SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
Technescan Sestamibi United Kingdom

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each vial contains 1 mg [Tetakis(2-methoxy-2-methylpropyl-1 isocyanide)copper(I)] tetrafluoroborate. The radionuclide is not part of the kit.

3. PHARMACEUTICAL FORM
Kit for radiopharmaceutical preparation.
White to almost white pellets or powder.
To be reconstituted with sodium pertechnetate (99mTc) solution for injection.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
This medicinal product is for diagnostic use only. It is indicated for adults. For paediatric population see section 4.2.
After radiolabelling with sodium pertechnetate (99mTc) solution, the solution of technetium (99mTc) sestamibi obtained is indicated for:
- Myocardial perfusion scintigraphy for the detection and localisation of coronary artery disease (angina pectoris 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 suspected breast cancer when mammography is equivocal, inadequate or indeterminate.
- Localisation of hyperfunctioning parathyroid tissue in patients with recurrent or persistent disease in both primary and secondary hyperparathyroidism, and in patients with primary hyperparathyroidism scheduled to undergo initial surgery of the parathyroid glands.

4.2 Posology and method of administration

Posology
Adults and elderly population
Posology may vary depending on gamma camera characteristics and reconstruction modalities. The injection of activities greater than local DRLs (Diagnostic Reference Levels) should be justified.
The recommended activity range for intravenous administration to an adult patient of average weight (70 kg) is for:

**Diagnosis of reduced coronary perfusion and myocardial infarction**
400 – 900 MBq
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 is usually sufficient.
For diagnosis of ischaemic heart disease two injections (stress and rest) are required in order to differentiate transient from persistently reduced myocardial uptake.

**Assessment of global ventricular function**
600 – 800 MBq injected as a bolus.

Scintimammography
700 – 1000 MBq injected as a bolus usually in the arm opposite to the lesion.

Localisation of hyperfunctioning parathyroid tissue
200 – 700 MBq injected as a bolus. The typical activity is between 500 – 700 MBq.
Posology may vary depending on gamma camera characteristics and reconstruction modalities.
The injection of activities greater than local DRLs (Diagnostic Reference Levels) should be justified.

Renal impairment
Careful consideration of the activity to be administered is required since an increased radiation exposure is possible in these patients.

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

Paediatric population
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 to children and adolescents may be calculated according to the recommendations of the European Association of Nuclear Medicine (EANM) paediatric dosage card; the activity administered to children and to adolescents may be calculated by multiplying a baseline activity (for calculation purposes) by the weight-dependent multiplies given in the table below.

<table>
<thead>
<tr>
<th>Weight [kg]</th>
<th>Multiple</th>
<th>Weight [kg]</th>
<th>Multiple</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>1</td>
<td>22</td>
<td>5.29</td>
</tr>
<tr>
<td>4</td>
<td>1.14</td>
<td>24</td>
<td>5.71</td>
</tr>
<tr>
<td>6</td>
<td>1.71</td>
<td>26</td>
<td>6.14</td>
</tr>
<tr>
<td>8</td>
<td>2.14</td>
<td>28</td>
<td>6.43</td>
</tr>
<tr>
<td>10</td>
<td>2.71</td>
<td>30</td>
<td>6.86</td>
</tr>
<tr>
<td>12</td>
<td>3.14</td>
<td>32</td>
<td>7.29</td>
</tr>
<tr>
<td>14</td>
<td>3.57</td>
<td>34</td>
<td>7.72</td>
</tr>
<tr>
<td>16</td>
<td>4.00</td>
<td>36</td>
<td>8.00</td>
</tr>
<tr>
<td>18</td>
<td>4.43</td>
<td>38</td>
<td>8.43</td>
</tr>
<tr>
<td>20</td>
<td>4.86</td>
<td>40</td>
<td>8.86</td>
</tr>
</tbody>
</table>

Method of administration
For intravenous use.
Because of potential tissue damage, extravasal injection of this radioactive product has to be strictly avoided.
For multidose use.

Precautions to be taken before handling or administration of the medicinal product
This medicinal product should be reconstituted before administration to the patient. For instructions on reconstitution and control of the radiochemical purity of the medicinal product before administration, see section 12.
For patient preparation, see section 4.4.

Image acquisition
Cardiac Imaging
Imaging should begin approximately after 30 - 60 min after injection to allow for hepatobiliary clearance. Longer delay can be required for resting images and for stress with vasodilators alone because of the risk of higher subdiaphragmatic technetium (99mTc) 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.

Scintimammography
Breast imaging is optimally initiated 5 to 10 minutes post injection with the patient in the prone position with breast freely pendant.
The product is administered in an arm vein contralateral to the breast with the suspected abnormality. If the disease is bilateral, the injection is ideally administered in a dorsal vein of the foot.
Parathyroid imaging

Parathyroid image acquisition depends on the protocol chosen. The most used studies are either the subtraction and/or the dual-phase techniques, which can be performed together.

For the subtraction technique either sodium iodide ($^{131}$I) or sodium pertechnetate ($^{99m}$Tc) can be used for imaging for the thyroid gland since these radiopharmaceuticals are trapped by functioning thyroid tissue. This image is subtracted from the technetium ($^{99m}$Tc) sestamibi image, and pathological hyperfunctioning parathyroid tissue remains visible after subtraction. When sodium iodide ($^{131}$I) is used, 10 to 20 MBq are orally administered. Four hours after the administration, neck and thorax images may be obtained. After sodium iodide ($^{131}$I) image acquisition, 200 to 700 MBq of technetium ($^{99m}$Tc) sestamibi are injected and images are acquired 10 minutes post injection in double acquisition with 2 peaks of gamma energy (140 keV for $^{99m}$Tc and 159 keV for iodine ($^{131}$I)). When sodium pertechnetate ($^{99m}$Tc) is used, 40-150 MBq are injected and neck and thorax images are acquired 30 minutes later. Then 200 to 700 MBq of technetium ($^{99m}$Tc) sestamibi are injected and a second acquisition of images is acquired 10 minutes later.

If the dual phase technique is used, 400 to 700 MBq of technetium ($^{99m}$Tc) sestamibi are injected and the first neck and mediastinum image is obtained 10 minutes later. After a wash-out period of 1 to 2 hours, neck and mediastinum imaging is again performed.

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

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 4.4.

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

4.4 Special warnings and precautions for use

Potential for hypersensitivity or anaphylactic reactions

Hypersensitivity to the active substance or to any of the excipients listed in section 4.3. Therefore, if the patient has a history of hypersensitivity reactions or anaphylaxis, 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.

Individual benefit/risk justification

For each patient, the radiation exposure must be justifiable by the likely benefit. The activity administered should in every case be as low as reasonably achievable to obtain the required diagnostic information.

Renal or hepatic impairment

Careful consideration of the benefit risk ratio in these patients is required since an increased radiation exposure is possible (see section 4.2).

Paediatric population

For information on the use in paediatric population, see section 4.2. Careful consideration of the indication is required since the effective dose per MBq is higher than in adults (see section 11).

Patient preparation

The patient should be well hydrated before the start of the examination and urged to void as often as possible during the first hours after the examination in order to reduce radiation.

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.

Interpretation of technetium ($^{99m}$Tc) sestamibi images

Interpretation of scintimammography

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 low. A negative examination does not exclude breast cancer especially in such a small lesion.

After the procedure

Close contact with infants and pregnant women should be restricted during the initial 24 hours following the injection.

Specific warnings

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

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

For precautions with respect to environmental hazard see section 6.6.

4.5 Interaction with other medicinal products and other forms of interaction

Medicinal products which affect myocardial function and/or blood flow may cause false negative results in the diagnosis of coronary arterial disease. Particularly beta-blockers and calcium antagonists reduce oxygen consumption and thus also affect perfusion and beta-blockers inhibit the increase of heart frequency and blood pressure under stress. For this reason, concomitant medication should be taken into consideration when interpreting the results of the scintigraphic examination. The recommendations of the applicable guidelines on ergonomic or pharmacological stress tests should be followed.

When the subtraction technique is used for imaging of hyperfunctioning parathyroid tissue, recent use of iodine containing radiologic contrast media, medicinal products used to treat hyper- or hypothyroidism or of several other medicinal products is likely to decrease the quality of thyroid imaging and even makes subtraction impossible. For a complete list of possibly interacting medicinal products refer to the SmPCs of sodium iodide ($^{131}$I) or sodium pertechnetate ($^{99m}$Tc).

Paediatric population

Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

When an administration of radiopharmaceuticals to a woman of childbearing potential is intended, it is important to determine whether or not she is pregnant. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. If in doubt about her potential pregnancy (if the woman has missed a period, if the period is very irregular, etc.), alternative techniques not using ionising radiation (if there are any) should be offered to the patient.

Pregnancy

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

Breastfeeding

Before administering radiopharmaceuticals to a mother who is breastfeeding consideration should be given to the possibility of delaying the administration of radionuclide until the mother has ceased breastfeeding, and to what is the most appropriate choice of radiopharmaceuticals, 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 infants should be restricted during the initial 24 hours following injection.

Fertility

No studies on fertility have been performed.

4.7 Effects on ability to drive and use machines

Technescan MIßI has no or negligible 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:

<table>
<thead>
<tr>
<th>Category</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very common</td>
<td>≥1/10</td>
</tr>
<tr>
<td>Common</td>
<td>≥1/100 to &lt;1/10</td>
</tr>
<tr>
<td>Uncommon</td>
<td>&lt;1/100</td>
</tr>
<tr>
<td>Rare</td>
<td>≥1/10,000 to &lt;1/1,000</td>
</tr>
<tr>
<td>Very rare</td>
<td>&lt;1/10,000</td>
</tr>
</tbody>
</table>

Not known (cannot be estimated from the available data)

**Immunologic disorders**
- Rare: Severe hypersensitivity reactions such as dyspnoea, hypotension, bradycardia, asthma and vomiting (usually within two hours of administration), angioedema. Other hypersensitivity reactions (allergic skin and mucosa reactions with exanthema (pruritus, urticaria, oedema), vasodilatation).

**Common disorders and administration site conditions**
- Common: After injection, a metallic or bitter taste, flushed.

**Other disorders**
- Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is 16.4 mSv when the maximal recommended activity of 2000 MBq (500 at rest and 1500 MBq at stress) for a 1-day-protocol is administered, these adverse reactions are expected to occur with a low probability.

**Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

00% of the injected dose is cleared through the faeces in 48 hours. The pharmacokinetics in patients with renal or hepatic impairment has not been characterised.

**Half-Life**

The biological myocardial half-life of technetium (99mTc) sestamibi is approximately 7 hours at rest and stress. The effective half-life (which includes biological and physical half-lives) is approximately 3 hours for the heart and approximately 30 minutes for the liver.

**Preclinical safety data**

In acute intravenous toxicity studies in mice, rats and dogs, the lowest dose of the reconstituted Sestamibi kit that resulted in any deaths was 7 mg/kg (expressed as Cu (MIBI), BF content) in female rats. This corresponds to 500 times the maximum human dose (MHD) of 0.014 mg/kg for adults (70 kg). Neither rats nor dogs exhibited treatment related effects at reconstituted Sestamibi 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), BF showed no genotoxic activity in the Ames, CHO/HPTRT 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. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: diagnostic radiopharmaceuticals, Technetium (99mTc) compounds, ATC code: V09GA01.

**Pharmacodynamic effects**

At the chemical concentrations used for diagnostic examinations, technetium (99mTc) sestamibi solution does not appear to have any pharmacodynamic activity.

**5.2 Pharmacokinetic properties**

After reconstitution with sodium pertechnetate (99mTc), the following technetium (99mTc) sestamibi complex is formed: [99mTc (MIBI)_2]+. Where: MIBI = 2-methoxyisobutyrylisonitrile

**Biodistribution**

Technetium (99mTc) sestamibi from the blood is rapidly distributed into the tissue: 5 minutes after injection only about 8% of the injected dose remains in the blood pool. In physiological distribution, evident concentration of technetium (99mTc) sestamibi can be seen in vivo in several organs. In particular, normal tracer uptake is evident in the salivary glands, thyroid, myocardium, liver, gallbladder, small and large intestine, kidneys, bladder, choroid plexuses and skeletal muscles, occasionally in the nipples. Faint homogeneous uptake in the breast or axilla is normal.

**Myocardial perfusion scintigraphy**

Technetium (99mTc) sestamibi is a cationic complex which diffuses passively through the capillary and cell membrane. Within the cell it is localised in the mitochondria, where it is trapped, and retention is based on intact mitochondria, reflecting viable myocytes. After intravenous injection, it is distributed within the myocardium according to myocardial perfusion and viability. 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. Irreversibly damaged cells however do not take up technetium (99mTc) sestamibi. The myocardial extraction level is reduced by hypoxia. It has very little redistribution and so separate injections are required for stress and resting studies.

**Scintimammography**

The tissue uptake of technetium (99mTc) sestamibi depends primarily on the vascularisation which is generally increased in tumor tissue. Technetium (99mTc) sestamibi accumulates in various neoplasms and most markedly in mitochondria. Its uptake is related to increased energy-dependent metabolism and cell proliferation. Its cellular accumulation is reduced when multidrug resistance proteins are overexpressed.

**Parathyroid imaging of hyperfunctioning tissue**

Technetium (99mTc) sestamibi localises in both parathyroid tissue and functioning thyroid tissue but usually washes out of normal thyroid tissue more rapidly than out of abnormal parathyroid tissue.

**Elimination**

Elimination of technetium (99mTc) sestamibi occurs mostly through the kidneys and the hepatobiliary system.

Activity of technetium (99mTc) sestamibi 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. The pharmacokinetics in patients with renal or hepatic impairment has not been characterised.

**Skin and subcutaneous tissue disorders:**
- Rare: reactions at the injection site, alopecia and paraesthesia, flushing.
- Not known: Erythema multiforme.

**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, dyspepsia.

**Cardiac disorders**
- Rare: Seizures (shortly after administration), syncope.

**Gastrointestinal disorders**
- Uncommon: Chest pain/angina pectoris, abnormal ECG.
- Rare: Arrhythmia.

**Other disorders**
- Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is 16.4 mSv when the maximal recommended activity of 2000 MBq (500 at rest and 1500 MBq at stress) for a 1-day-protocol is administered, these adverse reactions are expected to occur with a low probability.

**Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

**Yellow Card Scheme**
- Website: www.mhra.gov.uk/yellowcard

**0.7% of the injected dose is cleared through the faeces in 48 hours. The pharmacokinetics in patients with renal or hepatic impairment has not been characterised.**

**Half-Life**

The biological myocardial half-life of technetium (99mTc) sestamibi is approximately 7 hours at rest and stress. The effective half-life (which includes biological and physical half-lives) is approximately 3 hours for the heart and approximately 30 minutes for the liver.

**5.3 Preclinical safety data**

In acute intravenous toxicity studies in mice, rats and dogs, the lowest dose of the reconstituted Sestamibi kit that resulted in any deaths was 7 mg/kg (expressed as Cu (MIBI), BF 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 Sestamibi 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), BF showed no genotoxic activity in the Ames, CHO/HPTRT 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

Cysteine hydrochloride monohydrate
6.2 Incompatibilities
This medicinal product must not be mixed with other medicinal products except those mentioned in section 12.

6.3 Shelf life
2 years.
After radiolabelling: 10 hours. Do not store above 25°C after radiolabelling.

6.4 Special precautions for storage
Do not store above 25°C. Keep the vials in the outer carton in order to protect from light.
For storage conditions after radiolabelling of the medicinal product, see section 6.3.
Storage of radiopharmaceuticals should be in accordance with national regulations for radioactive materials.

6.5 Nature and contents of container
10 ml multi-dose glass vials, type 1 borosilicate glass (Ph. Eur.) sealed with a chlorobutyl rubber stopper.
Pack size: 5 vials.

6.6 Special precautions for disposal and other handling
General warnings
Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/ or appropriate licences of the competent official organisation.

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

Contents of the vial are intended only for use in the preparation of technetium (technetium) sestamibi and are not to be administered directly to the patient without first undergoing the preparative procedure.

For instructions on extemporary preparation of the medicinal product before administration, see section 12.

If at any time in the preparation of this product the integrity of this vial is compromised it should not be used.
Administration procedures should be carried out in a way to minimise risk of contamination of the medicinal product and irradiation of the operators. Adequate shielding is mandatory.
The content of the kit before extemporary preparation is not radioactive. However, after sodium pertechnetate (Na99mTc), 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 or any other biological fluids. Radiation protection precautions in accordance with national regulations must therefore be taken.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements for radioactive materials.

7. MARKETING AUTHORISATION HOLDER
Malinckrodt Medical B.V.
Westerduinweg 3
1755 LE Petten,
The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)
PL 12288/0002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
Date of first authorisation: 15/09/2008
Date of latest renewal: 08/05/2013

10. DATE OF REVISION OF THE TEXT
10/07/2014

11. DOSIMETRY
Technetium (99mTc) is produced by means of a (99Mo/99mTc) 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 (99mTc) which, in view of its long half-life of 2.13 x 105 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 taken up predominantly mainly in muscular tissues (including heart), liver, and kidneys, with 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 heart and skeletal muscles, with a correspondingly lower uptake in all other organs and tissues. The substance is excreted by the liver and kidneys in the proportions 75% and 25%, respectively.

Absorbed dose per unit activity administered (mGy/MBq) (Resting subject)

<table>
<thead>
<tr>
<th>Organ</th>
<th>Adult</th>
<th>15-years</th>
<th>10-years</th>
<th>5-years</th>
<th>1-year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenals</td>
<td>0.075</td>
<td>0.0099</td>
<td>0.015</td>
<td>0.022</td>
<td>0.033</td>
</tr>
<tr>
<td>Bladder</td>
<td>0.011</td>
<td>0.014</td>
<td>0.019</td>
<td>0.023</td>
<td>0.041</td>
</tr>
<tr>
<td>Bone surfaces</td>
<td>0.0082</td>
<td>0.010</td>
<td>0.016</td>
<td>0.021</td>
<td>0.038</td>
</tr>
<tr>
<td>Brain</td>
<td>0.0052</td>
<td>0.0071</td>
<td>0.011</td>
<td>0.016</td>
<td>0.027</td>
</tr>
<tr>
<td>Breast</td>
<td>0.0038</td>
<td>0.0053</td>
<td>0.0071</td>
<td>0.011</td>
<td>0.020</td>
</tr>
<tr>
<td>Gall bladder</td>
<td>0.039</td>
<td>0.045</td>
<td>0.058</td>
<td>0.10</td>
<td>0.32</td>
</tr>
<tr>
<td>Gastrointestinal tract</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stomach</td>
<td>0.0065</td>
<td>0.0090</td>
<td>0.015</td>
<td>0.021</td>
<td>0.035</td>
</tr>
<tr>
<td>Small intestine</td>
<td>0.015</td>
<td>0.018</td>
<td>0.029</td>
<td>0.045</td>
<td>0.080</td>
</tr>
<tr>
<td>Colon</td>
<td>0.024</td>
<td>0.031</td>
<td>0.050</td>
<td>0.079</td>
<td>0.15</td>
</tr>
<tr>
<td>Upper large intestine</td>
<td>0.027</td>
<td>0.035</td>
<td>0.057</td>
<td>0.089</td>
<td>0.17</td>
</tr>
<tr>
<td>Lower large intestine</td>
<td>0.019</td>
<td>0.025</td>
<td>0.041</td>
<td>0.065</td>
<td>0.12</td>
</tr>
<tr>
<td>Heart</td>
<td>0.0063</td>
<td>0.0082</td>
<td>0.012</td>
<td>0.018</td>
<td>0.030</td>
</tr>
<tr>
<td>Kidneys</td>
<td>0.036</td>
<td>0.043</td>
<td>0.059</td>
<td>0.085</td>
<td>0.15</td>
</tr>
<tr>
<td>Liver</td>
<td>0.011</td>
<td>0.014</td>
<td>0.021</td>
<td>0.030</td>
<td>0.052</td>
</tr>
<tr>
<td>Lungs</td>
<td>0.0046</td>
<td>0.0064</td>
<td>0.0097</td>
<td>0.014</td>
<td>0.025</td>
</tr>
<tr>
<td>Muscles</td>
<td>0.0029</td>
<td>0.0037</td>
<td>0.0054</td>
<td>0.0076</td>
<td>0.014</td>
</tr>
<tr>
<td>Oesophagus</td>
<td>0.0041</td>
<td>0.0057</td>
<td>0.0086</td>
<td>0.013</td>
<td>0.023</td>
</tr>
<tr>
<td>Ovaries</td>
<td>0.0091</td>
<td>0.012</td>
<td>0.018</td>
<td>0.025</td>
<td>0.045</td>
</tr>
<tr>
<td>Pancreas</td>
<td>0.0077</td>
<td>0.010</td>
<td>0.016</td>
<td>0.024</td>
<td>0.039</td>
</tr>
<tr>
<td>Red marrow</td>
<td>0.0055</td>
<td>0.0071</td>
<td>0.011</td>
<td>0.030</td>
<td>0.044</td>
</tr>
<tr>
<td>Salivary glands</td>
<td>0.014</td>
<td>0.017</td>
<td>0.022</td>
<td>0.015</td>
<td>0.026</td>
</tr>
<tr>
<td>Skin</td>
<td>0.0031</td>
<td>0.0041</td>
<td>0.0064</td>
<td>0.0098</td>
<td>0.019</td>
</tr>
<tr>
<td>Spleen</td>
<td>0.0065</td>
<td>0.0086</td>
<td>0.014</td>
<td>0.020</td>
<td>0.034</td>
</tr>
<tr>
<td>Testes</td>
<td>0.0038</td>
<td>0.0050</td>
<td>0.0075</td>
<td>0.011</td>
<td>0.021</td>
</tr>
<tr>
<td>Thymus</td>
<td>0.0041</td>
<td>0.0057</td>
<td>0.0086</td>
<td>0.013</td>
<td>0.023</td>
</tr>
<tr>
<td>Thyroid</td>
<td>0.0053</td>
<td>0.0079</td>
<td>0.012</td>
<td>0.024</td>
<td>0.045</td>
</tr>
<tr>
<td>Uterus</td>
<td>0.0078</td>
<td>0.010</td>
<td>0.015</td>
<td>0.022</td>
<td>0.038</td>
</tr>
<tr>
<td>Remaining organs</td>
<td>0.0031</td>
<td>0.0039</td>
<td>0.0060</td>
<td>0.0088</td>
<td>0.016</td>
</tr>
</tbody>
</table>

Effective dose (mSv/MBq) 0.0090 0.012 0.018 0.028 0.053
### Absorbed dose per unit activity administered (mGy/MBq)

<table>
<thead>
<tr>
<th>Organ</th>
<th>Adult</th>
<th>15-years</th>
<th>10-years</th>
<th>5-years</th>
<th>1-year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenals</td>
<td>0.0066</td>
<td>0.0087</td>
<td>0.013</td>
<td>0.019</td>
<td>0.033</td>
</tr>
<tr>
<td>Bladder</td>
<td>0.0098</td>
<td>0.013</td>
<td>0.017</td>
<td>0.021</td>
<td>0.036</td>
</tr>
<tr>
<td>Bone surfaces</td>
<td>0.0078</td>
<td>0.0097</td>
<td>0.014</td>
<td>0.020</td>
<td>0.030</td>
</tr>
<tr>
<td>Brain</td>
<td>0.0044</td>
<td>0.0060</td>
<td>0.0093</td>
<td>0.014</td>
<td>0.023</td>
</tr>
<tr>
<td>Breast</td>
<td>0.0034</td>
<td>0.0047</td>
<td>0.0062</td>
<td>0.0097</td>
<td>0.018</td>
</tr>
<tr>
<td>Gall bladder</td>
<td>0.033</td>
<td>0.038</td>
<td>0.049</td>
<td>0.086</td>
<td>0.26</td>
</tr>
</tbody>
</table>

### Gastrointestinal tract:

<table>
<thead>
<tr>
<th>Target Organ</th>
<th>Absorbed Dose (mGy/MBq)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomach</td>
<td>0.0059</td>
</tr>
<tr>
<td>Small intestine</td>
<td>0.012</td>
</tr>
<tr>
<td>Colon</td>
<td>0.019</td>
</tr>
<tr>
<td>Upper large intestine</td>
<td>0.022</td>
</tr>
<tr>
<td>Lower large intestine</td>
<td>0.016</td>
</tr>
</tbody>
</table>

#### Heart:

- Adult: 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, 0.027
- Pancreas: 0.0069, 0.0091, 0.014, 0.021, 0.035
- Red marrow: 0.0050, 0.0064, 0.0095, 0.013, 0.023
- Svalary glands: 0.0092, 0.011, 0.015, 0.020, 0.029
- Skin: 0.0079, 0.0093, 0.014, 0.020, 0.035
- Spleen: 0.0058, 0.0076, 0.012, 0.017, 0.030
- Testes: 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
- Remaining organs: 0.0033, 0.0043, 0.0064, 0.0098, 0.018

#### Effective dose (mSv/MBq)

- Cardiac imaging: 0.0079, 0.010, 0.016, 0.023, 0.045
- Parathyroid imaging: 0.0079, 0.010, 0.016, 0.023, 0.045

---

### Instructions for Preparation of Technetium (99mTc) Sestamibi

**Preparation of technetium (99mTc) sestamibi from the Technescan MIBI Kit**

1. The kit contains sodium pertechnetate (Na99mTcO4) solution max. 11.1 GBq in approximately 1 to 3 ml. Not more than 3 ml sodium pertechnetate (99mTc) solution will be used for the maximum activity of 11.1 GBq.

2. If the integrity of this vial is compromised, the product should not be used.

3. For Preparation of technetium (99mTc) sestamibi

4. Preparation of technetium (99mTc) sestamibi from the Technescan MIBI Kit 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:

#### Method of preparation

1. **Boiling procedure:**
   - Waterproof gloves should be worn during the preparation procedure. Remove the flip-off cap from the Technescan MIBI Kit vial and swab the top of the vial closure with alcohol to disinfect the surface.
   - Place the vial in a suitable radiation shield appropriately labelled with date, time of preparation, volume and activity.
   - With a sterile shielded syringe, aseptically obtain additive-free, sterile, non-pyrogenic sodium pertechnetate (99mTc) solution max. 11.1 GBq in approximately 1 to 3 ml. Not more than 3 ml sodium pertechnetate (99mTc) solution will be used for the maximum activity of 11.1 GBq.
   - Aseptically add the sodium pertechnetate (99mTc) 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.
   - Shake vigorously, about 5 to 10 quick upward-downward motions.

2. **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.

3. **Remove the shielded vial from the water bath and allow cooling for fifteen minutes.**

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

5. **If needed, a dilution with 0.9% saline solution is possible.**

6. **Aseptically withdraw material using a sterile shielded syringe. 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 a water bath where the stopper will be above the level of the water.**

11. **Remove the shielded vial from the water bath and allow cooling for fifteen minutes.**

---

### 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 Technescan MIBI 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 (99mTc) solution max. 11.1 GBq in approximately 3 ml. Not more than 3 ml sodium pertechnetate (99mTc) solution will be used for the maximum activity of 11.1 GBq.
4. Aseptically add the sodium pertechnetate (99mTc) 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 10 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.

Quality control

Radio-TLC Method for the Quantification of Technetium (99mTc) 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 0.7 - 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:
   % (99mTc) Sestamibi = (Activity top portion)/(Activity both pieces) x 100.
2.7 % (99mTc) Sestamibi should be ≥ 94%; otherwise the preparation should be discarded.

Note: Do not use material if the radiochemical purity is less than 94%.
Read all of this leaflet carefully before you are given this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your nuclear medicine doctor who will supervise the procedure.
- If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:
1. What Technescan MIBI is and what it is used for
2. What you need to know before Technescan MIBI is used
3. How Technescan MIBI is used
4. Possible side effects
5. How Technescan MIBI is stored
6. Contents of the pack and other information

1. WHAT TECHNESCAN MIBI IS AND WHAT IT IS USED FOR

This medicine is a radiopharmaceutical product for diagnostic use only. Technescan MIBI contains a substance called [tetraakis(2-methoxy-2-methylpropyl-1 isocyanide)copper(II)] tetrafluoroborate which is used to study the heart function and blood flow (myocardial perfusion) by making an image of the heart (scintigraphy), for example in the detection of heart attacks (myocardial infarctions) or when a disease causes reduced blood supply to (a part of) the heart muscle (ischaemia). Technescan MIBI is also used in the diagnosis of breast abnormalities in addition to other diagnostic methods when the results are unclear. Technescan MIBI can also be used to find the position of overactive parathyroid glands (glands that secrete the hormone that controls blood calcium levels).

After Technescan MIBI is injected, it temporarily collects in certain parts of the body. This radiopharmaceutical substance contains a small amount of radioactivity, which can be detected from outside of the body by using special cameras. Your nuclear medicine doctor will then take an image (scintigraphy) of the concerned organ which can give your doctor valuable information about the structure and the function of this organ or the location of e.g., a tumour.

The use of Technescan MIBI does involve exposure to small amounts of radioactivity. Your doctor and the nuclear medicine doctor have considered that the clinical benefit that you will obtain from the procedure with the radiopharmaceutical outweighs the risk due to radiation.

2. WHAT YOU NEED TO KNOW BEFORE TECHNESCAN MIBI IS USED

Technescan MIBI must not be used
- if you are allergic to tetrakis (1-isocyanide-2-methoxy-2-methylpropyl-) copper(II) tetrafluoroborate or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Take special care with Technescan MIBI
- if you are pregnant or believe you may be pregnant,
- if you are breastfeeding,
- if you have a kidney or liver disease.

You should inform your nuclear medicine doctor in case those apply to you. Your nuclear medicine doctor will inform you if you need to take any special precautions after using this medicine. Talk to your nuclear medicine doctor if you have any questions.

Before administration of Technescan MIBI you should
- be fasting for at least 4 hours if the product is going to be used to perform images of your heart,
- drink plenty of water before the start of the examination in order to urinate as often as possible during the first hours after the study.
4. POSSIBLE SIDE EFFECTS

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

Allergic reactions possibly with shortness of breath, extreme tiredness, being sick (usually within 2 hours after administration), swelling beneath the skin that can occur in areas such as the face and limbs (angioedema), and obstruct the airway, or leading to a dangerous decrease of blood pressure (hypotension) and slow heart beat (bradycardia) have been seen rarely.

Airway, or leading to a dangerous decrease of blood pressure (hypotension) and slow heart beat (bradycardia) have been seen rarely.

Other possible side effects are listed in the order of their frequency below:

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Possible side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>common: may affect up to 1 in 10 people</td>
<td>Metallic or bitter taste, smell alteration, and dry mouth immediately after injection.</td>
</tr>
<tr>
<td>uncommon: may affect up to 1 in 100 people</td>
<td>Headache, chest pain, abnormal ECG and feeling sick.</td>
</tr>
<tr>
<td>rare: may affect up to 1 in 1,000 people</td>
<td>Abnormal heart rhythm, local reactions at the injection site, stomach ache, fever, fainting, seizures, dizziness, flushing, skin numbness or tingling, tiredness, joint pains and stomach upset (dyspepsia).</td>
</tr>
<tr>
<td>not known: frequency cannot be estimated from the available data</td>
<td>Erythema multiforme, a widespread rash of skin and mucosa.</td>
</tr>
</tbody>
</table>

This radiopharmaceutical will deliver low amounts of ionising radiation associated with the least risk of cancer and hereditary abnormalities.

Reporting of side effects

If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system:

Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard
By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TECHNESCAN MIBI IS STORED

You will not have to store this medicine. This medicine is stored under the responsibility of the specialist in appropriate premises. Storage of radiopharmaceuticals will be in accordance with national regulation on radioactive materials.

The following information is intended for the specialist only.

This medicine must not be used after the expiry date, which is stated on the label.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Technescan MIBI contains

- The active substance is [Tetrakis(2-methoxy-2-methylpropyl-1 isocyanide)copper(I)] tetrafluoroborate.
- One vial contains 1 mg [Tetrakis(2-methoxy-2-methylpropyl-1 isocyanide)copper(I)] tetrafluoroborate.
- The other ingredients are stannous chloride dihydrate, cysteine hydrochloride monohydrate, sodium citrate, mannitol, hydrochloric acid and sodium hydroxide.

What Technescan MIBI looks like and contents of the pack

The product is a kit for radiopharmaceutical preparation.

Technescan MIBI consists of white to almost white pellets or powder which has to be dissolved in a solution and combined with radioactive technetium before use as an injection. Once the radioactive substance sodium pertechnetate \((^{99m}\text{Tc})\) is added to the vial, technetium \((^{99m}\text{Tc})\) sestamibi is formed. This solution is ready for injection.

Pack size
5 multi-dose vials

Marketing Authorisation Holder and Manufacturer
Mallinckrodt Medical B.V.
Westerduinweg 3
1755 LE PETTEN, The Netherlands

This leaflet was last revised in July 2014.