SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Technescan DMSA 1.2 mg kit for radiopharmaceutical preparation

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains:
Succimer (or dimercaptosuccinic acid or DMSA) 1.2 mg

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.
Off white to slightly yellow lyophilisate.

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 in adults and children for:

- Study of renal cortex morphology
- Study of individual kidney function
- Location of ectopic kidney.

4.2 Posology and method of administration

Posology
Adults
In adults, the recommended activity of technetium (^{99m}Tc) succimer, for a patient of average weight (70 kg), is 30 to 120 MBq. Other activities may be justifiable. It should be noted that in each country physicians should follow the Diagnostic Reference Levels and the rules set up by local law.

Elderly population
No special dosage regimen for elderly patients is required.

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 European Association of Nuclear Medicine dosage card (EANM 2016) by using the following formula:
A[MBq]Administered = Baseline Activity x *Multiple* (with a baseline activity of 6.8)

A minimum activity of 18.5 MBq is recommended in order to obtain images of sufficient quality.

The resulting activities to be administered may be found in the following table:

Weight (kg)	Activity (MBq)	Weight (kg)	Activity (MBq)	Weight (kg)	Activity (MBq)
3	18.5	22	36	42	62
4	18.5	24	39	44	65
6	18.5	26	42	46	68
8	18.5	28	44	48	70
10	18.5	30	47	50	73
12	21	32	50	52 - 54	77
14	24	34	52	56 - 58	82
16	27	36	54	60 - 62	86
18	30	38	57	64 - 66	91
20	33	40	60	68	95

Method of administration
Multidose vial.
For intravenous injection.

This medicinal product should be radiolabelled before administration to the patient.
For instructions on radiolabelling of the medicinal product before administration, see section 12.

For patient preparation, see section 4.4.

Image acquisition
Image acquisition may be started two to three hours post-injection. It can be performed using static (planar or tomographic) acquisition.
In case of renal insufficiency or renal obstruction, delayed acquisition (at 6 and 24 hours after tracer injection, respectively) may be necessary.
If significant hydronephrosis exists, delayed acquisition (4 to 24 hours after tracer injection) or furosemide injection may be useful.

4.3 Contraindications

Hypersensitivity to the active substance, or 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 section 4.2.
Careful consideration 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 to reduce radiation exposure.
Certain drug treatments should be discontinued (see section 4.5).

Interpretation of images
Tubular defects such as the Fanconi syndrome or nephronophthisis (medullary cystic kidney disease) may result in poor renal visualization (defective binding of the isotope within the tubular cell, increased bladder uptake and urinary excretion).

After the procedure
Close contact with infants and pregnant women is not restricted after the procedure.

Specific warnings
Injection should be strictly intravenous to avoid local deposit and irradiation. In the event of paravenous injection, the injection should be immediately stopped and the site of injection should be cooled and rested in elevated position.

This medicinal product contains less than 1 mmol sodium (23 mg) per vial, i.e. 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

Interference with the acid-base balance, e.g. by ammonium chloride and sodium bicarbonate, results *in vivo* in a change in valency of the technetium (^{99m}Tc) succimer complex, and consequently a reduced accumulation of this complex in the renal cortex in context of a marked concentration in the liver and faster urine excretion.

Mannitol causes dehydration and therefore a reduction in extraction of technetium (^{99m}Tc) succimer to the kidney.

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 medicinal products should be interrupted where possible.

Experimental research in animals has demonstrated that chemotherapy with methotrexate, cyclophosphamide or vincristine can affect the biodistribution of technetium (^{99m}Tc) succimer.

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 likely benefit exceeds the risks incurred by the mother and foetus.

Breast-feeding
Technetium (^{99m}Tc) succimer is excreted into breast milk.
Before administering radiopharmaceuticals 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, breast-feeding should be interrupted for at least 4 hours and the expressed feeds discarded.
Close contact with infants is not restricted during this period.

Fertility
The effect of administration of technetium (^{99m}Tc) succimer on fertility is unknown.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Information on adverse reactions is available from spontaneous reporting. The reports describe anaphylactoid, vasovagal and injection site reactions which were mild to moderate and usually resolved with either no or symptomatic treatment.

Tabulated list of adverse reactions
The following table includes the adverse reactions sorted by system organ classes according to MedDRA. The frequencies are defined as follows: very common ≥ 1/10; common from ≥ 1/100 to <1/10; uncommon from ≥ 1/1,000 to <1/100, rare from ≥ 1/10,000 to <1/1,000; very rare <1/10,000; frequency not known (cannot be estimated from the available data).

Adverse Reactions sorted by System Organ Class

System Organ Class (SOCs)	***Adverse reactions***	***Frequency***
Immune system disorders	Anaphylactoid reaction (e.g. rash, pruritus, urticaria, erythema, hyperhidrosis, periorbital oedema, conjunctivitis, laryngeal oedema, pharyngeal oedema, cough, dyspnoea, abdominal pain, vomiting, nausea, salivary hypersecretion, tongue oedema, hypotension, flushing)	Not known
Nervous system disorders	Vasovagal reaction (e.g. syncope, hypotension, headache, dizziness, pallor, asthenia, fatigue)	Not known
General disorders and administration site conditions	Injection site reaction (e.g. rash, swelling, inflammation, oedema)	Not known

Anaphylactoid reactions
Reported anaphylactoid reactions were mild to moderate, however the occurrence of severe reactions cannot be excluded (see section 4.4).

Vasovagal reactions
Vasovagal reactions are most probably caused by the procedure itself, especially in anxious patients, but a contribution of the product cannot be excluded.

Injection site reactions
Local reactions at the injection site may include rashes, swelling, inflammation and oedema. In most cases such reactions are probably caused by extravasation (see section 4.4).

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 authorization 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 national reporting system at Statens legemiddelverk.
Website: www.legemiddelverket.no/meldesjema

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, ATC code V09CA02.

Pharmacodynamic effects:
At the chemical concentrations used for diagnostic examinations, technetium (^{99m}Tc) succimer does not appear to have any pharmacodynamic activity.

5.2 Pharmacokinetic properties

Distribution and organ uptake
After intravenous injection of technetium (^{99m}Tc) succimer, binding to plasma proteins occurs rapidly in the blood; binding to erythrocytes is negligible. The technetium (^{99m}Tc) succimer localizes in high concentrations in the renal cortex. Maximal uptake occurs within 3-6 hours after intravenous injection, with about 40-50 % of the activity retained in the kidneys in patients with normal renal function. Less than 3 % of the administered activity localizes in the liver. However, this amount can be increased significantly and renal distribution decreased in patients with impaired renal functions.

The technetium (^{99m}Tc) succimer concentrates in the proximal renal tube, presumably as a result of peritubular reabsorption.

Elimination
After intravenous administration, technetium (^{99m}Tc) succimer is eliminated from the blood via the kidneys with a triphasic pattern in patients with normal renal function.
One hour after injection about 10 % of the activity appears in the urine. Within 24 hours, about 30 % is excreted in the urine.

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

5.3 Preclinical safety data

Toxicological studies in mice prove the safety of the single administration of technetium (^{99m}Tc) succimer in the indicated activity and amount (LD50 of succimer is 3.2 g/kg). Toxicity with repeated administration of 0.66 mg/kg/day succimer and 0.23 mg/kg/day of $SnCl_2$ over 14 days in rats was not observed. The maximal dose administered to human is 0.02 mg/kg succimer. 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

Inositol
Stannous chloride dihydrate (E 512)
Hydrochloric acid (E 507)
Sodium hydroxide (E 524)

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: 4 hours in the original glass vial. Do not store above 25 °C after radiolabelling.

6.4 Special precautions for storage

Store in a refrigerator (2 °C-8 °C). Keep the vials in the outer carton in order to protect from light.
For storage conditions after radiolabelling 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

10 ml glass vial (type I) closed with a bromobutyl stopper, sealed with an aluminium cap.
Pack size: five multidose vials in a carton box.

6.6 Special precautions for disposal and other handling

General warning
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 vial is intended only for use in the preparation of the technetium (^{99m}Tc) succimer solution and is not to be administered directly to the patient without first undergoing the preparative procedure.

For instructions on radiolabelling 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) 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

Curium Netherlands B.V.
Westerduinweg 3
1755 LE Petten
The Netherlands

8. MARKETING AUTHORISATION NUMBER

MTnr 8286

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

31 January 1995/10 May 2012

10. DATE OF REVISION OF THE TEXT

01.11.2024

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 International Commission on Radiological Protection (ICRP 128) and are calculated according to the following assumptions:
Total body retention is described by tri-exponential functions. A fraction of 0.5 is taken up in the renal cortex, with an uptake half-time of 1 h, and is assumed to be retained permanently. Fractions of 0.1 and 0.01 are taken up in liver and spleen, respectively, with a half-life of 1 h, and eliminated with half-times of 2 h (50 %) and 1.8 days (50 %).

Table 1: Dosimetry of technetium (^{99m}Tc) succimer

Organ	**Absorbed dose per unit activity administered (mGy/MBq)**				
	Adult	**15 years**	**10 years**	**5 years**	**1 year**
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
Gall bladder wall	0.0083	0.010	0.014	0.022	0.031
Gastro intestinal 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	0.0045	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 a (maximal recommended) 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 organs (urinary bladder wall, spleen, adrenals) are 2.2 mGy, 1.6 mGy and 1.4 mGy respectively.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Withdrawals should be performed under aseptic conditions. The vials must never be opened. 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
Prepare technetium (^{99m}Tc) succimer injection according to the following procedure using aseptic technique:
- Transfer an undiluted amount (1-5 mL) of sodium pertechnetate (^{99m}Tc) solution for injection (containing 1200 to 3700 MBq) to the Technescan DMSA vial.
- Do not use air vent needle as the vial content is under nitrogen: after introduction of the volume of sodium pertechnetate (^{99m}Tc) solution for injection, without removing the needle, withdraw an equivalent volume of nitrogen in order to avoid excess pressure in the vial.
- Invert the vial several times to ensure complete dissolution the powder.
- Incubate the vial for 15 minutes at room temperature.
The solution of technetium (^{99m}Tc) succimer is then ready for dilution or injection. It can be diluted with freshly opened 0.9 % saline solution to the required radioactive concentration. Do not introduce air into the vial.

Properties of the final radiolabelled preparation:
Colourless, clear to slightly opalescent solution
pH 2.3 – 3.5

Quality control
The radiochemical purity of the final radiolabelled preparation can be tested according to the following procedure:
- Examine by thin-layer chromatography (TLC) on silica gel coated glass-fibre sheets according to the European Pharmacopoeia (Ph.Eur.) (Monograph 643).
- Apply 5 to 10 µl of technetium (^{99m}Tc) succimer solution and develop 10-15 cm in methyl ethyl ketone R; the pertechnetate (^{99m}Tc) ion migrates near the solvent front, the technetium (^{99m}Tc) succimer complex remains at the start.
- Requirement:
Pertechnetate ≤ 2 %.
Percentage of total radioactivity found in the spot corresponding to technetium (^{99m}Tc) succimer complex: ≥ 95 %. The ^{99m}Tc binding generally exceeds 98 %.