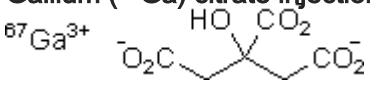
Gallium (^{67}Ga) citrate injection (Gallii (^{67}Ga) citratis injectio)



$C_6H_5{}^{67}GaO_7$

Chemical name. [^{67}Ga]gallium(III) 3-hydroxypropane-1,2,3-tricarboxylate.

Description. Gallium (^{67}Ga) citrate injection is a clear solution.

Gallium-67 has a half-life of 3.26 days.

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. Gallium (^{67}Ga) citrate injection is a sterile, aqueous solution of gallium-67 complexed with 2-hydroxypropane-1,2,3-tricarboxylate (citrate) with excess of citric acid, suitable for intravenous administration and that contains sufficient sodium chloride and sodium citrate to make the solution isotonic with blood. The injection contains not less than 90% and not more than 110% of the content of gallium-67 stated on the label at the reference date and hour stated on the label. Not less than 99% of the total radioactivity is due to gallium-67. Not less than 95% of the total gallium-67 radioactivity is present as gallium citrate. Not more than 0.2% of the total radioactivity is due to gallium-66.

Manufacture

Radionuclide production. Gallium-67 may be prepared by proton irradiation of zinc-68 or alpha irradiation of zinc-67 and processed in such a manner that gallium-67 obtained is carrier free. Gallium-67 may be separated from zinc by solvent extraction or column chromatography.

Production of radiopharmaceutical preparation. Gallium (^{67}Ga) citrate injection may contain a suitable antimicrobial preservative such as benzyl alcohol. The injection may be sterilized by "Heating in an autoclave" or it may 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 gallium-67, suitably diluted if needed. The spectrum is concordant with the *reference spectrum* of a specimen of gallium-67 in that it exhibits major peaks of 93, 185 and 300keV. Gallium-66 which is an impurity has a half-life of 9.4 hours with a main peak of 1039keV.
Standardized gallium-67 solutions are available from laboratories recognized by the relevant national or regional authority.

B. The half-life determined using a suitable detector system is 3.26 days or between 75 and 80 hours.

C. To 0.2 mL of the injection to be examined add 0.2 mL of a solution containing 1 g/l of ferric chloride R and 0.1 per cent v/v of hydrochloric acid R and mix. Compare the colour with that of a solution containing 9 g/l of benzyl alcohol R and 7 g/l of sodium chloride R treated in the same manner. A yellow colour develops in the test solution only.

pH value. Carry out the test as described in the monograph for "Radiopharmaceuticals". pH of the injection, 5.0 to 8.0.

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 spectrum using a suitable instrument and measure the half-life using a suitable

method. Determine the relative amounts of gallium-67, gallium-66 and other radionuclidic impurities that may be present. Not less than 99% of the total radioactivity is due to gallium-67 and not more than 0.2% of the total radioactivity is due to gallium-66.

Radiochemical purity. Carry out the test as described under 1.14.2 Paper chromatography, 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 with a solution prepared as follows: dissolve 1.36 g of sodium acetate R and 0.58 mL of glacial acetic acid R in 100 mL of water R. Allow the paper to dry in air and determine the radioactivity distribution by a suitable method. In this system, gallium citrate has an Rf value of about 0.9.

Not less than 95% of the total radioactivity is in the spot corresponding to gallium (^{67}Ga) citrate.

Chemical purity

Zinc. To 0.1 mL of the injection to be examined add 0.9 mL of water R, 5 mL of acetate buffer solution pH 4.7 R, 1 mL of a 250 g/l solution of sodium thiosulfate R and 5.0 mL of a dithizone solution prepared as follows: dissolve 10 mg of dithizone R in 100 mL of methyl ethyl ketone R allow to stand for 5 minutes, filter and immediately before use dilute the solution to 10 times its volume with methyl ethyl ketone R. Shake vigorously for 2 minutes and separate the organic layer. Measure the absorbance of the organic layer at 530 nm, using the organic layer of a blank solution as the compensation liquid. The absorbance is not greater than that of the organic layer obtained with 0.1 mL of zinc standard solution (5 ppm Zn) R treated in the same manner; not more than 5 ppm.

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 gallium-67 solution or by measurement in an instrument calibrated with the aid of such a solution.

Standardized gallium-67 solutions are available from laboratories recognized by the relevant national or regional authority.