GALLIUM (\(^{68}\text{Ga}\)) PSMA-11 INJECTION

Gallii (\(^{68}\text{Ga}\)) PSMA-11 solutio inyectabilis

\[
\text{C}_{44}\text{H}_{58}\text{GaN}_{6}\text{O}_{17}
\]

DEFINITION

Content:
– gallium-68: 90 per cent to 110 per cent of the declared gallium-68 radioactivity at the date and time stated on the label;
– PSMA-11: maximum 30 µg per maximum recommended dose in millilitres.

A reversible stereoisomerisation of \([^{68}\text{Ga}]\)gallium PSMA-11 takes place in solution depending on temperature, pH and time.

CHARACTERS
Appearance: clear, colourless solution.
 Half-life and nature of radiation of gallium-68: see general chapter 5.7. Table of physical characteristics of radionuclides.

IDENTIFICATION
A. Gamma-ray spectrometry.

\textit{Result}: the principal gamma photons have energies of 0.511 MeV and 1.077 MeV and, depending on the measurement geometry, a sum peak of 1.022 MeV may be observed; a peak corresponding to gamma photons with an energy of 1.883 MeV may be observed.

B. Approximate half-life: 62 min to 74 min.

C. Examine the chromatograms obtained in the test for impurities A and B and other radiochemical impurities (see Tests).

\textit{Result}: the 2 principal peaks in the radiochromatogram obtained with the test solution are similar in retention time to the 2 principal peaks in the chromatogram obtained with reference solution (a) using the spectrophotometer.
TESTS

pH (2.2.4): 4 to 8.

PSMA-11, gallium PSMA-11 and other related substances. Liquid chromatography (2.2.29).

Solvent mixture: trifluoroacetic acid R, water R (1:999 V/V).

Test solution. The preparation to be examined.

Reference solution (a). Dissolve a quantity of gallium PSMA-11 R corresponding to 50 µg of anhydrous and trifluoroacetic acid-free gallium PSMA-11 in 1.0 mL of water R.

Reference solution (b). Dissolve a quantity of PSMA-11 R corresponding to 30 µg of anhydrous and trifluoroacetic acid-free PSMA-11 in the solvent mixture and dilute to V with the solvent mixture, V being the maximum recommended dose in millilitres.

Reference solution (c). Dilute 1.0 mL of reference solution (b) to 10.0 mL with the solvent mixture.

Column:

- size: l = 0.15 m, Ø = 3.0 mm;
- stationary phase: base-deactivated octadecylsilyl silica gel for chromatography R (3 µm)(1).

Mobile phase:

- mobile phase A: trifluoroacetic acid R, water R for chromatography R (1:999 V/V);
- mobile phase B: trifluoroacetic acid R, acetonitrile R (1:999 V/V);

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Mobile phase A (per cent V/V)</th>
<th>Mobile phase B (per cent V/V)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 0.5</td>
<td>95 → 60</td>
<td>5 → 40</td>
</tr>
<tr>
<td>0.5 - 10</td>
<td>60 → 95</td>
<td>40 → 5</td>
</tr>
<tr>
<td>10 - 11</td>
<td>95</td>
<td>5</td>
</tr>
<tr>
<td>11 - 16</td>
<td></td>
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</tbody>
</table>

Flow rate: 0.6 mL/min.

Detection: spectrophotometer at 280 nm and radioactivity detector connected in series.

Injection: 20 µL.

Relative retention with reference to PSMA-11 (retention time = about 8 min): gallium PSMA-11 stereoisomer 1 = about 0.9; gallium PSMA-11 stereoisomer 2 = about 0.97.

System suitability: reference solution (a):

- resolution: minimum 1.5 between the peaks due to gallium PSMA-11 stereoisomers 1 and 2.

Limits: in the chromatogram obtained using the spectrophotometer:

- PSMA-11, gallium PSMA-11 and other related substances (the sum of the areas of the peaks due to compounds with a relative retention of not less than 0.8 and not more than 1.3 with reference to PSMA-11): not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (30 µg/V);
- disregard limit: the area of the principal peak in the chromatogram obtained with reference solution (c) (3 µg/V).

(1) ACE 3 C18 base deactivated is suitable.
The following chromatogram is shown for information but will not be published in the European Pharmacopoeia.

Figure 3044.-1. – Chromatogram for the test for PSMA-11, gallium PSMA-11 and other related substances: reference solution (a).

Figure 3044.-2. – Chromatogram for the test for PSMA-11, gallium PSMA-11 and other related substances: reference solution (b).

Figure 3044.-3. – Chromatogram for the test for PSMA-11, gallium PSMA-11 and other related substances: 10-fold dilution of reference solution (b).
The following chromatogram is shown for information but will not be published in the European Pharmacopoeia.

Figure 3044.-4. – Chromatogram for the test for PSMA-11 gallium PSMA-11 and other related substances: typical chromatogram of a test solution (10 µg PSMA-11/V, V = 10 mL).

Impurity C. Thin-layer chromatography (2.2.27).

Test solution. The preparation to be examined.

Reference solution. Dissolve 10 mg of HEPES R (impurity C) in water R and dilute to V with the same solvent, V being the maximum recommended dose in millilitres. Dilute 1.0 mL of the solution to 50.0 mL with water R.

Plate: TLC silica gel 60 plate F254(2).


Application: (V/1000 mL), V being the maximum recommended dose in millilitres; apply portions of 1 µL and dry with a current of warm air after each application.

Development: over 2/3 of the plate.

Detection: expose to iodine vapour for 4 min.

Retardation factor: impurity C = about 0.5.

System suitability: reference solution:
– the chromatogram shows a clearly visible spot.

Limit:
– impurity C: any spot due to impurity C is not more intense than the corresponding spot in the chromatogram obtained with the reference solution (200 µg/V).

Ethanol (2.4.24 or another suitable, validated method): maximum 10 per cent V/V and maximum 2.5 g per administration, taking the density (2.2.5) to be 0.790 g/mL.

Sterility. It complies with the test for sterility prescribed in the monograph Radiopharmaceutical preparations (0125). The preparation may be released for use before completion of the test.

Bacterial endotoxins (2.6.14): less than 175/V IU/mL, V being the maximum recommended dose in millilitres. The preparation may be released for use before completion of the test.

RADIOCHEMICAL PURITY

[68Ga]Gallium PSMA-11, impurities A and B and other radiochemical impurities. Liquid chromatography (2.2.29) as described in the test for PSMA-11, gallium PSMA-11 and other related substances. If necessary, dilute the test solution with water R to a radioactivity concentration suitable for the radioactivity detector.

Examine the chromatogram obtained using the radioactivity detector and locate the peaks due to [68Ga]gallium PSMA-11 by comparison with the chromatogram obtained with reference solution (a) using the spectrophotometer.

Relative retention with reference to [68Ga]gallium PSMA-11 stereoisomer 1 (retention time = about 7.5 min): impurities A and B = about 0.2.

(2) Merck ALUGRAM Xtra Nano SILGUR UV254 is suitable.
The following chromatogram is shown for information but will not be published in the European Pharmacopoeia.

Figure 3044.-5. – Chromatogram for the test for impurities A and B and other radiochemical impurities: typical radiochromatogram of a test solution.

Limits:

- sum of impurities A and B: not more than 3 per cent of the total radioactivity due to gallium-68;
- \([\text{\[^{68}\text{Ga}\]gallium}\]PSMA-11\): minimum 91 per cent of the total radioactivity due to gallium-68.

RADIOACTIVITY

Determine the radioactivity using a calibrated instrument.

IMPURITIES

A. \([\text{\[^{68}\text{Ga}\]gallium}\] in colloidal form,

B. \([\text{\[^{68}\text{Ga}\]gallium(III) ion},

C. 2-[4-(2-hydroxyethyl)piperazin-1-yl]ethanesulfonic acid (HEPES).

Reagents


White or almost white powder, freely soluble in water.

Content: minimum 96.0 per cent (anhydrous and trifluoroacetic acid-free substance).

**Gallium PSMA-11.** \(\text{C}_{44}\text{H}_{58}\text{GaN}_{6}\text{O}_{17}\). \(\text{M}, 1013\). \(\text{XXX}\text{XXX}\).


Colourless or almost white powder.

Content: minimum 95.0 per cent (anhydrous and trifluoroacetic acid-free substance).