THE INTERNATIONAL PHARMACOPOEIA

RADIOPHARMACEUTICALS: SPECIFIC MONOGRAPH

NATRIIODIDI (\(^{131}\)I) SOLUTIO
SODIUM IODIDE (\(^{131}\)I) SOLUTION

(June 2013)

DRAFT FOR REVISION

Should you have any comments on this draft, please send these to Dr Sabine Kopp, Medicines Quality Assurance Programme, Quality Assurance and Safety: Medicines, World Health Organization, 1211 Geneva 27, Switzerland; fax: (+41 22) 791 4730 or e-mail: kopps@who.int (with copies to gaspardin@who.int and bonnyw@who.int) by 15 August 2013.

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Monographs: Radiopharmaceuticals: Specific monographs: Natriiiodidi (\(^{131}\)I) solutio - Sodium iodide (\(^{131}\)I) solution

**Latin.** Natrii iodidi (\(^{131}\)I) solutio.

**English.** Sodium iodide (\(^{131}\)I) solution.

**Structural formula.** \( \text{Na}^+ \text{I} \)

**Relative molecular mass.** 153.895

**Empirical formula.** Na\(^{131}\)I

**Chemical name.** Sodium (\(^{131}\)I) iodide

**Other names.** Natrii radioiodidum, IodotopeSodium iodide I 131

**Description.** Sodium iodide (\(^{131}\)I) solution is a clear colourless solution. Iodine-131 has a half-life of 8.08 days.

**Category.** Diagnostic or therapeutic.
Storage. Stored at room temperature. Preserve in single-dose or multiple-dose containers that previously have been treated to prevent adsorption.

Labelling. State the date and the time of calibration; the amount of $^{131}\text{I}$ as iodide expressed as total MBq and the concentration expressed as MBq/ml, the expiration date, the name of any excipient, the name and quantity of any added preservative or stabilizer. The label states a statement of the intended use, whether oral or intravenous; a statement of whether the contents are intended for diagnostic or therapeutic use and the statement “Caution-Radioactive material”. The labelling indicates that in making dosage calculations, correction has to be made for radioactive decay, also indicates that the radioactive half-life of $^{131}\text{I}$ is 8.08 days.

Manufacture

Iodine-131 may be obtained by neutron bombardment of tellurium or by extraction from uranium fission products. There is no carrier iodide is added.

Sodium iodide ($^{131}\text{I}$) solution may contain sodium thiosulfate, sodium hydrogen carbonate or other suitable reducing agents and may contain a suitable buffer. Sodium iodide ($^{131}\text{I}$) solution may be sterilized by "Heating in an autoclave" (see 5.8 Methods of sterilization).

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 “Liquid preparations for oral use”, “Parenteral Preparations” and with that for “Radiopharmaceuticals” as appropriate.

Definition. Sodium iodide solution is an aqueous solution containing of radioactive ($^{131}\text{I}$) processed in the form of sodium iodide, suitable for either oral or intravenous administration. The solution contains not less than 90% and not more than 110% of the declared radioactivity due to iodine-131 stated on the label at the reference date and time. Not less than 99.9% of the total radioactivity is due to iodine-131. Not less than 95% of the total iodine-131 radioactivity is present as iodide. It contains minute amounts of naturally occurring iodine 127. The specific radioactivity is not less than 185 MBq (5 mCi) per microgram of iodine at the reference date and time stated on the label. The iodide content should not more than 20 µg in maximum recommended dose.
Identity tests

- Either tests A and C or tests B and C may be applied.

A. Record the gamma-ray and X-ray spectrum using a suitable instrument with a sample of iodine-131, suitably diluted if needed. The spectrum is concordant with the *reference spectrum* of a specimen of iodine-131 in that it exhibits a major peak of 364 keV. Standardized iodine-131 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 184 and 203 hours.

C. Examine the radiochromatogram obtained in the test for radiochemical purity. The principal peak in the chromatogram obtained with the test solution (a) is similar in retention time to the principal peak in the chromatogram obtained with the reference solution (a).

**pH value.** Carry out the test as described under 1.13 Determination of pH or R1.5 under the monograph for “Radiopharmaceuticals”. pH between 7.5 and 9.0 of the solutions intended for parenteral administration and between 7.5 and 10.0 of the solutions intended for oral administration.

**Sterility.** The solution complies with 3.2.1 Test for sterility of non-injectable preparations, modified as described in the monograph for “Radiopharmaceuticals”. If intended for intravenous administration it complies with 3.2 Test for sterility for injectable preparation, modified as described in the monograph for “Radiopharmaceuticals”. Test for sterility will be initiated on the day of manufacture. The solution 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, for solution intended for intravenous use modified as described in the monograph for “Radiopharmaceuticals”. The injection contains not more than 175/V (I.U of endotoxins per millilitre).

**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 iodine-131, iodine-133, iodine-135 and other radionuclidic impurities that may be present. Iodine-133 has a half-life of 20.8 hours and exhibits major peaks of 530 keV and 875 keV. Iodine-135 has a half-life of 6.55 hours and exhibits major peaks of 527 keV, 1132 keV and 1260 keV. Not less than 99.9% of the total radioactivity is due to iodine-131.

**Chemical purity**

**Iodide.** Carry out the test as described under 1.14.4 High-performance liquid chromatography. Prepare the test solution (a) which is the preparation to be examined. Prepare the test solution (b) by diluting test solution (a) using 0.05 M sodium
hydroxide until the radioactivity is equivalent to about 74 MBq/ml and add an equal volume of a solution containing 1 g/L of potassium iodide R, 2 g/L of potassium iodate R and 10 g/L of sodium hydrogen carbonate R and mix. The reference solution (a) is prepared by diluting 1 ml of a 26.2 mg/L solution of potassium iodide R to V with water R, (V being the maximum recommended dose in millilitres). Prepare the reference solution (b) by dilution 1 ml of a 24.5 mg/L solution of potassium iodate R to V with water R, (V being the maximum recommended dose in millilitres). Mix equal volumes of this solution and of reference solution (a). Prepare a solution containing 2 mg/ml of each of the components stated on the label, apart from iodide, used as blank solution. Use the column with (l = 0.25 m, Ø = 4.0 mm). The stationary phase is spherical base-deactivated end-capped octadecylsilyl silica gel for chromatography R (5 µm), maintain the temperature constant between 20 °C and 30 °C. Use stainless steel tubing.

Dissolve 5.844 g of sodium chloride R in 1000 mL of water R, add 680 µL of octylamine R and adjust to pH 7.0 with phosphoric acid R; add 50 mL of acetonitrile R and mix. Use the mixture as the mobile phase. The flow rate is 1.5 ml/min, the detector is spectrophotometer at 220 nm and radioactivity detector connected in series. Inject 25 µl of test solution (a), the blank solution and reference solutions (a) and (b). The run time is 12 minutes.

The relative retention with reference to iodide is 5 and to iodate is 0.2 to 0.3.

System suitability:
Regarding to the chromatogram due to the blank solution, none of obtained peaks shows a retention time similar to that of the peak due to iodide. The resolution is minimum of 2 between the peaks due to iodide and iodate in the chromatogram obtained with reference solution (b) recorded with the spectrophotometer. The limit of iodide is detected by studying the chromatogram obtained with the spectrophotometer and comparing the peak due to iodide with the chromatogram due to reference solution (a).

The area of the peak due to iodide is not more than the area of the corresponding peak in the chromatogram obtained with reference solution (a).

Radiochemical purity
• Either test A, B, or C may be applied:

A. Carry out the test as described under 1.14.2 Paper chromatography and ascending conditions, using paper for chromatography R (25- × 300-mm). Place a measured volume of a solution containing 100 mg of potassium iodide, 200 mg of potassium iodate, and 1 g of sodium bicarbonate and 25 mm from one end of the chromatographic paper. Allow the paper to dry. To the same area of the paper add an equal volume of appropriately diluted solution such that it provides a count rate of about 20,000 counts per minute, and allow to dry. Develop the chromatogram over a period of about 4 hours by ascending chromatography, using dilute methanol (7.0 in 10). Allow the paper to dry in air, and determine the radioactivity distribution by scanning with a suitable radiation detector: the radioactivity of the iodide $^{131}$I band is not less than 95% of the total radioactivity, and its
$R_F$ value falls within ±5% of the value found for sodium iodide when determined under parallel conditions. Confirmation of the identity of the iodide band is made by the addition to the suspected iodide band of 6 drops of acidified hydrogen peroxide solution (prepared by adding 6 drops of 1 N hydrochloric acid to 10 mL of hydrogen peroxide solution) followed by the dropwise addition of starch TS; the development of a blue color indicates presence of iodide.

B. Carry out the test [1.14.4 High-performance liquid chromatography](#) as described in the test for iodide with the following modification:

- Inject test solution (b),
- Detect iodide limit by examination of the radioactivity detector, not less than 95 per cent of the total radioactivity is due to $[^{131}\text{I}]$ iodide.

C. Carry out the test as described under [1.15 Electrophoresis, Paper-electrophoresis](#) Prepare paper strips, type Whatman No.3 MM for electrophoresis with dimensions of 65 x 3 cm.

Apply 10–20 µl samples in a distance of 10-13 cm from the end of the stripes. Use borate buffer with a concentration of 9 g/l and pH 9 ± 0.1. Carry out the electrophoresis on a potential of 900 V and time is 50 minutes.

The $R_f$ values for iodide is between 0.7 and 0.9, $R_f$ for iodate is 0.4, periodate from 0 to 0.1. Product can be accepted if the $[^{131}\text{I}]$ anion content is higher than 95% even on the expiration date.

**Radioactivity.** Measure the radioactivity as described under [R.1.1 Detection and measurement of radioactivity](#) in suitable calibrated counting equipment by comparison with a standardized iodine-131 solution or by measurement in an instrument calibrated with the aid of such a solution.

Standardized iodine-131 solutions are available from laboratories recognized by the relevant national or regional authority.

**Impurities**

$[^{131}\text{I}]$ iodate ion.