Thallous (^{201}Tl) chloride injection (Thallosi (^{201}Tl) chloridi injectio)

^{201}TlCl

Description. Thallous (^{201}Tl) chloride injection is a clear colourless, aqueous solution.

Thallium-201 has a half-life of 73.1 hours.

Category. Diagnostic.

Storage. After aseptic withdrawal of the first dose from a multidose container, the container should be stored at a temperature between 2°C to 8°C and the contents used within 7 days.

Labelling. State the date of withdrawal of the first dose for multidose containers.

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. Thallous (^{201}Tl) chloride injection is a sterile, isotonic, aqueous solution of thallium-201 as thallous chloride, 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 thallium-201 stated on the label at the reference date and time stated on the label. Not less than 97% of the total radioactivity is due to thallium-201. Not more than 2% of the total radioactivity is due to thallium-202. The specific radioactivity is not less than 3.7 GBq (100 mCi) of thallium-201 per milligram of thallium at the reference date and time stated on the label.

Manufacture

Radionuclide production. Thallium-201 is formed by the decay of lead-201. Lead-201 is a radioactive isotope of lead obtained from the irradiation with protons of suitable energy, of thallium which may be enriched in thallium-203. Separation of thallium-201 may be done using an ion-exchange resin.

Production of radiopharmaceutical preparation. Thallous (^{201}Tl) chloride injection may contain suitable antimicrobial preservatives such as benzyl alcohol or stabilizing agents. The injection may be sterilized by "Heating in an autoclave" (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 using a suitable instrument with a sample of thallium-201, suitably diluted if needed. The spectrum is concordant with the *reference spectrum* of a specimen of thallium-201 in that it exhibits major peaks of 135, 166, and 167keV and X-rays of 69 and 83keV.

Standardized thallium-201 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 70 and 75 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, 4.0 to 7.0.

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 and X-ray spectrum using a suitable instrument and measure the half-life using a suitable method. Determine the relative amounts of thallium-201, thallium-202 and other radionuclidic impurities that may be present. Thallium-202 has a half-life of 12.2 days and exhibits a main peak of 440 keV. Thallium-200 has a half-life of 1.09 days and exhibits main peaks of 368, 579, 828 and 1206 keV. Lead-201 has a half-life of 9.4 hours and exhibits a main peak of 331 keV. Lead-203 has a half-life of 2.17 days and exhibits a main peak of 270 keV. Not less than 97% of the total radioactivity is due to thallium-201. Not more than 2% of the total radioactivity is due to thallium-202.

Standardized solutions of thallium-201 and thallium-202, are available from laboratories recognized by the relevant national or

regional authority.

Radiochemical purity. Carry out the test as described under 1.14.2 Paper chromatography, ascending conditions, using a 2.5- x 15.0-cm cellulose polyacetate strip, as the support and disodium edetate (0.05 mol/l) VS as the electrolyte solution.

Soak the strip in the electrolyte solution for 45 to 60 minutes. Remove the strip with forceps, taking care to handle the outer edges only. Place the strip between 2 absorbent pads, and blot to remove excess solution.

Apply not less than 5 µl of a mixture of equal volumes of the injection and disodium edetate (0.05 mol/l) VS to the centre of the blotted strip, and mark the point of application. Attach the strip to the support bridge of an electrophoresis chamber containing equal volumes of disodium edetate (0.05 mol/l) VS in each side of the chamber. Ensure that each end of the strip is in contact with the disodium edetate (0.05 mol/l) VS. Attach the chamber cover, and perform the electrophoresis at 250 volts for 30 minutes. Remove the strip from the chamber, and allow it to dry in air without blotting. Determine the radioactivity distribution by a suitable method.

Not less than 95% of the radioactivity on the strip migrates towards the cathode as a single peak.

Chemical purity

Thallium. Transfer 1.0 mL of the injection and 1.0 mL of thallium standard (2 µg/mL Tl) TS to separate screw-cap test tubes.

To each tube, add the following five solutions (A, B, C, D and E) and mix after each addition: 2 drops of a solution prepared by carefully mixing 18 mL of nitric acid (~1000 g/l) TS and 82 mL of hydrochloric acid (~250 g/l) TS (solution A); 1.0 mL of sulfosalicylic acid (0.1 mol/l) VS (solution B); 2 drops of hydrochloric acid (~250 g/l) TS (solution C); 4 drops of a solution prepared by dissolving 50 mg of rhodamine B R in hydrochloric acid (~250 g/l) TS and diluting to 100.0 mL (solution D); 1.0 mL of diisopropyl ether R (solution E).

Screw the caps on tightly, shake the tubes by hand for exactly 1 minute, releasing any pressure build-up by loosening the caps slightly. Recap the tubes and allow the phases to separate. Transfer 0.5 mL of the ether layer from each tube to clean tubes.

The colour of the ether layer obtained from the injection is not darker than that from the thallium standard (2 µg/mL Tl) TS.

Iron. Into separate cavities of a spot plate, place 0.1 mL of the injection and 0.1 mL of iron standard FeTS diluted with water R to a concentration of 5 µg/mL. Add to each cavity 0.1 mL of a solution of hydroxylamine hydrochloride R (1 in 10), 1 mL of a solution of sodium acetate R (1 in 4), and 0.1 mL of a 0.5% dipyridyl solution prepared by dissolving 0.5 g of 2,2'-dipyridyl R in 100 mL of water R containing 0.15 mL of hydrochloric acid (~250 g/l) TS, and mix. After 5 minutes, the colour obtained from the injection is not darker than that of the iron standard solution.

Copper. Into separate cavities of a spot plate, place 0.2 mL of the injection and 0.2 mL of copper standard (5 µg/mL Cu) TS. Add to each cavity the following 3 solutions (A, B and C) and mix after each addition: 0.2 mL of water R (solution A) and 0.1 mL of a solution of iron thiocyanate prepared by dissolving 1.5 g of ferric chloride R and 2 g of potassium thiocyanate R in water R and diluting to 100.0 mL with the same solvent (solution B); 0.1 mL of a solution of sodium thiosulphate R (1 in 100) (solution C). The time required for the injection to decolorize is equal to or longer than that observed for the copper standard solution.

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 thallium-201 solution or by measurement in an instrument calibrated with the aid of such a solution.

Standardized thallium-201 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 guinea pigs. At 1 hour post injection not less than 85% of the injected radioactivity should be found in the heart.