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 (dimercaptosuccinic acid).

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 lyophilised powder.

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 obtained is indicated for:

- the study of the renal cortex morphology.
- the study of individual kidney function.
- the location of ectopic kidney.

4.2 Posology and method of administration

Posology

Adults

The recommended activity is 30 to 120 MBq for a patient of 70 kg bodyweight.

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 the recommendations of the European Association of Nuclear Medicine (EANM 2016) paediatric dosage card, by multiplying a baseline activity (for calculation purposes) by the weight-dependent multiples given in the table below:

A**[**MBq**]**Administered = Baseline Activity x Multiple (with a baseline activity of 6.8)

Body Mass	**Multiple**	Body Mass	**Multiple**	Body Mass	**Multiple**
3 kg	**1***	22 kg	**5.29**	42 kg	**9.14**
4 kg	**1.14***	24 kg	**5.71**	44 kg	**9.57**
6 kg	**1.71***	26 kg	**6.14**	46 kg	**10.00**
8 kg	**2.14***	28 kg	**6.43**	48 kg	**10.29**
10 kg	**2.71***	30 kg	**6.86**	50 kg	**10.71**
12 kg	**3.14**	32 kg	**7.29**	52-54 kg	**11.29**
14 kg	**3.57**	34 kg	**7.72**	56-58 kg	**12.00**
16 kg	**4.00**	36 kg	**8.00**	60-62 kg	**12.71**
18 kg	**4.43**	38 kg	**8.43**	64-66 kg	**13.43**
20 kg	**4.86**	40 kg	**8.86**	68 kg	**14.00**

*) If the result of the calculation is less than 18.5 MBq, the recommended minimum activity of 18.5 MBq should be used in order to obtain images of sufficient quality.

Method of administration

For intravenous use.
For multidose use.

Precautions to be taken before handling or administration of the medicinal product
This medicinal product should be radiolabelled before administration to the patient.

For instructions on radiolabelling and control of the radiochemical purity of the medicinal product before administration, see section 12.

For patient preparation, see section 4.4.

Image acquisition

The images can be obtained by static (planar or tomographic) acquisitions between 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.

Renal impairment

Careful consideration of the benefit risk ratio in these patients is required since an increased radiation exposure is possible (see section 4.2).

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.

After the procedure

Close contact with infants and pregnant women should be restricted during 4 hours.

Specific warnings

This medicinal product contains less than 1 mmol of sodium (23 mg) per vial, i.e. is essentially 'sodium- free'.

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 (^{99m}Tc) succimer i.e:

- ammonium chloride: may substantially reduce renal uptake and increase hepatic uptake of technetium (^{99m}Tc) succimer

- sodium bicarbonate: reduction of renal uptake of technetium (^{99m}Tc) succimer,

- mannitol: reduction of renal uptake of technetium (^{99m}Tc) succimer.

- ACE inhibitors (e.g. captopril) may cause reversible failure of tubule function as a result of the reduction in filtration pressure in a kidney that is affected by renal artery stenosis. This in turn leads to reduced renal concentration of technetium (^{99m}Tc) succimer.

To avoid these influences, treatment with any of the above chemical products should be interrupted where possible.

Chemotherapy : Experimental research in animals has demonstrated that methotrexate, cyclophosphamide or vincristine can affect the biodistribution of technetium (^{99m}Tc) succimer. Nephrotoxic chemotherapy increases the renal retention of technetium (99mTc) succimer by alteration of renal function.

Adsorption to plastic syringes has been reported in literature. The consequence of adsorption of technetium (99mTc) succimer (and subsequent inadequate dosing) is an increased duration

of the acquisition, and an inappropriate diagnosis. It is therefore recommended to dispense in the syringe shortly before injection

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 doses to the foetus. Only essential investigations should therefore be carried out during pregnancy, when the likely benefit 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 4 hours and the expressed feeds discarded.

Close contact with infants should be limited during this period.

Fertility
No study on fertility has been performed.

4.7 Effects on ability to drive and use machines

Renocis has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The adverse events are presented in the table below by the MedDRA System Organ Class and with a not known frequency (cannot be estimated from the available data):

MedDRA Body system SOCs	**Preferred term**	**Frequency**
Immune system disorders	Hypersensitivity	Not known

Allergic reactions have been reported in the literature.

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

As the effective dose is 1.06 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 or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

In the event of administration of a radiation overdose with technetium (^{99m}Tc) succimer 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. It might be helpful to estimate the effective dose that was applied.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Diagnostic radiopharmaceuticals for the renal system, Technetium (^{99m}Tc) compounds

ATC code: V09CA02

Pharmacodynamic effects

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

5.2 Pharmacokinetic properties

Distribution

Technetium (^{99m}Tc) succimer is cleared 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.

Elimination

Excretion is exclusively via the kidneys.

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 and 0.23 mg/kg/day $SnCl_2$ over 14 days in rats was not observed. The dose usually administered to humans is 0.14 mg/kg succimer.

This agent 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 (E 512)
Inositol
Ascorbic acid (E 300)
Sodium hydroxide (E 524) (for pH adjustment)
Nitrogen atmosphere (E 941)

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.

After radiolabelling: 8 hours. Do not store above 25°C after radiolabelling.

6.4 Special precautions for storage

Store the kit in a refrigerator (2°C – 8°C).

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

Colourless, type I 15-ml glass vials closed with bromobutyl stopper and polypropylene lid welded to an aluminium crimp capsule.

Pack size: 5 multidose vials

6.6 Special precautions for disposal and other handling

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.

Content of the vials is intended only for use in the preparation of technetium (^{99m}Tc) succimer injection and is 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, vomit, or any other biological fluids. 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

04/02/2026

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 10^5 years, can be regarded as quasi stable.

The data listed below are from ICRP 128. and are calculated according to the following assumptions:
After intravenous injection of technetium (^{99m}Tc) succimer, half (0.5) is deposited in the renal cortex, with an uptake half-time of 1 h, and is assumed to be retained permanently. A further fraction is temporarily retained in liver (0.1) and spleen (0.01) with a half-time of 1 h, and eliminated with half-times of 2 h (0.5) and 1.8 days (0.5). Excretion is exclusively via the kidneys.

^{99m}Tc-DMSA	**Absorbed dose per unit activity administered (mGy/MBq)**				
Organ	**Adult**	**15 year old**	**10 year old**	**5 year old**	**1 year old**
Adrenals	0.012	0.016	0.024	0.035	0.060
Bone surfaces	0.005	0.0062	0.0092	0.014	0.026
Brain	0.0012	0.0015	0.0025	0.0040	0.0072
Breast	0.0013	0.0018	0.0028	0.0045	0.0084
Gallbladder wall	0.0083	0.010	0.014	0.022	0.031
Gastrointestinal tract					
Stomach wall	0.0052	0.0063	0.010	0.014	0.020
Small intestine wall	0.0050	0.0064	0.010	0.014	0.024
Colon wall	0.0043	0.0055	0.0082	0.012	0.020
(Upper large intestine wall	0.0050	0.0064	0.0095	0.014	0.023
Lower large intestine wall)	0.0033	0.0043	0.0065	0.0096	0.016
Heart wall	0.0030	0.0038	0.0058	0.0086	0.014
Kidneys	0.18	0.22	0.30	0.43	0.76
Liver	0.0095	0.012	0.018	0.025	0.041
Lungs	0.0025	0.0035	0.0052	0.0080	0.015
Muscles	0.0029	0.0036	0.0052	0.0077	0.014
Oesophagus	0.0017	0.0023	0.0034	0.0054	0.0094
Ovaries	0.0035	0.0047	0.0070	0.011	0.019
Pancreas	0.0090	0.011	0.016	0.023	0.037
Red marrow	0.0039	0.0047	0.0068	0.0090	0.014
Skin	0.0015	0.0018	0.0029	00045	0.0085
Spleen	0.013	0.017	0.026	0.038	0.061

Testes	0.0018	0.0024	0.0037	0.0053	0.010
Thymus	0.0017	0.0023	0.0034	0.0054	0.0094
Thyroid	0.0015	0.0019	0.0031	0.0052	0.0094
Urinary bladder wall	0.018	0.023	0.029	0.031	0.057
Uterus	0.0045	0.0056	0.0083	0.011	0.019
Remaining organs	0.0029	0.0037	0.0052	0.0077	0.014
Effective dose (mSv/MBq)	**0.0088**	**0.011**	**0.015**	**0.021**	**0.037**

The effective dose resulting from the administration of an activity of 120 MBq for an adult weighing 70 kg is about 1.06 mSv.
For an administered activity of 120 MBq the typical radiation dose to the target organ (kidneys) is about 22 mGy and the typical radiation doses to the critical organs are: urinary bladder wall: 2.2 mGy, spleen: 1.6 mGy and adrenals: 1.4 mGy.

12 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Withdrawals should be performed under aseptic conditions. The vial must never be opened and must be kept inside the lead shielding. After disinfecting 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

Usual precautions regarding sterility and radioprotection should be respected.

- 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 sodium pertechnetate (^{99m}Tc) injection corresponding to **maximum 3.7 GBq**. Sodium pertechnetate (^{99m}Tc) injection should comply with European Pharmacopoeia specifications.
- 0.9% sodium chloride solution for injection may be used as a diluent during the radiolabeling procedure to achieve the desired activity. The total volume of the radiolabelled solution **must not exceed 6 mL**.
- Do not use a breather needle as the content is under nitrogen: after introduction of the volume of sodium pertechnetate (^{99m}Tc) injection or 0.9% sodium chloride solution, without removing the needle, withdraw an equivalent volume of nitrogen in order to avoid overpressure in the vial.
- Swirl the vial gently until complete dissolution of the powder then leave to stand for 10 minutes before use.

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 radiochemical purity of the final radiolabelled preparation can be tested according to the following procedure:

Method

Thin-layer chromatography

Materials and reagents

1. TLC Fibre glass plate coated with silica gel R of sufficient length and not less than 2.5 cm wide, heated at 110°C for 30min.

Trace two thin 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 R

3. Glass tank

Glass tank of suitable size for the chromatographic plate used, ground at the top to take a closely fitting lid. In the top of the tank is a device which suspends the chromatographic plate 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 plate using a syringe and needle and dry in air.

3. Using forceps, insert the plate into the tank. Lower the plate into the mobile phase and close the lid. Then allow the solvent to migrate to the "solvent line".

4. Remove the plate 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 (^{99m}Tc) succimer is 0.0 to 0.1, and that of pertechnetate ion (free (^{99m}Tc) technetium) is 0.9 to 1.0.

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

6. Calculations

Calculate the percentage of technetium (^{99m}Tc) succimer (radiochemical purity)

$$\%\ \text{technetium } (^{99m}\text{Tc})\ \text{succimer} = \frac{\text{Radioactivity of the spot at Rf 0.0 to 0.1}}{\text{Total radioactivity of the plate}} \times 100$$

Calculate the percentage of free (^{99m}Tc) technetium

$$\%\ \text{free } (^{99m}\text{Tc})\ \text{technetium} = \frac{\text{Radioactivity of the spot at Rf 0.9 to 1.0}}{\text{Total radioactivity of the plate}} \times 100$$

7. The percentage of technetium (^{99m}Tc) succimer (radiochemical purity) should be at least 95.0 % and the percentage of free (^{99m}Tc) technetium should not be greater than 2.0 %.

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