

BRAZILIAN

Pharmacopeia

7th edition





BRAZILIAN Pharmacopeia

7th edition

Brazilian Health Regulatory Agency

Brazilian Pharmacopeia

7th edition

Volume II - Monographs

Radiopharmaceuticals

Brasília
2026

Copyright © 2026. Brazilian Health Regulatory Agency

Full or partial reproduction of this work is allowed provided that the source is cited. The printing, distribution, reproduction of this work for commercial purposes is prohibited without the prior and express consent of Anvisa.

Available at: < <https://www.gov.br/anvisa/pt-br> >

Director-President

Antônio Barra Torres

Directors

Meiruze Sousa Freitas

Daniel Meirelles Fernandes Pereira

Romison Rodrigues Mota

Frederico Augusto de Abreu Fernandes (Diretor substituto)

Manager of Public Health Laboratories

Graziela Costa Araújo

Pharmacopeia Coordinator

Thaís Corrêa Rocha

Approved by Resolution – RDC No. 940, of November 14, 2024

Elaboration and edition:

Brazilian Health Regulatory Agency

SIA Ward 5, Special Area 57, Lot 200

71205-050 Brasília – DF

Cover Graphic Design

Igor Viana Coelho Henriques

Dados Internacionais de Catalogação na Publicação (CIP)
(Câmara Brasileira do Livro, SP, Brasil)

Agência Nacional de Vigilância Sanitária Brasil
Brazilian pharmacopeia [livro eletrônico] :
volume II : monographs : radiopharmaceuticals /
Agência Nacional de Vigilância Sanitária Brasil. --
7. ed. -- Brasília, DF : ANVISA, 2026.
PDF

ISBN 978-65-89701-63-7

1. Farmacopeia - Brasil 2. Medicina nuclear
I. Título.

26-374618.0

CDD-615.1181

Índices para catálogo sistemático:

1. Brasil : Farmacopeia 615.1181

Maria Alice Ferreira - Bibliotecária - CRB-8/7964



RADIOPHARMACEUTICALS

COLLOIDAL TIN (^{99m} Tc) INJECTABLE SOLUTION	RF006-00
FLUDEOXYGLUCOSE (18 F), INJECTION	RF001-02
SODIUM IODIDE (123 I) ORAL SOLUTION	RF007-00
SODIUM IODIDE (131 I) CAPSULES	RF008-00
SODIUM IODIDE (131 I) ORAL SOLUTION	RF009-00
SODIUM MEDRONATE (^{99m} Tc), INJECTION	RF002-01
SODIUM PENTETATE (^{99m} Tc), Injection	RF003-01
SODIUM PERTECHNETATE (^{99m} Tc), INJECTION	RF004-01
SESTAMIBI (^{99m} Tc), INJECTION	RF005-01

COLLOIDAL TIN ($^{99\text{m}}\text{Tc}$) INJECTABLE SOLUTION

Stanni colloidalis et technetii ($^{99\text{m}}\text{Tc}$) solutio iniectabilis

[$^{99\text{m}}\text{Tc}$] (SnF_2)

colloidal tin ($^{99\text{m}}\text{Tc}$); 11311

$\text{Sn(II)-}^{99\text{m}}\text{Tc}$; stannous fluoride ($^{99\text{m}}\text{Tc}$)

Contains not less than 90.0% and not more than 110.0% of the declared radioactivity of technetium- $^{99\text{m}}$ colloidal tin ($^{99\text{m}}\text{Tc}$), expressed in MBq/mL (or mCi/mL), at the date and time stated on the label.

DESCRIPTION

Sterile, clear, colorless colloidal dispersion of tin labeled with technetium- $^{99\text{m}}$, obtained from Sodium Pertechnetate ($^{99\text{m}}\text{Tc}$) Injectable Solution. Contains a variable amount of tin, not exceeding 1 mg/mL; contains fluoride ions. It may contain a protective stabilizing colloid and an appropriate buffering solution.

IDENTIFICATION

Identification test B. may be omitted if tests A. and C. are performed. Identification test C. may be omitted if tests A. and B. are performed.

A. The product must meet the requirements of the *Radionuclidic Identification Test* and *Radionuclidic Purity* as described under *Sodium Pertechnetate ($^{99\text{m}}\text{Tc}$) Injectable Solution*.

B. Mix 0.05 mL of zirconyl nitrate RS with 0.05 mL of alizarin red TS. Add 0.05 mL of the injectable solution to be examined. A yellow color is produced.

C. Examine the chromatogram obtained in the radiochemical purity test. The distribution of activity contributes to the identification of the preparation.

PURITY TESTS

pH (5.2.19). 4.0 to 7.0.

Radiochemical purity. Proceed as described under *Paper Chromatography (5.2.17.2)*, ascending type.

Stationary phase: a strip of chromatography paper.

Mobile phase: acetone.

Test solution: colloidal tin ($^{99\text{m}}\text{Tc}$) injectable solution to be examined.

Procedure: Apply 2–5 μL of a dilution of the *Test solution* appropriate to the sensitivity of the detection equipment onto the paper strip. Develop the chromatogram immediately, for sufficient time to resolve the species, and allow it to air-dry. Determine the distribution of radioactivity using a suitable detector. Free pertechnetate migrates with the solvent front ($R_f = 0.9\text{--}1.0$). Colloidal tin ($^{99\text{m}}\text{Tc}$) remains at the point of origin ($R_f = 0.0\text{--}0.1$). Not less than 95.0% of the radioactivity is due to technetium- $^{99\text{m}}$ ($^{99\text{m}}\text{Tc}$) in the colloidal form.

BIOLOGICAL SAFETY TESTS

Sterility (5.5.3.2.1). Complies with the test.

Bacterial endotoxins test (5.5.2.7.3). Must contain less than 175 IU/V, where V is the maximum injected volume, in mL, at the expiry date or time.

Biological distribution. Administer, intravenously, a maximum volume of 0.2 mL of colloidal tin (^{99m}Tc) injectable solution into the tail vein of three mice (20–25 g). Measure the syringe activity before and after administration. Euthanize the animals 20 minutes after injection and carefully remove the liver, spleen and lungs. Excise the tail. Determine the percentage of radioactivity in each organ according to:

$$(A/B) \times 100$$

where,

A is the radioactivity of the organ and B is the total radioactivity, which corresponds to the difference between the two syringe measurements minus the activity remaining in the tail.

The sum of the percentages of radioactivity found in the liver and spleen must be at least 80.0% of the injected activity, and not more than 5.0% of the injected activity must be found in the lungs in not fewer than two of the three animals.

RADIOACTIVITY

Proceed as described under *Radiopharmaceuticals* (8.3). Use an appropriate, calibrated counting system to determine the radioactivity in Bq (Ci), or their multiples and submultiples, per unit volume.

PACKAGING AND STORAGE

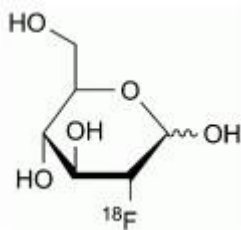
Proceed as described under *Radiopharmaceuticals* (8.3). Store in a tightly closed container with appropriate radiation shielding.

LABELING

Comply with current regulations.

USE

Diagnostic.

FLUDEOXYGLUCOSE (18 F), INJECTION*Fludeoxyglucosi (¹⁸F) injectio*C₆H₁₁¹⁸FO₅; 181.15

fludeoxyglucose (18 F); 04114

2-[¹⁸F]fluoro-2-deoxy-D-glucopyranose (2-[¹⁸F]fluoro-2-deoxy-D-glucose); 2-deoxy-2-[¹⁸F]fluoro-Dglucose; FDG-¹⁸F
[105851-17-0]

It contains not less than 90 percent and not more than 110 percent of fludeoxyglucose (18 F) radioactivity, at the date and time stated on the label.

DESCRIPTION

Fludeoxyglucose (18 F) is a sterile, clear or slightly yellow solution of 2-deoxy-2-[¹⁸F]fluoro-D-glucose. It may contain preservative, stabilizing agents or buffering agents. Fluorine-18 (18 F) is positron-emitting radionuclide with half-life of 109.77 minutes. It may be prepared by proton irradiation of oxygen-18 (18 O) in cyclotron accelerators and processed in a manner that 18 F obtained is carrier free.

IDENTIFICATION

A. Radionuclidic identity: proceed according to *Radiopharmaceuticals* (8.3). The physical half-life of 18 F determined using a suitable detector system, is between 105 and 115 minutes. In the gamma-ray spectrum obtained in the Radionuclidic purity test, the gamma emissions must correspond to the 0.511 MeV peak and also to the 1.022 MeV sum peak, depending on the measurement geometry.

B. Radiochemical identity: the R_f value of fludeoxyglucose (18 F) on the chromatogram of the *Sample solution* must correspond to the chromatogram of the *Standard solution*, as obtained in the *Radiochemical purity test*.

PURITY TESTS

pH (5.2.19). 4.5 to 7.5.

Radiochemical purity. Carry out of the test as described in *Thin-layer chromatography* (5.2.17.1). *Standard solution:* dissolve 10 mg of fludeoxyglucose (non-radioactive 2-deoxy-2-fluoro-D-glucose; MW 182.15) CRS in 100 mL of acetonitrile:water (95:5).

Sample solution: fludeoxyglucose (18 F) injection to be analyzed.

Stationary phase: activated chromatographic silica gel TLC-plate with adequate dimensions.

Mobile phase: acetonitrile: water (95:5).

Procedure: Place an aliquot of the diluted Sample solution in order to obtain an adequate counting rate for the radioactivity detection system. Approximately 10 µL of the Standard solution is applied on the same TLC-plate. Develop the chromatogram until the mobile phase has moved about ¾ of the length of the plate. Remove the plate and allow it to air-dry. Determine the radioactivity distribution on the plate with a suitable radiation detector.

In order to determine the position of fludeoxyglucose, spray the chromatographic plate with 1 M sulfuric acid solution, followed by heating until a spot appears. The R_f value of the Sample solution corresponds to that of the Standard solution (approximately 0.4). At least, 90 % of the total radioactivity correspond to fludeoxyglucose (18 F).

Chemical purity.

Note: the methods and limits described in this section are related to potential impurities that are associated to the synthesis process. The following tests are not necessary when those specific substances are not used or generated in the synthesis process.

Aminopolyether limit. Carry out the test as described in *Thin-layer chromatography* (5.2.17.1).

Sample solution: fludeoxyglucose (18 F) injection to be analyzed.

Standard solution: weigh the appropriate amount of aminopolyether (4,7,13,16,21,24-hexaoxa-1,10diazabicyclo[8.8.8]hexacosane) CRS and dissolve in 0.9 % sodium chloride solution (w/v) to obtain solution at 50 µg/mL.

Stationary phase: chromatographic silica gel TLC-plate.

Mobile phase: methanol:ammonium hydroxide 30% (9:1).

Procedure: Separately apply about 2.5 µL of the Sample solution and the Standard solution on the TLC-plate. Develop the chromatogram. Remove the plate and let it dry at room temperature. Place the plate in a chamber containing iodine crystals until a spot is visible on the chromatogram of the Standard solution.

The size and intensity of the aminopolyether spot of the *Sample solution* must not exceed that of the *Standard solution*.

2-chloro-2-deoxy-D-glucose. Carry out the test as described in *High performance liquid chromatography* (5.2.17.4). Use a high performance liquid chromatograph equipped with a pulsed amperometric detector and a 250 mm (L) x 4 mm (internal diameter) column, 10 µm packing strongly alkaline anionic resin; 0.5 mL/min of flow rate.

Mobile phase: prepare 1000 mL of a 0.2 M sodium hydroxide solution, filter and degas with helium.

System suitability: weigh appropriate amounts of fludeoxyglucose CRS and 2chloro-2-deoxy-D-glucose CRS and dissolve in the mobile phase to obtain 1 mg/mL and 0.1 mg/mL solutions, respectively.

Sample solution: fludeoxyglucose (18 F) injection to be analyzed.

Standard solution: 0.1 mg/mL 2-chloro-2-deoxy-D-glucose CRS solution.

System suitability: separately inject the Standard solution and the System suitability solution and record the chromatogram according to the Procedure. The resolution between fludeoxyglucose and 2-chloro-2-deoxy-D-glucose must be at least 1.5, and the relative standard deviation for repeated injections must be at most 5 %.

Procedure: Separately inject equal volumes (approximately 100 µL) of the *Standard solution* and the *Sample solution*. Record the chromatograms and measure the area of the main peaks.

Calculate the amount in mg of 2-chloro-2-deoxy-D-glucose, in each mL of the *Sample solution* (C_a) using the following formula:

$$C_a = C_p (r_a/r_p)$$

where:

C_p is the concentration of 2-chloro-2-deoxy-D-glucose in the *Standard solution* (mg/ml);
 r_a and r_p are the areas of peaks of 2-chloro-2-deoxy-D-glucose, from the *Sample solution* and the *Standard solution*, respectively.

The amount of 2-chloro-2-deoxy-D-glucose in the *Sample solution* (C_a) should be not more than 1 mg per dose.

Residual solvents. Carry out the test as described in Gas chromatography (5.2.17.5). The gas chromatograph is equipped with a flame ionization detector, split mode injection system (1:20 rate) and a 0.25 mm (internal diameter) x 30 m (L) fused-silica column coated with a 0.50 µm film thickness cross-linked polyethylene glycol (MW around 15000). Helium is the carrier gas with 2 mL/min of flow rate. The method program is the following: initially the temperature is maintained at 40 °C for one minute. Then increase 40 °C/min until reaching 100 °C and keep for one minute. The injector and detector temperature must be maintained at 250 °C and 300 °C, respectively.

Sample solution: fludeoxyglucose (18 F) injection to be analyzed.

Standard solution: an aqueous solution containing 0.01 % acetonitrile (w/v), 0.1 % ethanol (w/v) and 0.1 % ethyl ether (w/v).

System suitability: inject approximately 1 µL of the *Standard solution* in triplicate and record the peak response. The resolution between any two components must be at least 1.0 and the relative standard deviation for the areas of the injection replicates must be at most 5 %.

Procedure: separately inject equal volumes (approximately 1 µL) of the *Sample solution* and the *Standard solution*. Record the chromatograms and measure the peak areas

Calculate the concentration of residual solvent in the *Sample solution* as follows:

$$C_a = C_p (r_a/r_p)$$

where:

C_a = percentage of solvent in the *Sample solution* (%);
 C_p = percentage of solvent in the *Standard solution* (%);
 r_a/r_p = peak area of *Sample solution*/peak area of the *Standard solution*.

maximum, 0.04% of acetonitrile, 0.5% of ethanol and 0.5% of ethyl ether.

Radionuclidic purity. Carry out the test as describing in *Radiopharmaceuticals* (9). Determine using a suitable calibrated gamma-ray spectrometer. In the resultant gamma spectrum, at least 99.5 % must correspond to 0.511 MeV main peak, 1.022 MeV sum peak or Compton-scattering peaks of 18 F.

BIOLOGICAL SAFETY TESTS

Sterility (5.5.3.2.1). Meets the requirements. The product can be used before the conclusion of sterility test.

Bacterial endotoxins test (5.5.2.7.3). It must contain less than 175 UE/V, where *V* is the maximum recommended dose, in mL, at the expiration date or time.

RADIOACTIVITY

Carry out the test as described in *Radiopharmaceuticals* (8.3). Use a suitable and calibrated counting instrument, determine the radioactivity in Bq (Ci) or its multiples and sub-multiples, per volume unit.

PACKAGING AND STORAGE

Carry out as described in *Radiopharmaceuticals* (8.3). Keep in a perfectly closed container, in a radiation protection shield.

LABELING

Following the current legislation.

USE

Diagnostic.

SODIUM IODIDE (123 I) ORAL SOLUTION

Natrii iodidi (¹²³I) solutio

Na-¹²³I; 145.89
sodium iodide (¹²³I); 09741
[¹²³I] sodium iodide
[41927-88-2]

Contains not less than 90.0% and not more than 110.0% of the radioactivity of sodium iodide (123 I) at the date and time stated on the label.

DESCRIPTION

Clear, colorless oral solution containing iodine-123 in the form of sodium iodide. It may contain a reducing agent, such as sodium thiosulfate, and an appropriate buffer solution. Iodine-123 is a gamma-emitting radionuclide and has a physical half-life of 13.2 hours. Iodine-123 may be obtained by proton irradiation of enriched xenon-124 (minimum 98.0%), followed by decay of xenon-123 originating from cesium-123.

IDENTIFICATION

A. The gamma spectrum shows a principal peak at an energy of 0.159 MeV.

B. Examine the chromatogram obtained in the test for *Radiochemical purity*. The R_f of the principal species in the *Test solution* is between 0.8 and 1.0.

PURITY TESTS

pH (5.2.19). 7.5 to 10.0.

Radiochemical purity. Proceed as described under *Paper Chromatography (5.2.17.2)*, ascending type.

Stationary phase: a strip of chromatographic paper.

Mobile phase: methanol–water (85:15).

Test solution: dilute the sodium iodide (¹²³I) solution to be examined with 0.01 M sodium hydroxide to obtain a count rate suitable for the radioactivity detection system.

Reference solution: prepare a solution containing 2 g/L potassium iodide, 2 g/L potassium iodate, and 10 g/L of sodium bicarbonate.

Revealing solution A: 20 g/L potassium iodate solution.

Revealing solution B: glacial acetic acid.

Procedure: Apply 2–5 µL of the *Reference solution* onto the paper strip and allow to dry. At the same point, apply 2–5 µL of an appropriate dilution of the *Test solution* for the sensitivity of the detector. Develop the chromatogram through 10 cm from the application point and allow to air dry. Confirm the identity of iodide by applying *Revealing solution A* followed by *Revealing solution*

B to the upper half of the strip. Determine the distribution of radioactivity using an appropriate detector, considering the entire revealed region for calculating the percentage of sodium iodide (¹²³I). Not less than 95.0% of the total radioactivity corresponds to sodium iodide (¹²³I).

Radionuclidic purity. Proceed as described under *Radiopharmaceuticals* (8.3). Determine radionuclides by gamma-ray spectrometry (γ) using a properly calibrated instrument. Determine the relative amounts of iodine-123, iodine-125, tellurium-121, and other radionuclidic impurities. For detection of tellurium-121 and iodine-125, retain the preparation for a sufficient period to allow decay of iodine-123. Not less than 90.0% of the total radioactivity must correspond to iodine-123.

BIOLOGICAL SAFETY TESTS

Total count of mesophilic microorganisms (5.5.3.1.2). Complies with the test.

Test for pathogenic microorganisms (5.5.3.1.3). Complies with the test.

Note: the absence of biological safety tests in the final product must be technically justified.

RADIOACTIVITY

Proceed as described under *Radiopharmaceuticals* (8.3). Use an appropriate and calibrated counting system to determine activity in Bq (Ci), or their multiples or submultiples, per unit volume.

PACKAGING AND STORAGE

Proceed as described under *Radiopharmaceuticals* (8.3). Store in a tightly closed container with appropriate radiation shielding.

LABELING

Comply with current regulations.

USE

Diagnostic and therapeutic.

SODIUM IODIDE (131 I) CAPSULES*Natrii iodidi (¹³¹I) capsula*Na¹³¹I; 153.89sodium iodide (¹³¹I); 04972[¹³¹I] sodium iodide

[7790-26-3]

Each oral capsule contains not less than 90.0% and not more than 110.0% of the radioactivity of sodium iodide (131 I) at the date and time stated on the label. Each capsule contains not more than 20 µg of iodide.

DESCRIPTION

Oral capsule containing iodine-131 in the form of sodium iodide. It may contain a reducing agent, such as sodium thiosulfate. Iodine-131 is a gamma- and beta-emitting radionuclide with a physical half-life of 8.06 days. Iodine-131 may be obtained as a fission product of uranium-235 or by neutron bombardment of tellurium-130 targets, processed into sodium iodide.

IDENTIFICATION

A. Proceed as described under *Identification* test **A.** of the monograph *Sodium Iodide (¹³¹I) Oral Solution*.

B. Proceed as described under *Identification* test **B.** of the monograph *Sodium Iodide (¹³¹I) Oral Solution*.

PURITY TESTS

Note: The methods and limits in this section relate to potential impurities associated with the production of iodine-131 by fission of uranium-235. Additional purity tests may be necessary for iodine-131 obtained by neutron bombardment of tellurium targets.

Disintegration. Proceed as described under *Disintegration Test (5.1.4.1)*. Using a water bath at 37 °C, heat a vessel containing 20 mL of 0.2% potassium iodide solution. Add the capsule to be examined, ensuring it is fully submerged. Maintain agitation at 20 rpm. Perform the test on 3 non-radioactive capsules. The contents of the capsule must completely dissolve within 15 minutes in at least two of the capsules.

Content Uniformity Test for diagnostic-use capsules. Determine the mean activity using a sample of not fewer than ten capsules. The activity of each capsule must not differ by more than 10% from the mean, and the relative standard deviation must not exceed 3.5%.

Radiochemical purity. Homogenize the capsule in a water:methanol solution (1:1). Proceed as described under *Radiochemical purity* in the monograph *Sodium Iodide (¹³¹I) Solution*, using an aliquot of the supernatant. Not less than 95% of the total radioactivity corresponds to sodium iodide (¹³¹I).

Radionuclidic purity. Proceed as described under *Radiopharmaceuticals (8.3)*. Determine by gamma-ray spectrometry (γ) using a properly calibrated instrument. Determine the relative amounts

of iodine-131, iodine-133, iodine-135, and other radionuclidic impurities. Not less than 99.9% of the total radioactivity must correspond to iodine-131.

BIOLOGICAL SAFETY TESTS

Total count of mesophilic microorganisms (5.5.3.1.2). Complies with the test.

Test for pathogenic microorganisms (5.5.3.1.3). Complies with the test.

***Note:** the absence of biological safety tests in the final product must be technically justified.*

RADIOACTIVITY

Proceed as described under *Radiopharmaceuticals (8.3)*. Use an appropriate and calibrated counting system to determine the activity in Bq (Ci) or their multiples and submultiples per capsule.

PACKAGING AND STORAGE

Proceed as described under *Radiopharmaceuticals (8.3)*. Store in a tightly closed container with appropriate radiation shielding.

LABELING

Comply with current regulations.

USE

Diagnostic and therapeutic.

SODIUM IODIDE (131 I) ORAL SOLUTION

Natrii iodidi (¹³¹I) solutio

Na¹³¹I; 153.89
sodium iodide (¹³¹I); 04972
[¹³¹I] sodium iodide
[7790-26-3]

Contains not less than 90.0% and not more than 110.0% of the radioactivity of sodium iodide (131 I) at the date and time stated on the label.

DESCRIPTION

Clear, colorless oral solution containing iodine-131 as sodium iodide. It may contain a reducing agent, such as sodium thiosulfate, and an appropriate buffer solution. Iodine-131 is a gamma- and beta-emitting radionuclide with a physical half-life of 8.06 days. Iodine-131 may be obtained as a fission product of uranium-235 or by neutron bombardment of tellurium-130 targets, processed into sodium iodide.

IDENTIFICATION

- A.** The gamma spectrum exhibits a principal peak at 0.364 MeV.
- B.** Examine the chromatogram obtained in the test for *Radiochemical Purity*. The R_f of the principal species in the *Test solution* is between 0.8 and 1.0.

PURITY TESTS

Note: The methods and limits described in this section relate to potential impurities associated with the production of iodine-131 from uranium-235 fission. Additional purity tests may be necessary for iodine-131 obtained by neutron bombardment of tellurium targets.

pH (5.2.19). 7.5 to 10.0.

Radiochemical purity. Proceed as described under *Paper Chromatography (5.2.17.2)*, ascending type.

Stationary phase: a strip of chromatographic paper.

Mobile phase: mixture of methanol and water (85:15).

Test solution: dilute the sodium iodide (¹³¹I) solution to be analyzed in 0.01 M sodium hydroxide to obtain a count rate suitable for the radioactivity detection system employed.

Reference solution: prepare a solution containing 2 g/L of potassium iodide, 2 g/L of potassium iodate and 10 g/L of sodium bicarbonate.

Reagent solution A: potassium iodate solution, 20 g/L.

Reagent solution B: glacial acetic acid.

Procedure: apply 2–5 µL of the *Reference solution* to the paper strip and allow to dry. On the same spot, apply 2–5 µL of a suitable dilution of the *Test solution*. Develop the chromatogram for 10 cm from the point of application and allow to air dry. Confirm the identity of iodide by applying *Reagent solution A* followed by *Reagent solution B* on the upper half of the strip. Determine the radioactivity distribution on the strip with a suitable detector, considering the entire developed region for the calculation of the percentage of sodium iodide (¹³¹I). Not less than 95% of the total radioactivity corresponds to sodium iodide (¹³¹I).

Radionuclidic purity. Proceed as described under *Radiopharmaceuticals (8.3)*. Determine by gamma-ray spectrometry (γ) using a properly calibrated instrument. Determine the relative amounts of iodine-131, iodine-133, iodine-135, and other radionuclidic impurities present. Not less than 99.9% of the total radioactivity must correspond to iodine-131.

BIOLOGICAL SAFETY TESTS

Total mesophilic microorganism count (5.5.3.1.2). Complies with the test.

Test for pathogenic microorganisms (5.5.3.1.3). Complies with the test.

Note: the absence of biological safety tests in the final product must be technically justified.

RADIOACTIVITY

Proceed as described under *Radiopharmaceuticals (8.3)*. Use an appropriate and calibrated counting system to determine the activity in Bq (Ci) or their multiples and submultiples per unit volume.

PACKAGING AND STORAGE

Proceed as described under *Radiopharmaceuticals (8.3)*. Store in a tightly closed container with appropriate radiation shielding.

LABELING

Comply with current regulations.

USE

Diagnostic and therapeutic.

SODIUM MEDRONATE (99m Tc), INJECTION

Technetii (^{99m}Tc) medronati injectio

[^{99m}Tc](CH₆O₈P₂)_n

sodium medronate (99m Tc); 09794

MDP-^{99m}Tc; sodium methylene diphosphonate (99m Tc)

[121524-79-6]

It contains not less than 90 percent and not more than 110 percent sodium medronate (99m Tc), expressed in MBq/mL (mCi/mL), at the date and time stated on the label.

DESCRIPTION

Technetium-99m sodium medronate injection is a sterile, clear aqueous solution. It is a complex formed by sodium medronate and technetium-99m, from the sodium pertechnetate (99m Tc) injection solution, in presence of a reducing agent. Other chemicals forms of radioactivity do not exceed 10 percent of the total radioactivity. It may contain preservatives, stabilizers, antimicrobial agents and suitable buffer solutions.

IDENTIFICATION

A. The product must meet the requirements of the Radionuclidic Identification test and of Radionuclidic Purity from the monograph Sodium pertechnetate (99m Tc), injection.

B. Examine the chromatogram obtained in the radiochemical purity test. The radioactivity distribution contributes to the identification of the preparation.

PURITY TESTS

pH (5.2.19). 4.0 to 8.0.

Radiochemical purity Carry out the test as described in *Paper chromatography (5.2.17.2)*, ascending type.

Sample solution: sodium medronate (99m Tc) injection to be analyzed.

A. Stationary phase: use a chromatographic paper strip.

Mobile phase: sodium chloride solution 0.9% (w/v).

Procedure: Place 2 to 5 µL of a dilution of the *Sample solution* on the paper strip suitable to the sensitivity of the detection equipment. Develop the chromatogram immediately and over a suitable period to allow the specimens to separate and allow it to air-dry. Determine the distribution of radioactivity using an appropriate detector. Free pertechnetate and the sodium medronate (99m Tc) migrate with the solvent front (R_f 0.9-1.0). Technetium-99m in colloidal form is located at origin (R_f 0.0-0.1).

B. Stationary phase: use a chromatographic paper strip.

Mobile phase: acetone.

Procedure: place 2 to 5 µL of a dilution of the *Sample solution* on the paper strip suitable to the sensitivity of the detection equipment. Develop the chromatogram immediately and over a suitable period to allow the specimens to separate and allow it to air-dry. Determine the distribution of radioactivity using an appropriate detector. Free pertechnetate migrates with the solvent front (R_f 0.9-

1.0). Sodium medronate (99m Tc) and technetium-99m in colloidal form are located at origin (Rf 0.0-0.1).

The percentage of radioactivity corresponding to the sum of percentages of radioactivity due to technetium in colloidal form, determined in the test A and free technetium-99m, determined in the test B, must not exceed 10.0%.

BIOLOGICAL SAFETY TESTS

Sterility (5.5.3.2.1). Meets the requirements.

Bacterial endotoxins test (5.5.2.7.3). It must contain less than 175 UE/V, where *V* is the maximum recommended dose, in mL, at the expiration date or time.

Biological distribution. Inject intravenously in a volume not exceeding 0.2 mL, equivalent to, at most, 0.05 mg of sodium medronate, on the caudal or saphenous vein of three rats (150-250 g). Measure the syringe activity before and after administering. Sacrifice the animals one hour after the injection and carefully remove a femur, the liver, and the kidneys. Extirpate the tail if the vein was used for injection. Determine the percentage of radioactivity in each organ according to the expression:

$$(A/B) \times 100$$

where:

A is the organ radioactivity and B is the total radioactivity, equivalent to the difference between the two measures from the syringe, less the tail activity.

A minimum of 1% of the injected radioactivity must be found on the femur and a maximum of 5% on the liver or kidneys in at least two of the three animals.

RADIOACTIVITY

Carry out of the test as described in *Radiopharmaceuticals (8.3)*. Using an suitable and calibrated counting instrument, determine the activity in Bq (Ci) or its multiples and sub-multiples, per volume unit.

PACKAGING AND STORAGE

Carry out as described in *Radiopharmaceuticals (8.3)*. Keep in a perfectly closed container, in a radiation protection shield.

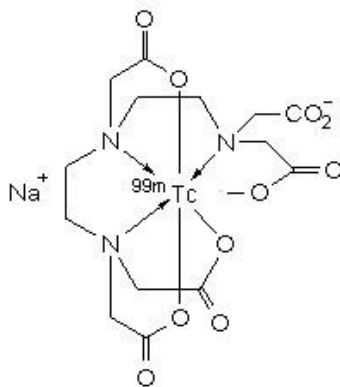
LABELING

Following the current legislation.

USE

Diagnostic.

SODIUM PENTETATE (99m Tc), Injection
Technetii (^{99m}Tc) pentetatis injectio



[^{99m}Tc]C₁₄H₁₈N₃NaO₁₀; 510.20

sodium pentetate (99m Tc); 09748

[N, N-bis{2-[bis(carboxymethyl)amino]ethyl} glycinate(5-)]sodium [^{99m}Tc]technetate(1-);
 DTPA-99mTc

[65454-61-7]

It contains not less than 90 percent and not more than 110 percent of sodium pentetate (99m Tc), expressed in MBq/mL (mCi/mL), at the date and time stated on the label.

DESCRIPTION

Technetium-99m sodium pentetate injection is a sterile, clear aqueous solution. It is a complex formed by sodium pentetate and technetium-99m, from the sodium pertechnetate (99m Tc) injection solution, in presence of a reducing agent. Other chemicals forms of radioactivity do not exceed 10 percent of the total radioactivity. It may contain preservatives, stabilizers, antimicrobial agents and suitable buffer solutions.

IDENTIFICATION

A. The product must meet the requirements of the Radionuclidic Identification test and of Radionuclidic Purity from the monograph *Sodium pertechnetate (99m Tc), injection*.

B. Examine the chromatogram obtained in the radiochemical purity test. The radioactivity distribution contributes to the identification of the preparation.

PURITY TESTS

pH (5.2.19). 3.8 to 7.5.

Radiochemical purity. Carry out the test as described in *Paper chromatography (5.2.17.2)*, ascending type.

Sample solution: sodium pentetate (99m Tc) injection to be analyzed.

A. Stationary phase: use a chromatographic paper strip.

Mobile phase: sodium chloride solution at 0.9% (w/v).

Procedure: place 2 to 5 µL of a dilution of the *Sample solution*, on the paper strip, suitable to the sensitivity of the detection equipment. Develop the chromatogram immediately and over a suitable period to allow the specimens to separate and allow it to air-dry. Determine the distribution of radioactivity using an appropriate detector. Free pertechnetate and the sodium pentetate (99m Tc) migrate with the solvent front (Rf 0.9-1.0). Technetium-99m in colloidal form located at origin (Rf 0.0-0.1).

B. Stationary phase: use a chromatographic paper strip.

Mobile phase: acetone.

Procedure: place 2 to 5 µL of a dilution of the *Sample solution*, on the paper strip, suitable to the sensitivity of the detection equipment. Develop the chromatogram immediately and over a suitable period to allow the specimens to separate and allow it to air-dry. Determine the distribution of radioactivity using an appropriate detector. Free pertechnetate migrates with the solvent front (Rf 0.9-1.0). Sodium pentetate (99m Tc) and technetium-99m in colloidal form are located at origin (Rf 0.0-0.1).

The percentage of radioactivity corresponding to the sum of percentages of radioactivity due to technetium in colloidal form, determined in the test A and free technetium-99m, determined in the test B, must not exceed 10.0 %.

BIOLOGICAL SAFETY TESTS

Sterility (5.5.3.2.1). Meets the requirements

Bacterial endotoxins test (5.5.2.7.3). It must contain less than 175 UE/V, where V is the maximum recommended dose, in mL, at the expiration date or time.

Biological distribution. Inject intravenously in a volume not exceeding 0.2 mL of sodium pentetate (99m Tc) injection on the caudal or saphenous vein of three rats (150-250 g). Measure the syringe activity before and after administering. Extirpate the tail, if the caudal vein was used for injection. Determine the percentage of radioactivity in each organ according to the expression:

$$(A/B) \times 100$$

where:

A is the organ radioactivity and B is the total radioactivity, equivalent to the difference between the two measures from the syringe, less the tail activity.

Two hours after the injection, the sum of percentages of radioactivity found in the urine and bladder must be higher than 85% of the injected radioactivity and less than 1% of the radioactivity injected must be found in the liver of at minimum two of the three animals.

RADIOACTIVITY

Carry out the test as described in Radiopharmaceuticals (**8.3**). Using a suitable and calibrated counting instrument, determine the activity in Bq (Ci) or its multiples and sub-multiples, per volume unit.

PACKAGING AND STORAGE

Carry out as described in Radiopharmaceuticals (**8.3**). Keep in a perfectly closed container, in a radiation protection shield.

LABELING

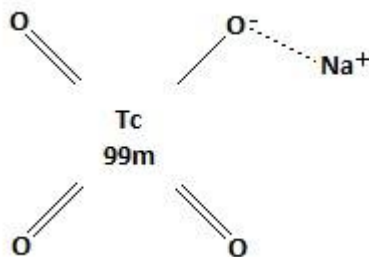
Following the current legislation.

USE

Diagnostic.

SODIUM PERTECHNETATE (99m Tc), INJECTION

Technetii (^{99m}Tc) injectio



Na[^{99m}Tc]O₄; 185.89
 sodium pertechnetate (99m Tc); 09750
 pertechnetetic acid (H^{99m}TcO₄), sodium salt
 [23288-60-0]

It contains not less than 90 percent and not more than 110 percent of sodium pertechnetate (99m Tc) expressed in MBq/mL (mCi/mL), at the date and time stated on the label.

DESCRIPTION

Sterile and colorless solution of sodium pertechnetate (99m Tc), prepared from isotonic sodium chloride solution. Sodium pertechnetate (99m Tc) injection is produced by chemical separation of the radioactive decay of parent radionuclide molybdenum-99.

At least 95% of the total technetium-99m (99m Tc) radioactivity should be present as pertechnetate ion.

Technetium-99m is a gamma emitting radionuclide, with a half-life of 6,007 hours, formed by the decay of molybdenum-99 (99 Mo).

Molybdenum-99 is a radioactive isotope of molybdenum and may be formed as a product of uranium fission or by the neutron bombardment of molybdenum-98 (98 Mo).

IDENTIFICATION

The gamma spectrum, obtained with a properly calibrated gamma spectrometry system, must correspond to the spectrum of technetium-99m concerning its energies and intensities, as indicated under *Radiopharmaceuticals* (8.3). The main gamma photon of 99m Tc has an energy of 140 keV.

PURITY TESTS

pH (5.2.19). 4.0 to 8.0.

Aluminum.

Note: To be determined if, in obtaining the sodium pertechnetate (99m Tc) solution, separation is accomplished by an alumina column in the preparation of the Injection.

Sample solution: dilute 1 mL of the sodium pertechnetate (99m Tc) injection to 2.5 mL, with water.

Reference solution: prepare at the same time as the *Sample solution* and use 2 mL of the standard aluminum solution (2 ppm Al).

Aluminum standard solution: dissolve in water 35.17 mg of aluminum potassium sulfate dodecahydrate (CRS) accurately weighed, dilute to 1000 mL. Each mL of this solution contains 2 µg of Al.

Procedure: in a test tube of about 12 mm in internal diameter, mix 1 mL of 0.5 M acetate buffer solution, pH 4.6 and 2 mL of the *Sample solution*. Add 50 µL of a 10 g per liter chrome azurol solution. After three minutes, the color of the solution is not more intense than that of an aluminum standard. The concentration of aluminum ion in the Injection is not greater than 5 ppm Al.

Methyl ethyl ketone.

Note: *determine if the separation is accomplished by liquid-liquid extraction in the preparation of the injection*

Procedure: place 1 mL of the injectable solution to an adequate container and dilute with water to 20 mL. Add 2 mL of 1 M sodium hydroxide, mix, then add 2 mL of 0.1 M iodine, dropwise, and again mix. At the same time, prepare a standard by placing 1 mL of a methyl ethyl ketone solution (1 in 1000) to a similar container and diluting with water to 20 mL. Add 2 mL of 1 M sodium hydroxide, mix, then add 2 mL of 0.1 M iodine, dropwise, and again mix. After two minutes, the turbidity of the *Sample solution* does not exceed that of the standard (0.1%).

Radionuclidic purity.

Preliminary assay obtain an approximate estimate, before using the sodium pertechnetate (99m Tc) injection, using a volume of technetium-99m solution that has approximately 370 MBq (10 mCi) and determine its activity with a properly calibrated activity meter using the technetium-99m scale, as indicated in *Radiopharmaceuticals (9)*. Register the activity. Measure the activity of molybdenum-99 in the same *Sample solution*, changing the activity meter scale to molybdenum-99 and placing the *Sample solution* inside the 6 mm lead shielding, necessary for such determination. The maximum activity of molybdenum-99 is not more than 0.15 kBq per MBq (0.15 µCi per mCi) of technetium-99m, from the previously determined measure.

Purity assay in the decayed test solution: keep a sample of the sodium pertechnetate (99m Tc) injection to be analyzed, for a sufficient interval (three to five days) so that the activity of technetium-99m decreases and enables the detection of radionuclidic impurities. All activity measurements must refer to the date and time of administration. Obtain the gamma radiation spectrum of the test solution using a high resolution gamma spectrometry system.

For the injectable solution prepared from technetium-99m derived of the precursor molybdenum-99 as the result of neutron bombardment of stable molybdenum, proceed with the following tests:

MOLYBDENUM-99: the presence of molybdenum-99 in the injectable solution is evident by its characteristic gamma ray spectrum. The most prominent photopeaks of this radionuclide have energies of 0.181; 0.740 and 0.780 MeV. The activity of molybdenum-99 is no grater than 0.15 kBq per MBq (0.15µCi per mCi) of technetium-99m, per administered dose, at the time of administration.

OTHER GAMMA RAY-EMITTING RADIONUCLIDIC IMPURITIES: the total activity of other emitting radionuclidic impurities does not exceed 0.5 kBq per MBq (0.5 µCi per mCi) of technetium-99m, or 92 kBq (2.5 µCi) per administered dose at the time of administration.

For the injectable solution prepared from technetium-99m derived of the precursor molybdenum-99 obtained as the result of fission of uranium, proceed to the tests described below:

MOLYBDENUM-99: the injectable solution must meet the requirements established for injection prepared by irradiation of stable molybdenum with neutrons (as previously described).

IODINE-131: the most prominent photopeak of this radionuclide has 0.364 MeV of energy. The maximum activity of iodine-131 is not more than 0.05 kBq per MBq (0.05 µCi per mCi) of technetium-99m, at the time of administration.

RUTHENIUM-103: the most prominent photopeak of this radionuclide has 0.497 MeV of energy. The maximum activity of ruthenium-103 is not more than 0.05 kBq per MBq (0.05 µCi per mCi) of technetium-99m, in the moment of administration.

STRONTIUM-89: determine the presence of strontium-89 in the injection by a suitable and calibrated counting instrument for detecting corpuscular radiation. Strontium-89 disintegrates by beta emission, with maximum energy of 1.463 MeV. The maximum activity of strontium-89 is not more than 0.0006 kBq per MBq (0.0006 µCi per mCi) of technetium-99m, at the time of administration.

STRONTIUM-90: determine the presence of strontium-90 in the injection by using an counting system adequate for detecting corpuscular radiation. Strontium-90 disintegrates by beta emission, with maximum energy of 0.546 MeV. The maximum activity of strontium-90 is not more 0.00006 kBq per MBq (0.00006 µCi per mCi) of technetium-99m, at the time of administration.

OTHER RADIONUCLIDIC IMPURITIES: the activities of other radionuclidic impurities that emit gamma and beta rays must correspond to a maximum of 0.01% at the time of administration. The total alpha activity is not more than 0.001 Bq per 1 MBq (or 0.001 µCi per 1 mCi) of technetium-99m, at the time of administration.

Radiochemical purity. Carry out the test as described in *Paper chromatography (5.2.17.2)*, ascending type.

Sample solution: dilute the sodium pertechnetate (99m Tc) injection with water to obtain an adequate radioactive concentration to the detection system.

Stationary phase: use a chromatographic paper strip.

Mobile phase: methyl alcohol and water (85:15).

Procedure: Place on the paper strip 2 to 5 µL of the *Sample solution*. Develop the chromatogram immediately and for a sufficient period of time that enables the separation of the specimens and allow it to air-dry. Determine the distribution of radioactivity using an appropriate instrument. The value of R_f corresponding to pertechnetate ion is between 0.9 and 1.0. The radioactivity of the pertechnetate ion is not less than 95% of the total radioactivity in the test specimen.

BIOLOGICAL SAFETY TESTS

Sterility (5.5.3.2.1).

Meets the requirements

Bacterial endotoxins test (5.5.2.7.3). It must contain less than 175 UE/V, where *V* is the maximum recommended dose in mL, at the expiration date or time.

RADIOACTIVITY

Carry out the test as described in Radiopharmaceuticals (8.3). Use a suitable and calibrated counting instrument, determine the activity in Bq (Ci) or its multiples and sub-multiples, per volume unit.

PACKAGING AND STORAGE

Carry out as described in Radiopharmaceuticals (**8.3**). Keep in a perfectly closed container, in a radiation protection shield.

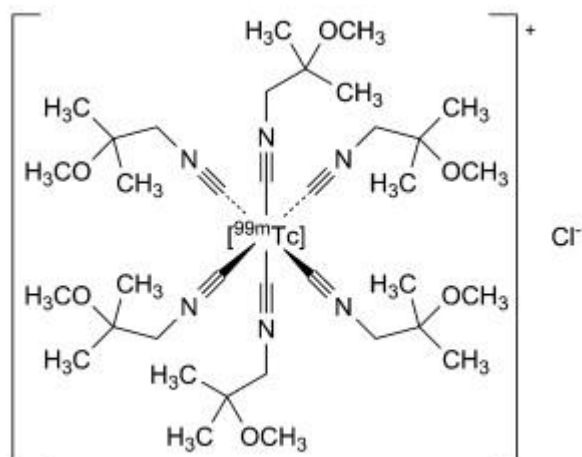
LABELING

Following the current legislation.

USE

Diagnostic.

SESTAMIBI (^{99m}Tc), INJECTION
Technetii (^{99m}Tc) sestamibi injectio



[^{99m}Tc]C₃₆H₆₆N₆O₆; 775.41

Technetium (99m) Sestamibi; 08338

(OC-6-11)-hexakis[1-(isocyane-κC)-2-methoxy-2-methylpropane] [^{99m}Tc]technetium(I) chloride; MIBI-^{99m}Tc

[109581-73-9]

It contains not less than 90 percent and not more than 110 percent of labeled amount of the radioactivity of sestamibi (^{99m}Tc), at the date and time stated on the label.

DESCRIPTION

Sestamibi (^{99m}Tc) injection is a sterile, clear solution of tetrakis(2-methoxy-2-methylpropyl-1-isocyanide) copper (I) tetrafluoroborate that is labeled with technetium-99m from sodium pertechnetate (^{99m}Tc) injection, in the presence of a reducing agent and a weak chelating agent. Other chemical forms of radioactivity do not exceed 10% of the total radioactivity. It may contain preservatives, stabilizers, antimicrobial agents and suitable buffer solutions.

IDENTIFICATION

A. The product must comply with the requirements from the Radionuclidic identification test and of Radionuclidic purity from the monograph *Sodium pertechnetate (^{99m}Tc), injection*.

B. Examine the chromatogram obtained in the radiochemical purity test. The radioactivity distribution contributes to the identification of the preparation.

PURITY TESTS

pH (5.2.19). 5.0 to 6.0.

Radiochemical purity.

A. Carry out the test as described in *Thin-layer chromatography (5.2.17.1)*.

Sample solution: sestamibi (^{99m}Tc) injection to be analyzed.

Stationary phase: reverse phase chromatographic plate (silica chemically linked to octadecylsilane group) with adequate dimensions.

Mobile phase: solution of acetonitrile : methanol: ammonium acetate 3.85%: tetrahydrofuran (4:3:2:1).

Procedure: Place on the chromatographic plate 2 to 5 µL of a dilution of the *Sample solution*, suitable for the sensitivity of the detection equipment. Develop the chromatogram immediately for a sufficient period of time that allows separating the specimens and allow it to air-dry. Determine the distribution of radioactivity using an appropriate detector.

The Rf value corresponding to sestamibi (99m Tc) and to the impurity (OC-6-22)-pentakis[1-(isocyanekC)-2-methoxy-2-methylpropane][1-(isocyanekC)-2-methylprop-1-ene][^{99m}Tc]technetium(1+), also known as pentamibi (99m Tc), is between 0.3 and 0.6. Per technetate (99m Tc) ion is located at about the Rf 0.8 and 1.0 and technetium-99m in colloidal form is located at about Rf 0.0 and 0.1 minimum 90% of the total radioactivity must be between Rf 0.3 and 0.6. The maximum percentage of radioactivity corresponding to the sum of percentages of radioactivity of the impurities free per technetate (99m Tc) ion and technetium-99m in colloidal form must be 10%.

B. Carry out the test as described in *High performance liquid chromatography (5.2.17.4)*. Use a liquid chromatograph equipped with radioactivity detector; analytical column with 300 mm of length and 3.9 mm of diameter, packaged with silica chemically linked to octadecylsilane group (10 µm); Mobile phase flow of approximately 2 mL per minute. If the peak impurity pentamibi (99m Tc) is present, its relative retention in relation to the peak sestamibi (99m Tc) is from 1.3 to 1.5.

Sample solution: sestamibi (99m Tc) injection to be analyzed.

Mobile phase: prepare a filtered and degassed mixture of methanol, ammonium sulfate solution 0.05 M and acetonitrile (45:35:20).

Procedure: inject approximately 5 µL (9.375 MBq or 250 µCi) of sestamibi (99m Tc) injection in the liquid chromatograph and adjust the integrator/recording device so that the peak is between 25% and 100% of the fullscale. separately, inject equal volumes (approximately 5 µL, 9.375 MBq or 250 µCi) of the *Sample solution* in the chromatograph, record the chromatograms, and measure the area percentage for all the peaks presented. The retention time of sestamibi (99m Tc) is about 5 to 10 minutes. the retention time of the impurity pentamibi (99m Tc) is about 6 to 13 minutes. Correct for the presence of technetium-99m in colloidal form, which is not determined by this method, using the following equation:

$$F = (100\% - P) / 100$$

Where *F* is the correction factor and *P* is the percentage of technetium-99m in colloidal form acquired by this method **A**. Obtain the corrected area percentage by multiplying *F* by the percentage area of the peaks presented in the chromatogram.

A mean of not less than 90% (corrected area percentage) of the total radioactivity is represented by sestamibi (99m Tc), and a mean of not more than 5% (corrected area percentage) of the total radioactivity is present as pentamibi (99m Tc).

BIOLOGICAL SAFETY TESTS

Sterility (5.5.3.2.1). Meets the requirements

Bacterial endotoxins test (5.5.2.7.3). It must contain less than 175 UE/V, where *V* is the maximum recommended dose in mL, at the expiration date or time.

RADIOACTIVITY

Carry out the test as described in *Radiopharmaceuticals (8.3)*. Using an suitable and calibrated counting instrument, determine the activity in Bq (Ci) or its multiples and sub-multiples, per volume unit.

PACKAGING AND STORAGE

Carry out as described as in *Radiopharmaceuticals (8.3)*. Keep in a perfectly closed container, in a radiation protection shield.

LABELING

Following the current legislation.

USE

Diagnostic.