SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Technescan DTPA kit for radiopharmaceutical preparation 20.8 mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Pentetic acid 20.8 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
White lyophilised powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

a) After radiolabelling with sodium pertechnetate (^{99m}Tc) solution, the obtained solution may be used for:
- dynamic renal scintigraphy for examination of the blood flow, function and urinary tract.
- determination of the glomerular filtration rate.
- cerebral angiography and brain scintigraphy. As an alternative method when computed tomography and/or nuclear magnetic resonance imaging are not available.

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

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

4.2 Posology and method of administration

Posology
Adults
In adults the doses listed below are recommended for administration (other doses may be justifiable):

For intravenous use
- determination of the glomerular filtration rate based on plasma: 1.8-3.7 MBq.
- determination of the glomerular filtration rate using a gamma camera in combination with sequential dynamic renal scans: 37-370 MBq. brain scintigraphy: 185-740 MBq.

For inhalation
- Lung ventilation imaging: 500-1000 MBq in nebulizer. 50-100 MBq in the lung.

For oral application
- assessment of gastro-oesophageal reflux and gastric emptying: 10-20 MBq.

Renal impairment
In case of renal impairment, the radiation exposure may be increased. This must be taken into account when determining the amount of activity to be administered.

Elderly
There is no special dosing regimen for elderly patients.

Paediatric population
The use in children and adolescents must be considered carefully based on the clinical need and an assessment of the benefit/risk balance in this patient group.

Posology for children. The dose for children is determined on the basis of their body weight:

$$\text{paediatric dose (MBq)} = \frac{\text{dose for adults (MBq) x child's weight (kg)}}{70}$$

Under certain circumstances, dose adjustment on the basis of the body surface area may be indicated.

$$\text{paediatric dose (MBq)} = \frac{\text{dose for adults (MBq) x child's body surface area } (m^2)}{1.73}$$

In very young children (aged up to one year old), a minimum dose of 20 MBq is required for imaging of sufficient quality, when technetium (^{99m}Tc) pentetate (DTPA) is used for renal assessment.

Method of administration
For multiple doses.

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

For instructions on reconstitution and radiolabelling of the medicinal product, see section 8.

For patient preparation see section 4.4.

Imaging
For intravenous use
- Determination of the glomerular filtration rate using a gamma camera in combination with sequential dynamic renal scans. The sequential scintigraphy must be started immediately after the injection; the most suitable time for static imaging is one hour after injection.
- For a brain assessment, static images are acquired one hour to possibly several hours after injection. Sequential dynamic scintigraphy must be started immediately after the injection.

Oral application
- assessment of gastro-oesophageal reflux and gastric emptying: Dynamic images must be acquired within the first minutes (up to 120 minutes before gastroduodenal passage).

4.3 Contraindications
Hypersensitivity to the active substance, to any of the excipients mentioned in section 6.1 or to any of the components of the radiolabelled product.

4.4 Special warnings and precautions for use

Potential for hypersensitivity or anaphylactic reactions

If any hypersensitivity or anaphylactic reactions occur, administration of the medicinal product must be discontinued immediately and the patient should be started on intravenous treatment, if necessary. Appropriate medicinal products and equipment, such as endotracheal tubes and mechanical ventilation must be available within reach to ensure that emergency care can be given immediately.

Individual risk/benefit analysis

For each individual patient, exposure to ionising radiation must be justified based on the anticipated benefit. The activity administered must be the lowest possible activity that achieves the intended diagnostic result.

Renal impairment

In case of renal impairment, the radiation exposure may be increased. This must be taken into account when determining the amount of activity to be administered.

Paediatric population

For information about the use in the paediatric population, see section 4.2. It is necessary to carefully consider the indication, as the effective dose per MBq is higher than for 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 in order to reduce radiation.

After the procedure

There is no need to limit contact between the patient and children or pregnant women after the patient has left the hospital.

Specific warnings
Technescan DTPA cannot be administered in the subarachnoid space because it should never be used for scintigraphy of the cerebrospinal fluid flow.

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

Precautions with respect to environmental hazards, see section 6.6.

4.5 Interaction with other medicinal products and other forms of interaction

Many medicinal products may affect the function of the examined organ and may change the uptake of technetium (^{99m}Tc) pentetate (DTPA), such as:

Diagnostic use of captopril: Under specific circumstances and when performed again one hour after oral administration of captopril (25-50 mg), dynamic renal scintigraphy may reveal haemodynamic abnormalities in a kidney affected by renal artery stenosis. The blood pressure must be monitored closely, because patients with vascular disease run the risk of developing serious hypotension and renal impairment.

Diagnostic use of furosemide: Administration of intravenous furosemide during dynamic renal scintigraphy increases the elimination of technetium (^{99m}Tc) pentetate (DTPA), which may help determine whether there is an actual obstruction in a dilated renal vessel.

Cerebral angiography: Psychopharmaceuticals increase the blood flow in the area of the external carotid artery. This may result in rapid uptake of the isotope in the nasopharynx during the arterial and capillary phases (hot-nose phenomenon).

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

When administration of radiopharmaceuticals to a woman of childbearing potential is necessary, 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 a potential pregnancy (if the woman has missed a period, if the period is very

irregular, etc.), alternative techniques not using any ionising radiation (if any are available) should be offered to the patient.

Pregnancy
Radionuclide procedures performed on pregnant women also cause radiation doses for the foetus. During pregnancy, only highly urgent examinations should be performed, where the expected benefit strongly outweighs the risk run by mother and foetus.

Breast-feeding
^{99m}Tc is secreted in breast milk. 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 after the mother has ceased breast-feeding and as to whether the most appropriate radiopharmaceutical has been chosen, considering the secretion of radioactivity in breast milk. If the administration is considered necessary, breast-feeding should be interrupted for at least 12 hours and the expressed feeds must be discarded. Normally, the recommendation is to only resume breast-feeding when the level in the milk does not cause a radiation dose of over 1 mSv for the child.

Fertility
No studies have been performed into the effects of Technescan DTPA on fertility.

4.7 Effects on ability to drive and use machines
Technescan DTPA has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects
Anaphylactoid and vasovagal reactions have been reported. Intolerance reactions may consist of skin reactions, like pruritus and urticaria, nausea or vomiting, oedema or dyspnoea (see section 4.4 for further advice concerning allergic reactions).

System organ class	Frequency	Symptoms
Immune system disorders	Not known*	Anaphylactoid reactions (e.g. skin reactions, like pruritus and urticaria, nausea, vomiting, facial flushing, oedema, dyspnoea)
Nervous system disorders	Not known*	Vasovagal reaction (e.g. hypotension)

* The frequency cannot be estimated from the available data.
Adverse reactions from spontaneous reports.

Exposure to ionising radiation is associated with cancer induction and a potential of development of hereditary defects. Because the effective radiation dose is 1.8 mSv when the maximum recommended activity of 370 MBq is administered for determination of the glomerular filtration rate, these adverse reactions are not expected to occur.

4.9 Overdose
In the event of administration of a radiation overdose of technetium (^{99m}Tc) pentetate (DTPA), the dose absorbed by the patient should be reduced where possible by increasing elimination of the radionuclide from the body through forced diuresis and frequent miction.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group:
diagnostic radiopharmaceuticals for the renal system, Technetium (^{99m}Tc) pentetate, ATC code: V09CA01;

diagnostic radiopharmaceuticals for the respiratory system, Technetium (^{99m}Tc) pentetate inhalant, ATC code: V09EA01.

In the chemical concentrations and activities used for diagnostic procedures, technetium (^{99m}Tc) pentetate (DTPA) does not appear to have any pharmacodynamic effect.

5.2 Pharmacokinetic properties

- After intravenous injection, technetium (^{99m}Tc) pentetate (DTPA) is distributed quickly within the extracellular fluid. Less than 5% of the injected dose is bound to the plasma proteins. The binding of technetium (^{99m}Tc) pentetate (DTPA) to erythrocytes is negligible as well. Technetium (^{99m}Tc) pentetate (DTPA) does not pass the normal blood-cerebrospinal fluid barrier but diffuses somewhat into breast milk. The plasma clearance is multi-exponential with a very fast component. The complex remains stable in vivo; more than 98% of the radioactivity in urine comes in the form of a chelate.

  Elimination

  About 90% of the injected dose is excreted in urine during the first 24 hours mainly through glomerular filtration. In the kidneys no retention of the compound has been demonstrated.

  Renal impairment

  The plasma clearance may be delayed in patients with kidney disease. In patients showing oedema and ascites, the distribution of the radionuclide in the extracellular space may be changed.

- During lung ventilation examinations, technetium (^{99m}Tc) pentetate (DTPA) diffuses rapidly from the lung alveoli to the vascular bed, where it is diluted. The half-life of technetium (Tc99m) pentetate (DTPA) in the lungs is just under one hour. There are many factors that are likely to change the permeability of the lung epithelium, such as smoking cigarettes.
- After oral administration, technetium (^{99m}Tc) pentetate (DTPA) does not pass the barrier of the gastrointestinal tract.

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 during 14 days of doses which were (respectively) 100 and 1000 times higher than the normal dose for humans did not result in any signs of toxicity. The minimum dose of CaDTPA causing abortion and foetal death in mice was about 3600 times higher than the dose of $CaNa_3DTPA$ proposed for diagnostics in women. Mutagenicity studies and long-term carcinogenicity studies have not been carried out.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Gentisic acid, stannous (II)chloride dihydrate, calcium chloride dihydrate, hydrochloric acid and 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: 8 hours. After radiolabelling, store below 25°C.
The product does not contain any preservatives. If the product is intended for multiple administrations, each aliquot should be removed under aseptic conditions.

6.4 Special precautions for storage

Store below 25°C. For storage conditions after radiolabelling of the product, see section 6.3. Storage must be in accordance with the national regulations for radioactive substances.

6.5 Nature and contents of container

10 ml glass injection vial (Type I, Ph.Eur.) closed with a bromobutyl rubber stopper, sealed with an aluminium crimp cap. Technescan DTPA is supplied as five vials per 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 the appropriate licences of the competent official authority.

Radiopharmaceuticals should be prepared by the user in a manner which satisfies both radiological safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken.

The contents of the vial are solely intended for the preparation of Technescan DTPA and are not intended to be administered to the patient directly.

For instructions on radiolabelling of the pharmaceutical product before administration, see section 8.

If at any time during the preparation of this product the integrity of the vial is compromised, it should no longer be used.

Administration procedures must be performed in a way that minimizes the risk of contamination of the medicinal product and radiation exposure of the users. Adequate shielding is mandatory.

The contents of the kit for reconstitution are not radioactive. After the addition of sodium pertechnetate (^{99m}Tc) the product must be shielded adequately.

Patients who have been treated with radiopharmaceuticals are a risk factor for other people because of the external radiation exposure or because of contamination through splashes of urine, vomit, etc. Precautions in accordance with national regulations concerning radiation safety must therefore be adhered to.

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

7 DOSIMETRY

(^{99m}Tc) Technetium is produced using a (^{99}Mo/^{99m}Tc) generator and disintegrates with the emission of gamma radiation with an average energy of 140 keV and a half-life of 6.02 hours to (^{99m}Tc) technetium, which can be regarded as quasi-stable, considering its long half-life of 2.23 x 10^5 years. For this product the effective dose / EDE is as follows:

- 3.6 mSv as a result of an activity of 740 MBq administered intravenously to a patient with a

normal kidney function (for a person weighing 70 kg).

- 0.7 mSv as a result of inhalation (nebulizer) of 100 MBq (for a person weighing 70 kg).
- 0.5 mSv as a result of oral administration of 20 MBq (for a person weighing 70 kg).

According to the International Commission of Radiological Protection the radiation doses absorbed by patients are as follows:

Normal kidney function (ICRP 80)

Absorbed dose per unit activity administered (mGy/MBq)

Organ	Adult	15 years	10 years	5 years	1 year
Adrenal glands	1.4E-03	1.8E-03	2.6E-03	3.8E-03	7.0E-03
Bladder	6.2E-02	7.8E-02	9.7E-02	9.5E-02	1.7E-01
Bone surface	2.3E-03	2.8E-03	4.0E-03	5.5E-03	9.9E-03
Brain	8.4E-04	1.0E-03	1.7E-03	2.7E-03	4.8E-03
Breast	7.1E-04	9.0E-04	1.3E-03	2.1E-03	4.0E-03
Gall bladder	1.5E-03	2.0E-03	3.6E-03	4.6E-03	6.0E-03
Gastrointestinal tract:					
Stomach	1.3E-03	1.7E-03	2.8E-03	3.7E-03	6.7E-03
Small intestine	2.5E-03	3.1E-03	4.5E-03	5.7E-03	9.8E-03
Colon	3.0E-03	3.8E-03	5.4E-03	6.4E-03	1.1E-02
(Wall u.p.[1] of colon	2.1E-03	2.7E-03	4.0E-03	5.4E-03	9.0E-03)
(Wall l.p.[2] of colon	4.3E-03	5.3E-03	7.3E-03	7.7E-03	1.3E-02)
Heart	1.1E-03	1.4E-03	2.1E-03	3.2E-03	5.8E-03
Kidneys	3.9E-03	4.7E-03	6.7E-03	9.6E-03	1.7E-02
Liver	1.2E-03	1.5E-03	2.4E-03	3.5E-03	6.3E-03
Lungs	9.9E-04	1.3E-03	1.9E-03	2.9E-03	5.3E-03
Muscles	1.6E-03	2.0E-03	2.8E-03	3.7E-03	6.7E-03
Oesophagus	1.0E-03	1.3E-03	1.9E-03	2.9E-03	5.3E-03
Ovaries	4.2E-03	5.3E-03	6.9E-03	7.8E-03	1.3E-02
Pancreas	1.4E-03	1.8E-03	2.7E-03	4.0E-03	7.2E-03
Red marrow	1.4E-03	1.8E-03	2.6E-03	3.3E-03	5.6E-03
Skin	8.5E-04	1.0E-03	1.6E-03	2.3E-03	4.3E-03
Spleen	1.2E-03	1.6E-03	2.4E-03	3.6E-03	6.6E-03
Testicles	2.9E-03	4.0E-03	6.0E-03	6.9E-03	1.3E-02
Thymus	1.0E-03	1.3E-03	1.9E-03	2.9E-03	5.3E-02
Thyroid	1.0E-03	1.3E-03	2.0E-03	3.2E-03	5.8E-03
Uterus	7.9E-03	9.5E-03	1.3E-02	1.3E-02	2.2E-02
Other organs	1.7E-03	2.0E-03	2.8E-03	3.7E-03	6.4E-03
Effective dose (mSv/MBq)	6.3E-03	7.8E-03	1.1E-02	1.7E-02	3.0E-02

[1] u.p. = upper part
[2] l.p. = lower part

Abnormal kidney function (ICRP 53)

Absorbed dose per unit of administered activity (mGy/MBq)

Organ	Adult	15 years	10 years	5 years	1 year
Adrenal glands	4.1E-03	5.1E-03	7.8E-03	1.2E-02	2.1E-02
Bladder wall	2.1E-02	2.7E-02	4.0E-02	5.8E-02	1.1E-01
Bone surface	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
Gastrointestinal tract:					
Gastric wall	3.8E-03	5.0E-03	7.9E-03	1.1E-02	2.0E-02
Small intestine	4.7E-03	5.6E-03	8.6E-03	1.3E-02	2.3E-02
Wall u.p. of colon	4.4E-03	5.6E-03	8.1E-03	1.3E-02	2.2E-02
Wall l.p. of colon	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
Testicles	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
EDE (mSv/MBq)	5.3E-03	6.6E-03	9.7E-03	1.5E-02	2.6E-02

The radiation doses for humans in case of administration of Tc99m-DTPA via aerosol are as follows (ICRP 53):
Absorbed dose per unit of administered activity (mGy/MBq)

Organ	Adult	15 years	10 years	5 years	1 year
Adrenal glands	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 surface	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
Gastrointestinal tract:					
Gastric wall	1.7E-03	2.2E-03	3.5E-03	5.1E-03	8.9E-03
Small intestine	2.1E-03	2.6E-03	4.1E-03	6.3E-03	1.1E-02
Wall u.p. of colon	1.9E-03	2.4E-03	3.8E-03	6.1E-03	1.0E-02
Wall l.p. of colon	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
Testicles	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
EDE (mSv/MBq)	7.0E-03	9.1E-03	1.3E-02	2.0E-02	3.6E-02

The radiation doses for humans in case of oral administration of ^{99m}Tc -DTPA are as follows: (D.J. Gambini, R. Garnier: Manuel pratique de Médecine Nucléaire).

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

8 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Use the aseptic technique for all procedures. Add the required amount of sodium pertechnetate (^{99m}Tc) injection (fission or non-fission), with a maximum of 11.1 GBq (300 mCi), in a volume of 2-10 ml to a vial of Technescan DTPA and mix until complete dissolution has been obtained. After 15-30 minutes of incubation at 15-25°C the preparation will be ready for injection.

Quality control
Studies by means of thin layer chromatography (TLC) on glass fibre strips coated with silica gel.

a) Develop 5 to 10 µl in a solution of 0.9% sodium chloride (m/V) R; the technetium pentetate complex and the pertechnetate ion migrate to the same level as the liquid front. Contaminations in colloidal form remain at the start.

b) Develop 5 to 10 µl with methyl ketone R; the pertechnetate ion migrates to the same level as the liquid front. Technetium pentetate and contaminations in colloidal form remain at the start.
For details, see the European Pharmacopoeia (Ph.Eur.) (Monograph 642).