Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

DRAXMIBI 1 mg kit for radiopharmaceutical preparation

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 vial contains:

Active substance

Tetrakis(2-methoxyisobutylisonitrile)copper(I) Tetrafluoroborate 1 mg

Excipients:
This medicinal product contains 0.61 mg of Sodium per vial.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Kit for radiopharmaceutical preparation.
Lyophilized, white 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 pertechnetate (^{99m}Tc) solution for injection, the solution of technetium (^{99m}Tc) sestamibi obtained is indicated for:

Myocardial perfusion scintigraphy
Detection and localization of coronary artery disease 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.

Scinti-mammography for the detection of suspected breast cancer
Detection of suspected 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:

Diagnosis of reduced coronary perfusion and myocardial infarction:
400 - 900 MBq

Assessment of global ventricular function:
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 ischemic 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 by these two injections which 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).

In each country nuclear medicine physicians should respect the diagnostic reference levels (DRLs) and the rules laid down by the local legislation. The injection of activities greater than local DRLs should be justified.

For diagnosis of myocardial infarction one injection at rest may be sufficient.
For breast imaging: 740 - 925 MBq injected as a bolus in the arm opposite to the lesion.

For parathyroid imaging: 185 - 740 MBq injected as a bolus.

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

Safety and efficacy in children below the age of 18 years have not been established. Where appropriate and practical, an investigation that does not involve radiation should be employed.
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 children 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	22 kg = 0.50	42 kg = 0.78
4 kg = 0.14	24 kg = 0.53	44 kg = 0.80
6 kg = 0.19	26 kg = 0.56	46 kg = 0.82
8 kg = 0.23	28 kg = 0.58	48 kg = 0.85
10 kg = 0.27	30 kg = 0.60	50 kg = 0.88
12 kg = 0.32	32 kg = 0.62	52 - 54 kg = 0.90
14 kg = 0.36	34 kg = 0.64	56 - 58 kg = 0.92
16 kg = 0.40	36 kg = 0.66	60 - 62 kg = 0.96
18 kg = 0.44	38 kg = 0.68	64 - 66 kg = 0.98
20 kg = 0.46	40 kg = 0.70	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) sestamibi resulting in less liver activity in the image.

Imaging should begin approximately after 60 min after injection to allow for hapatobiliary 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. Tests may be done in a one day or two days protocol.

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

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 depends on whether subtraction technique or wash-out technique is used. For the subtraction technique either ^{123}I, ^{99m}Tc or ^{201}TI can be used and should be performed according to literature, guideline and recommended activites:

If double phase wash-out technique is used, 370 to 740 MBq of technetium (^{99m}Tc) sestamibi 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. Between the two images SPECT or SPECT/CT can be performed.

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 12.

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) sestamibi 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 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 1cm in diameter may not all be detected with scintimammography as the sensitivity of technetium (^{99m}Tc) sestamibi for the detection of these lesions is 52 % relative to histological diagnosis. 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. Their 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. Appropriate aseptic precautions should be taken, complying with the requirements of Good Manufacturing Practice for pharmaceuticals.

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

If hypersensitivity 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 Fertility, 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 be considered.

Pregnancy
Radionuclide procedures carried out on pregnant women also involve radiation to the foetus. Only imperative investigations should therefore be carried out during pregnancy, when the likely benefit far exceeds the risk incurred by the mother and foetus.

Lactation
Before administering a 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 infant should be restricted during this period.

4.7 Effects on ability to drive and use machines

DRAXMIBI 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)

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

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

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

Gastrointestinal disorders:
Uncommon: Nausea
Rare: Abdominal pain.

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.
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.

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.

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 an average amount of activity of 2000 MBq (500 MBq at rest and 1500 MBq at stress) for a 1-day-protocol is 16.4 mSv (4.5 mSv at rest and 11.9 mSv at stress). The effective dose is 8.32 mSv when the maximal recommended activity of 925 MBq is administered.

4.9 Overdose

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Technetium (^{99m}Tc) compounds
ATC code: V09GA01

Pharmacodynamic effects are not expected after administration of technetium (^{99m}Tc) sestamibi.

After reconstitution with Sodium Pertechnetate (^{99m}Tc) Injection, the following complex forms (technetium (^{99m}Tc) sestamibi):
^{99m}Tc-$(MIBI)_6^+$ Where: MIBI = 2-methoxyisobutylisonitrile

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

5.2 Pharmacokinetic properties

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

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

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

<u>Cardiac indication</u>
Technetium (^{99m}Tc) sestamibi binds to the mitochondrial membrane and an intact mitochondrial membrane potential is important for intracellular binding.

The uptake of technetium (^{99m}Tc) Sestamibi 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) sestamibi averaged 0.38 +/- 0.09. Technetium (^{99m}Tc) sestamibi from the blood is rapidly distributed into the tissue. Five minutes after injection only about 8 percent of the injected dose is still in circulation.

Technetium (^{99m}Tc) sestamibi 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.

<u>Mastology indication</u>
The cellular concentration of technetium (^{99m}Tc) sestamibi 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) sestamibi is a substrate of P glycoprotein. A direct correlation between the P-glycoprotein expression and the elimination of technetium (^{99m}Tc) sestamibi 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) sestamibi in parathyroid adenoma. Localization of technetium (^{99m}Tc) sestamibi appears to be dependent on blood flow to the tissue, the concentration of technetium (^{99m}Tc) sestamibi presented to the tissue, and the size of the parathyroid adenoma.

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) sestamibi. 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 ischemia in the dog. Technetium (^{99m}Tc) sestamibi 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) sestamibi 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 technetium (^{99m}Tc) sestamibi 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 technetium (^{99m}Tc) sestamibi 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.

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 cytoxic 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 DRAXMIBI have not been conducted.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Citrate Dihydrate
L-Cysteine Hydrochloride Monohydrate
Mannitol
Stannous Chloride Dihydrate
Hydrochloric Acid (for pH-adjustment)
Sodium Hydroxide (for pH-adjustment)

6.2 Incompatibilities

The technetium labelling reactions involved depend on maintaining the stannous level in the reduced state. Hence, Sodium Pertechnetate (^{99m}Tc) Injection containing oxidants should not be employed.

This medicinal product must not be mixed with other medicinal products except those mentioned in section 12.

6.3 Shelf life

Before reconstitution: 12 months.
After reconstitution: 10 hours. Do not store above 25°C. Do not refrigerate or freeze.

6.4 Special precautions for storage

Store in the original package in order to protect from light.
Unlabelled product: Do not store above 25°C. Do not refrigerate or freeze.
For storage conditions of the reconstituted medicinal product, see section 6.3.
Storage should be in accordance with national regulations for radioactive material.

6.5 Nature and contents of container

10 ml glass vials, type I borosilicate glass sealed with a butyl rubber stopper. Pack sizes: 2, 5 and 10 vials in a carton.

Not all pack size may be marketed.

This product is in multi-dose vials.

6.6 Special precautions for disposal

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

7 MARKETING AUTHORISATION HOLDER

DRAXIMAGE (UK) Limited
5 Old Bailey
2nd Floor
London EC4M 7BA
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA1419/1/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10th July 2009

10 DATE OF REVISION OF THE TEXT

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 mean energy of 140 keV and half-life of 6.02 hours to technetium (^{99m}Tc) which, in view of its long half-life of 2.13 x 10^5 years can be regarded as quasi stable.

The data listed below are from ICRP 80 and 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)**				
	Adults	15-year-olds	10-year-olds	5-year-olds	1-year-olds
Adrenal glands	0.0075	0.009	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	0.015
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
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 [mSv/MBq]	**0.0090**	**0.012**	**0.018**	**0.028**	**0.053**

Organ	**Dose absorbed per activity administered [mGy/MBq] (exercise test)**				
	Adults	15-year-olds	10-year-olds	5-year-olds	1-year-olds
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 [mSv/MBq]	**0.0079**	**0.010**	**0.016**	**0.023**	**0.045**

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

Myocardial perfusion scintigraphy
The effective dose calculated with an average amount of activity of 1800 MBq (900 MBq at stress and 900 MBq at rest) for a 2-day-protocol is 15.2 mSv.

The effective dose calculated with an average amount of activity of 2000 MBq (500 MBq at rest and 1500 MBq at stress) for a 1-day-protocol is 16.4 mSv.

Evaluation of ventricular function
After injection of 800 MBq, the effective dose is 7.2 mSv at rest. After injection of 800 MBq, the effective dose is 6.3 mSv at stress.

Scinti-mammography
After injection of 925 MBq, the effective dose is 8.32 mSv.

Parathyroid imaging of hyperfunctioning tissue
The effective dose after administration of 740 MBq is 6.7 mSv.

12 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

The contents of the kit before preparation are not radioactive. However, after Sodium Pertechnetate (^{99m}Tc) Injection 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.

The medicinal product should not come into contact with air.

The labelling of the kit should be made according to either method A or method B.

Instructions for Preparation of technetium (^{99m}Tc) sestamibi

A. Boiling procedure:

Preparation of technetium (^{99m}Tc) sestamibi from DRAXMIBI is to be done according to the following aseptic procedure:

1 Waterproof gloves should be worn during the preparation procedure. Remove the plastic disc from the DRAXMIBI 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 1 to 3 ml. Not less than 3 ml sodium pertechnetate (^{99m}Tc) solution will be use 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 10 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 Aseptically withdraw material using a sterile shielded syringe. Use within ten (10) hours of preparation.

10 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.

B. Thermal Cycler procedure:

Preparation of technetium (^{99m}Tc) sestamibi from DRAXMIBI is to be done according to the following aseptic procedure:

1 Waterproof gloves should be worn during the preparation procedure. Remove the plastic disc from the DRAXMIBI 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 1 to 3 ml. Not less than 3 ml sodium pertechnetate (^{99m}Tc) solution will be use 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 shield in the sample block. While slightly pressing downwards, give the shield a quarter turn to make certain there is a firm fit between the shield and the sample block.

7 Press the proceed button to initiate the program (the thermal cycler automatically heats & cools the vial and contents). Please see the Recon-o-stat Instruction Manual for further details.

8 Inspect visually for the absence of particulate matter and discoloration prior to administration.

9 Aseptically withdraw material using a sterile shielded syringe. Use within ten (10) hours of preparation.

10 Radiochemical purity should be checked prior to patient administration according to the Radio-TLC Method as detailed below.

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

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 0.74 – 11.12 GBq 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 Develop the plate a distance of 5.0 cm from the spot.

2.5 Cut the strip 2.5 cm (one third) from the bottom of the strip, and measure each piece in your dose calibrator.

2.6 Calculate the % radiochemical purity as:
% (^{99m}Tc) sestamibi = (Activity top portion)/(Activity both pieces) x 100.

2.7 % (^{99m}Tc) sestamibi should be ≥ 94%; otherwise the preparation should be discarded.

Note: Do not use material if the radiochemical purity is less than 94%.

After reconstitution the container and any unused contents should be disposed of in accordance with local requirements for radioactive materials.