	3–4 April 2014

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Compilation of feedback to IAEA	May 2014
Presentation to forty-ninth WHO Expert Committee on Specifications for Pharmaceutical Preparations	13–17 October 2014
Update during the fiftieth WHO Expert Committee on Specifications for Pharmaceutical Preparations	12–16 October 2015
Review and discussion of situation regarding monograph development for radiopharmaceuticals at informal consultation on quality control laboratory tools and specifications for medicines	9–11 May 2016
IAEA update during the fifty-first WHO Expert Committee on Specifications for Pharmaceutical Preparations	17–21 October 2016
Review and discussion during informal consultation on quality control laboratory tools and specifications for medicines	2–4 May 2017
IAEA delegated final review and modifications to Professor Alain Nicolas, France	May–September 2017
Mailing of revised monograph for public consultation	September 2017
Presentation to the fifty-second WHO Expert Committee on Specifications for Pharmaceutical Preparations	16–20 October 2017
Any further action as necessary	

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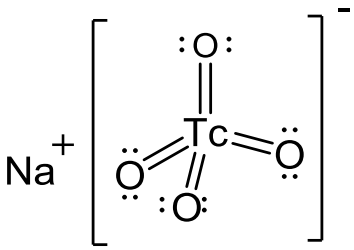
Monograph for Sodium pertechnetate (^{99m}Tc) injection (non-fission)
(Natrii pertechnetatis (^{99m}Tc) sine fissione formati injectio)

This monograph applies to sodium pertechnetate (^{99m}Tc) injection obtained from generators containing molybdenum-99. (^{99}Mo) is produced by neutron irradiation of molybdenum and extracted from generator columns.

Latin. Natrii pertechnetatis (^{99m}Tc) sine fissione formati injectio.

English. Sodium pertechnetate (^{99m}Tc) injection (non-fission).

Structural formula



Molecular formula. $Na^{99m}TcO_4$

Relative molecularmass. 185.99

Chemical name. Sodium oxido(trioxo)technetium-99m

Other names. Sodium tetraoxotechnetate (VII)

Description. Sodium pertechnetate (^{99m}Tc) injection (non-fission) is a clear, colourless solution. Technetium-99m has a half-life of 6.02 hours.

Category. Diagnostic.

Labelling. The label complies with the General monograph *Radiopharmaceuticals*.

Manufacture

Sodium pertechnetate is produced in ^{99}Mo/^{99m}Tc generator by the radioactive decay of parent radionuclide molybdenum-99 which is adsorbed on a column of alumina. Sodium pertechnetate (^{99m}Tc) is eluted from the column by a sterile 0.9% sodium chloride 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

Sodium pertechnetate [^{99m}Tc] injection (non-fission) is a sterile solution, made isotonic by sodium chloride and suitable for intravenous administration. The injection contains not less than 90% and not more than 110% of the declared technetium-99m activity stated on the label at the reference date and time. Not less than 95% of the total technetium-99m radioactivity is present as pertechnetate ion. Not more than 0.1% of the total radioactivity is due to molybdenum-99 breakthrough. Not more than 0.01% of the total radioactivity is due to other gamma-emitting radionuclides, apart from that due to technetium-99 resulting from the decay of technetium-99m.

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 141 keV.

Standardized technetium-99m solution is 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. In the test for Radiochemical purity, the Rf of the principal peak in the radiochromatogram obtained with the test solution is about 0.6.

Tests

pH. Perform the test as described under *1.13 Determination of pH* or *R1.5* under the monograph for *Radiopharmaceuticals*.

The pH of the injection should be between 4.0 and 8.0.

Aluminium

Test solution. In a test tube about 12 mm in internal diameter, mix 1 mL of acetate buffer solution pH 4.6 R and 2 mL of a 1 in 2.5 dilution of the preparation to be examined in water R. Add 0.05 mL of a 10 g/L solution of chromazurol S R.

Reference solution. Prepare at the same time and in the same manner as the test solution and using 2 mL of aluminium standard solution (2 ppm Al) R.

After 3 minutes, the colour of the test solution is not more intense than that of the reference solution.

The concentration of the aluminium ion in the injection is not greater than 5 µg per mL.

Sterility

The test for sterility will be initiated on the day of manufacture. The injection may be released for use before completion of the test.

The injection complies with *3.2 Test for sterility*, modified as described in the monograph for *Radiopharmaceuticals*.

Bacterial endotoxins. The test must be completed prior the product release.

Perform 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 mL.

Radionuclidic purity

Molybdenum-99 (impurity A) and other gamma-emitting impurities. Molybdenum-99 and other gamma-emitting impurities can be determined by gamma-ray spectrometry. Molybdenum-99 is the principal radionuclidic impurity in test solution. It needs to be determined only for first elution of ^{99}Mo/^{99m}Tc generators.

Retain a sample of the preparation to be examined for a sufficient time to allow the technetium-99m radioactivity to decay to a sufficiently low level to permit the detection of radionuclidic impurities. All measurements of radioactivity are expressed with reference to the date and time of administration.

Molybdenum-99 (Impurity A). Record the gamma-ray spectrum of the decayed material. The most prominent gamma photons have energies of 0.181 MeV, 0.740 MeV and 0.778 MeV; molybdenum-99 has a half-life of 66.0 h. Compare the radioactivity with that of a standardized molybdenum-99 solution.

The radioactivity due to Molybdenum-99 (Impurity A) does not exceed 0.1% of the total radioactivity of the test solution.

Other gamma-emitting impurities

Examine the gamma-ray spectrum of the decayed material for the presence of other radionuclidic impurities, which should, where possible, be identified and quantified.

The total radioactivity due to other gamma-emitting impurities does not exceed 0.01% of the total radioactivity of the test solution.

Radiochemical purity

Either Method A or Method B to be applied

Not less than 95% due to Technetium-99m as [^{99m}Tc] pertechnetate ion.

Method A. Perform the test as described under *1.14.2 Paper chromatography* and ascending conditions, using paper for chromatography R. A mixture of methanol R and water R (80:20, v/v) to be used as a mobile phase. The injection to be examined is used as a test solution, and is diluted with water or saline (0.9% sodium chloride w/v solution) to a suitable radioactive concentration. Apply to the paper about 5 µL of the test solution. Develop for 90 minutes and allow the paper to dry in air. Determine the radioactivity distribution by scanning using a radiochromatogram scanner with a collimator suitably adjusted to measure ^{99m}Tc or cut into 1 cm sections and count in a well type NaI(Tl) scintillation counter and corrected for background counts. In this system [^{99m}Tc] pertechnetate ion has an Rf value of about 0.6.

Method B. Perform the test as described under *1.14.2 Paper chromatography* and ascending conditions, using Whatman No 1 paper strip R. Use acetone or methyl ethyl ketone as a mobile phase. The injection to be examined is used as test solution, and is diluted with water or saline (0.9% sodium chloride w/v solution) to a suitable radioactive concentration. Apply 2 to 5 µL of the test solution at 1 cm above the bottom of the strip. Run the chromatogram up to a distance of 6 cm. The Rf value for (^{99m}Tc) pertechnetate ion is 0.9–1.0 and Rf value for reduced hydrolysed ^{99m}Tc is 0.0–0.1. The chromatographic strip is dried in air. Determine the radioactivity distribution by scanning using a radiochromatogram scanner with a collimator suitably adjusted to measure ^{99m}Tc or cut into two equal sections at 4.0 cm. The upper half section (section A) and bottom half section (section B) are counted separately in counting tubes in NaI(Tl) scintillation counter and corrected for background counts. Radiochemical purity is calculated as:

$$\text{per cent RCP} = \frac{\text{Counts in section A}}{\text{Counts in section A} + \text{Counts in section B}} \times 100$$

Radioactivity

Measure the radioactivity using a suitable calibrated counting instrument as described under *R.1.1 Detection and measurement of radioactivity*.

Impurities

A. Molybdenum-99

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