technetium-99m radioactivity at the date and hour stated on the label. Not less than 95.0 per cent of the radioactivity corresponds to technetium-99m complexed with etifenin.

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

CHARACTERS

A clear, colourless solution.

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 by liquid chromatography (*2.2.29*).

Test solution. Dilute the injection to be examined with *methanol R* to obtain a solution containing about l mg of etifenin per millilitre.

Reference solution. Dissolve 5.0 mg of *etifenin CRS* in *methanol R* and dilute to 5.0 ml with the same solvent.

The chromatographic procedure may be carried out using:

- a column 0.25 m long and 4.6 mm in internal diameter packed with *octadecylsilyl silica gel for chromatography R* (5 µm to 10 µm),
- as mobile phase at a flow rate of 1 ml/min a mixture of 20 volumes of *methanol R* and 80 volumes of a 14 g/l solution of *potassium dihydrogen phosphate R* adjusted to pH 2.5 by the addition of *phosphoric acid R*,
- a spectrophotometer set at 230 nm.

Inject 20 µl of each solution. The principal peak in the chromatogram obtained with the test solution has a similar retention time to the principal peak in the chromatogram obtained with the reference solution.

TESTS

pH (*2.2.3*). The pH of the injection is 4.0 to 6.0.

Physiological distribution. Inject 0.1 ml (equivalent to about 3.7 MBq) into a caudal vein of each of three mice, each weighing 20 g to 25 g. Kill the mice l h after the injection. Remove the liver, gall-bladder, small intestine, large intestine and kidneys, collecting excreted urine. Measure the radioactivity in the organs using a suitable instrument. Measure the radioactivity of the rest of the body, after having removed the tail. Determine the percentage of radioactivity in each organ from the expression:

$$\frac{A}{B} \times 100$$

A = radioactivity of the organ concerned,

B = radioactivity of all organs and the rest of the body, excluding the tail.

In not fewer than two mice the sum of the percentages of radioactivity in the gall-bladder and small and large intestine is not less than 80 per cent. Not more than 3 per cent of the radioactivity is present in the liver, and not more than 2 per cent in the kidneys

Tin

Test solution. Dilute 1.0 ml of the injection to be examined to 5.0 ml with *1 M hydrochloric acid*.

Reference solution. Prepare a reference solution containing 0.075 mg of *stannous chloride R* per millilitre in *1 M hydrochloric acid*.

To 1.0 ml of each solution add 0.4 ml of a 20 g/l solution of *sodium laurilsulfate R*, 0.05 ml of *thioglycollic acid R*, 0.l ml of *dithiol reagent R* and 3.0 ml of *0.2 M hydrochloric acid*. Mix. Measure the absorbance (*2.2.25*) of each solution at 540 nm, using *0.2 M hydrochloric acid* as the compensation liquid. The absorbance of the test solution is not greater than that of the reference solution (0.2 mg of Sn per millilitre).

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

Examine by thin-layer chromatography (*2.2.27*) using silicic acid as the coating substance on a glass-fibre sheet. Heat the plate at 110 °C for l0 min. The plate used should be such that during development the mobile phase moves over a distance of 10 cm to 15 cm in about 15 min.

Apply to the plate 5 µl to 10 µl of the injection to be examined. Develop immediately over a path of 10 cm to 15 cm using a 9 g/l solution of *sodium chloride R*. Allow the plate to dry. Determine the distribution of radioactivity using a suitable detector. Technetium-99m complexed with etifenin migrates almost to the middle of the chromatogram and pertechnetate ion migrates with the solvent front. Impurities in colloidal form remain at the starting point. The radioactivity corresponding to technetium-99m complexed with etifenin represents not less than 95.0 per cent of the total radioactivity of the chromatogram.

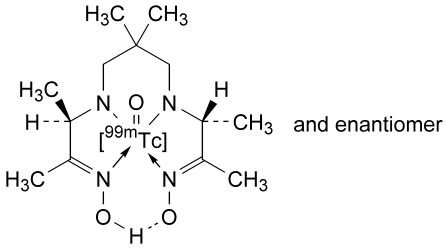
RADIOACTIVITY

Measure the radioactivity using suitable counting equipment by comparison with a standardised technetium-99m solution or by measurement in an instrument calibrated with the aid of such a solution.

01/2005:1925

TECHNETIUM (^{99m}TC) EXAMETAZIME INJECTION

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



and enantiomer

DEFINITION

Sterile solution of lipophilic technetium-99m exametazime which may be prepared by dissolving a racemic mixture of (3*RS*,9*RS*)-4,8-diaza-3,6,6,9-tetramethylundecane-2,10-dione bisoxime in the presence of a stannous salt in *Sodium pertechnetate (^{99m}Tc) injection (fission) (0124)* or *Sodium pertechnetate (^{99m}Tc) injection (non-fission) (0283)*. It may contain stabilisers and inert additives.

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

Purity: minimum of 80 per cent of the total radioactivity corresponds to lipophilic technetium-99m exametazime and its *meso* isomer.

CHARACTERS

Appearance: clear solution.

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

IDENTIFICATION

A. Gamma-ray spectrometry.

Comparison: standardised technetium-99m solution, or by using a calibrated instrument. Standardised technetium-99m solutions and/or standardisation services are available from the competent authority.

Results: the spectrum obtained with the solution to be examined does not differ significantly from that obtained with a standardised technetium-99m solution. The most prominent gamma photon has an energy of 0.141 MeV.

B. Examine the chromatograms obtained in the test Impurity A under Radiochemical purity.

Results: the principal peak in the chromatogram obtained with the test solution is similar in retention time to the peak due to lipophilic technetium-99m exametazime in the chromatogram obtained with the reference solution.

TESTS

pH (*2.2.3*): 5.0 to 10.0.

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

Impurity C. Thin-layer chromatography (*2.2.27*).

Test solution. The preparation to be examined.

Plate: *TLC silica gel plate R*; use a glass-fibre plate.

Mobile phase: 9 g/l solution of *sodium chloride R*.

Application: about 5 µl.

Development: immediate, over 2/3 of the plate.

Drying: in air.

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

Retention factors: impurity C = 0.8 to 1.0; lipophilic technetium-99m exametazime and impurities A, B, D and E do not migrate.

Limits:

– *impurity C*: maximum 10 per cent of the total radioactivity.

Total of lipophilic technetium-99m exametazime and impurity A. Thin-layer chromatography (*2.2.27*).

Test solution. The preparation to be examined.

Plate: *TLC silica gel plate R*; use a glass-fibre plate.

Mobile phase: *methyl ethyl ketone R*.

Application: about 5 µl.

Development: immediate, over 2/3 of the plate.

Drying: in air.

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

Retention factors: lipophilic technetium-99m exametazime = 0.8 to 1.0, impurity A = 0.8 to 1.0, impurity C = 0.8 to 1.0; impurities B, D and E do not migrate.

Limits: calculate the percentage of radioactivity due to impurities B, D and E from test B (*B*) and the percentage of the radioactivity due to impurity C from test A (*A*). Calculate the total percentage of lipophilic technetium-99m exametazime and impurity A from the expression:

$$100 - A - B$$

– *total of lipophilic technetium-99m exametazime and impurity A*: minimum 80 per cent of the total radioactivity.

Impurity A. Liquid chromatography (*2.2.29*).

Test solution. The preparation to be examined.

Reference solution. Dissolve the contents of a vial of *meso-rich exametazime CRS* in 0.5 ml of a 9 g/l solution of *sodium chloride R* and transfer to a lead-shielded, nitrogen-filled vial. Add 6 µl of a freshly prepared 1 g/l solution of *stannous chloride R* in *0.05 M hydrochloric acid* and 2.5 ml of sodium pertechnetate (^{99m}Tc) injection (fission or non-fission) containing 370-740 MBq. Mix carefully and use within 30 min of preparation.

Column:

– *size*: *l* = 0.25 m, Ø = 4.6 mm,

– *stationary phase*: *spherical base-deactivated end-capped octadecylsilyl silica gel for chromatography R* (5 µm) with a pore size of 13 nm and a carbon loading of 11 per cent.

Mobile phase: mix 33 volumes of *acetonitrile R* and 67 volumes of *0.1 M phosphate buffer solution pH 3.0 R*.

Flow rate: 1.5 ml/min.

Detection: radioactivity detector.

Injection: loop injector.

Run time: 20 min.

Relative retention with reference to lipophilic technetium-99m exametazime: impurity A = about 1.2.

System suitability: reference solution:

– chromatogram similar to the chromatogram provided with *meso-rich exametazime CRS*,

– *resolution*: minimum of 2 between the peaks due to lipophilic technetium-99m exametazime and to impurity A.

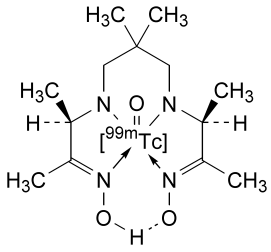
Limits:

– *impurity A*: maximum 5 per cent of the radioactivity due to lipophilic technetium-99m exametazime and impurity A.

RADIOACTIVITY

Measure the radioactivity using suitable equipment by comparison with a standardised technetium-99m solution or by using a calibrated instrument.

IMPURITIES



A. *meso* isomer of lipophilic technetium-99m exametazime,

B. technetium-99m in colloidal form,

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

D. non lipophilic technetium-99m exametazime complex,

E. *meso* isomer of non lipophilic technetium-99m exametazime complex.

01/2005:1047

TECHNETIUM (^{99m}Tc) GLUCONATE INJECTION

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

DEFINITION

Technetium (^{99m}Tc) gluconate injection is a sterile solution, which may be prepared by mixing solutions of calcium gluconate and a stannous salt or other suitable reducing agent with sodium pertechnetate (^{99m}Tc) injection (fission or non-fission). 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 90 per cent of the radioactivity corresponds to technetium-99m gluconate complex.

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

CHARACTERS

A slightly opalescent solution.

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. 5 µl of the solution complies with identification A prescribed in the monograph on *Calcium gluconate (0172)*.

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

TESTS

pH (*2.2.3*). The pH of the solution is 6.0 to 8.5.

Physiological distribution. Inject a volume not greater than 0.2 ml into the caudal vein of each of three rats weighing 150 g to 250 g. Measure the radioactivity of the syringe before and after injection. Sacrifice the rats 30 min after the injection. Remove at least 1 g of blood by a suitable method and remove the kidneys, the liver, the bladder plus voided urine and the tail. Weigh the sample of blood.

Determine the radioactivity in the organs, the blood sample and the tail using a suitable instrument. Calculate the percentage of radioactivity in each organ and in 1 g of blood with respect to the total radioactivity calculated as the difference between the two measurements made on the syringe minus the activity in the tail. Correct the blood concentration by multiplying by a factor of $m/200$ where m is the body mass of the rat in grams.

In not fewer than two of the three rats used, the radioactivity in the kidneys is not less than 15 per cent, that in the bladder plus voided urine is not less than 20 per cent and that in the liver is not more than 5 per cent. The radioactivity in the blood, after correction, is not more than 0.50 per cent.

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

Examine by thin-layer chromatography (*2.2.27*) using silica gel as the coating substance on a glass-fibre sheet. Heat the plate at 110 °C for 10 min. Use a plate such that during development the mobile phase migrates over a distance of 10 cm to 15 cm in about 10 min.

a) Apply to the plate 5 µl to 10 µl of the solution to be examined. Develop immediately over a path of 10 cm to 15 cm using a 9 g/l solution of *sodium chloride R*. Allow the plate to dry. Determine the distribution of radioactivity using a suitable detector. Impurities in colloidal form remain at the starting point. Technetium gluconate complex and pertechnetate ion migrate near to the solvent front.

b) Apply to the plate 5 µl to 10 µl of the solution to be examined and allow to dry. Develop over a path of 10 cm to 15 cm using *methyl ethyl ketone R*. Dry in a current of warm air. Determine the distribution of radioactivity using a suitable detector. Pertechnetate ion impurity migrates near to the solvent front. Technetium gluconate complex and technetium in colloidal form remain at the starting point.

The sum of the percentages of radioactivity corresponding to impurities in the chromatograms obtained in test (a) and (b) does not exceed 10 per cent.

RADIOACTIVITY

Measure the radioactivity using suitable counting equipment by comparison with a standardised technetium-99m solution or by measurement in an instrument calibrated with the aid of such a solution.

01/2005:0640

TECHNETIUM (^{99m}Tc) HUMAN ALBUMIN INJECTION

Technetii (^{99m}Tc) humani albumini solutio iniectabilis

DEFINITION

Technetium (^{99m}Tc) human albumin injection is a sterile, apyrogenic solution of human albumin labelled with technetium-99m. It contains a reducing substance, such as a tin salt in an amount not exceeding 1 mg of Sn per millilitre;