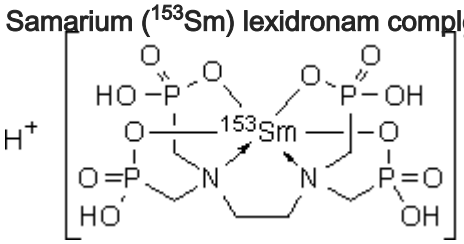
Samarium (^{153}Sm) lexidronam complex injection (Samarii (^{153}Sm) lexidronami multiplex injectio)



$C_6H_{17}N_2O_{12}P_4{}^{153}Sm$

Chemical names. Hydrogen (*OC-6-21*)-[(ethylenedinitrilo-κ^2*N,N'*)tetrakis(methylenephosphonato)-κ^4*O^P,O$^{P'}$,O$^{P''}$,O$^{P'''}$*][^{153}Sm]samarate(1-); samarium (^{153}Sm) ethylenediamine tetramethylene phosphonate.

Other names. Samarium (^{153}Sm) ethylenediamine tetramethylene phosphonate injection; (^{153}Sm)-EDTMP injection.

Description. Samarium (^{153}Sm) lexidronam complex injection is a clear colourless solution.

Samarium-153 has a half-life of 46.3 hours.

Category. Therapeutic.

Storage. Samarium (^{153}Sm) lexidronam complex injection should be kept at a temperature between 2°C to 8°C, protected from light and during transportation, at a temperature below -10°C.

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. Samarium (^{153}Sm) lexidronam complex injection is a sterile solution of samarium-153 complexed with ethylenediamine tetramethylene phosphonate (EDTMP) present in excess. The injection is suitable for intravenous administration and contains sufficient sodium chloride to make the solution isotonic with blood. (^{153}Sm)-EDTMP complex injection contains not less than 90% and not more than 110% of the content of samarium-153 stated on the label at the reference date and time stated on the label. Not less than 99.8% of the total radioactivity is due to samarium-153. Not less than 95% of the total samarium-153 radioactivity is present as EDTMP complex.

Manufacture

Radionuclide production. Samarium-153 may be obtained by neutron irradiation of enriched samarium oxide (152Sm) Sm2O3 in quartz ampoule.

Production of radiopharmaceutical preparation. Samarium (^{153}Sm) chloride is complexed by addition to a solution of EDTMP that is present in excess. EDTMP may be previously synthesized from phosphorous acid, ethylenediamine and formaldehyde using the Mannich-type reaction. It is then purified by successive re-crystallizations and identified by infrared spectroscopy. The pH of the stock solution of EDTMP in sodium hydroxide is adjusted to 7-7.5 for complexation with samarium-153. (^{153}Sm)-EDTMP complex injection may contain stabilizing agents as well as buffers and it 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 and X-ray spectra using a suitable instrument with a sample of samarium-153, suitably diluted if needed. The spectrum is concordant with the *reference spectrum* of a specimen of samarium-153 in that it exhibits major peaks of 70 and 103 keV.

Standardized samarium-153 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 44 and 49 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, 7.0 to 8.5.

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 samarium-153, europium-154 and other radionuclidic impurities that may be present. Not less than 99.8% of the total radioactivity is due to samarium-153 and not more than 0.01% of the total radioactivity is due to europium-154. The sum of all gamma-emitting impurities is less than 0.2%.

Radiochemical purity. Carry out the test as described under 1.14.2 Paper chromatography and ascending conditions, using cellulose paper strips. Apply to the paper about 5 µl of the injection to be examined, suitably diluted to give an optimum count rate and develop for a distance of 20 cm with a mixture of 0.2 volumes of ammonia (260 g/l) TS and 40 volumes of water R. Allow the paper to dry in air and determine the radioactivity distribution by a suitable method. In this system, samarium-153 has an Rf value of about 0 and the (^{153}Sm)-EDTMP complex has an Rf value of about 0.6. Not less than 95% of the total radioactivity is in the spot corresponding to the (^{153}Sm)-EDTMP complex.

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 samarium-153 solution or by measurement in an instrument calibrated with the aid of such a solution.

Standardized samarium-153 solutions are available from laboratories recognized by the relevant national or regional authority.