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:

Dimercaptosuccinic acid 1.2 mg.

The radionuclide is not part of the kit.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Kit for radiopharmaceutical preparation.
Greyish white to slightly yellow pellets or powder.
To be reconstituted with sodium pertechnetate (^{99m}Tc) solution for injection (not included in this kit).

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 obtained 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. 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
There is no special dosage regimen for the elderly patient.

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 paediatric 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 were calculated according to the EANM dosage card (2008) by using the following formula:
***A*[*MBq*]Administered =** *Baseline Activity* x *Multiple* (with a baseline activity of 17.0)

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

Please see also guidelines on ^{99m}TcDMSA scintigraphy in children.

Weight (kg)	Activity (MBq)	Weight (kg)	Activity (MBq)	Weight (kg)	Activity (MBq)
3	17	22	52	42	75
4	19	24	54	44	77
6	25	26	57	46	79
8	29	28	59	48	81
10	33	30	62	50	83
12	37	32	64	52 - 54	85
14	40	34	66	56 - 58	89
16	43	36	68	60 - 62	93
18	46	38	71	64 - 66	96
20	49	40	73	68	98

Method of administration
This medicinal product is for multidose use.
Administration is by intravenous injection. This medicinal product should be reconstituted before administration to the patient.

For instruction on reconstitution of the medicinal product before administrations, see section 12.

For patient preparation, see section 4.4.

Image acquisition
The image acquisitions may be performed two to three hours post-injection. Where there is renal impairment or obstruction, delayed views may be needed (6 to 24 hours respectively).
In case of significant hydronephrosis late images or furosemide injection may then be useful (4 to 24 hours).

4.3 Contraindications

Hypersensitivity to dimercaptosuccinic acid 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, exposure to ionising radiation must be justifiable on the basis of likely benefit. The activity administered must be such that the resulting radiation dose is as low as reasonably achievable bearing in mind the need to obtain the intended diagnostic information.

Renal impairment
Careful consideration of the benefit risk ratio in these patients is required since an increased radiation exposure is possible.

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 study in order to reduce radiation.

Specific warnings
Tubular defects such as the Fanconi syndrome or nephronophtisis may result in poor renal visualization (defective binding of the isotope within the tubular cell and urinary excretion).

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

Precautions with respect to environmental hazard see section 6.6.

General warning

Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings. Its receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the local 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.

4.5 Interaction with other medicinal products and other forms of interactions

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

Mannitol causes dehydration and therefore a reduction in extraction of DMSA-[^{99m}Tc]technetium to the kidney.

ACE inhibitors 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 DMSA-[^{99m}Tc]technetium.

Experimental research in animals has demonstrated that chemotherapy with methotrexate, cyclophosphamide or vincristine can affect the biodistribution of DMSA -[^{99m}Tc]technetium.

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 far exceeds the risks incurred by mother and foetus.

Breast-feeding
^{99m}Tc will be excreted into breast milk.
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 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, breast-feeding should be interrupted for at least 4 hours and the expressed feeds discarded.

Fertility
The effect of administration of ^{99m}Tc-DMSA on pregnant women and 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.

Anaphylactoid reactions
Reported anaphylactoid reactions were mild to moderate, however the occurrence of severe reactions cannot be excluded. If anaphylactoid reactions occur, the medicinal product must no longer be administered. Appropriate instruments (including endotracheal tube and ventilator) and medications should be to hand so as to be able to react immediately in an emergency.

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 edema. In most cases such reactions are probably caused by extravasation. Extended extravasation may necessitate surgical treatment.

Adverse Reactions sorted by System Organ Class
Immune system disorders
Frequency unknown*: 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)

Nervous system disorders
Frequency unknown*: Vasovagal reaction (e.g. syncope, hypotension, headache dizziness, pallor, asthenia, fatigue)

General disorders and administration site conditions
Frequency unknown*: Injection site reaction

* Adverse reactions derived from spontaneous reporting

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 effects are expected to occur with a low probability.
In all cases it is necessary to ensure that the risks of the radiation are less than from the disease itself.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

In the event of the administration of a radiation overdose with DMSA-[^{99m}Tc]technetium 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 codeV09CA02

At the chemical concentrations and activities used for diagnostic procedures DMSA-[^{99m}Tc]technetium does not appear to exert any pharmacodynamic activity.

5.2 Pharmacokinetic properties

Distribution
The DMSA-[^{99m}Tc]technetium localizes in high concentrations in the renal cortex. Maximal localization 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 decreases in patients with impaired renal functions.

DMSA-[^{99m}Tc]technetium concentrates in the proximal renal tube, presumably as a result of peritubular reabsorption.

Elimination
After intravenous administration DMSA-[^{99m}Tc]technetium is eliminated from the blood with a triphasic pattern in patients with normal renal function.

Half-life
The effective half-life of DMSA-[^{99m}Tc]technetium 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 of $SnCl_2$ over 14 days in rats was not observed. The dose usually administered to human is 0.14 mg/kg succimer (DMSA). 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

Inositol
Stannous chloride dihydrate
Hydrochloric acid
Sodium hydroxide

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 a glass vial. Do not store above 25˚C after radiolabelling. Do not refrigerate or freeze.

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 radiolabeling 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 closed with a bromobutyl rubber stopper and an aluminium crimp cap.
Technescan DMSA is supplied as five vials in a carton.

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. Its receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the local 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 Technescan DMSA and are not to be administered directly to the patient without first undergoing the preparative procedure.

For instructions on reconstitution 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 this kit before extemporary preparation is not radioactive. However, after sodium pertechnetate (99mTc) 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 product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Curium Netherlands B.V.
Westerduinweg 3
P.O. Box 3
1755 ZG Petten
The Netherlands

8 MARKETING AUTHORISATION NUMBER

PA0690/011/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22 January 1999

Date of last renewal: 22 January 2009

10 DATE OF REVISION OF THE TEXT

November 2020

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.

The data listed below are from ICRP 80.

^{99m}Tc-DMSA	Absorbed dose per unit activity administered (mGy/MBq)				
Organ	**Adult**	**15 years**	**10 years**	**5 years**	**1 year**
Adrenals	0.012	0.016	0.024	0.035	0.060
Bladder	0.018	0.023	0.029	0.031	0.057
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	0.083	0.010	0.014	0.022	0.031
GI-tract					
Stomach	0.0052	0.0063	0.010	0.014	0.020
SI	0.0050	0.0064	0.010	0.014	0.024
Colon	0.0043	0.0055	0.0083	0.012	0.020
(ULI LLI)	0.0050 0.0033	0.0064 0.0043	0.0095 0.0065	0.0096	0.023 0.016
Heart	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
Uterus	0.0015	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 120MBq for an adult weighing 70 kg is about 1.06 mSv.

12 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

If the integrity of this vial is compromised, the product should not be used.

Method of preparation

Add aseptically an undiluted amount of sodium pertechnetate (^{99m}Tc) solution for injection (containing 1.2 to 3.7 GBq) in a volume of 5 ml to a DMSA vial and shake for 1 minute. After incubation for 15 minutes at room temperature, the preparation is ready for dilution or injection.

The preparation can be diluted with freshly opened 0.9 % saline solution. 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.

The reconstituted product is a colourless, clear to slightly opalescent solution.

Quality control
Examine by TLC on silica gel coated glass-fibre sheets according the European pharmacopoeia (Ph.Eur.) (Monograph 643). Apply 5 to 10 µl and develop 5-10 cm in methyl ethyl ketone R; the pertechnetate ion migrates near the solvent front, technetium succimer complex remains at the start. Requirement: pertechnetate $\leq$ 2 %. Percentage of the total radioactivity found in the spot corresponding to technetium succimer complex: $\geq$ 95 %. The ^{99m}Tc binding generally exceeds 98%.