SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

TechneScan MAG3, kit for radiopharmaceutical preparation

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains 1mg betiatide.
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.
Powder for solution for injection.
Off-white to slightly yellow lyophilizate.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.
After reconstitution and labelling with sodium pertechnetate (^{99m}Tc) solution, the diagnostic agent technetium (^{99m}Tc) mertiatide may be used for the evaluation of nephrological and urological disorders in particular for the study of morphology, perfusion, function of the kidney and characterisation of urinary outflow.

4.2 Posology and method of administration

Posology

Adults
The recommended activity for an adult weighing 70 kg is 40 to 200 MBq, depending on the pathology to be studied and the method to be used. Other activities may be justifiable. Studies of renal blood flow or transport through the ureters generally require a larger dose than studies of intra-renal transport, whereas renography requires smaller activities than sequential scintigraphy.

Elderly population
No special dosage-scheme is required 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 children and adolescents has to be considered carefully, based upon clinical needs and assessing the risk/benefit ratio in this patient group.

The activity to be administered in children and adolescents is determined according to the EANM dosage card (2016) using the following formula:

The activity to be administered A[MBq] = Baseline activity (of 11.9 MBq) x Multiple

The activities to be applied are listed in the following table:

Weight (kg)	Activity (MBq)	Weight (kg)	Activity (MBq)	Weight (kg)	Activity (MBq)
3	15	22	36	42	52
4	15	24	38	44	54
6	18	26	40	46	55
8	20	28	41	48	57
10	23	30	43	50	58
12	26	32	45	52 - 54	60
14	28	34	46	56 - 58	62
16	30	36	48	60 - 62	65
18	32	38	50	64 - 66	67
20	34	40	51	68	69

In very young children, a minimum dose of 15 MBq is necessary in order to obtain images of sufficient quality.

Concomitant medicinal products for diagnostic tests
The administration of a diuretic or an ACE inhibitor during the diagnostic procedure is sometimes used for differential diagnosis of nephrological and urological disorders.

Method of administration
Multidose vial.
For intravenous injection.
This medicinal product should be reconstituted before administration to the patient.
For instructions regarding reconstitution, see section 12.
For patient preparation, see section 4.4.

Image acquisition
The scintigraphic investigation is usually performed immediately after administration.

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 be 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.

Paediatric population
For information on the use in the paediatric population, see section 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 study to reduce radiation.

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

Specific warnings
Flow measurement
The agent is not suited for exact monitoring of effective renal plasma flow or effective renal blood flow in patients with seriously impaired renal function.

Excretion via gall bladder
Small amounts of technetium (^{99m}Tc)-labelled impurities may be present and/or are formed during the labelling process. As some of these impurities are distributed to the liver and excreted via the gall bladder they may influence the late phase (after 30 minutes) of a dynamic renal study due to the overlap of kidney and liver in the region of interest.

Sodium content
This medicinal product contains less than 1 mmol sodium (23 mg) per vial, i. e. essentially ‘sodium-free’.

Environmental hazard
Precautions with respect to environmental hazard see section 6.6.

4.5 Interaction with other medicinal products and other forms of interaction

Technetium (^{99m}Tc) mertiatide has not been described to interfere with agents commonly prescribed to patients requiring the above-mentioned investigations (e.g. antihypertensives and medicinal agents used to treat or prevent organ transplant rejection). However, the single administration of a diuretic or ACE inhibitor is sometimes used in the differential diagnosis of nephrological and urological disorders.

All products having an impact on the renal blood flow (e.g. acetylsalicylic acid) or on the tubular renal excretion (e.g. administered contrast media, probenecid, hydrochlorothiazide, NSAIDS such as diclofenac, sulfonamides) may impair tubular renal excretion and thereby influence the technetium (^{99m}Tc) mertiatide clearance.

Calcium antagonists can cause false-positive captopril renograms. These medications should be stopped before captopril renography, and physicians should be aware of this possible drug interaction if bilateral symmetrical renal function deterioration is seen on a patient's captopril renogram.

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 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 radiopharmaceutical, bearing in mind the secretion of activity in breast milk.
Sodium pertechnetate (^{99m}Tc) is excreted in human milk. If the administration is considered necessary, breast-feeding should at least be interrupted for four hours, and the expressed feeds discarded.
Close contact with infants is not restricted during this period.

Fertility
There are no data on possible harmful effects of TechneScan MAG3 on fertility.

4.7 Effects on ability to drive and use machines

TechneScan MAG3 has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is 1.4 mSv when the maximal recommended activity of 200 MBq is administered these adverse reactions are expected to occur with a low probability.

Information on adverse reactions is available from spontaneous reporting.

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	Hypersensitivity reactions including anaphylaxis (e.g. urticarial rash, swelling of eyelids, cough, nausea, vomiting,)	Not known
Nervous System disorders	Vasovagal reaction (e.g. seizure, dyspnoea, flushing, headache, facial oedema, pain, abnormal sensation, dizziness, hypotension, tachycardia,).	Not known
General disorders and administration site conditions	Injection site reactions (e.g. skin rash, pain, swelling)	Not known

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:
HPRA Pharmacovigilance
Website: www.hpra.ie.

4.9 Overdose

The risk of an excessive technetium (^{99m}Tc)-mertiatide dose is largely theoretical and most likely to be due to excessive radiation exposure.
In the event of an administration of a radiation overdose with TechneScan MAG3, the absorbed dose to the patient should be reduced where possible by increasing 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 renal system, technetium (^{99m}Tc) compounds. ATC code: V09CA03.

Pharmacodynamic effects
At the chemical concentration used for diagnosis examinations, technetium (^{99m}Tc) mertiatide does not appear to have any pharmacodynamic activity.

Measuring the activity over the kidneys allows renal blood flow, intrarenal tubular transit times and excretion via the outflow tracts to be recorded separately for both kidneys.

5.2 Pharmacokinetic properties

Distribution
(^{99m}Tc)-mertiatide has a relatively high binding to plasma proteins, but this binding is reversible and (^{99m}Tc)-mertiatide is rapidly excreted from the kidneys.

Elimination
After intravenous injection (^{99m}Tc)-mertiatide is rapidly cleared from the blood by the kidneys predominantly via tubular secretion. Glomerular filtration accounts for 11% of total clearance. In normal renal function, 70% of the administered dose has been excreted in the urine after 30 minutes and more than 95% after 3 hours. These latter percentages are dependent on the pathology of the kidneys and the urogenital system.

Half-life
Technetium-99m (^{99m}Tc) has a physical half-life of 6.01 hours.

5.3 Preclinical safety data

Toxicology studies with mice have demonstrated that a single intravenous injection of 1.43 and 14.3 mg/kg, no deaths were observed. This corresponds to about 1000 times the maximum human dose. Toxicity with repeated administration of 0.43 mg/kg/day over 14 days in rats was not observed. This medicinal product is not intended for regular or continuous administration.
No mutagenicity effects have been observed.
Long-term carcinogenicity studies have not been carried out.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium tartrate dihydrate
Stannous chloride dihydrate
Hydrochloric acid (for pH adjustment)

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 in a refrigerator (2-8 °C).
For storage conditions after reconstitution 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 Type 1 Ph.Eur glass vial closed with a rubber stopper and sealed with an aluminium crimp cap.
Pack size: 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. 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 vial are intended only for use in the preparation of technetium (^{99m}Tc) mertiatide and are not to be administered directly to the patient without first undergoing the preparative procedure.

For instructions on preparation of the medicinal product, 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 reconstitution 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

PA0690/018/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 2nd March 1992
Date of last renewal: 2nd March 2007

10. DATE OF REVISION OF THE TEXT

May 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 6.01 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 128 and are calculated according to the following assumptions:

- In the normal case, following intravenous administration of MAG3, the substance is rapidly distributed in the extracellular fluid and excreted entirely by the renal system according to the kidney–bladder model. Total body retention is described by tri-exponential functions (Stabin et al., 1992). The renal transit time is assumed to be 4 min, as for Hippuran.
- When renal function is bilaterally impaired, it is assumed that the clearance rate of the substance is one-tenth of that for the normal case, that the renal transit time is increased to 20 min, and that a fraction of 0.04 is taken up in the liver.
- As an example of acute unilateral renal blockage, it is assumed that a fraction of 0.5 of the administered radiopharmaceuticals is taken up by one kidney, slowly released to the blood with a half-time of 5 days, and subsequently excreted by the other kidney, which is assumed to function normally.

Absorbed doses: ^{99m}Tc MAG3 (Normal renal function)

	Absorbed dose per unit activity administered (mGy/MBq)				
Organ	Adult	15 years	10 years	5 years	1 year
Adrenals	3.9E-04	5.1E-04	8.2E-04	1.2E-03	2.5E-03
Bone surfaces	1.3E-03	1.6E-03	2.1E-03	2.4E-03	4.3E-03
Brain	1.0E-04	1.3E-04	2.2E-04	3.5E-04	6.1E-04
Breast	1.0E-04	1.4E-04	2.4E-04	3.9E-04	8.2E-04
Gall bladder wall	5.7E-04	8.7E-04	2.0E-03	1.7E-03	2.8E-03
GI-tract					
Stomach wall	3.9E-04	4.9E-04	9.7E-04	1.3E-03	2.5E-03
SI wall	2.3E-03	3.0E-03	4.2E-03	4.6E-03	7.8E-03
Colon wall	3.4E-03	4.3E-03	5.9E-03	6.0E-03	9.8E-03
(ULI wall	1.7E-03	2.3E-03	3.4E-03	4.0E-03	6.7E-03)
(LLI wall	5.7E-03	7.0E-03	9.2E-03	8.7E-03	1.4E-02)
Heart wall	1.8E-04	2.4E-04	3.7E-04	5.7E-04	1.2E-03
Kidneys	3.4E-03	4.2E-03	5.9E-03	8.4E-03	1.5E-02
Liver	3.1E-04	4.3E-04	7.5E-04	1.1E-03	2.1E-03
Lungs	1.5E-04	2.1E-04	3.3E-04	5.0E-04	1.0E-03
Muscles	1.4E-03	1.7E-03	2.2E-03	2.4E-03	4.1E-03
Oesophagus	1.3E-04	1.8E-04	2.8E-04	4.4E-04	8.2E-04
Ovaries	5.4E-03	6.9E-03	8.7E-03	8.7E-03	1.4E-02
Pancreas	4.0E-04	5.0E-04	9.3E-04	1.3E-03	2.5E-03
Red marrow	9.3E-04	1.2E-03	1.6E-03	1.5E-03	2.1E-03
Skin	4.6E-04	5.7E-04	8.3E-04	9.7E-04	1.8E-03
Spleen	3.6E-04	4.9E-04	7.9E-04	1.2E-03	2.3E-03
Testes	3.7E-03	5.3E-03	8.1E-03	8.7E-03	1.6E-02
Thymus	1.3E-04	1.8E-04	2.8E-04	4.4E-04	8.2E-04
Thyroid	1.3E-04	1.6E-04	2.7E-04	4.4E-04	8.2E-04
Urinary bladder wall	1.1E-01	1.4E-01	1.7E-01	1.8E-01	3.2E-01
Uterus	1.2E-02	1.4E-02	1.9E-02	1.9E-02	3.1E-02
Remaining Organs	1.3E-03	1.6E-03	2.1E-03	2.2E-03	3.6E-03
Effective dose (mSv/MBq)	**7.0E-03**	**9.0E-03**	**1.2E-02**	**1.2E-02**	**2.2E-02**
The urinary bladder wall contributes up to 80% of the effective dose.					
Effective dose if urinary bladder is emptied 1 or 0,5 hours after administration:					
1 hour	2.5E-03	3.1E-03	4.5E-03	6.4E-03	6.4E-03
30 min	1.7E-03	2.1E-03	2.9E-03	3.9E-03	6.8E-03

The effective dose resulting from the administration of an activity of 200 MBq for an adult weighing 70 kg is about 1.4 mSv.
For an administered activity of 200 MBq the typical radiation dose to the target organ (kidneys) is 0.68 mGy and the typical radiation dose to the critical organ (urinary bladder wall) is 22 mGy.

Absorbed doses: ^{99m}Tc MAG3 (Abnormal renal function)

	Absorbed dose per unit activity administered (mGy/MBq)				
Organ	Adult	15 years	10 years	5 years	1 year
Adrenals	1.6E-03	2.1E-03	3.2E-03	4.8E-03	8.6E-03
Bone surfaces	2.2E-03	2.7E-03	3.8E-03	5.0E-03	9.1E-03
Brain	6.1E-04	7.7E-04	1.3E-03	2.0E-03	3.6E-03
Breast	5.4E-04	7.0E-04	1.1E-03	1.7E-03	3.2E-03
Gall bladder wall	1.6E-03	2.2E-03	3.8E-03	4.6E-03	6.4E-03
GI-tract					
Stomach wall	1.2E-03	1.5E-03	2.6E-03	3.5E-03	6.1E-03
SI wall	2.7E-03	3.5E-03	5.0E-03	6.0E-03	1.0E-02
Colon wall	3.5E-03	4.4E-03	6.1E-03	6.9E-03	1.1E-02
(ULI wall	2.2E-03	3.0E-03	4.3E-03	5.6E-03	9.3E-03)
(LLI wall	5.1E-03	6.3E-03	8.5E-03	8.6E-03	1.4E-02)
Heart wall	9.1E-04	1.2E-03	1.8E-03	2.7E-03	4.8E-03
Kidneys	1.4E-02	1.7E-02	2.4E-02	3.4E-02	5.9E-02
Liver	1.4E-03	1.8E-03	2.7E-03	3.8E-03	6.6E-03
Lungs	7.9E-04	1.1E-03	1.6E-03	2.4E-03	4.5E-03
Muscles	1.7E-03	2.1E-03	2.9E-03	3.6E-03	6.4E-03
Oesophagus	7.4E-04	9.7E-04	1.5E-03	2.3E-03	4.1E-03
Ovaries	4.9E-03	6.3E-03	8.1E-03	8.7E-03	1.4E-02
Pancreas	1.5E-03	1.9E-03	2.9E-03	4.3E-03	7.4E-03
Red marrow	1.5E-03	1.9E-03	2.6E-03	3.1E-03	5.0E-03
Skin	7.8E-04	9.6E-04	1.5E-03	2.0E-03	3.8E-03
Spleen	1.5E-03	1.9E-03	2.9E-03	4.3E-03	7.4E-03
Testes	3.4E-03	4.7E-03	7.1E-03	7.8E-03	1.4E-02
Thymus	7.4E-04	9.7E-04	1.5E-03	2.3E-03	4.1E-03
Thyroid	7.3E-04	9.5E-04	1.5E-03	2.4E-03	4.4E-03
Urinary bladder wall	8.3E-02	1.1E-01	1.3E-01	1.3E-01	2.3E-01
Uterus	1.0E-02	1.2E-02	1.6E-02	1.6E-02	2.7E-02
Remaining Organs	1.7E-03	2.1E-03	2.8E-03	3.4E-03	6.0E-03
Effective dose (mSv/MBq)	**6.1E-03**	**7.8E-03**	**1.0E-02**	**1.1E-02**	**1.9E-02**

The effective dose resulting from the administration of a maximum recommended activity of 200 MBq for an adult weighing 70 kg is about 1.22 mSv.
For an administered activity of 200 MBq the typical radiation dose to the target organ (kidney) is 2.8 mGy and the typical radiation dose to the critical organ (urinary bladder wall) is 16.6 mGy.

Absorbed doses: ^{99m}Tc MAG3 (Acute unilateral renal blockage)

	Absorbed dose per unit activity administered (mGy/MBq)				
Organ	Adult	15 years	10 years	5 years	1 year
Adrenals	1.1E-02	1.4E-02	2.2E-02	3.2E-02	5.5E-02
Bone surfaces	3.1E 03	4.0E-03	5.8E-03	8.4E-03	1.7E-02
Brain	1.1E-04	1.4E-04	2.3E-04	3.9E-04	7.5E-04
Breast	3.8E-04	5.1E-04	1.0E-03	1.6E-03	3.0E-03
Gall bladder wall	6.2E-03	7.3E-03	1.0E-02	1.6E-02	2.3E-02
GI-tract					
Stomach wall	3.9E-03	4.4E-03	7.0E-03	9.3E-03	1.2E-02
SI wall	4.3E-03	5.5E-03	8.5E-03	1.2E-02	1.9E-02
Colon wall	3.9E-03	5.0E-03	7.2E-03	9.2E-03	1.5E-03
(ULI wall	4.0E-03	5.1E-03	7.6E-03	1.0E-02	1.6E-02)
(LLI wall	3.8E-03	4.8E-03	6.7E-03	8.2E-03	1.3E-02)
Heart wall	1.3E-03	1.6E-03	2.7E-03	4.0E-03	6.1E-03
Kidneys	2.0E-01	2.4E-01	3.3E-01	4.7E-01	8.1E-01
Liver	4.4E-03	5.4E-03	8.1E-03	1.1E-02	1.7E-02
Lungs	1.1E-03	1.6E-03	2.5E-03	3.9E-03	7.2E-03
Muscles	2.2E-03	2.7E-03	3.7E-03	5.1E-03	8.9E-03
Oesophagus	3.8E-04	5.4E-04	8.5E-04	1.5E-03	2.3E-03
Ovaries	3.8E-03	5.1E-03	7.1E-03	9.2E-03	1.5E-02
Pancreas	7.4E-03	9.0E-03	1.3E-02	1.8E-02	2.9E-02
Red marrow	3.0E-03	3.6E-03	5.0E-03	6.0E-03	8.3E-03
Skin	8.2E-04	1.0E-03	1.5E-03	2.2E-03	4.2E-03
Spleen	9.8E-03	1.2E-02	1.8E-02	2.6E-02	4.0E-02
Testes	2.0E-03	2.9E-03	4.5E-03	5.0E-03	9.8E-03
Thymus	3.8E-04	5.4E-04	8.5E-04	1.5E-03	2.3E-03
Thyroid	1.7E-04	2.3E-04	4.5E-04	9.2E-04	1.6E-03
Urinary bladder wall	5.6E-02	7.1E-02	9.1E-02	9.3E-02	1.7E-01
Uterus	7.2E-03	8.7E-03	1.2E-02	1.3E-02	2.2E-02
Remaining Organs	2.1E-03	2.6E-03	3.6E-03	4.7E-03	8.0E-03
Effective dose (mSv/MBq)	**1.0E-02**	**1.2E-02**	**1.7E-02**	**2.2E-02**	**3.8E-02**

The effective dose resulting from the administration of a maximum recommended activity of 200 MBq for an adult weighing 70 kg is about 2.0 mSv.
For an administered activity of 200 MBq the typical radiation dose to the target organ (kidney) is 40 mGy and the typical radiation dose to the critical organ (urinary bladder wall) is 11.2 mGy.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Withdrawals should be performed under aseptic conditions. The vials must never be opened before 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 authorized automated application system.

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

The contents of the vial must be labelled with sodium pertechnetate (^{99m}Tc) solution. After reconstitution, the diagnostic agent technetium (^{99m}Tc) mertiatide is obtained upon heating.
The formation of labelled impurities is minimal, when using an eluate with the smallest possible volume. Therefore, labelling should be done using an eluate with the highest possible radioactive concentration. Only eluates obtained from a (^{99m}Tc)-generator, which has been eluted within the preceding 24 hours should be used. Moreover, only eluates obtained from a (^{99m}Tc)-generator, which has been in use for less than one week, have to be used. Dilution of the preparation should be done with sodium chloride 9 mg/mLsolution for

injection. After reconstitution and labelling the solution may be used for one or more administrations.

Method of preparation
Elute a (^{99m}Tc) generator in a 5 mL volume, according to the fractionated elution technique and follow the directions for use for the generator. Use maximum 3 mL eluate. The desired amount of (^{99m}Tc), with a maximum of 2960 MBq must be diluted to a volume of 10 mL with a sodium chloride 9 mg/mL solution for injection. Add this volume to a vial of TechneScan MAG3.

For this a thin needle must be used (G20 or higher) so that the puncture hole closes again. This prevents the water from entering the vial during the heating and cooling steps that follow.

Heat immediately during 10 minutes in a dry heating device previously heated to 120 °C or boiling water bath. During heating the vial should be standing upright in order to prevent traces of metal coming off the rubber stopper, so influencing the labelling procedure unfavourably.
Cool down the vial to room temperature in cold water. The preparation is ready for administration. If needed, a dilution with sodium chloride 9 mg/mL solution for injection is possible.
This technetium (^{99m}Tc) mertiatide preparation can be used until 8 hours after completion of the heating step.

Properties of the medicinal product after labelling:
Clear to slightly opalescent, colourless, aqueous solution.
pH : 5.0-6.0
Osmolality : slightly hypertonic.

Precaution during the labelling procedure
To indicate that during the heating and the cooling step no contamination of the contents of the vial has occurred, the user is advised to add a suitable dyestuff to the heating bath and to the cooling bath (e.g. methylene blue to make a concentration of 1 % or sodium fluorescein to make a concentration of 0.1 %).
The radiolabelled product vial should be examined (taking appropriate radiological protective measures) prior to use.

Instructions for quality control
The following methods may be used:

1. HPLC method:
The radiochemical purity of the labelled substance is examined by high performance liquid chromatography (HPLC) using a suitable detector of radioactivity, on a 25 cm RP18 column, flow rate 1.0 mL/min. Mobile phase A is a 93:7 mixture of phosphate solution (1.36 g KH_2PO_4, adjusted with 0.1 M NaOH to pH 6) and ethanol. Mobile phase B is a 1: 9 mixture of water and methanol.

Use a gradient elution program with the following parameters:

Time (min):	Flow (mL/min):	% A	% B
10	1	100	0
15	1	0	100

The technetium (^{99m}Tc) mertiatide peak appears at the end of the passage of mobile phase A.
The injection volume is 20 µL and the total count rate per channel must not exceed 30.000.

Requirement:

	T=0	after 8 hours
Technetium (^{99m}Tc) mertiatide	≥ 95.0%	≥ 94.0%
Total front fractions	≤ 3.0%	≤ 3.0%
Methanol fraction	≤ 4.0%	≤ 4.0%

2. Simplified Sep-Pak rapid procedure:
The method may be used as an alternative for the above mentioned method. The purpose of this method is to check the labelling procedure, as performed by the user in the hospital.
The method is based on cartridges, which are widely used as sample pretreatment of aqueous solutions for chromatography.

Material

- 1 mL and 10 mL syringes
- Waters Sep-Pak C18 Plus short cartridge, 360 mg sorbent per cartridge; product number WAT020515
- Ethanol absolute
- 0.001 M Hydrochloric acid (HCl)
- Ethanol/Saline (Ethanol - Sodium chloride solution 9 g/L (ratio 1:1))

Stepwise process

The cartridge (e.g. Sep-Pak C18 Plus short) is washed with 10 mL absolute ethanol, followed by 10 mL 0.001 M HCl. Remaining residues of the solutions are removed by 5 mL of air.
The technetium (^{99m}Tc) mertiatide solution (0.1 mL) is applied on the cartridge. It is important that the column is not dried out during all the different steps. Elute dropwise with 10 mL 0.001 M HCl and collect the eluate. This first eluate contains all hydrophilic impurities.

Next, elute the cartridge dropwise with 10 mL of a solution of ethanol/saline (1:1 v/v). This second eluate contains technetium (^{99m}Tc) mertiatide. The cartridge contains all non-elutable impurities.

Calculation of radiochemical purity/impurities

Use the combined eluted radioactivity plus cartridge as 100 %.

$$\text{Radiochemical purity} = \frac{\text{Activity } 2^{nd} \text{ eluate} * 100\%}{\text{Combined eluted activity } (1^{st} \text{ and } 2^{nd} \text{ eluates}) + \text{cartridge}}$$

$$\text{Radiochemical impurities} = \frac{\text{Activity } (1^{st} \text{ eluate or cartridge}) * 100\%}{\text{Combined eluted activity } (1^{st} \text{ and } 2^{nd} \text{ eluates}) + \text{cartridge}}$$

Requirement

	T = 0	after 8 hours
Technetium (^{99m}Tc) mertiatide (2^{nd} eluate)	≥ 94.0 %	≥ 94.0 %
Hydrophilic impurities (1^{st} eluate)	≤ 3.0 %	≤ 3.0 %
Non-elutable impurities (cartridge)	≤ 4.0 %	≤ 4.0 %