410902

ENGLISH

PACKAGE LEAFLET: INFORMATION FOR THE USER

DRAXMIBI 1 mg

Kit for radiopharmaceutical preparation

Tetrakis (2-methoxy isobutyl isonitrile) copper(I) tetrafluoroborate

Read all of this leaflet carefully before you start using this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others as it may harm them.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT DRAXMIBI IS AND WHAT IT IS USED FOR

This medicinal product is for diagnostic use only.

DRAXMIBI is used to study the blood circulation, especially the blood circulation in the heart. It is also used to determine if any areas of the heart muscle have been damaged because of an insufficient blood supply to the heart. DRAXMIBI is also used in the diagnosis of breast cancer when the results of other diagnostic methods are unclear. DRAXMIBI can also be used to check for overactivity of the parathyroid gland, which may be causing an abnormally high activity of this organ.

After injecting DRAXMIBI, your doctor will then take an image (scan) of the concerned organ. The area where the radioactive compound accumulated will show up in the scan and help the doctor make the diagnosis.

2. BEFORE YOU ARE INJECTED WITH DRAXMIBI

Do not use DRAXMIBI

If you are allergic (hypersensitive) to the active substance or any of the other ingredients of DRAXMIBI (see Section 6 for a list of ingredients).

Take special care with DRAXMIBI

This product is hardly ever used in patients under 18 years because it has not been fully investigated in this age group. If you are younger than 18 years, the doctor may still decide to use this product if the risks are smaller than the benefits. Please tell your doctor, if you know you are suffering from a kidney and/or liver disease and/or malformation of your gallbladder. Your doctor will explain to you the details of the applied doses and procedures.

Please also read the information under 'Pregnancy and breastfeeding'.

DRAXMIBI contains a small amount of radioactive medicine and will be injected in your body. The risk associated with this procedure is very small. Your doctor will only carry out the examination if he/she believes that the risk is smaller than the potential benefit of the examination.

Using other medicines

Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Pregnancy and breastfeeding

Ask your doctor for advice before taking any medicine.

It is important to tell your doctor if you are or may be pregnant or if you are breastfeeding. The use of medicinal products which contain radioactivity during pregnancy must be considered carefully. Your doctor will only administer this product during pregnancy if a benefit is expected that outweighs the risks.

If you are breastfeeding, please tell your doctor. He/she may decide either to postpone the examination until you have stopped breastfeeding or ask you to stop breastfeeding temporarily.

Breastfeeding should be stopped for 24 hours after injection and the expressed milk within this period of time should be discarded.

Driving and using machines

DRAXMIBI does not affect the ability to drive or use machines.

Important information about some ingredients of DRAXMIBI

This medicinal product contains less than 1 mmol Sodium (23 mg) per vial. This means that this product is practically 'sodium-free'.

3. HOW TO USE DRAXMIBI

This product may only be used in accordance with your doctor's instructions and under his/her supervision.

DRAXMIBI is administered by injection into a vein. The doctor may give you 2 injections for heart imaging, one at rest and one with exercise. If 2 injections are needed, they will be given at least 2 hours apart. Scans can be made until 6 hours after the injection.

If DRAXMIBI is used to study the blood flow in your heart, you should not eat for at least four hours prior to the examination. Your doctor may ask you to have a light fatty meal or drink one or two glasses of milk after each injection, prior to making the scan.

Your doctor may advise you to drink a lot of fluid so that the traces of radioactivity will leave your body more quickly. This is normal when using medicinal products which contain radioactivity. Your doctor will also tell you about any other steps you may need to take following the use of this product.

Because there are strict laws covering the use, handling and disposal of radioactivity, DRAXMIBI will always be used in a hospital or in similar settings. It will only be handled and administered by people who have been trained and are qualified in the safe handling of radioactive material.

If you are injected with more DRAXMIBI than you should

Since DRAXMIBI is administered under strictly controlled circumstances by a doctor, it is unlikely that you will be given an overdose. Should this happen nonetheless, the doctor will take appropriate measures.

Your doctor may then also advise you to drink a lot of fluid so that the traces of radioactivity will leave your body more quickly.

If you have any further questions on the use of this product, ask your doctor.

4. POSSIBLE SIDE EFFECTS

Like all medicines, DRAXMIBI can cause side effects, although not everybody gets them.

The following terms are used to describe how often side effects have been reported.

very common: affects more than 1 user in 10
common: affects 1 to 10 users in 100
uncommon: affects 1 to 10 users in 1,000
rare: affects 1 to 10 users in 10,000
very rare: affects less than 1 user in 10,000
not known: frequency cannot be estimated from the available data

Common side effects that have occurred in patients who have been injected with DRAXMIBI include:

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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-methoxy isonitrile) 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 localisation 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 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.

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 Tl-201 can be used and should be performed according to literature, guideline and recommended activites:

If double phase 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 1 cm 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. 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. 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 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 breastfeeding consideration should be given as to whether the investigation could be reasonably delayed until after the mother has ceased breastfeeding 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, breastfeeding 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-methoxy isobutyl isonitrile

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.

Cardiac indication

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.

Mastology indication

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.

Localisation 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 $T_{1/2}$ is approximately 7 hours at rest and stress. The effective $T_{1/2}$ (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 $Cu(MIBI)_4BF_4$ 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.

$Cu(MIBI)_4BF_4$ 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: 15 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 1 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 and other handling

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

7 MARKETING AUTHORISATION HOLDER

DRAXIMAGE (UK) LIMITED
125 Old Broad Street, 26th Floor, London
United Kingdom EC2N 1AR

8 MARKETING AUTHORISATION NUMBER(S)

PL 29620/0003

9 DATE OF FIRST AUTHORISATION

02/09/2009

10 DATE OF REVISION OF THE TEXT

14/03/2013

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 (^{99}Tc) which, in view of its long half-life of 2.13×10^5 years can be regarded as quasi stable.

The data listed below are from ICRP 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-old	10-year-old	5-year-old	1-year-old
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-old	10-year-old	5-year-old	1-year-old
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 the 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.

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metallic or bitter taste, alteration of smell, and dry mouth immediately after injection.

Uncommon side effects that have occurred in patients who have been injected with DRAXMIBI include: headache, chest pain, abnormal ECG and feeling sick.

Rare side effects that have occurred in patients who have been injected with DRAXMIBI include: hypersensitivity reactions, abnormal heart rhythm, oedema, local reactions at the injection site, stomach pain, vomiting, itching, hives, fever, fainting, seizures, dizziness, flushing, rash, skin numbness or tingling, fatigue, shortness of breath (dyspnoea), low blood pressure (hypotension), and joint pains.

Exposure to ionising radiation can cause cancer and can possibly cause hereditary defects in children you may later wish to have. However, like most radioactive medicinal products that are used for diagnostic examinations, DRAXMIBI has low radiation doses of less than 20 mSv therefore these risks are very small.

If any of the side effects gets serious or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE DRAXMIBI

DRAXMIBI will be stored by the hospital pharmacist. The pharmacist and the doctor will follow the advice listed below:

Keep out of the reach and sight of children.

Do not use DRAXMIBI after the expiry date which is stated on the vial and the box after EXP. The expiry date refers to the last day of that month.

Store in the original package in order to protect from light. Unlabelled and labelled product: Do not store above 25°C. Do not refrigerate or freeze.

Storage should be in accordance with national regulations for radioactive material.

Shelf-life after reconstitution: 10 hours.

Do not use DRAXMIBI if you notice cracks or any other indication that the product is no longer vacuum-sealed.

DRAXMIBI should be disposed according to local regulations.

6. FURTHER INFORMATION

What DRAXMIBI contains

The **active substance** is Tetrakis (2-methoxy isobutyl isonitrile) copper(I) tetrafluoroborate

Each vial contains 1 mg.

The **other ingredients** are: sodium citrate dihydrate, L-cysteine hydrochloride monohydrate, mannitol, stannous chloride dihydrate, hydrochloric acid and sodium hydroxide.

What DRAXMIBI looks like and contents of the pack

DRAXMIBI 1 mg kit for radiopharmaceutical preparation is a white, freeze-dried powder.

Pack sizes: 2, 5 or 10 vials.
Not all pack sizes may be marketed.

This product is in multi-dose vials.

Marketing authorisation holder

DRAXIMAGE (UK) Limited
125 Old Broad Street, 26th Floor
London, EC2N 1AR
United Kingdom

Manufacturer responsible for batch release

Diagnostic Imaging Limited (DIL)
Elkington Lodge
Welford
Northamptonshire, NN6 6HE
United Kingdom

This medicinal product is authorised in the member states of the EEA under the following names:

- Belgium
  DRAXMIBI 1 mg trousse pour préparation radiopharmaceutique
- Denmark
  DRAXMIBI
- Germany
  DRAXMIBI 1 mg kit für ein radioaktives Arzneimittel
- The Netherlands
  DRAXMIBI 1 mg kit voor radiofarmaceutisch preparaat
- United Kingdom
  DRAXMIBI 1 mg kit for radiopharmaceutical preparation

This leaflet was last approved in 02/2013.

The following information is intended for healthcare professionals only:

The complete Summary of Products Characteristics is added as a tear-off section at the end of this package leaflet.

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