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SUMMARY OF PRODUCT CHARACTERISTICS (MIBI)

1. NAME OF THE MEDICINAL PRODUCT

Technetril, kit for radiopharmaceutical preparation (MIBI)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains 1 mg [Tetrakis (2-methoxyisobutylisonitrile) copper (I)] tetrafluoroborate. For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Kit for radiopharmaceutical preparation.
White to slightly yellow 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 reconstitution with sodium technetium (^{99m}Tc) pertechnetate solution for injection, the solution of Technetium (^{99m}Tc) Technetril obtained is indicated:

- Myocardial perfusion scintigraphy
  Detection and localisation of coronary artery disease (angina and myocardial infarction)
- Assessment of global ventricular function
  First-pass technique for determination of ejection fraction and/or ECG-triggered, gated SPECT for evaluation of left ventricular ejection fraction, volumes and regional wall motion.
- Scintimammography for the detection of breast cancer
  Detection of breast cancer when mammography is equivocal, inadequate or indeterminate.
- Localisation of hyperfunctioning parathyroid tissue in patients with recurrent or persistent hyperparathyroidism, and in patients scheduled to undergo surgery of the parathyroid glands.

4.2 Posology and method of administration

For intravenous use.
The suggested activity range for intravenous administration to a patient of average weight (70 kg) is:

<u>Diagnosis of reduced coronary perfusion and myocardial infarction</u>:
400 – 900 MBq

<u>Assessment of global ventricular function:</u>
600 – 800 MBq
Injected as a bolus

For diagnosis of ischaemic heart disease two injections (stress and rest) are required in order to differentiate transiently from persistently reduced myocardial uptake.

The recommended activity range for diagnosis of ischaemic heart disease according to the European procedural guideline is:

– Two-day protocol: 600–900 MBq/study
– One-day protocol: 400–500 MBq
for the first injection, three times more for the second injection.

Not more than a total of 2000 MBq should be administered for a one-day protocol and 1800 MBq for a two-day-protocol. For a one day protocol, the two injections (stress and rest) should be done at least **two hours** apart but may be performed in either order. After the stress injection, exercise should be encouraged for an additional one minute (if possible).

For diagnosis of myocardial infarction one injection at rest may be sufficient.

The injection of activities greater than local DRLs (Diagnostic Reference Levels) should be justified.

For breast imaging: 740 - 925 MBq
Injected as a bolus in the arm opposite to the lesion

For parathyroid imaging: 200 - 750 MBq
Injected as a bolus

The activity used should in every case be as low as reasonably practical.

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 for paediatric patients should be modified according to the recommendations of the Paediatric Task Group of the EANM (1990). This activity can be determined from the recommended activity for adults on the basis of body mass, using the following multiplying coefficient:

3 kg = 0.10	12 kg = 0.32	22 kg = 0.50	32 kg = 0.62	42 kg = 0.78	52-54 kg = 0.90
4 kg = 0.14	14 kg = 0.36	24 kg = 0.53	34 kg = 0.64	44 kg = 0.80	56-58 kg = 0.92
6 kg = 0.19	16 kg = 0.40	26 kg = 0.56	36 kg = 0.66	46 kg = 0.82	60-62 kg = 0.96
8 kg = 0.23	18 kg = 0.44	28 kg = 0.58	38 kg = 0.68	48 kg = 0.85	64-66 kg = 0.98
10 kg = 0.27	20 kg = 0.46	30 kg = 0.60	40 kg = 0.70	50 kg = 0.88	68 kg = 0.99

Cardiac Imaging
If possible, patients should fast for at least four hours prior to the study. It is recommended that patients eat a light fatty meal or drink a glass or two of milk after each injection, prior to imaging. This will promote rapid hepatobiliary clearance of Technetium (^{99m}Tc) Technetril resulting in less liver activity in the image.

Imaging should begin approximately after 60 min after injection to allow for hepatobiliary clearance. Longer delay can be required for resting images and for stress with vasodilatators alone because of the risk of higher subdiaphragmatic ^{99m}Tc activity. There is no evidence for significant changes in myocardial tracer concentration or redistribution, therefore imaging for up to 6 hours post injection is possible. Test may be done in a one day or two days protocol.

Preferably tomographic imaging (SPECT) with or without ECG gating should be performed according to current international guidelines.

Breast imaging
Breast imaging is optimally initiated 5 to 10 minutes post injection with the patient in the prone position with breast freely pendant. A 10 minute lateral image of the breast suspected of containing cancer should be obtained with the camera face as close to the breast as practical.

The patient should then be repositioned so that the contralateral breast is pendant and a lateral image of it should be obtained. An anterior supine image may then be obtained with the patient's arms behind her head.

Parathyroid imaging:
Parathyroid imaging depends on whether subtraction technique or wash-out technique is used. For the subtraction technique either ^{123}I or ^{99m}Tc can be used and should be performed according to literature, guidelines and recommended activities.

If the double phase technique is used, 370 to 740 MBq of Technetium (^{99m}Tc) Technetril are injected and the first neck and thorax image obtained 10 minutes later. After a wash-out period of 1 to 2 hours, neck and thorax imaging is again performed.

The planar images may be complemented by early and delayed SPECT or SPECT/CT.

Safety and efficacy in children and adolescents below the age of 18 have not been fully established. Alternative techniques which do not involve ionising radiation should be especially considered.

In case of kidney failure, exposure to ionising radiation can be increased. This must be taken into account when calculating the activity to be administered.

In general, activity selection for patients with a decreased hepatic function should be cautious, usually starting at the low end of the dosing range.

For the instruction for preparation and control of the radiochemical purity of the radiopharmaceutical, see section 9.

4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings and precautions for use
Pregnancy, see section 4.6
Contents of the vial are intended only for use in the preparation of Technetium (^{99m}Tc) Technetril and are not to be administered directly to the patient without first undergoing the preparative procedure.

Newborns, infants, children and adolescents, see section 4.2

In myocardial scintigraphy investigations under stress conditions, the general contraindications and precautions associated with the induction of ergometric or pharmacological stress should be considered.

Because of potential tissue damage extravasal injection of this radioactive product has to be strictly avoided.
In case of kidney failure, exposure to ionising radiation can be increased. This must be taken into account when calculating the activity to be administered.

In patients with reduced hepatobiliary function, a very careful consideration is required since an increased radiation exposure is possible in these patients.

Breast lesions less than 1 cm in diameter may not all be detected with scintimammography as the sensitivity of Technetium (^{99m}Tc) Technetril for the detection of these lesions is low. A negative examination does not exclude breast cancer especially in such a small lesion.

Proper hydration and frequent urination are necessary to reduce bladder irradiation.

Radiopharmaceutical agents should be used only by qualified personnel with the appropriate government authorisation for use and manipulation of radionuclides. Its receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the local competent official organisation.

For each patient, exposure to ionising radiation must be justified 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.

Radiopharmaceuticals should be prepared by the user in a manner which satisfies both radiation safety and pharmaceutical quality requirements.
This medicinal product contains less than 1 mmol sodium (23 mg) per vial, i.e. essentially 'sodium- free'.
If hypersensitivity or anaphylactoid 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.

4.5 Interaction with other medicinal products and other forms of interaction

No drug interactions have been described to date.
Medicinal products which affect myocardial function and/or blood flow may cause false negative results in the diagnosis of coronary arterial disease. For this reason, concomitant medication should be taken into consideration when interpreting the results of the scintigraphic examination.

4.6 Pregnancy and lactation

Women of childbearing potential

When it is necessary to inject radiopharmaceuticals 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 minimum consistent with achieving the desired clinical information.
Alternative techniques, which do not involve ionising radiation should always be considered.

Pregnancy

Radionuclide procedures carried out on pregnant women also involve radiation dose to the fetus. Only imperative investigations should therefore be carried out during pregnancy, when the likely benefit far exceeds the risk incurred by the mother and fetus. An effective dose to fetus of 1 mSv should not be exceeded, unless clinically justified. However, it should be taken into consideration that any reduction in administered activity must not impact on the likelihood of achieving a diagnostic outcome.

Lactation

Before administering radiopharmaceuticals 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 choice of radiopharmaceuticals has

been made, bearing in mind the secretion of activity in breast milk. If the administration is considered necessary, breast-feeding should be interrupted for 24 hours and the expressed feeds discarded. Close contact with infants should be restricted during this period.

4.7 Effects on ability to drive and use machines

Technetril has no influence on the ability to drive and use machines.

4.8 Undesirable effects

The following table presents how the frequencies are reflected in this section:

Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100)
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000)
Not known (cannot be estimated from the available data)

General disorders and administration site conditions:
Common: Immediately after injection, a metallic or bitter taste, partly in combination with dry mouth and an alteration in the sense of smell may be observed.
Rare: Fever, fatigue, dizziness, transient arthritic-like pain.

Cardiac disorders
Uncommon: Chest pain/angina pectoris, abnormal ECG.
Rare: Arrhythmia.

Gastrointestinal disorders:
Uncommon: Nausea
Rare: Abdominal pain.

Nervous system disorders:
Uncommon: Headache
Rare: Seizures (shortly after administration), syncope.

Immune system disorders:
Rare: Severe hypersensitivity reactions such as dyspnoea, hypotension, bradycardia, asthenia and vomiting (usually within two hours of administration), angioedema.

Skin and subcutaneous tissue disorders:
Rare: Allergic skin and mucosa reactions with exanthema (pruritus, urticaria, oedema), vasodilatation, local reactions at the injection site, hypoaesthesia and paraesthesia, flushing.
Very rare: Other hypersensitivity reactions have been described in predisposed patients.
Not known (cannot be estimated from the available data): Erythema multiforme.

If hypersensitivity reactions occur, the administration of the medicinal product must be discontinued immediately and, if necessary, intravenous treatment initiated. Respective medicinal products and equipment (e.g. endotracheal tube and ventilator) have to be readily available.

Other disorders

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects.

As most diagnostic nuclear medicinal product investigations are done with low radiation doses of less than 20 mSv these adverse events are expected to occur with a low probability. The effective dose calculated with a maximal recommended activity of 2000 MBq (500 at rest and 1500 MBq at stress) for a 1-day-protocol is 16.3 mSv.

4.9 Overdose

In the event of administration of a radiation overdose with Technetium (^{99m}Tc) Technetril the absorbed dose to the patient should be reduced where possible by increasing the elimination of the radionuclide from the body by frequent micturition and defaecation.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: diagnostic radiopharmaceuticals, Technetium (^{99m}Tc). Pharmacodynamic effects are not expected after administration of Technetium (^{99m}Tc) Technetril.

Technetium (^{99m}Tc) Technetril, when administrated in usual activities and by the usual way, has no pharmacodynamic effects detectable clinically.

The tissue uptake of Technetium (^{99m}Tc) Technetril depends primarily on the vascularisation which is generally increased in tumor tissue. Due to its lipophilicity and its positive charge, the Technetium (^{99m}Tc) Technetril complex crosses the cell membrane and concentrates in the most negatively charged compartment of the cell, the mitochondria.

Cardiac indication

Technetium (^{99m}Tc) Technetril binds to the mitochondrial membrane and an intact mitochondrial membrane potential is important for intracellular binding.

The uptake of Technetium (^{99m}Tc) Technetril in the myocardium is proportional to blood flow in the physiologic flow range. The rate of passive uptake is determined by the membrane permeability of the drug and the surface area of the vascular beds to which it is exposed. Since the radiotracer enters the cell via diffusion, it will underestimate blood flow at high flow rates (>2.0 ml/g/min).

When coronary flow varied from 0.52 to 3.19 ml/g/min, myocardial extraction for Technetium (^{99m}Tc) Technetril averaged 0.38 +/- 0.09. Technetium (^{99m}Tc) Technetril from the blood is rapidly distributed into the tissue. Five minutes after injection only about 8 percent of the injected activity is still in circulation.

Technetium (^{99m}Tc) Technetril undergoes minimal redistribution over time. This may impact on lesion detection as the differential washout between the normal and ischemic myocardium may result in a reduction in defect size or severity with time.

Mastology indications

The cellular concentration of Technetium (^{99m}Tc) Technetril was demonstrated to be increased in mammary tumour tissue probably because of the high content of mitochondria in tumour cells and the high membrane potential of tumour cells.

Several in vitro studies demonstrated that Technetium (^{99m}Tc) Technetril is a substrate of P-glycoprotein. A direct correlation between the P-glycoprotein expression and the elimination of Technetium (^{99m}Tc) Technetril from tumours has been established. The cellular over-expression of P-glycoprotein could result in false negative images of tumours, especially of tumours larger than 1 cm.

Parathyroid indication

In adenoma of the parathyroid glands blood flow and the number of mitochondria are increased. This fact may explain the elevated uptake and trapping of Technetium (^{99m}Tc) Technetril in parathyroid adenoma.

Localization of Technetium (^{99m}Tc) Technetril appears to be dependent on blood flow to the tissue, the concentration of Technetium (^{99m}Tc) Technetril presented to the tissue, and the size of the parathyroid adenoma.

5.2 Pharmacokinetic properties

Technetium (^{99m}Tc) Technetril is a cationic complex which accumulates in the viable myocardial tissue proportional to the regional coronary blood flow.

Technetium (^{99m}Tc) Technetril from the blood is rapidly distributed into the tissue: 5 minutes after injection only about 8% of the injected dose is still in circulation.

Myocardial uptake

Myocardial uptake which is coronary flow dependent is 1.5% of the injected dose at stress and 1.2% of the injected dose at rest. Animal experiments have shown that uptake is not dependent on the functional capability of the Sodium-potassium pump. Irreversibly damaged cells however do not take up Technetium (^{99m}Tc) Technetril. The myocardial extraction level is reduced by hypoxia. The clearance of the myocardial fraction is minimal and the redistribution is insignificant during at least 4 hours after an induced ischaemia in the dog. Technetium (^{99m}Tc) Technetril is rapidly distributed from the blood into the tissue: 5 minutes after injection only about 8% of the injected dose is still in circulation.

However some experimental and clinical studies indicated a redistribution in severely ischaemic areas. A potential influence on the diagnostic quality of the test has not been established.

Elimination

The major metabolic pathway for clearance of Technetium (^{99m}Tc) Technetril is the hepatobiliary system. Activity from the gallbladder appears in the intestine within one hour of injection. About 27% of the injected dose is cleared through renal elimination after 24 hours and approximately 33% of the injected dose is cleared through the faeces in 48 hours.

Half-Life

The biological myocardial T½ is approximately 7 hours at rest and stress. The effective T½ (which includes biological and physical half-lives) is approximately 3 hours.

5.3 Preclinical safety data

In acute intravenous toxicity studies in mice, rats and dogs, the lowest dose of the reconstituted Technetril kit that resulted in any deaths was 7 mg/kg (expressed as Cu $(MIBI)_4$ BF_4 content) in female rats. This corresponds to 500 times the maximal human dose (MHD) of 0.014 mg/kg for adults (70 kg). Neither rats nor dogs exhibited treatment related effects at reconstituted Technetril kit doses of 0.42 mg/kg (30 times MHD) and 0.07 mg/kg (5 times MHD) respectively for 28 days. At repeated dose administration, the first toxicity symptoms appeared during the administration of 150 times the daily dose during 28 days.

Extravasation administration in animals showed acute inflammation with oedema and haemorrhages at the injected site.

Studies on reproductive toxicity have not been conducted.

Cu $(MIBI)_4$ BF_4 showed no genotoxic activity in the Ames, CHO/HPRT and sister chromatid exchange tests. At cytotoxic concentrations, an increase in chromosome aberration was observed

in the in vitro human lymphocyte assay. No genotoxic activity was observed in the in vivo mouse micronucleus test at 9 mg/kg.

Studies to assess the carcinogenic potential of the radiopharmaceutical kit have not been conducted.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Stannous chloride dihydrate
L-Cysteine hydrochloride monohydrate
Sodium citrate
Mannitol
Hydrochloric acid (for pH-adjustment)
Sodium Citrate dihydrate (for pH-adjustment)

6.2 Incompatibilities

The Technetium labelling reactions involved depend on maintaining the tin content at the reduced state. Hence, sodium pertechnetate (^{99m}Tc) injection or saline solution, containing oxidants should not be employed. In order not to interfere with the stability of the ^{99m}Tc complex, the radioactive product must not be mixed with other medicinal products or components.

6.3 Shelf life

1 years. After reconstitution: 5 hours. Do not store above 25°C after reconstitution.

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

The labelled 10 ml injection vials are closed with rubber stopper and aluminum cap. One box contains six (5) vials, one Instruction Manual and one Quality Certificate.

6.6 Special precautions for disposal and other handling

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

7. 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 calculated according to the following assumptions: After intravenous injection the substance is rapidly cleared from the blood and accumulates mainly in muscular tissues (including heart), liver, kidneys, and a smaller amount in salivary glands and thyroid. When the substance is injected in conjunction with a stress test, there is a considerable increase of the uptake in organs and tissues. The substance is excreted by the liver and kidneys in the proportions 75% and 25%, respectively.

Organ	Dose absorbed per activity administered [mGy/MBq] (resting test)				
	Adult	15-years	10-years	5-years	1-year
Adrenal glands	0.0075	0.0099	0.015	0.022	0.038
Bladder walls	0.011	0.014	0.019	0.023	0.041
Bone surface	0.0082	0.010	0.016	0.021	0.038
Brain	0.0052	0.0071	0.011	0.016	0.027
Breasts	0.0038	0.0053	0.0071	0.011	0.020
Gall bladder	0.039	0.045	0.058	0.10	0.32
Alimentary tract:					
Stomach	0.0065	0.0090	0.015	0.021	0.035
Small intestine	0.015	0.018	0.029	0.045	0.080
Colon	0.024	0.031	0.050	0.079	0.015
ULI	0.027	0.035	0.057	0.089	0.17
LLI	0.019	0.025	0.041	0.065	0.12
Heart	0.0063	0.0082	0.012	0.018	0.030
Kidneys	0.036	0.043	0.059	0.085	0.15
Liver	0.011	0.014	0.021	0.030	0.052
Lungs	0.0046	0.0064	0.0097	0.014	0.025
Muscles	0.0029	0.0037	0.0054	0.0076	0.014
Oesophagus	0.0041	0.0057	0.0086	0.013	0.023
Ovaries	0.0091	0.012	0.018	0.025	0.045
Pancreas	0.0077	0.010	0.016	0.024	0.039
Bone marrow	0.0055	0.0071	0.011	0.030	0.044
Salivary glands	0.014	0.017	0.022	0.015	0.026
Skin	0.0031	0.0041	0.0064	0.0098	0.019
Spleen	0.0065	0.0086	0.014	0.020	0.034
Testicles	0.0038	0.0050	0.0075	0.011	0.021
Thymus	0.0041	0.0057	0.0086	0.013	0.023
Thyroid	0.0053	0.0079	0.012	0.024	0.045

Organ	Dose absorbed per activity administered [mGy/MBq] (resting test)				
	Adult	15-years	10-years	5-years	1-year
Uterus	0.0078	0.010	0.015	0.022	0.038
Other organs	0.0031	0.0039	0.0060	0.0088	0.016
Effective dose	0.0090	0.012	0.018	0.028	0.053
[mSv/MBq]					

Organ	Dose absorbed per activity administered [mGy/MBq] (exercise test)				
	Adult	15-years	10-years	5-years	1-year
Adrenal glands	0.0066	0.0087	0.013	0.019	0.033
Bladder walls	0.0098	0.013	0.017	0.021	0.038
Bone surface	0.0078	0.0097	0.014	0.020	0.036
Brain	0.0044	0.0060	0.0093	0.014	0.023
Breasts	0.0034	0.0047	0.0062	0.0097	0.018
Gall bladder	0.033	0.038	0.049	0.086	0.26
Alimentary tract:					
Stomach	0.0059	0.0081	0.013	0.019	0.032
Small intestine	0.012	0.015	0.024	0.037	0.066
Colon	0.019	0.025	0.041	0.064	0.12
ULI	0.022	0.028	0.046	0.072	0.13
LLI	0.016	0.021	0.034	0.053	0.099
Heart	0.0072	0.0094	0.010	0.021	0.035
Kidneys	0.026	0.032	0.044	0.063	0.11
Liver	0.0092	0.012	0.018	0.025	0.044
Lungs	0.0044	0.0060	0.0087	0.013	0.023
Muscles	0.0032	0.0041	0.0060	0.0090	0.017
Oesophagus	0.0040	0.0055	0.0080	0.012	0.023
Ovaries	0.0081	0.011	0.015	0.023	0.040
Pancreas	0.0069	0.0091	0.014	0.021	0.035
Bone marrow	0.0050	0.0064	0.0095	0.013	0.023
Salivary glands	0.0092	0.011	0.0015	0.0020	0.0029
Skin	0.0029	0.0037	0.0058	0.0090	0.017
Spleen	0.0058	0.0076	0.012	0.017	0.030
Testicles	0.0037	0.0048	0.0071	0.011	0.020
Thymus	0.0040	0.0055	0.0080	0.012	0.023
Thyroid	0.0044	0.0064	0.0099	0.019	0.035
Uterus	0.0072	0.0093	0.014	0.020	0.035
Other organs	0.0033	0.0043	0.0064	0.0098	0.018
Effective dose	0.0079	0.010	0.016	0.023	0.045
[mSv/MBq]					

The effective dose per unit of administered activity has been calculated according to a voiding frequency of 3.5 hours in adults.

Myocardial imaging:
The effective dose resulting from the administration of a maximal recommended activity of 2000 MBq Technetium (^{99m}Tc) Technetril for an adult weighing 70 kg is approximately 16.3 mSv (500 MBq for rest and 1500 MBq for exercise test) for a one-day protocol, and 15.2 mSv (900 MBq for rest and 900 MBq for stress) for a two-day protocol.

Scintimammography:
The effective dose after administration of maximal 925 MBq is 8.3 mSv.

Parathyroid imaging:
The effective dose after administration of maximal 750 MBq is 6.75 mSv.

8. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Instructions for Preparation of Technetium (^{99m}Tc) Technetril

Preparation of Technetium (^{99m}Tc) Technetril is to be done according to the following aseptic procedure. The heating of the preparation can either be done using a water bath or in a heating block. Both methods are described underneath:

Boiling procedure:

1 Waterproof gloves should be worn during the preparation procedure. Remove the cap from the Technetril vial and swab the top of the vial closure with alcohol to disinfect the surface.
2 Place the vial in a suitable radiation shield appropriately labelled with date, time of preparation, volume and activity.
3 With a sterile shielded syringe, aseptically obtain additive-free, sterile, non-pyrogenic sodium pertechnetate (^{99m}Tc) solution max. 11.1 GBq in approximately 3 ml. Not more than 3 ml sodium pertechnetate (^{99m}Tc) solution will be used for the maximum activity of 11.1 GBq.
4 Aseptically add the sodium pertechnetate (^{99m}Tc) solution to the vial in the lead shield. Without withdrawing the needle, remove an equal volume of headspace to maintain atmospheric pressure within the vial.
5 Shake vigorously, about 5 to 10 quick upward-downward motions.
6 Remove the vial from the lead shield and place upright in an appropriately shielded and contained boiling water bath, such that the vial is suspended above the bottom of the bath, and boil for 10 minutes. The bath must be shielded. Timing for the 15 minutes commences as soon as the water begins to boil again.
Note: The vial must remain upright during the boiling step. Use a water bath where the stopper will be above the level of the water.
7 Remove the shielded vial from the water bath and allow cooling for fifteen minutes.
8 Inspect visually for the absence of particulate matter and discoloration prior to administration.
9 If needed, a dilution with 0.9 % saline solution is possible.
10 Aseptically withdraw material using a sterile shielded syringe. Use within ten (10) hours of preparation.
11 Radiochemical purity should be checked prior to patient administration according to the Radio TLC Method as detailed below.

Heating block procedure:

1 Waterproof gloves should be worn during the preparation procedure. Remove the flip-off cap from the Technetril Kit vial and swab the top of the vial closure with alcohol to disinfect the surface.
2 Place the vial in a suitable radiation shield appropriately labelled with date, time of preparation, volume and activity.

3 With a sterile shielded syringe, aseptically obtain additive-free, sterile, non-pyrogenic sodium pertechnetate (^{99m}Tc) solution max. 11.1 GBq in approximately 3 ml. Not more than 3 ml sodium pertechnetate (^{99m}Tc) solution will be used for the maximum activity of 11.1 GBq.
4 Aseptically add the sodium pertechnetate (^{99m}Tc) solution to the vial in the lead shield. Without withdrawing the needle, remove an equal volume of headspace to maintain atmospheric pressure within the vial.
5 Shake vigorously, about 5 to 10 quick upward-downward motions.
6 Place the vial into the heating block previously heated to 120°C, and incubate for 15 minutes. The heating block should be adapted to the size of the vial in order to ensure a correct transfer of heat from the heating device to the content of the vial.
7 Remove the vial for the heating block and allow cooling to room temperature.
8 Inspect visually for the absence of particulate matter and discoloration prior to administration.
9 If needed, a dilution with 0.9 % saline solution is possible.
10 Aseptically withdraw material using a sterile shielded syringe. Use within ten (10) hours of preparation.
11 Radiochemical purity should be checked prior to patient administration according to the Radio TLC Method as detailed below.

Note: the potential for cracking and significant contamination exists whenever vials containing radioactive material are heated.

Radio-TLC Method for the Quantification of Technetium (^{99m}Tc) Technetril

1. Materials
   - 1.1 Baker-Flex-Aluminium Oxide plate, # 1 B-F, pre-cut to 2.5 cm x 7.5 cm.
   - 1.2 Ethanol, > 95%.
   - 1.3 Capintec, or equivalent instrument for measuring radioactivity in the 0.7 - 11.1GBq range.
   - 1.4 1 ml syringe with a 22-26 gauge needle.
   - 1.5 Small developing tank with cover, (100 ml beaker covered with Parafilm is sufficient).
2. Procedure
   - 2.1 Pour enough ethanol into the developing tank (beaker) to have a depth of 3-4 mm of solvent. Cover the tank (beaker) with Parafilm® and allow it to equilibrate for approximately 10 minutes.
   - 2.2 Apply 1 drop of ethanol, using a 1 ml syringe with a 22-26 gauge needle on to the Aluminium Oxide TLC plate, 1.5 cm from the bottom. **Do not allow the spot to dry**.
   - 2.3 Apply 1 drop of the kit solution on top of the ethanol spot. Dry the spot. **Do not heat!**
   - 2.4 Allow the solvent front to travel for a distance of 5.0 cm from the spot.
   - 2.5 Cut the strip at 4.0 cm from the bottom, and measure each piece in your dose calibrator.
   - 2.6 Calculate the % Radiochemical purity as:
     % (^{99m}Tc) Technetril = (Activity top portion)/(Activity both pieces) x 100.
   - 2.7 % (^{99m}Tc) Technetril should be ≥ 90%; otherwise the preparation should be discarded.

The content of the kit before preparation is not radioactive. However, after sodium pertechnetate (^{99m}Tc) Injection, Ph. Eur., 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.
As with any pharmaceutical product, if at any time in the preparation of this product the integrity of this vial is compromised it should not be used.