SUMMARY OF PRODUCT CHARACTERISTICS

PRODUCT SUMMARY

1 TRADE NAME OF THE MEDICINAL PRODUCT

Trade name: TechneScan® DTPA
(Mallinckrodt Medical catalogue number: DRN 4362).
Non-proprietary name: Technetium (^{99m}Tc) Pentetate Solution.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One vial contains
Pentetic acid 20.8 mg

3 PHARMACEUTICAL FORM

Powder for solution for injection.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

a After reconstitution with sodium pertechnetate (^{99m}Tc) solution the agent may be used for:
- Dynamic renal scintigraphy for perfusion, function and urinary tract studies
- Measurement of glomerular filtration rate
- Cerebral angiography and brain scanning; as an alternative method when computed tomography and/or magnetic resonance imaging are not available

b After inhalation of the nebulized technetium (^{99m}Tc) labelled substance:
- Lung ventilation imaging

c After oral administration of the technetium (^{99m}Tc) labelled substance:
- Studies of gastro-oesophageal reflux and gastric emptying

4.2 Posology and Method of Administration

In adults the following administered doses are recommended (other doses may be justifiable):

For intravenous use:
- Measurement of glomerular filtration rate from plasma: 1.8-3.7 MBq.
- Measurement of glomerular filtration rate using gamma camera combined with sequential dynamic renal scanning: 37-370 Mbq. Sequential scanning should begin immediately after injection. Optimal static imaging time is 1 hour post injection.
- Brain scanning: 185-740 Mbq. For cerebral examinations static images are obtained 1 hour and, if necessary, several hours after injection. Sequential dynamic scanning should begin immediately after injection.

For inhalation:
- Lung ventilation imaging: 500-1000 MBq in nebuliser; 50-100 MBq in lung.

For oral use:

- Study of gastro-oesophageal reflux and gastric emptying: 10-20 MBq. Dynamic recording should be performed during the first minutes (up to 120 minutes for gastroduodenal transit).

Paediatric dose:

- The dose for children is adjusted according to body weight:

$$\text{Paediatric dosage (MBq)} = \frac{\text{Adult dosage (MBq) x Child weight (kg)}}{70}$$

In some circumstances, dose adjustment according to surface area may be appropriate:

$$\text{Paediatric dosage (MBq)} = \frac{\text{Adult dosage (MBq) x Child body surface } (m^2)}{1.73}$$

In very young children (up to 1 year) a minimum dose of 20 MBq is necessary in order to obtain images of sufficient quality, when technetium (^{99m}Tc) pentetate (DTPA) is used for kidney studies.

4.3 Contra-indications

TechneScan® DTPA should not be used in patients with a known allergy to sodium pentetate or any of the excipients.

4.4 Special Warnings and Special Precautions for Use

4.4.1 Special warnings

TechneScan® DTPA must not be administered into the subarachnoidal space as it should never be used for scintigraphy of the cerebrospinal flow. This radiopharmaceutical may 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 organisations. 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, complying with the requirements of Good Manufacturing Practice for pharmaceuticals.

4.4.2 Special precautions for use

In case of reduced renal function the radiation exposure can be increased; this should be considered in the assessment of the activity to be administered. To reduce the radiation dose to the bladder, good hydration and frequent voiding of urine is recommended.

4.5 Interactions with other Medicinal Product and other forms of Interaction

Many drugs may affect the function of tested organ and modify the uptake of technetium (^{99m}Tc) pentetate (DTPA) i.e.:

Diagnostic use of captopril

Dynamic renal scanning performed under control conditions and again one hour after

oral administration of captopril (25-50 mg) may reveal haemodynamic changes in a kidney affected by renal artery stenosis. The blood pressure should be carefully monitored as patients with vascular disease are at risk of significant hypotension and renal impairment.

Diagnostic use of frusemide
The administration of intravenous frusemide during dynamic renal scanning increase elimination of technetium (^{99m}Tc) pentetate (DTPA) which may help to distinguish whether true obstruction exists in a dilated renal tract.

Cerebral angiography
Psychotropic drugs increase blood flow in the territory of the external carotid artery. This may lead to the rapid uptake of tracer in the nasopharyngeal area during the arterial and capillary phases (hot nose phenomenon).

4.6 Pregnancy and Lactation

When it is necessary to administer radioactive medicinal products to women of childbearing potential, information should always be sought about pregnancy. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. Where uncertainty exists it is important that radiation exposure should be the minimal consistent with achieving the desired clinical information. Alternative techniques which do not involve ionising radiation should be considered. Radionuclide procedures carried out on pregnant women also involve radiation doses to the foetus. Only imperative investigations should be carried out during pregnancy, when the likely benefit exceeds the risk incurred by mother and foetus.

Before administering a radioactive medicinal product to a mother who is breast-feeding consideration should be given as to whether the investigation could be reasonably delayed until the mother has ceased breast-feeding and as to whether the most appropriate choice of radiopharmaceutical has been made, bearing in mind the secretion of activity in breast milk. If the administration is considered necessary the breast-feeding should be interrupted for 12 hours and the expressed feeds discarded. Breast-feeding can be restarted when the level in the milk will not result in a radiation dose to the child greater than 1 mSv.

4.7 Effects on Ability to Drive and Use Machines

Effects on ability to drive or use machines have not been described and are not expected.

4.8 Undesirable Effects

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 or therapeutic result. Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. For diagnostic nuclear medicine investigations the current evidence suggests that these adverse effects will occur with low frequency because of the low radiation doses incurred. For most diagnostic investigations using a nuclear medicine procedure the radiation dose delivered (EDE) is less than 20 mSv. Higher doses may be justified in

some clinical circumstances. In isolated cases, allergic or allergoid reactions and vasovagal reactions have been reported. Intolerance reactions may consist of skin reactions, nausea or vomiting, oedema, hypotension, or further allergy-type symptoms.
This product contains no excipients that have a recognised action or effect, or knowledge of which is important for safe and effective use of the product.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard

4.9 Overdose

In the event of the administration of a radiation overdose with technetium (^{99m}Tc) pentetate (DTPA) 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

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

5.2 Pharmacokinetic Properties

Following intravenous injection, technetium (^{99m}Tc) pentetate (DTPA) rapidly distributes throughout the extracellular fluid. Less than 5% of the injected dose is bound to the plasma proteins. There is also a negligible binding of technetium (^{99m}Tc) pentetate (DTPA) to red blood cells. Technetium (^{99m}Tc) pentetate (DTPA) does not cross the normal blood-brain barrier but diffuse weakly in breast milk. Plasma clearance is multi-exponential with an extremely fast component. The complex remains stable in vivo, more than 98% of urine radioactivity is in the form of a chelate. Approximately 90% of the injected dose is eliminated in the urine within the first 24 hours mainly by glomerular filtration. No retention of the compound has been demonstrated in the kidneys. Plasma clearance may be delayed in patients with renal disease. In subjects exhibiting oedema or ascites, distribution of the radionuclide in the extracellular space may be modified.

In lung ventilation studies, after inhalation, technetium (^{99m}Tc) pentetate (DTPA) diffuses rapidly from the pulmonary alveoles towards the vascular space where it is diluted. The half-life of technetium (^{99m}Tc) pentetate (DTPA) in the lungs is slightly less than 1 hour. Many factors are likely to modify the permeability of the pulmonary epithelium like cigarette smoking.

Following oral administration, technetium (^{99m}Tc) pentetate (DTPA) does not pass through the digestive barrier.

5.3 Preclinical Safety Data

This agent is not intended for regular or continuous administration. Repeated intravenous administration of $CaNa_3DTPA$ to rabbits and dogs for 14 days of doses that were 100 and 1000 times (respectively) the normal dose for human, produced no evidence of toxicity. The minimum dose of CaDTPA causing abortion and fetal death in mice was approximately 3600 times the dose of $CaNa_3DTPA$ that is proposed for diagnosis in women. Mutagenicity studies and long-term carcinogenicity studies have not been carried out.

5.4 Radiation dosimetry

(^{99m}Tc) technetium decays with the emission of gamma radiation with a mean energy of 140 keV and a half-life of 6 hours to (^{99}Tc) technetium, which can be regarded as quasi stable. For this product the effective dose equivalent resulting from:

- An intravenous administered activity of 740 MBq to a patient with normal renal function is 4.7 mSv (per 70 kg individual).
- An inhalation (nebuliser) of 100 MBq is 0.7-7 mSv (per 70 kg individual).
- An oral administration of 20 MBq is 0.5 mSv (per 70 kg individual). According to ICRP (International Commission of Radiological Protection) the radiation doses absorbed by the patients are the following:

Normal renal function
Absorbed dose per unit activity administered (mGy/MBq)

Organ	**Adult**	**15 year**	**10 year**	**5 year**	**1 year**
Adrenals	1.4E-03	1.8E-03	2.7E-03	4.2E-03	7.8E-03
Bladder wall	6.5E-02	8.1E-02	1.2E-01	1.7E-01	3.2E-01
Bone surfaces	1.7E-03	2.1E-03	3.1E-03	4.6E-03	8.5E-03
Breast	9.4E-04	9.4E-04	1.4E-03	2.2E-03	4.3E-03
GI-tract					
Stomach wall	1.3E-03	1.7E-03	2.8E-03	4.1E-03	7.5E-03
Small intest	2.6E-03	3.1E-03	5.0E-03	7.5E-03	1.3E-02
ULI wall	2.2E-03	2.9E-03	4.4E-03	7.1E-03	1.2E-02
LLI wall	4.2E-03	5.4E-03	8.2E-03	1.1E-02	1.9E-02
Kidneys	4.4E-03	5.4E-03	7.7E-03	1.1E-02	2.0E-02
Liver	1.3E-03	1.6E-03	2.5E-03	3.9E-03	7.0E-03
Lungs	1.0E-03	1.3E-03	2.0E-03	3.1E-03	5.7E-03
Ovaries	4.3E-03	5.3E-03	7.8E-03	1.1E-02	1.8E-02
Pancreas	1.5E-03	1.8E-03	2.9E-03	4.5E-03	8.1E-03
Red marrow	2.5E-03	3.0E-03	4.2E-03	5.7E-03	8.7E-03
Spleen	1.4E-03	1.7E-03	2.5E-03	4.0E-03	7.2E-03
Testes	2.8E-03	4.1E-03	6.8E-03	1.0E-02	1.9E-02
Thyroid	7.9E-04	1.3E-03	2.1E-03	3.4E-03	6.1E-03
Uterus	7.9E-03	9.6E-03	1.5E-02	2.1E-02	3.5E-02
Other tissue	1.7E-03	2.0E-03	3.1E-03	4.6E-03	8.3E-03
Effective dose equivalent (mSv/MBq)					
	6.3E-03	**7.8E-03**	**1.1E-02**	**1.7E-02**	**3.0E-02**

Abnormal renal function
Absorbed dose per unit activity administered (mGy/MBq)

Organ	**Adult**	**15 year**	**10 year**	**5 year**	**1 year**
Adrenals	4.1E-03	5.1E-03	7.8E-03	1.2E-02	2.1E-02
Bladder wall	2.2E-02	2.7E-02	4.0E-02	5.8E-02	1.1E-01
Bone surfaces	4.4E-03	5.3E-03	7.9E-03	1.2E-02	2.1E-02
Breast	3.0E-03	3.0E-03	4.3E-03	6.9E-03	1.3E-02
GI-tract					
Stomach wall	3.8E-03	5.0E-03	7.9E-03	1.1E-02	2.0E-02
Small intest	4.7E-03	5.6E-03	8.6E-03	1.3E-02	2.3E-02
ULI wall	4.4E-03	5.6E-03	8.1E-03	1.3E-02	2.2E-02
LLI wall	4.7E-03	6.2E-03	9.6E-03	1.4E-02	2.5E-02
Kidneys	7.9E-03	9.6E-03	1.4E-02	2.0E-02	3.4E-02
Liver	3.8E-03	4.6E-03	7.1E-03	1.1E-02	1.9E-02
Lungs	3.3E-03	4.2E-03	6.2E-03	9.5E-03	1.7E-02
Ovaries	4.9E-03	6.3E-03	9.4E-03	1.4E-02	2.4E-02
Pancreas	4.3E-03	5.4E-03	8.1E-03	1.2E-02	2.2E-02
Red marrow	5.2E-03	6.3E-03	9.0E-03	1.3E-02	2.2E-02
Spleen	4.0E-03	4.8E-03	7.2E-03	1.1E-02	2.0E-02
Testes	3.3E-03	4.5E-03	6.9E-03	1.1E-02	2.0E-02
Thyroid	2.5E-03	4.3E-03	6.8E-03	1.1E-02	1.9E-02
Uterus	6.3E-03	7.5E-03	1.1E-02	1.7E-02	2.9E-02
Other tissue	3.3E-03	4.0E-03	6.1E-03	9.4E-03	1.7E-02
Effective dose equivalent (mSv/MBq)					
	5.3E-03	**6.6E-03**	**9.7E-03**	**1.5E-02**	**2.6E-02**

The radiation doses given to man on administration by aerosol of ^{99m}Tc DTPA are the following:

Absorbed dose per unit activity administered (mGy/MBq)

Organ	**Adult**	**15 year**	**10 year**	**5 year**	**1 year**
Adrenals	2.1E-03	2.9E-03	4.4E-03	6.7E-03	1.2E-02
Bladder wall	4.7E-02	5.8E-02	8.4E-02	1.2E-01	2.3E-01
Bone surfaces	1.9E-03	2.4E-03	3.5E-03	5.3E-03	9.8E-03
Breast	1.9E-03	1.9E-03	3.3E-03	4.8E-03	7.8E-03
GI-tract					
Stomach wall	1.7E-03	2.2E-03	3.5E-03	5.1E-03	8.9E-03
Small intest	2.1E-03	2.6E-03	4.1E-03	6.3E-03	1.1E-02
ULI wall	1.9E-03	2.4E-03	3.8E-03	6.1E-03	1.0E-02
LLI wall	3.2E-03	4.2E-03	6.3E-03	8.8E-03	1.5E-02
Kidneys	4.1E-03	5.1E-03	7.2E-03	1.1E-03	1.9E-02
Liver	1.9E-03	2.5E-03	3.7E-03	5.5E-03	9.7E-03
Lungs	1.7E-02	2.6E-02	3.6E-02	5.4E-02	1.0E-01
Ovaries	3.3E-03	4.1E-03	6.1E-03	8.9E-03	1.5E-02
Pancreas	2.1E-03	2.6E-03	4.0E-03	6.1E-03	1.1E-02
Red marrow	2.7E-03	3.4E-03	4.7E-03	6.2E-03	9.6E-03
Spleen	1.9E-03	2.4E-03	3.6E-03	5.6E-03	9.9E-03
Testes	2.1E-03	3.1E-03	5.2E-03	7.9E-03	1.5E-02
Thyroid	9.9E-04	1.7E-03	2.7E-03	4.4E-03	7.8E-03
Uterus	5.9E-03	7.2E-03	1.1E-02	1.6E-02	2.7E-02
Other tissue	1.8E-03	2.2E-03	3.2E-03	4.9E-03	8.6E-03
Effective dose equivalent (mSv/MBq)					
	7.0E-03	**9.1E-03**	**1.3E-02**	**2.0E-02**	**3.6E-02**

The radiation doses given to man on administration per os of ^{99m}Tc DTPA are the following (D.J. Gambini, R. Granier: Manuel pratique de Médecine Nucléaire)

Organ	**Absorbed dose per unit activity administered (mGy/MBq)**
Stomach	8.6E-02
Small intest	7.0E-02
Red marrow	1.2E-03
Ovaries	3.5E-03
Testes	1.7E-03
Effective dose equivalent (mSv/MBq)	**2.5E-02**

6 PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Gentisic acid
Stannous chloride dihydrate
Calcium chloride dihydrate
Sodium hydroxide
Hydrochloric acid

Properties of the labelled compound:
Clear to slightly opalescent, colourless aqueous solution.

pH : 4.0-5.0
Labelling yield : ≥ 95%

6.2 Incompatibilities

None known.

6.3 Shelf Life

TechneScan® DTPA expires 12 months after the day of production. The expiry date is stated on the label of each vial and on the carton box. The labelled product should be injected within 8 hours after reconstitution.

6.4 Special Precautions for Storage

TechneScan® DTPA is to be stored in the dark. Do not store above 25ºC.
Chemical and physical in-use stability has been demonstrated for 8 hours/day at 25 ºC. From a microbiological point of view, the product should be used immediately. If not used immediately, in use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours below 25 ºC, unless reconstitution / dilution (etc) has taken place in controlled and validated aseptic conditions.

6.5 Nature and Contents of Container

Carton box containing 5 glass vials of 10 ml. The vials are closed with a bromobutyl rubber lyophilisation stopper sealed with an aluminium cap.

6.6 Instruction for Use, Handling and Disposal

6.6.1 Instructions for labelling

Use aseptique technique throughout all procedures. Add the required amount of Sodium Pertechnetate(^{99m}Tc) Injection (Fission or Non-Fission), maximum 11.1 GBq (300 mCi), in a volume of 2-10 ml to a vial of TechneScan® DTPA and mix until the contents have dissolved. After 15-30 minutes incubation at 15-25ºC the preparation is ready for injection.

6.6.2 Instructions for quality control

Examine by TLC on silica gel coated glass-fibre sheets.

a Develop 5 to 10 µl in 0.9% m/V solution of sodium chloride R; technetium pentetate complex and pertechnetate ion migrate near the solvent front, impurities in colloidal form remain at the start.

b Develop 5 to 10 µl in methyl ethyl ketone R; pertechnetate ion migrates near the solvent front, technetium pentetate complex and impurities in colloidal form remain at the start. For particulars consult the European Pharmacopoeia (Monograph 642). The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spills of urine, vomiting, etc. National regulations for radioactive materials must be applied in the radiation protection precautions and waste disposal.

ADMINISTRATIVE DATA

7 MARKETING AUTHORISATION HOLDER

Mallinckrodt Medical B.V.
Westerduinweg 3
1755 LE Petten
Netherlands

8 MARKETING AUTHORISATION NUMBER

PL 12288/0011

9 DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

21 March 2001

10 DATE OF (PARTIAL) REVISION OF THE TEXT

March 2015