SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
RENOCIS 1 mg kit for radiopharmaceutical preparation

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each vial contains 1 mg of succimer (or dimercaptosuccinic acid, DMSA). The radionuclide is not part of the kit.
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.
After radiolabelling with sodium pertechnetate ($^{99m}$Tc) solution, the solution of technetium ($^{99m}$Tc) succimer is indicated for:
- Static (planar or tomographic) renal imaging.
- morphological studies of renal cortex.
- individual kidney function.
- location of ectopic kidney.

4.2 Posology and method of administration
Posology
Adults
In adults, the recommended activity is 30 to 120 MBq
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 by using the following formula:
Paediatric dosage (MBq) = \frac{\text{Adult dosage (MBq)} \times \text{Child weight (kg)}}{70}

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

\[
\text{Paediatric dosage (MBq)} = \frac{\text{Adult dosage (MBq)} \times \text{Child body surface (m}^2\text{)}}{1.73}
\]

Method of administration

Multidose use.

This medicinal product should be reconstituted before administration to the patient.

Intravenous use.

For instructions on extemporaneous preparation of the medicinal product before administration, see section 12.

For patient preparation, see section 4.4.

Image acquisition

The image acquisitions may be performed as soon as 1 to 3 hours post-injection. Where there is renal impairment or obstruction, delayed views may be needed (6 to 24 hours respectively).

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 labelled 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.

Paediatric population

For information on the use in paediatric population, see sections 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 as often as possible during the first hours after the examination in order to reduce radiation.

Precautions with respect to environmental hazard see section 6.6.
4.5 Interaction with other medicinal products and other forms of interaction
Some chemical compounds or medicaments may affect the function of tested organs and influence the uptake of technetium (\(99mTc\)) succimer i.e:

- ammonium chloride: may substantially reduce renal uptake and increase hepatic uptake of technetium (\(99mTc\)) succimer
- sodium bicarbonate: reduction of renal uptake of technetium (\(99mTc\)) succimer,
- mannitol: reduction of renal uptake of technetium (\(99mTc\)) succimer.

To avoid these influences, treatment with any of the above chemical products should be interrupted where possible. Care should be taken to ensure the patient is adequately hydrated before scanning.

- Captopril: In patients with unilateral renal artery stenosis, uptake of technetium (\(99mTc\)) succimer will be impaired in the affected kidney. This is usually reversible after discontinuation of captopril.

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.

Breast-feeding
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
Effects on ability to drive and use machines have not been described and are not expected.

4.8 Undesirable effects
Allergic reactions have been reported in the literature although to date these have been inadequately described.

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects.

As the effective dose is 1.1 mSv when the maximal recommended activity of 120 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 Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard.

4.9 Overdose

In the event of administration of a radiation overdose with technetium ($^{99m}$Tc) succimer ($^{99m}$Tc DMSA) 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: Diagnostic Radiopharmaceuticals, ATC code: V09CA02

Pharmacodynamic effects

At the chemical concentrations and activities used for diagnostic procedures technetium ($^{99m}$Tc) succimer ($^{99m}$Tc DMSA) does not appear to exert any pharmacodynamic effects.

5.2 Pharmacokinetic properties

Distribution

After intravenous administration technetium ($^{99m}$Tc) succimer is eliminated from blood with a triphasic pattern in patients with normal renal function.

Organ uptake

The technetium ($^{99m}$Tc) succimer localizes in high concentrations in renal cortex. Maximal localisation occurs within 3-6 hours after intravenous injection, with about 40-50 % of the dose retained in the kidneys. Less than 3 % of the administered dose localizes in the liver. However, this amount can be increased significantly and renal distribution decreased in patients with impaired renal functions.

Half-life

The effective half-life of technetium ($^{99m}$Tc) succimer in blood is around 1 hour.

5.3 Preclinical safety data

Toxicity with repeated administration of 0.66 mg/kg/day succimer (DMSA) and 0.23 mg/kg/day SnCl2 over 14 days in rats was not observed. The dose usually administered to humans is 0.14 mg/kg succimer (DMSA). This medicinal product is not intended for regular or continuous administration.
Mutagenicity studies and long-term carcinogenicity studies have not been carried out.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Stannous chloride dihydrate
Inositol
Ascorbic acid

6.2 Incompatibilities
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: do not store above 25°C and use within 8 hours.

6.4 Special precautions for storage
Store the kit at 2°C – 8°C (in a refrigerator).
For storage conditions after labelling of the medicinal product, 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: 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 vials are intended only for use in the preparation of technetium ($^{99m}$Tc) succimer 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 minimize risk of contamination of the medicinal product and irradiation of the operators. Adequate shielding is mandatory.

The content of the kit before reconstitution is not radioactive. However, after sodium pertechnetate ($^{99m}$Tc), 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 11876/0008

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
Date of first authorisation: 13 March 1997
Date of latest renewal: 29 March 2011

10 DATE OF REVISION OF THE TEXT
26/11/2015

11 DOSIMETRY
Technetium ($^{99m}$Tc) is produced by means of a ($^{99}$Mo/$^{99m}$Tc) 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 ($^{99}$Tc) which, in view of its long half-life of 2.13 x 105 years, can be regarded as quasi stable.

The data listed below are from ICRP (International Commission of Radiological Protection, Publication 80) and are calculated according to the following assumptions:

<table>
<thead>
<tr>
<th>Organ</th>
<th>Absorbed dose per unit activity administered (mGy/MBq)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tissue</td>
<td>Adult</td>
</tr>
<tr>
<td>-------------------</td>
<td>-------</td>
</tr>
<tr>
<td>Adrenals</td>
<td>0.012</td>
</tr>
<tr>
<td>Bladder</td>
<td>0.018</td>
</tr>
<tr>
<td>Bone surfaces</td>
<td>0.0050</td>
</tr>
<tr>
<td>Brain</td>
<td>0.0012</td>
</tr>
<tr>
<td>Breast</td>
<td>0.0013</td>
</tr>
<tr>
<td>Gall bladder</td>
<td>0.0083</td>
</tr>
<tr>
<td>GI-tract Stomach</td>
<td>0.0052</td>
</tr>
<tr>
<td>SI</td>
<td>0.0050</td>
</tr>
<tr>
<td>Colon</td>
<td>0.0043</td>
</tr>
<tr>
<td>(ULI)</td>
<td>0.0050</td>
</tr>
<tr>
<td>(LLI)</td>
<td>0.0033</td>
</tr>
<tr>
<td>Heart</td>
<td>0.0030</td>
</tr>
<tr>
<td>Kidneys</td>
<td>0.18</td>
</tr>
<tr>
<td>Liver</td>
<td>0.0095</td>
</tr>
<tr>
<td>Lungs</td>
<td>0.0025</td>
</tr>
<tr>
<td>Muscles</td>
<td>0.0029</td>
</tr>
<tr>
<td>Oesophagus</td>
<td>0.0017</td>
</tr>
<tr>
<td>Ovaries</td>
<td>0.0035</td>
</tr>
<tr>
<td>Pancreas</td>
<td>0.0090</td>
</tr>
<tr>
<td></td>
<td>0.0039</td>
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<tr>
<td>----------------</td>
<td>--------</td>
</tr>
<tr>
<td>Red marrow</td>
<td></td>
</tr>
<tr>
<td>Skin</td>
<td>0.0015</td>
</tr>
<tr>
<td>Spleen</td>
<td>0.013</td>
</tr>
<tr>
<td>Testes</td>
<td>0.0018</td>
</tr>
<tr>
<td>Thymus</td>
<td>0.0017</td>
</tr>
<tr>
<td>Thyroid</td>
<td>0.0015</td>
</tr>
<tr>
<td>Uterus</td>
<td>0.00454</td>
</tr>
<tr>
<td>Remaining organs</td>
<td>0.0029</td>
</tr>
<tr>
<td><strong>Effective dose (mSv/MBq)</strong></td>
<td><strong>0.0088</strong></td>
</tr>
</tbody>
</table>

The effective dose resulting from the administration of an activity of 120 MBq for an adult weighing 70 kg is about 1.1 mSv.
For an administered activity of 120 MBq the typical radiation dose to the target organ (kidneys) is 21.6 mGy and the typical radiation dose to the critical organ (bladder) is 2.2 mGy respectively.

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**
Take a vial from the kit and put it in an appropriate lead shielding.
Using a hypodermic syringe, introduce through the rubber stopper 1 to 6 mL of sterile pyrogen-free sodium pertechnetate ($^{99m}$Tc) injection corresponding to maximum 3.7 GBq.
Sodium pertechnetate ($^{99m}$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 ($^{99m}$Tc) injection, without removing the
needle, withdraw an equivalent volume of nitrogen in order to avoid excess pressure in the vial.

Shake for 5 to 10 minutes.

The obtained preparation is a clear and colourless solution, with a pH ranging between 2.3 and 3.5.

Before use, limpidity of the solution after preparation, pH, radioactivity and gamma spectrum will be checked.

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

Method
Ascending paper chromatography

Materials and reagents
1. Chromatographic paper
   Whatman 1 strip of sufficient length and not less than 2.5 cm wide.
   Trace two fine lines parallel to the ends of the strips, the one being called "deposit line" at 2.5 cm, the other one being called "solvent line" at 10 cm from the "deposit line".

2. Mobile phase
   Methyl ethyl ketone

3. Glass tank
   Glass tank of suitable size for the chromatographic paper used, ground at the top to take a closely fitting lid. In the top of the tank is a device which suspends the chromatographic paper and is capable of being lowered without opening the chamber.

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

Procedure
1. Place into the glass tank a layer 2 cm deep of the mobile phase.

2. Apply a spot of the preparation to the "deposit line" of the paper strip using a syringe and needle and dry in air.

3. Using forceps, insert the paper strip into the tank and close the lid. Lower the paper into the mobile phase and allow the solvent to migrate to the "solvent line".
4. Remove the paper strip with forceps and dry in air.

5. Determine distribution of radioactivity with an appropriate detector. Identify each radioactive spot by calculating the Rf. The Rf of technetium (99mTc) succimer is 0, and that of pertechnetate ion (free (99mTc) technetium) is 1. Measure the radioactivity of each spot by integration of the peaks.

6. Calculations
Calculate the percentage of technetium (99mTc) succimer (radiochemical purity)

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

Calculate the percentage of free (99mTc) technetium

\[
\% \text{ free (99mTc) technetium} = \frac{\text{Radioactivity of the spot at Rf 1}}{\text{Total radioactivity of the paper strip}} \times 100
\]

7. The percentage of technetium (99mTc) succimer (radiochemical purity) should be at least 95 % and the percentage of free (99mTc) technetium should not be greater than 2 %. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.