SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

NANOCIS
Kit for the preparation of technetium (^{99m}Tc) colloidal rhenium sulphide injection
(Nanocolloid)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial A contains 0.24 mg of rhenium sulphide, corresponding to 0.15 mg of elemental rhenium.

The radionuclide is not part of the kit.

For a full list of excipients, see 6.1.

3. PHARMACEUTICAL FORM

Kit for radiopharmaceutical preparation.
Powder and solvent for solution for injection.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

After labelling with sodium pertechnetate (^{99m}Tc) solution for injection:

- Lymphoscintigraphy for the purpose of visualising the regional lymphatic system:
  - **imaging and intraoperative detection of sentinel lymph node (SLN)** in the following tumours: breast cancer, malignant melanoma, vulvar carcinoma, penile carcinoma, prostate cancer and head and neck squamous cell carcinoma.
  - **imaging of regional lymphatic flow** for individualised radiation therapy.
  - **lymphatic flow scintigraphy** for diagnosing lymphatic oedema in the limbs.
- Digestive exploration (gastroesophageal scintigraphy).

4.2 Posology and method of administration

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

Lymphoscintigraphy:
Imaging and detection of sentinel lymph node
The activity of technetium (^{99m}Tc) colloidal rhenium sulphide in adults depends upon the indication, the anatomical region that is to be investigated and the time between the injection and imaging.

The injection site is selected according to the anatomical area to be investigated. The injection is made without pressure into loose connective tissue, which should not be poorly vascularised. Before the injection, an aspiration test should ascertain that no blood vessel was inadvertently punctured.

Melanoma: 10 - 100 MBq intradermally at least four depots around the tumour. It is recommended to not exceed 0.2 ml of volume for each site.
Lymphoscintigraphic images are obtained starting after the injection and regularly thereafter until the SLN is visualised.

Breast: 5 – 20 MBq (0.2 mL) divided into one or more injections under palpation or ultrasound.
The injected activity varies depending on the time elapsed between the scintigraphic imaging and surgery.
A maximum volume of 0.5 mL may be justified in cases of deep tumor.
In case of superficial tumor, route of administration may be either intradermal next to the tumor or subcutaneous peri-tumoral.
The injection can be performed peri-areolar when tumor is in upper quadrants.
In case of deep tumor, peri-tumor route of administration is recommended.
Scintigraphic scans of breast and axillary region can be acquired 15 to 30 minutes and 3 hours after injection.

Prostate cancer: 200 MBq through the rectum in prostate lobes under ultrasound (an injection of 100 MBq in 0.3 mL for each prostatic lobe).
The tracer is injected the day before operation. The patient has previously received prophylactic broad-spectrum antibiotic (as for any prostate biopsy).
The scintigraphic images are performed immediately after the patient has emptied his bladder.

Penile cancer: On the day before operation, 60 MBq is administered intradermally 2 cm proximal to the penile tumour.
Lymphoscintigraphic images are obtained starting after the injection and every 30 minutes thereafter until the SLN is visualised.

Vulvar cancer: On the day before operation, 0.2 mL with a 60 - 120 MBq activity is administered intradermally at four sites around the tumor.
Lymphoscintigraphic images are obtained starting after the injection and every 30 minutes thereafter until the SLN is visualised.

Head and neck cancer: After the patient has received topical anesthesia, 20 - 40 MBq in 0.5 - 1.0 mL is injected submucosally around the circumference of the tumor. A non-alcoholic mouthwash is used immediately after the injection to minimize the possibility that the patient might swallow residual radioactive material.
Scintigraphy is performed immediately and up to 2 hours after injection.

- **Lymphatic flow scintigraphy**

20 - 200 MBq given by single or multiple subcutaneous injection(s). The activity is usually below 20 MBq per injection site, depending on the anatomical areas to be investigated and the time interval between injection and imaging. Recommended volumes are 0.2 - 0.3 mL. A maximum volume of 0.5 mL per injection site should not be exceeded.

Paediatric population
The activity to be administered in children should be a fraction of the adult activity and should be calculated according to the following equation:

$$\text{Paediatric activity (MBq)} = \frac{\text{Adult dose (MBq)} \times \text{child weight (kg)}}{70\ \text{(kg)}}$$

Although body weight is the more used factor on which to base the adjustment of the activity administered, in a limited number of cases the body surface area may be considered to be more appropriate.

$$\text{Paediatric activity (MBq)} = \frac{\text{Adult dose (MBq)} \times \text{child surface } (m^2)}{1.73}$$

A minimum activity, about 5 - 10 MBq per injection site is, however, needed to achieve uptake of sufficient quality.

Study of the gastro oesophageal reflux:
For adults, the patient receives an oral activity of 3.5 to 12 MBq of technetium (^{99m}Tc) colloidal rhenium sulphide (other activities may be justifiable) in a liquid phase in accordance with local practice.

Dynamic scintigraphy may be performed along with static imaging.

For children 3.5 to 12 MBq is given in a liquid phase according to local practice.
For instructions on reconstitution of the medicinal product before administration, see section 12.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings and precautions for use

Pregnancy, see section 4.6.

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.

In patients with complete obstruction of the lymphatic system,lymphoscintigraphy is not advised in patients, particularly in the lower extremities, because of the potential radiation hazard at the injection sites.

Paediatric population
Paediatric population, see sections 4.2. or 5.1., as appropriate.
Careful consideration of the indication is required since the effective dose per MBq is higher than in adults (see section 11 “Dosimetry”).

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 study in order to reduce radiation.

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 by the user 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 NANOCIS and are not to be administered directly to the patient without first undergoing the preparative procedure.

Specific warnings
This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially 'sodium- free'.

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.

Technetium (^{99m}Tc)-labelled NANOCIS must be handled with care and appropriate safety measures should be used to minimise radiation exposure to the patient and to the healthcare professionals (see section 11), consistent with proper patient management.

Precautions with respect to environmental hazard are in Section 6.6.

4.5 Interaction with other medicinal products and other forms of interaction

The use of local anaesthetic agents or hyaluronidase prior to administering the labelled preparation have shown to disturb lymphatic uptake.

4.6 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 imperative investigations should therefore be carried out during pregnancy, when the likely benefit far exceeds the risk incurred by the mother and foetus.

Lactation
Before administering a radioactive medicinal product to a mother who is breast feeding, consideration should be given to the possibility of delaying the administration of radionuclide until the mother has ceased breast feeding 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, the breast feeding should be interrupted for 24 hours and the expressed feeds discarded.

4.7 Effects on ability to drive and use machines

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

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4.8 Undesirable effects

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

Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100)
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000)
Not known (cannot be estimated from the available data)

MedDRA System Organ Class	Preferred Term
General disorders and administration site conditions Very rare	Injection site pain.
Immune system disorders Very rare	Hypersensitivity.

In very rare cases, administration of the product can involve allergic side effects.
The injection of the hypertonic technetium (^{99m}Tc) rhenium sulphide colloidal solution can produce pain at the injection site.

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is 1.32 mSv when the maximal recommended activity of 200 MBq is administered, these adverse events 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:

Denmark
Danish Medicines Agency
Axel Heides Gade 1
2300 Copenhagen S
Website: www.meldenbivirkning.dk
Email: dkma@dkma.dk

Norway
Statens legemiddelverk
Nettside: www.legemiddelverket.no/meldeskjema

4.9 Overdose

In the event of administration of a radiation overdose after oral administration, the absorbed dose to the patient undergoing gastroesophageal scintigraphy should be reduced by increasing the elimination of the radionuclide from the body by using laxatives to promote faecal excretion.

In the event of administration of a radiation overdose after subcutaneous injection, the absorbed dose to the patient undergoing lymphography can not be reduced due to poor elimination of the radionuclide from the body.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: radiopharmaceutical preparation for diagnostic use.
ATC code: V09DB06 – Diagnostic radiopharmaceuticals, hepatic and reticulo endothelial system, technetium (^{99m}Tc), particles and colloids.

At the chemical concentrations used for diagnostic examinations, technetium (^{99m}Tc) colloidal rhenium sulphide does not appear to exert any pharmacodynamic activity.

5.2 Pharmacokinetic properties

* **Subcutaneous injection:**

Distribution / Organ uptake

Technetium (^{99m}Tc) colloidal rhenium sulphide is administered by subcutaneous injection, in general in the region of the interdigital space of the hand or foot, or in the marginal area of a tumour.

The lymphatic capillaries have a discontinuous wall with pores and no basal membrane, so that colloids because of their small size can be rapidly taken up into the lymph capillaries from the interstitial fluid. During transport of the lymph through lymph nodes, some of the colloidal particles are phagocytosed by bordering cells of the reticuloendothelial system in the lymph nodes. This is repeated from one lymph node to the next.

The radiopharmaceutical preparation is a metal colloid, which is partly phagocytosed and stored in the first lymph node group.
Following injection, the activity in the lymph node corresponds to 3.06 $\pm$ 0.10 % of the administered activity at the first hour, and 3.83 $\pm$ 0.16 % at the third hour.

Passage into the blood vessels is insignificant during the first few hours after administration.

Elimination

Experimental data show urinary and hepatic elimination of the injected product.
11 % of the injected activity is retrieved in the liver parenchyma after 3 hours. Urinary elimination gradually increases and reaches 14.6 % of the injected activity at one hour.

* **Administration *per os*:**

Technetium (^{99m}Tc) colloidal rhenium sulphide administered per os is not absorbed from the gastro-intestinal tract.

5.3 Preclinical safety data

The intraperitoneal LD_{50} for potassium perrhenate is about 2.8 g/kg in mice. Expressed with reference to rhenium, the LD_{50} is 180 mg/kg.

Acute intravenous toxicity in mice of rhenium sulphide nanocolloid gives no abnormal reaction neither after injection of the preparation containing 2.5 mg rhenium sulphide/kg and 50 mg sodium pyrophosphate/kg nor for the 7 days following this injection.

In rat, the LD_{50} after intravenous injection of stannous pyrophosphate is 41.0 $\pm$ 1.6 mg/kg.

For a subcutaneous injection of 185 MBq in man, the quantity of sodium pyrophosphate is 0.007 mg/kg, i.e. 12,500 times less than the LD_{50} by the intravenous route in the mouse. The corresponding quantity of stannous chloride is 0.001 mg/kg, i.e. 23,000 times less than the LD_{50} in the mouse.

Sodium pyrophosphate in the presence of stannous chloride: Acute intravenous toxicity in the mouse gives a LD_{50} of 100 mg $Na_4P_2O_7$, 10 H_2O/kg.

No teratogenicity and mutagenicity studies or long-term studies of carcinogenesis have been carried out.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Vial A (under nitrogen atmosphere):

Gelatin
Ascorbic acid
Sodium hydroxide (pH adjustement)
Concentrated hydrochloric acid
Water for injections

Vial B (under nitrogen atmosphere):

Sodium pyrophosphate decahydrate
Stannous chloride dihydrate
Sodium hydroxide (pH adjustement)
Concentrated hydrochloric acid (pH adjustement)

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 12.

6.3 Shelf life

6 months from the date of manufacture.
The expiry date is indicated on the outer packaging and on each vial.
Do not store the labelled product above 25°C and used within 4 hours after labelling.

6.4 Special precautions for storage

Store the kit in a refrigerator (2°C - 8°C).
For storage conditions of the reconstituted 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

a) 15 mL, type I Ph. Eur. clear, colourless glass vial, containing 1 mL of sterile solution;

and

b) 15 mL, type I Ph. Eur. clear, colourless glass vial, containing a freeze-dried powder intended for reconstitution with the solution in vial (A) above and then labelled with Sodium Pertechnetate (^{99m}Tc) Solution Ph. Eur.

Pack size: Kit containing 5 vials A and 5 vials B.

6.6 Special precautions for disposal and other handling

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 or urine, vomiting, etc. Suitable precautions should be taken concerning the radioactivity eliminated by the patients in order to avoid any contamination. Radiation protection precautions in accordance with national regulations must therefore be taken.

All lumpectomy specimens should be stored for decontamination until the dose rate equals background levels.
The residues may be put in an ordinary waste bin so far as long as the activity of vials and syringes does not exceed that of background when measured with a low level radiation detector.
Any unused 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

DENMARK: DK R 1042
NORWAY: MT nr 99-4546

9. DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

DENMARK First authorisation: 31. January 1995

NORWAY First authorisation: 08. May 2001
Date of latest renewal: 08. May 2011

10. DATE OF REVISION OF THE TEXT

December 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 2.13×10^5 years, can be regarded as quasi stable.

*** Dosimetry data after subcutaneous administration:**

The absorbed radiation dose for a patient (70 kg body weight) after administration of technetium (^{99m}Tc) colloidal rhenium sulphide has been calculated using a dosimetric model assuming a subcutaneous injection in the breast and a lymphogenic outflow of 20 % of the activity.

Table 1: Absorbed radiation dose (mGy/MBq injected activity) and effective dose (mSv/MBq injected activity) after subcutaneous injection in the breast by gamma rays emanating from injections depot and by absorption in RES in case of lymphogenic outflow.**

Organ	Absorbed dose resulting from the subcutaneous injection depot (mGy/MBq)***	Absorbed dose per percentage of outflow (mGy/MBq/% flow)****	Total absorbed dose for injected activity of 200 MBq and assumption of lymphogenic outflow of 20 %*****
Breast	5.6×10^{-2}	2.58×10^{-5}	11.30
Heart	1.04×10^{-2}	8.36×10^{-5}	2.41
Thymus	9.94×10^{-3}	2.56×10^{-5}	2.09
Lungs	7.85×10^{-3}	7.70×10^{-5}	1.88
Bone surfaces	2.97×10^{-3}	1.10×10^{-4}	1.03
Skin	2.80×10^{-3}	1.53×10^{-5}	0.62
Liver	2.77×10^{-3}	8.91×10^{-4}	4.12
Stomach wall	2.49×10^{-3}	8.17×10^{-5}	0.82
Pancreas	2.34×10^{-3}	1.67×10^{-4}	1.14
Adrenal	1.88×10^{-3}	1.51×10^{-4}	0.98
Red bone marrow	1.85×10^{-3}	1.04×10^{-4}	0.79
Muscles	1.69×10^{-3}	3.30×10^{-5}	0.47
Spleen	1.61×10^{-3}	8.66×10^{-4}	3.79
Gallbladder	1.39×10^{-3}	2.40×10^{-4}	1.24
Thyroid gland	1.22×10^{-3}	1.02×10^{-5}	0.29
Kidneys	7.71×10^{-4}	1.14×10^{-4}	0.61
Upper large intestine	4.72×10^{-4}	6.84×10^{-5}	0.37
Small intestine	3.05×10^{-4}	5.07×10^{-5}	0.26
Uterus	1.21×10^{-4}	2.39×10^{-5}	0.12
Lower large intestine	1.13×10^{-4}	2.26×10^{-5}	0.11
Ovaries	1.11×10^{-4}	2.92×10^{-5}	0.14
Brain	1.02×10^{-4}	8.09×10^{-6}	0.05
Bladder wall	7.86×10^{-5}	1.27×10^{-5}	0.07
Testes*	0.10×10^{-4}	3.92×10^{-6}	0.02
Whole body	4.06×10^{-3}	6.13×10^{-5}	1.06
Effective dose (mSv)	**4.7×10^{-3}**	**9.59×10^{-5}**	**1.32**

- Testes values calculated as per “adult male model”.
- ** RES: reticulo-endothelial system
- *** **Absorbed dose per applied activity from the subcutaneous injection depot (mGy/MBq) with the hypothesis that the depot stays at the injection site.**
- ****** Absorbed dose per percentage of outflowing colloid in the RES (mGy/MBq/% flow) with the hypothesis that the depot does not stay totally at the injection site but migrates to RES.**
- ******* Total absorbed dose as a total of column 1 and 2 for injected activity of 200 MBq and assumption of lymphogenic outflow of 20 %**

After subcutaneous administration of 200 MBq (maximal activity) in adults and with an assumed lymphogenic outflow of 20%, the effective dose is 1.32 mSv.
The absorbed dose in the target organ (lymph nodes) is mostly range from 100 to 400 mGy.
Mean absorbed doses in the critical organs are : breast 11.30 mGy, liver 4.12mGy, spleen 3.79 mGy, lungs 1.88 mGy, gallbladder 1.24 mGy, red bone marrow 0.79 mGy; kidneys 0.61 mGy, and bladder wall 0.07 mGy.

Radiation exposure to healthcare professionals

The radiation exposure to operating room personnel, and pathologist during breast sentinel lymph node biopsy has been estimated after a peritumoral injection of 25 to 40 MBq in breast cancer of ^{99m}Tc sulphide colloid 1.5 to 3 hours before lumpectomy.The results are presented in the table below.

Table 2: radiation exposure to operating room personnel, and pathologist during breast sentinel lymph node biopsy

	Operating room and pathologist exposure (mSv/h)		
	Breast injection site	Lumpectomy	Sentinel lymph node
3 cm (surgeon's hands)	0.34 (0.20-0.42)	0.018	0.0006
30 cm (surgeon's torso)	0.013	0.003	0.0004
300 cm (scrub nurse's torso)	0.001	NA	NA
3 cm (pathologist's hands)		0.018	0.0006
30 cm (pathologist's torso)		0.003	0.0004

* **Dosimetry data on *per os* administration:**

The doses of radiation absorbed from technetium (^{99m}Tc) colloidal rhenium sulphide are laid down by the International Commission of Radiological Protection, ICRP Publication 80 (Radiation dose to patients from radiopharmaceuticals).

Table 2: Tc-LABELLED NON-ABSORBABLE MARKERS
Oral administration of fluids

Absorbed dose per unit activity administered (mGy/MBq)

Organ	Adult	15 years	10 years	5 years	1 year
Adrenals	2.5×10^{-3}	3.3×10^{-3}	5.5×10^{-3}	8.9×10^{-3}	1.5×10^{-2}
* Bladder wall	6.9×10^{-3}	9.1×10^{-3}	1.4×10^{-2}	2.2×10^{-2}	3.5×10^{-2}
Bone surfaces	4.2×10^{-3}	5.2×10^{-3}	7.4×10^{-3}	1.1×10^{-3}	2.1×10^{-2}
Brain	1.8×10^{-6}	3.4×10^{-6}	1.2×10^{-5}	4.0×10^{-5}	1.0×10^{-4}
Breast	2.8×10^{-4}	4.2×10^{-4}	9.4×10^{-4}	2.0×10^{-3}	3.8×10^{-3}
Gall bladder	1.4×10^{-2}	1.8×10^{-2}	3.0×10^{-2}	4.3×10^{-2}	7.1×10^{-2}
GI-tract					
* Stomach	2.2×10^{-2}	2.9×10^{-2}	4.1×10^{-2}	6.6×10^{-2}	1.2×10^{-1}
* SI	6.0×10^{-2}	7.6×10^{-2}	1.2×10^{-1}	1.9×10^{-1}	3.5×10^{-1}
* Colon	1.0×10^{-1}	1.3×10^{-1}	2.2×10^{-1}	3.5×10^{-1}	6.6×10^{-1}
* (ULI	1.2×10^{-1}	1.5×10^{-1}	2.5×10^{-1}	4.0×10^{-1}	7.5×10^{-1} 1)
* (LLI	8.3×10^{-2}	1.1×10^{-1}	1.8×10^{-1}	2.9×10^{-1}	5.4×10^{-1} 1)
Heart	1.0×10^{-3}	1.4×10^{-3}	2.5×10^{-3}	4.3×10^{-3}	8.6×10^{-3}
Kidneys	5.5×10^{-3}	6.7×10^{-3}	1.0×10^{-2}	1.5×10^{-2}	2.3×10^{-2}
Liver	3.7×10^{-3}	4.8×10^{-3}	9.3×10^{-3}	1.5×10^{-2}	2.7×10^{-2}
Lungs	5.7×10^{-4}	9.1×10^{-4}	1.6×10^{-3}	2.9×10^{-3}	5.7×10^{-3}
Muscles	3.2×10^{-3}	4.0×10^{-3}	6.0×10^{-3}	9.0×10^{-3}	1.5×10^{-2}
Oesophagus	1.9×10^{-4}	3.0×10^{-4}	5.0×10^{-4}	1.2×10^{-3}	2.6×10^{-3}
Ovaries	2.5×10^{-2}	3.2×10^{-2}	4.8×10^{-2}	6.8×10^{-2}	1.1×10^{-1}
Pancreas	5.9×10^{-3}	7.9×10^{-3}	1.2×10^{-2}	1.8×10^{-2}	3.1×10^{-2}
Red marrow	4.7×10^{-3}	5.7×10^{-2}	7.5×10^{-2}	9.2×10^{-2}	1.1×10^{-2}
Skin	9.3×10^{-4}	1.1×10^{-3}	1.7×10^{-3}	2.9×10^{-3}	5.4×10^{-3}
Spleen	4.0×10^{-3}	5.0×10^{-3}	7.8×10^{-3}	1.2×10^{-2}	2.0×10^{-2}
Testes	1.3×10^{-3}	2.0×10^{-3}	3.8×10^{-3}	6.5×10^{-3}	1.2×10^{-2}
Thymus	1.9×10^{-4}	3.0×10^{-4}	5.0×10^{-4}	1.2×10^{-3}	2.6×10^{-3}
Thyroid	2.0×10^{-5}	4.8×10^{-5}	1.5×10^{-4}	3.0×10^{-4}	1.2×10^{-3}
Uterus	1.6×10^{-2}	2.0×10^{-2}	3.1×10^{-2}	4.7×10^{-2}	7.6×10^{-2}
Remaining organs	5.2×10^{-3}	7.2×10^{-3}	1.1×10^{-2}	2.0×10^{-2}	3.0×10^{-2}
Effective dose (mSv/MBq)	1.9×10^{-2}	2.5×10^{-2}	3.9×10^{-2}	6.2×10^{-2}	1.1×10^{-1}

For this product the effective dose resulting from a *per os* administered activity of 12 MBq is typically 0.23 mSv (per 70 kg individual).

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

As with any pharmaceutical product, if at any time in the preparation of this product the integrity of this vial is compromised it should not be used.
The product is to be used after reconstitution of the kit and labelling with addition of sodium pertechnetate (^{99m}Tc) solution for injection, allowing the preparation of technetium (^{99m}Tc) colloidal rhenium sulphide injection (Nanocolloid).

The mean diameter of the colloidal particles is around 100 nm (Brownian notion and Photon correlation spectroscopy measuring principles).

Method of preparation

Usual precautions regarding sterility and radioprotection should be respected.

Take a vial B from the kit and introduce through the asepticized rubber cap 2 mL of water for injection with a hypodermic syringe (do not use a breather needle). Shake the vial to dissolve the product.
Introduce without breather needle 0.5 mL of solution from the vial B into a vial A. Shake.
Put vial A in an appropriate lead shielding. Introduce without breather needle 1 to 2 mL of (^{99m}Tc) sodium pertechnetate injection with an activity of 370 to 5550 MBq.
Put vial A in a boiling water-bath during 15 to 30 minutes without lead shielding.
Cool the vial under running water.

Quality control

The quality of labeling (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 at 2 cm from one of the ends of the paper strip a fine line called "deposit line" and an other line called "front line" at 10 cm from the "deposit line".

2. Mobile phase
Methylethylketone.

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
The method of preparation of the kit is described above § 6.6.

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

2. Remove a spot of the preparation and apply it 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 until the "front line".

4. Remove the paper strip with forceps and dry in air.

5. Determine distribution of activity with an appropriate detector.
Identify each radioactive spot by calculating the Rf. The Rf of technetium (^{99m}Tc) complex is 0, and that of impurities ((^{99m}Tc) pertechnetate) is 1.
Measure the activity of each spot by integration of the peaks.

6. Calculations
Calculate the percentage of technetium (^{99m}Tc) complex (radiochemical purity)

$$\% \text{ technetium } (^{99m}\text{Tc}) \text{ complex} = \frac{\text{Activity of the spot at Rf 0}}{\text{Total Activity of the paper strip}} \times 100$$

Calculate the percentage of impurities

$$\% \text{ of impurities} = \frac{\text{Activity of the spot at Rf 1}}{\text{Total activity of the paper strip}} \times 100$$

7. The percentage of technetium (^{99m}Tc) complex (radiochemical purity) should be at least 95 % and the percentage of impurities should not be greater than 5 %.

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