SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

PENTACIS 9.10 mg, kit for radiopharmaceutical preparation

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains 9.10 mg of trisodium and calcium pentetate (DTPA).

The radionuclide is not part of the kit.

Excipient with known effect:
Each vial contains 2.2 mg of sodium.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Kit for radiopharmaceutical preparation.
White pellet.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

a) After radiolabelling with sodium pertechnetate (\(^{99m}\text{Tc}\)) solution, the solution obtained is indicated for:
Dynamic renal scintigraphy for perfusion, function and urinary tract studies.
Measurement of glomerular filtration rate.
Cerebral angiography and brain scanning. As an alternative method, when computed tomography and/or magnetic resonance imaging are not available.

b) After inhalation of the nebulized technetium (\(^{99m}\text{Tc}\)) labelled substance:
Lung ventilation imaging.

c) After oral administration of the technetium (\(^{99m}\text{Tc}\)) labelled substance:
Studies of gastro-oesophageal reflux and gastric emptying.
4.2 Posology and method of administration

This medicinal product is intended for use in designated nuclear medicine facilities only, and should only be handled by authorised personnel.

Posology

**Adults**

The following administered activities are recommended on a patient of average weight (70 kg). Other activities may be justifiable:

- Measurement of glomerular filtration rate from plasma: 2-4 MBq
- Measurement of glomerular filtration rate using gamma camera combined with sequential dynamic renal scanning: 37-370 MBq
- Brain scanning: 185-740 MBq
- Lung ventilation imaging: 500-1000 MBq in nebuliser. 50-100 MBq in lung.

Researchers can study gastro-oesophageal reflux and gastric emptying: 10-20 MBq

**Renal impairment**

Careful consideration of the activity to be administered is required since an increased radiation exposure is possible in these patients.

**Paediatric population**

The use in children and adolescents has to be considered carefully, based upon clinical needs and assessing the risk/benefit ratio in this patient group.

The activities to be administered to children and to adolescents may be calculated according to body weight:

\[
\text{Pediatric activity (MBq)} = \frac{\text{Adult dosage (MBq)} \times \text{Child weight (kg)}}{70}
\]

In some circumstances, dose adjustment according to surface area may be appropriate.

\[
\text{Pediatric activity (MBq)} = \frac{\text{Adult dosage (MBq)} \times \text{Child body surface (m²)}}{1.73}
\]

In very young children (up to 1 year) a minimum dose of 20 MBq is necessary in order to obtain images of sufficient quality, when technetium (\(^{99m}\)Tc) pentetate (DTPA) is used for kidney studies.

Method of administration

This medicinal product should be reconstituted before administration to the patient:
- by intravenous injection for measurement of glomerular filtration rate and brain scanning,
- by inhalation in lung or in nebuliser for lung ventilation imaging,
- by oral use for study of gastro-oesophageal reflux and gastric emptying.

For instructions on reconstitution of the medicinal product before administration, see section 12.
For patient preparation, see section 4.4.

**Image acquisition**
Measurement of glomerular filtration rate from plasma: Sequential scanning should begin immediately after injection. Optimal static imaging time is 1 hour post injection.

Brain scanning: static images are obtained 1 hour and, if necessary, several hours after injection. Sequential dynamic scanning should begin immediately after injection.

Study of gastro-oesophageal reflux and gastric emptying: dynamic recording should be performed during the first minutes (up to 120 minutes for gastroduodenal transit).

### 4.3 Contraindications

Hypersensitivity to the active substance, to any of the excipients listed in section 6.1 or to any of the components of the labeled radiopharmaceutical.

### 4.4 Special warnings and precautions for use

**Potential for hypersensitivity or anaphylactic reactions**
If hypersensitivity or anaphylactic reactions occur, the administration of the medicinal product must be discontinued immediately and intravenous treatment initiated, if necessary. To enable immediate action in emergencies, the necessary medicinal products and equipment such as endotracheal tube and ventilator must be immediately available.

**Individual benefit/risk justification**
For each patient, the radiation exposure must be justifiable by the likely benefit. The activity administered should in every case be as low as reasonably achievable to obtain the required diagnostic information.

**Renal impairment**
Careful consideration of the benefit/risk ratio in these patients is required since an increased radiation exposure is possible. This must be taken into account when calculating the activity to be administered (see section 11”).

**Paediatric population**
For information on the use in paediatric population, see section 4.2.
Careful consideration of the indication is required since the effective dose per MBq is higher than in adults (see section 11).

**Patient preparation**
The patient should be well hydrated before the start of the examination and urged to void before scanning and as often as possible during the first hours after the examination in order to reduce radiation to the bladder wall.

**Specific warnings**
When labelling kit, the sodium content of the dose administered must take into account the sodium derived from the eluate and the kit. Please refer to the package leaflet of the generator of technetium (99mTc) used.
Depending on the time when you administer the injection, the content of sodium given to the patient may in some cases be greater than 1 mmol (23 mg). This should be taken into account in patient on low sodium diet.

For precautions with respect to environmental hazard, see section 6.6.

4.5 Interaction with other medicinal products and other forms of interaction

Many drugs may affect the function of tested organ and modify the uptake of technetium \(^{99m}\text{Tc}\) pentetate (DTPA) i.e.

**Diagnostic use of captopril:** Dynamic renal scanning performed under controlled conditions and again one hour after oral administration of captopril (25-50 mg) may reveal haemodynamic changes in a kidney affected by renal artery stenosis. The blood pressure should be carefully monitored as patients with vascular disease are at risk of significant hypotension and renal impairment.

**Diagnostic use of furosemide:** The administration of intravenous furosemide during dynamic renal scanning increases elimination of technetium \(^{99m}\text{Tc}\) pentetate (DTPA) which may help to distinguish whether true obstruction exists in a dilated renal tract.

**Cerebral angiography:** Psychotropic drugs increase blood flow in the territory of the external carotid artery. This may lead to the rapid uptake of tracer in the nasopharyngeal area during the arterial and capillary phases (hot nose phenomenon).

4.6 Fertility, pregnancy and lactation

**Women of childbearing potential**
When an administration of radiopharmaceuticals to a woman of childbearing potential is intended, it is important to determine whether or not she is pregnant. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. If in doubt about her potential pregnancy (if the woman has missed a period, if the period is very irregular, etc.), alternative techniques not using ionising radiation (if there are any) should be offered to the patient.

**Pregnancy**
Radionuclide procedures carried out on pregnant women also involve radiation dose to the foetus. Only essential investigations should therefore be carried out during pregnancy, when the likely benefit far exceeds the risk incurred by the mother and foetus.

**Breastfeeding**
Before administering radiopharmaceuticals to a mother who is breastfeeding consideration should be given to the possibility of delaying the administration of radionuclide until the mother has ceased breastfeeding, and to what is the most appropriate choice of radiopharmaceuticals, bearing in mind the secretion of activity in breast milk. If the administration is considered necessary, breastfeeding should be interrupted for 12 hours and the expressed feeds discarded.

4.7 Effects on ability to drive and use machines

Pentacis has no or negligible influence on the ability to drive and use machines.
4.8 Undesirable effects

The following presents how the frequencies are reflected in this section:

Very rare (<1/10,000).

In this table the undesirable effects are classified in accordance with the MedDRA SOCs.

<table>
<thead>
<tr>
<th>MedDRA Body system</th>
<th>Preferred term</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervous system disorders</td>
<td>Dizziness</td>
<td>Very rare</td>
</tr>
<tr>
<td>Vascular disorders</td>
<td>Hypotension</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Flushing</td>
<td></td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>Dyspnoea</td>
<td></td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Urticaria</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pruritus</td>
<td></td>
</tr>
</tbody>
</table>

In isolated cases the following adverse reactions have been reported: flushing, dizziness, dyspnoea, itch, urticaria and hypotension.

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is 3.6 mSv when the maximal recommended activity of 740 MBq is administered these adverse reactions are expected to occur with a low probability.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme, Website: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard).

4.9 Overdose

In the event of administration of a radiation overdose with technetium (99mTc) pentetate (DTPA) the absorbed dose to the patient should be reduced where possible by increasing the elimination of the radionuclide from the body by forced diuresis and frequent bladder voiding.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Radiopharmaceutical preparation for diagnostic use: renal system and respiratory system. ATC codes: V09CA01 and V09EA01

Pharmacodynamic effects
At the chemical concentrations used for diagnostic examinations technetium (99mTc) pentetate (DTPA) does not appear to have any pharmacodynamic activity.
5.2 Pharmacokinetic properties

Distribution
Following intravenous injection, technetium (\textsuperscript{99m}Tc) pentetate (DTPA) rapidly distributes throughout the extracellular fluid. In subjects exhibiting oedema or ascites, distribution of the radionuclide in the extracellular space may be modified.

Organ uptake
Less than 5% of the injected dose is bound to the plasma proteins. There is also a negligible binding of technetium (\textsuperscript{99m}Tc) pentetate (DTPA) to red blood cells. Technetium (\textsuperscript{99m}Tc) pentetate (DTPA) does not cross the normal blood-brain barrier but diffuses weakly in breast milk.

Elimination / Half-Life
Plasma clearance is multiexponential with an extremely fast component. The complex remains stable in vivo, more than 98% of urine radioactivity is in the form of a chelate. Approximately 90% of the injected dose is eliminated in the urine within the first 24 hours mainly by glomerular filtration. No retention of the compound has been demonstrated in the kidneys. Plasma clearance may be delayed in patients with renal disease.

In lung ventilation studies, after inhalation, technetium (\textsuperscript{99m}Tc) pentetate (DTPA) diffuses rapidly from the pulmonary alveoles towards the vascular space where it is diluted. The half-life of technetium (\textsuperscript{99m}Tc) pentetate (DTPA) in the lungs is slightly less than 1 hour. Many factors are likely to modify the permeability of the pulmonary epithelium like cigarette smoking. Following oral administration, technetium (\textsuperscript{99m}Tc) pentetate (DTPA) does not pass through the digestive barrier.

5.3 Preclinical safety data

Repeated intravenous administration of CaNa\textsubscript{3}DTPA to rabbits and dogs for 14 days of doses that were 100 and 1000 times (respectively) the normal dose for humans, produced no evidence of toxicity. This medicinal product is not intended for regular or continuous administration.

The minimum dose of CaDTPA causing abortion and fetal death in mice was approximately 3600 times the dose of CaNa\textsubscript{3}DTPA that is proposed for diagnosis in women. Mutagenicity studies and long-term carcinogenicity studies have not been carried out.
6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Stannous chloride dihydrate

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products except those mentioned in section 12.

6.3 Shelf life

1 year.
The expiry date is indicated on the outer packaging and on each vial.
After radiolabelling: store in a refrigerator (2°C-8°C) and use within 4 hours, with a maximum of 5 withdrawals per vial.

6.4 Special precautions for storage

Store the kit in a refrigerator (2°C-8°C).
For storage conditions after radiolabelling, see section 6.3.
Storage of radiopharmaceuticals should be in accordance with national regulation on radioactive materials.

6.5 Nature and contents of container

15 mL, colourless, European Pharmacopoeia type I, drawn glass vials, closed with rubber stoppers and aluminium capsules.
Pack size: kit of 5 multidose vials.

6.6 Special precautions for disposal

General warnings
Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the competent official organisation.
Radiopharmaceuticals should be prepared in a manner which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken.
Contents of the vial are intended only for use in the preparation of technetium (\(^{99m}\text{Tc}\))-DTPA injection and are not to be administered directly to the patient without first undergoing the preparative procedure.
For instructions on extemporaneous preparation of the medicinal product before administration, see section 12.

If at any time in the preparation of this product the integrity of this vial is compromised it should not be used.

Administration procedures should be carried out in a way to minimise risk of contamination of the medicinal product and irradiation of the operators. Adequate shielding is mandatory.

The content of the kit before extemporary preparation is not radioactive. However, after sodium pertechnetate ($^{99m}$Tc) Injection, Ph. Eur. is added, adequate shielding of the final preparation must be maintained. The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spill of urine, vomiting, etc. Radiation protection precautions in accordance with national regulations must therefore be taken.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

CIS bio international
B.P. 32
91192 Gif-sur-Yvette Cedex
FRANCE

8 MARKETING AUTHORISATION NUMBER(S)

PL 11876/0011

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 15 July 1996
Date of latest renewal: 16 November 2006

10 DATE OF REVISION OF THE TEXT

07/07/2016
11 DOSIMETRY

Technetium (99mTc) is produced by means of a (99Mo/99mTc) generator and decays with the emission of gamma radiation with a mean energy of 140 keV and a half-life of 6.02 hours to technetium (99Tc) which, in view of its long half-life of 2.13 x 10^5 years can be regarded as quasi stable.

The data listed below are from ICRP publications 53 and 80 for technetium-DTPA and are calculated according to the following assumptions:

Intravenous administration of Tc-diethylenetriaminepentaacetic acid (DTPA) gives rise to an initial distribution in the extracellular fluid. Following this initial distribution phase, the substance is excreted exclusively by the renal system according to the model for glomerular filtration rate substances and the kidney-bladder model.

In the normal case, total body retention is described by a double exponential function with component half-times of 100 min (0.99) and 7 d (0.01). The fraction excreted by the kidneys is 1.0, and the renal transit time is 5 min.

For the abnormal case, it is assumed that the retention half-time of the major component is 1000 min and that the renal transit time is increased to 20 min.

Inhalation of aerosols consisting of particles smaller than 2-3 pm in diameter in well-defined respiratory breathing patterns results in a deposition mainly in the alveoli, with only minimal deposition in bronchi and upper airways. In free breathing, such particles are deposited in the bronchi and upper airways. Particles made of readily soluble substances are rapidly cleared from the lungs via the blood stream, while particles made of slowly dissolving or insoluble material are retained for longer times, up to several weeks or months, depending upon type of material. During this time the label is slowly released to the bloodstream. Soluble particles are usually prepared from DTPA, although pertechnetate may also be used. The biological half-time of Tc-DTPA in the lungs is 60-80 min in normal non-smokers; it is shortened in smokers and in most patients with lung disease. A value of 60 min is adopted here. Substance reaching the blood is eliminated according to the model for intravenously administered Tc-DTPA.
Organ absorbed doses and effective doses for normal renal function after intravenous administration of technetium-DTPA, have been recalculated in Publication 80.

**Normal renal function (ICRP 80)**

<table>
<thead>
<tr>
<th>ORGAN</th>
<th>Absorbed Dose Per Unit of Administered Activity (mGy/MBq)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adult</td>
</tr>
<tr>
<td>Adrenals</td>
<td>0.0013</td>
</tr>
<tr>
<td>Bladder wall</td>
<td>0.062</td>
</tr>
<tr>
<td>Bone surfaces</td>
<td>0.0023</td>
</tr>
<tr>
<td>Brain</td>
<td>0.00084</td>
</tr>
<tr>
<td>Breast</td>
<td>0.00071</td>
</tr>
<tr>
<td>Gall bladder</td>
<td>0.0015</td>
</tr>
<tr>
<td>Gastrointestinal tract</td>
<td></td>
</tr>
<tr>
<td>Stomach</td>
<td>0.0013</td>
</tr>
<tr>
<td>Small intestine</td>
<td>0.0025</td>
</tr>
<tr>
<td>Colon</td>
<td>0.0030</td>
</tr>
<tr>
<td>Upper large intestine wall</td>
<td>0.0021</td>
</tr>
<tr>
<td>Lower large intestine wall</td>
<td>0.0043</td>
</tr>
<tr>
<td>Heart</td>
<td>0.0011</td>
</tr>
<tr>
<td>Kidneys</td>
<td>0.0039</td>
</tr>
<tr>
<td>Liver</td>
<td>0.0012</td>
</tr>
<tr>
<td>Lungs</td>
<td>0.00099</td>
</tr>
<tr>
<td>Muscles</td>
<td>0.0016</td>
</tr>
<tr>
<td>Oesophagus</td>
<td>0.0010</td>
</tr>
<tr>
<td>Ovaries</td>
<td>0.0042</td>
</tr>
<tr>
<td>Pancreas</td>
<td>0.0014</td>
</tr>
<tr>
<td>Red marrow</td>
<td>0.0014</td>
</tr>
<tr>
<td>Skin</td>
<td>0.00085</td>
</tr>
<tr>
<td>Spleen</td>
<td>0.0012</td>
</tr>
<tr>
<td>Testes</td>
<td>0.0029</td>
</tr>
<tr>
<td>Thymus</td>
<td>0.0010</td>
</tr>
<tr>
<td>Thyroid</td>
<td>0.0010</td>
</tr>
<tr>
<td>Uterus</td>
<td>0.0079</td>
</tr>
<tr>
<td>Other tissue</td>
<td>0.0017</td>
</tr>
<tr>
<td><strong>Effective dose (mSv/MBq)</strong></td>
<td><strong>0.0049</strong></td>
</tr>
</tbody>
</table>

The effective dose resulting from the administration of an activity of 740 MBq for an adult weighing 70 kg with normal renal function is about 3.6 mSv.
### Abnormal renal function (ICRP 53)

<table>
<thead>
<tr>
<th>ORGAN</th>
<th>ADSORBED DOSE PER UNIT OF ADMINISTERED ACTIVITY (mGy/MBq)</th>
<th>Adult</th>
<th>15 years</th>
<th>10 years</th>
<th>5 years</th>
<th>1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenals</td>
<td></td>
<td>0.0041</td>
<td>0.0051</td>
<td>0.0078</td>
<td>0.012</td>
<td>0.021</td>
</tr>
<tr>
<td>Bladder wall</td>
<td></td>
<td>0.022</td>
<td>0.027</td>
<td>0.040</td>
<td>0.058</td>
<td>0.11</td>
</tr>
<tr>
<td>Bone surfaces</td>
<td></td>
<td>0.0044</td>
<td>0.0053</td>
<td>0.0079</td>
<td>0.012</td>
<td>0.021</td>
</tr>
<tr>
<td>Breast</td>
<td></td>
<td>0.0030</td>
<td>0.0030</td>
<td>0.0043</td>
<td>0.0069</td>
<td>0.013</td>
</tr>
<tr>
<td>Gastrointestinal tract</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stomach wall</td>
<td></td>
<td>0.0038</td>
<td>0.0050</td>
<td>0.0079</td>
<td>0.011</td>
<td>0.020</td>
</tr>
<tr>
<td>Small intestine</td>
<td></td>
<td>0.0047</td>
<td>0.0056</td>
<td>0.0086</td>
<td>0.013</td>
<td>0.023</td>
</tr>
<tr>
<td>Upper large intestine wall</td>
<td></td>
<td>0.0044</td>
<td>0.0056</td>
<td>0.0081</td>
<td>0.013</td>
<td>0.022</td>
</tr>
<tr>
<td>Lower large intestine wall</td>
<td></td>
<td>0.0047</td>
<td>0.0062</td>
<td>0.0096</td>
<td>0.014</td>
<td>0.025</td>
</tr>
<tr>
<td>Kidneys</td>
<td></td>
<td>0.0079</td>
<td>0.0096</td>
<td>0.014</td>
<td>0.020</td>
<td>0.034</td>
</tr>
<tr>
<td>Liver</td>
<td></td>
<td>0.0038</td>
<td>0.0046</td>
<td>0.0071</td>
<td>0.011</td>
<td>0.019</td>
</tr>
<tr>
<td>Lungs</td>
<td></td>
<td>0.0033</td>
<td>0.0042</td>
<td>0.0062</td>
<td>0.0095</td>
<td>0.017</td>
</tr>
<tr>
<td>Ovaries</td>
<td></td>
<td>0.0049</td>
<td>0.0063</td>
<td>0.0094</td>
<td>0.014</td>
<td>0.024</td>
</tr>
<tr>
<td>Pancreas</td>
<td></td>
<td>0.0043</td>
<td>0.0054</td>
<td>0.0081</td>
<td>0.012</td>
<td>0.022</td>
</tr>
<tr>
<td>Red marrow</td>
<td></td>
<td>0.0052</td>
<td>0.0063</td>
<td>0.0090</td>
<td>0.013</td>
<td>0.022</td>
</tr>
<tr>
<td>Spleen</td>
<td></td>
<td>0.0040</td>
<td>0.0048</td>
<td>0.0072</td>
<td>0.011</td>
<td>0.020</td>
</tr>
<tr>
<td>Testes</td>
<td></td>
<td>0.0033</td>
<td>0.0045</td>
<td>0.0069</td>
<td>0.011</td>
<td>0.020</td>
</tr>
<tr>
<td>Thyroid</td>
<td></td>
<td>0.0025</td>
<td>0.0043</td>
<td>0.0068</td>
<td>0.011</td>
<td>0.019</td>
</tr>
<tr>
<td>Uterus</td>
<td></td>
<td>0.0063</td>
<td>0.0075</td>
<td>0.011</td>
<td>0.017</td>
<td>0.029</td>
</tr>
<tr>
<td>Other tissue</td>
<td></td>
<td>0.0033</td>
<td>0.0040</td>
<td>0.0061</td>
<td>0.0094</td>
<td>0.017</td>
</tr>
<tr>
<td><strong>Effective dose equivalent</strong></td>
<td><strong>Total dose equivalent (mSv/MBq)</strong></td>
<td>0.0053</td>
<td>0.0066</td>
<td>0.0097</td>
<td>0.015</td>
<td>0.026</td>
</tr>
</tbody>
</table>
The radiation doses given to man on administration by aerosol of (\(^{99m}\text{Tc}\)) DTPA are the following (ICRP 53):

<table>
<thead>
<tr>
<th>ORGAN</th>
<th>ABSORBED DOSE PER UNIT OF ADMINISTERED ACTIVITY (mGy/MBq)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adult</td>
</tr>
<tr>
<td>Adrenals</td>
<td>0.0021</td>
</tr>
<tr>
<td>Bladder wall</td>
<td>0.047</td>
</tr>
<tr>
<td>Bone surfaces</td>
<td>0.0019</td>
</tr>
<tr>
<td>Breast</td>
<td>0.0019</td>
</tr>
<tr>
<td>Gastrointestinal tract</td>
<td></td>
</tr>
<tr>
<td>Stomach wall</td>
<td>0.0017</td>
</tr>
<tr>
<td>Small intestine</td>
<td>0.0021</td>
</tr>
<tr>
<td>Upper large intestine wall</td>
<td>0.0019</td>
</tr>
<tr>
<td>Lower large intestine wall</td>
<td>0.0032</td>
</tr>
<tr>
<td>Kidneys</td>
<td>0.0041</td>
</tr>
<tr>
<td>Liver</td>
<td>0.0019</td>
</tr>
<tr>
<td>Lungs</td>
<td>0.017</td>
</tr>
<tr>
<td>Ovaries</td>
<td>0.0033</td>
</tr>
<tr>
<td>Pancreas</td>
<td>0.0021</td>
</tr>
<tr>
<td>Red marrow</td>
<td>0.0027</td>
</tr>
<tr>
<td>Spleen</td>
<td>0.0019</td>
</tr>
<tr>
<td>Testes</td>
<td>0.0021</td>
</tr>
<tr>
<td>Thyroid</td>
<td>0.00099</td>
</tr>
<tr>
<td>Uterus</td>
<td>0.0059</td>
</tr>
<tr>
<td>Other tissue</td>
<td>0.0018</td>
</tr>
<tr>
<td>Effective dose equivalent</td>
<td>0.0070</td>
</tr>
</tbody>
</table>

For this product the effective dose equivalent resulting from an inhalation (nebuliser) of 100 MBq is 0.7 mSv (per 70 kg individual).
The radiation doses given to man on administration per os of \(^{99m}\text{Tc}\) DTPA are the following (D.J. GAMBINI, R. GRANIER : Manuel pratique de Médecine Nucléaire)

<table>
<thead>
<tr>
<th>ORGAN</th>
<th>ABSORBED DOSE PER UNIT OF ADMINISTERED ACTIVITY (mGy/MBq)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomach</td>
<td>0.086</td>
</tr>
<tr>
<td>Small intestine</td>
<td>0.07</td>
</tr>
<tr>
<td>Red marrow</td>
<td>0.0012</td>
</tr>
<tr>
<td>Ovaries</td>
<td>0.0035</td>
</tr>
<tr>
<td>Testes</td>
<td>0.0017</td>
</tr>
<tr>
<td>Effective dose equivalent (mSv/MBq)</td>
<td>0.025</td>
</tr>
</tbody>
</table>

For this product the effective dose equivalent resulting from an oral administration of 20 MBq is 0.5 mSv (per 70 kg individual).

12 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Usual precautions regarding sterility and radioprotection must be respected.
Withdrawals should be performed under aseptic conditions. The vial must not be opened and must be kept inside the lead shielding. After disinfection of the stopper, the solution should be withdrawn via the stopper using a single dose syringe fitted with suitable protective shielding and a disposable sterile needle or using an authorised automated application system.
If the integrity of this vial is compromised, the product should not be used.

Method of preparation of technetium \(^{99m}\text{Tc}\)-DTPA

Take a vial from the kit and put it in an appropriate lead shielding.
Using a hypodermic syringe, introduce through the rubber stopper 5 mL of sterile pyrogen-free sodium pertechnetate \(^{99m}\text{Tc}\) injection, activity varying from 3.7 MBq to maximum 2000 MBq.
Sodium pertechnetate \(^{99m}\text{Tc}\) injection should comply with European Pharmacopoeia specifications. Do not use a breather needle as the contents are under nitrogen: after introduction of the volume of sodium pertechnetate \(^{99m}\text{Tc}\) injection, without removing the needle, withdraw an equivalent volume of nitrogen in order to avoid excess pressure in the vial.
Shake for about 2 minutes.
The solution of technetium \(^{99m}\text{Tc}\)-DTPA obtained is a clear and colourless solution, free from visible particles, with a pH ranging between 4.0 and 7.5.
Before use, limpidity of the solution after preparation, pH, radioactivity and gamma spectrum will be checked.
A maximum of 5 withdrawals per vial is recommended.
Quality control

The quality of labelling (radiochemical purity) could be checked according to the following procedure.

Methods

Thin-layer chromatography or ascending paper chromatography

Thin-layer chromatography

Materials and reagents

1. Chromatographic sheets
2. Fiber-glass sheet strips (2.5 x 20 cm) A and B coated with silica gel and previously heated at 110 °C for 10 minutes.

On each strip trace two fine lines parallel to the ends of the strips, the one being called "deposit line" at 2 cm, the other one being called "solvent line" at 10 cm from the "deposit line".

2. Mobile phases
   - Solvent A: 0.9 % sodium chloride solution
   - Solvent B: methyl ethyl ketone

3. Chromatographic tanks
   - 2 glass tanks A and B of suitable size for the chromatographic sheets used and provided with a tightly fitting lid.

4. Miscellaneous
   - Forceps, syringes, needles, appropriate counting assembly.

Procedure

1. Respectively place into the chromatographic tanks A and B a sufficient volume of the mobile phases A and B and let equilibrate at room temperature for a few minutes.

2. Apply 5 to 10 µL of the preparation to the "deposit line" of strips A and B using a syringe and needle.

3. Using forceps, introduce each strip vertically into the corresponding chromatographic tank for development with the "deposit line" downward. Close the chromatographic tanks and allow the solvent to migrate to the "solvent line".

4. Remove the strips with forceps and dry in the air.

5. Determine distribution of radioactivity with an appropriate detector.

6. Calculations
   - With the mobile phase A, impurities in colloidal form (hydrolysed technetium (99mTc)) remain at the "deposit line" (Rf 0). Technetium (99mTc) pentetate complex and pertechnetate ion (free technetium (99mTc)) migrate near to the "solvent line".
   - Calculate the percentage of hydrolysed (99mTc) technetium

\[
\% \text{ hydrolysed technetium (99mTc)} = \frac{\text{Radioactivity at Rf 0}}{\text{Total radioactivity of strip A}} \times 100
\]

   - With mobile phase B, pertechnetate ion (free technetium (99mTc)) migrates near to the "solvent line" (Rf 1). Technetium (99mTc) pentetate complex and impurities in colloidal form remain at the "deposit line".
   - Calculate the percentage of free technetium (99mTc)

\[
\% \text{ free technetium (99mTc)} = \frac{\text{Radioactivity at Rf 1}}{\text{Total radioactivity of strip B}} \times 100
\]
The sum of the percentages of radioactivity corresponding to hydrolysed \(^{99m}\text{Tc}\) technetium and free technetium \(^{99m}\text{Tc}\) should not be greater than 5.0 %.

*Paper chromatography (alternative method)*

**Materials and reagents**

1. Paper chromatography
2. “Whatman 1” type sheets (2.5 x 20 cm) A and B
   
   On each paper strip, trace two thin lines parallel to the ends of the strip: one is called “deposit line” at 2 cm from the bottom, the other one is called “solvent line” at 10 cm above from the deposit line.

3. Mobile phases
   
   A: 0.9 % sodium chloride solution
   
   B: methyl ethyl ketone

4. 2 glass tanks A and B (as a chromatographic chamber) provided with a device allowing to suspend the chromatographic paper and also to lower it without opening the chamber.

5. Forceps, scissors, syringes, needles, appropriate counting assembly

**Procedure**

1. Respectively place a sufficient volume of the mobile phases A and B into the glass tanks A and B and let equilibrate for about 5-10 minutes.

2. Apply 5 to 10 µL of the radiolabelled preparation to the deposit line of each of the paper strip A and B using a syringe and needle. **Do not let dry the spot.**

3. Using forceps, suspend a paper strip into each of the tanks and close the lids. In both cases, lower the paper into the mobile phase (the deposit line should be above the solvent surface) and allow the solvent to migrate to the solvent line.

4. Remove the paper strips and dry in the air.

5. Determine distribution of radioactivity with an appropriate detector. Identify each radioactive spot by calculating the Rf.

6. Calculations
   
   In system A, impurities in colloidal form (hydrolised technetium \(^{99m}\text{Tc}\)) remain at the starting point, whereas pertechnetate ion (free technetium \(^{99m}\text{Tc}\)) and technetium \(^{99m}\text{Tc}\) pentetate complex migrate around Rf 0.7 and 1.0 respectively.

   In system B, impurities in colloidal form and technetium \(^{99m}\text{Tc}\) pentetate complex remain at the starting point, whereas pertechnetate ion (free technetium \(^{99m}\text{Tc}\)) migrates around Rf 1.0.

   Measure the radioactivity of each considered impurity spot by integration of the peaks.

   Calculate the percentage of hydrolysed technetium \(^{99m}\text{Tc}\):
   
   \[
   \% \text{ hydrolysed technetium } (^{99m}\text{Tc}) = \frac{\text{Radioactivity at Rf 0}}{\text{Total radioactivity of strip A}} \times 100
   \]

   Calculate the percentage of free technetium \(^{99m}\text{Tc}\):
   
   \[
   \% \text{ free technetium } (^{99m}\text{Tc})= \frac{\text{Radioactivity at Rf 1}}{\text{Total radioactivity of strip B}} \times 100
   \]

   Calculate the sum of the percentages of radioactivity corresponding to impurities in the chromatograms obtained in systems A and B (% hydrolysed technetium \(^{99m}\text{Tc}\) + % free technetium \(^{99m}\text{Tc}\)).
7- The sum of the percentages of radioactivity corresponding to impurities in the chromatograms obtained in systems A and B should not exceed 5.0%.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.