Reference solutions. Prepare the reference solutions using *aluminium standard solution (10 ppm Al) R* diluted as necessary with *dilute nitric acid R*.

Iron. Not more than 5.0 µg/ml, determined by atomic emission spectrometry (plasma or arc method) (*2.2.22, Method I*).

Test solution. Dilute 0.2 ml of the injection to be examined to a suitable volume with *dilute nitric acid R*.

Reference solutions. Prepare the reference solutions using *iron standard solution (20 ppm Fe) R* diluted as necessary with *dilute nitric acid R*.

Lead. Not more than 5.0 µg/ml, determined by atomic emission spectrometry (plasma or arc method) (*2.2.22, Method I*).

Test solution. Dilute 0.2 ml of the injection to be examined to a suitable volume with *dilute nitric acid R*.

Reference solutions. Prepare the reference solutions using *lead standard solution (10 ppm Pb) R* diluted as necessary with *dilute nitric acid R*.

Strontium. 6.0 mg/ml to 12.5 mg/ml. Examine by atomic emission spectrometry (*2.2.22, Method I*).

Test solution. Dilute 0.2 ml of the injection to be examined to a suitable volume with *dilute nitric acid R*.

Reference solutions. Prepare the reference solutions using *strontium standard solution (1.0 per cent Sr) R* diluted as necessary with *dilute nitric acid R*.

Sterility. It complies with the test for sterility prescribed in the monograph on *Radiopharmaceutical preparations (0125)*.

RADIONUCLIDIC PURITY

Gamma emitters. Record the gamma-ray and X-ray spectrum of the injection to be examined using a suitable instrument. Not more than 0.4 per cent of the total radioactivity in the preparation to be examined is due to gamma emitting radionuclides other than yttrium-89m.

Beta emitters. Evaporate to dryness 100 µl of the injection to be examined under a radiant heat source. Dissolve the residue in 2 ml of *47 per cent hydrobromic acid R*, evaporate to dryness under the radiant heat source and dissolve the residue in 2 ml of *dilute hydrobromic acid R1*. Transfer the solution to the top of a column, 5 mm to 6 mm in diameter, packed with approximately 2 ml of *cationic exchange resin R1* (100 µm to 250 µm), previously conditioned with *dilute hydrobromic acid R1* and elute the column with the same solvent until 10 ml of eluate has been collected into a container containing 50 µl of a 15 g/l solution of *anhydrous sodium sulphate R* in *1 M hydrochloric acid*.

To a liquid scintillation vial add an appropriate volume of scintillation liquid followed by 1 ml of *water R*, 0.1 ml of a 15 g/l solution of *anhydrous sodium sulphate R* in *1 M hydrochloric acid* and 100 µl of eluate. Shake to obtain a clear solution. Using suitable counting equipment determine the radioactivity due to sulphur-35 and phosphorus-32 in the sample.

Taking into account the recovery efficiency of the separation, counting efficiency and radioactive decay, determine the radioactive concentration of sulphur-35 and phosphorus-32 in the sample and hence the percentage of total beta emitting impurities in the injection to be examined. Not more than 0.2 per cent of the total radioactivity in the injection to be examined is due to the sum of sulphur-35 and phosphorus-32 radioactivities.

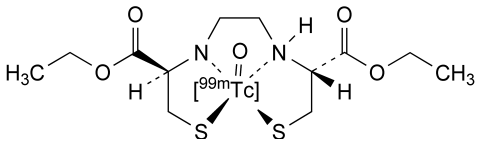
RADIOACTIVITY

Measure the radioactivity using suitable equipment by comparison with a standardised strontium-89 solution or by measurement in an instrument calibrated with the aid of such a solution.

01/2008:2123

TECHNETIUM (^{99m}Tc) BICISATE INJECTION

Technetii (^{99m}Tc) bicisati solutio iniectabilis



DEFINITION

Sterile solution of a complex of technetium-99m with diethyl *N,N'*-ethylenedi-L-cysteinate. It may contain stabilisers and inert additives such as *Mannitol (0559)* and *Disodium edetate (0232)*.

Content: 90 per cent to 110 per cent of the declared technetium-99m radioactivity at the date and hour stated on the label.

PRODUCTION

It is prepared from *N,N'*-(1,2-ethylenediyl)bis[(2*R*)-2-amino-3-sulphanylpropanoic acid] diethyl ester and *Sodium pertechnetate (^{99m}Tc) injection (fission) (0124)* or *Sodium pertechnetate (^{99m}Tc) injection (non-fission) (0283)* in the presence of reducing agents such as a stannous salt.

CHARACTERS

Appearance: clear, colourless solution.

Half-life and nature of radiation of technetium-99m: see general chapter *5.7. Table of physical characteristics of radionuclides*.

IDENTIFICATION

A. Gamma-ray spectrometry.

Results: the most prominent gamma photon of technetium-99m has an energy of 0.141 MeV.

B. Examine the chromatograms obtained in the test for radiochemical purity (see Tests).

Results: the principal peak in the chromatogram obtained with the test solution is similar in retardation factor to the principal peak in the chromatogram obtained with reference solution (a).

TESTS

pH (*2.2.3*): 6.5 to 7.5.

Sterility. It complies with the test for sterility prescribed in the monograph on *Radiopharmaceutical preparations (0125)*. The injection may be released for use before completion of the test.

RADIOCHEMICAL PURITY

Impurities A, B, C, D, E, F. Thin-layer chromatography (*2.2.27*).

Test solution. The preparation to be examined.

Reference solution (a). To vial B of *bicisate labelling kit CRS* in lead shielding add 2 ml of sodium pertechnetate (^{99m}Tc) injection (fission or non-fission) containing 400-800 MBq. Dissolve the contents of vial A of *bicisate labelling kit CRS* in 3 ml of a 9 g/l solution of *sodium chloride R*. Immediately transfer 1.0 ml of the solution contained in vial A to vial B. Mix and allow to stand for 30 min at room temperature.

Reference solution (b). Sodium pertechnetate (^{99m}Tc) injection (fission or non fission).

Plate: *TLC silica gel plate R*.

Mobile phase: *ethyl acetate R*.

Application: 5 µl, allow the spots to dry for 5-10 min.

Development: over 4/5 of the plate.

Drying: in air.

Detection: determine the distribution of radioactivity using a suitable detector.

Retardation factors: technetium-99m bicisate = more than 0.4; impurities A, B, C, D, E and F = less than 0.2.

System suitability: the retardation factor of the principal peak in the chromatogram obtained with reference solution (a) is clearly different from the retardation factor of the peak in the chromatogram obtained with reference solution (b).

Limit:

– *sum of impurities A, B, C, D, E and F*: not more than 6 per cent of the total radioactivity.

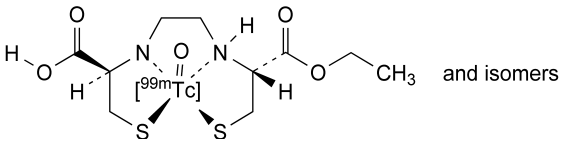
RADIOACTIVITY

Determine the radioactivity using a calibrated instrument.

IMPURITIES

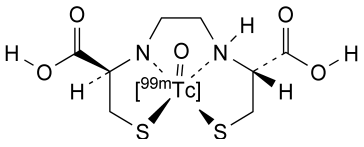
A. technetium-99m in colloidal form,

B. [^{99m}Tc]pertechnetate ion,



and isomers

C. complex of technetium-99m with ethyl hydrogen *N*,*N*′-ethylenedi-L-cysteinate,



D. complex of technetium-99m with *N*,*N*′-ethylenedi-L-cysteine,

E. complex of technetium-99m with mannitol,

F. complex of technetium-99m with disodium edetate.

01/2008:0126

TECHNETIUM (^{99m}Tc) COLLOIDAL RHENIUM SULPHIDE INJECTION

Rhenii sulfidi colloidalis et technetii (^{99m}Tc) solutio iniectabilis

DEFINITION

Technetium (^{99m}Tc) colloidal rhenium sulphide injection is a sterile, apyrogenic colloidal dispersion of rhenium sulphide the micelles of which are labelled with technetium-99m. It is stabilised with gelatin. The injection contains not less than 90.0 per cent and not more than 110.0 per cent of the declared technetium-99m radioactivity at the date and hour stated on the label. Not less than 92 per cent of the radioactivity corresponds to technetium-99m in colloidal form. The pH of the injection may be adjusted by the addition of a suitable buffer such as a citrate buffer solution. The injection contains a variable amount of colloidal rhenium sulphide, not exceeding 0.22 mg of rhenium (Re) per millilitre, according to the method of preparation.

It is prepared from sodium pertechnetate (^{99m}Tc) injection (fission or non-fission) using suitable sterile, apyrogenic ingredients and calculating the ratio of radionuclidic impurities with reference to the date and hour of administration.

CHARACTERS

A light-brown liquid.

Technetium-99m has a half-life of 6.02 h and emits gamma radiation.

IDENTIFICATION

A. Record the gamma-ray spectrum using a suitable instrument. The spectrum does not differ significantly from that of a standardised technetium-99m solution either by direct comparison or by using an instrument calibrated with the aid of such a solution. Standardised technetium-99m and molybdenum-99 solutions are available from laboratories recognised by the competent authority. The most prominent gamma photon of technetium-99m has an energy of 0.140 MeV.

B. Examine the chromatogram obtained in the test for radiochemical purity. The distribution of radioactivity contributes to the identification of the injection.

C. To 1 ml add 5 ml of *hydrochloric acid R*, 5 ml of a 50 g/l solution of *thiourea R* and 1 ml of a 200 g/l solution of *stannous chloride R* in *hydrochloric acid R*. A yellow colour is produced.

TESTS

pH (*2.2.3*). The pH of the injection is 4.0 to 7.0.

Rhenium

Test solution. Use 1 ml of the injection to be examined.

Reference solutions. Using a solution containing 100 µg of *potassium perrhenate R* (equivalent to 60 ppm of Re) and 240 µg of *sodium thiosulphate R* per millilitre, prepare a suitable range of solutions and dilute to the same final volume with *water R*.

To the test solution and to 1 ml of each of the reference solutions add 5 ml of *hydrochloric acid R*, 5 ml of a 50 g/l solution of *thiourea R* and 1 ml of a 200 g/l solution of *stannous chloride R* in *hydrochloric acid R* and dilute to 25.0 ml with *water R*. Allow to stand for 40 min and measure the absorbance (*2.2.25*) of each solution at 400 nm, using a reagent blank as the compensation liquid. Using the absorbances obtained with the reference solutions, draw a calibration curve and calculate the concentration of rhenium in the injection to be examined.

Physiological distribution. Inject a volume not greater than 0.2 ml into the caudal vein of each of three mice each weighing 20 g to 25 g. Euthanise the mice 20 min after the injection, remove the liver, spleen and lungs and measure the radioactivity in the organs using a suitable instrument.