After administration of Myoview, you should:
- urinate frequently in order to eliminate the product from your body.

The nuclear medicine doctor will inform you if you need to take any special precautions after receiving this medicine. Contact the nuclear medicine doctor if your have any questions.

4. Possible side effects

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

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

Serious side effects
If you have an allergic reaction when you are in hospital or a clinic having the scan, tell the nuclear medicine doctor straight away. The signs and symptoms may include:

Uncommon – may affect up to 1 in 100 people
- Flushing

Rare – may affect up to 1 in 1000 people
- skin rash

Not known – frequency cannot be estimated from the available data
- itching, redness or hives
- swelling of the face, local swelling
- difficulty breathing, wheezing, throat tightness, coughing

In more severe cases(severe allergic reaction or anaphylaxis), reactions may include:
- passing out (unconsciousness), feeling dizzy or lightheaded.

If any of the side effects above happen after you leave the hospital or clinic, go straight to the casualty department of your nearest hospital.

Other side effects include
Uncommon – may affect up to 1 in 100 people
- changes in taste, such as a metallic taste
- uncomfortable feeling of warmth beginning where the injection was given
- vomiting

Rare – may affect up to 1 in 1000 people
- changes in smell
- visual impairment
- abdominal pain, feeling sick (nausea), burning sensation in mouth

Not known – frequency cannot be estimated from the available data
- headache, dizziness
- heart pounding (palpitations), chest pain
- fever
- white blood cell count increased (seen in certain types of blood test)

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

5. How to store Myoview

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 the national regulations for radioactive materials.

Hospital staff will ensure that the product is stored and disposed of correctly and not used after the expiry date stated on the label.

This following information is intended for healthcare or medical professionals only.

Keep this medicine out of the sight and reach of children
- Do not use Myoview after the expiry date which is stated on the label, after EXP.
- Store the product in a refrigerator at 2-8°C. Store in the original package in order to protect from light.
- Chemical and physical in-use stability of the reconstituted solution for injection has been demonstrated for 12 hours at 2°C-25°C. Store the reconstituted product below 25°C. Do not freeze.

6. Contents of the pack and other information

This following information is intended for healthcare or medical professionals only

What Myoview contains
- The active ingredient is tetrofosmin. Each vial of Myoview contains 230 micrograms of tetrofosmin.
- The other ingredients are stannous chloride dihydrate, disodium sulphosalicylate, sodium D-gluconate and sodium hydrogen carbonate.

What Myoview looks like and contents of the pack
Myoview is a kit for radio-pharmaceutical preparation, it is supplied as a single colourless glass vial containing a powder for solution for injection. Pack sizes of
2 or 5 vials are available, not all pack sizes may be marketed.

Marketing Authorisation Holder
GE Healthcare Limited, Pollards Wood, Nightingales Lane, Chalfont St Giles, Buckinghamshire, HP8 4SP, United Kingdom.

Manufacturer
GE Healthcare AS
Nycoveien 1
NO-0485 Oslo
Norway

This leaflet was last revised in
May 2024.

Marketing Authorisations
PL 00221/0142

GE Healthcare

PATIENT INFORMATION

MYOVIEW™
230 micrograms kit for radiopharmaceutical preparation

Tetrofosmin

1206680

1206680 GBR

PACKAGE LEAFLET: INFORMATION FOR THE USER

Myoview 230 micrograms kit for radiopharmaceutical preparation

Tetrofosmin

Read all of this leaflet carefully before you are given Myoview, 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.
- 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.

In this leaflet:

1. What Myoview is and what it is used for

This medicine is for diagnostic use only. It is used only to help identify illness.

Myoview is a 'radio-pharmaceutical' medicine. It is given before a scan and helps a special camera see inside a part of your body.

- It contains an active ingredient called 'tetrofosmin'. This is mixed with a radioactive ingredient called 'technetium 99m' before it is used.
- Once injected it can be seen from outside your body by a special camera used in the scan.
- The scan can help your nuclear medicine doctor see how well the heart is working, or see damage to the heart after a heart attack.
- Some other people are given this medicine before a scan to look at lumps in the breast.

Your nuclear medicine doctor will explain which part of your body will be scanned.

The use of Myoview 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. Ask your nuclear medicine doctor if you have any questions.

2. What you need to know before you are given Myoview

Do not use Myoview:

- If you are allergic (hypersensitive) to Myoview or any other ingredient (listed in Section 6).
- If you are pregnant or think you might be pregnant.

Do not take Myoview if any of the above applies to you. If you are not sure talk to your nuclear medicine doctor.

Warnings and Precautions

Talk to your nuclear medicine doctor before using Myoview:

- If the person who will be given this medicine is a child or adolescent.
- If you have missed your last period. This may indicate that you are pregnant and therefore unable to be given Myoview (see section Pregnancy and breast-feeding).
- If you are on a low sodium diet.
- If you are breast-feeding.

Before administration of Myoview you should:

Drink plenty of water before the start of the examination in order to urinate as often as possible during the first hours after the scan.

Children and adolescents

Efficacy and safety in patients below 18 years has not been established.

Other medicines and Myoview

Please tell your nuclear medicine doctor, who will supervise the procedure, if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. This includes herbal medicines. This is because some medicines can affect the way Myoview works.

If you are having a heart scan tell your nuclear medicine doctor if you are taking any of the types of medicine below.

This is because they may affect the results of your scan:

- Beta blockers such as atenolol, bisoprolol or propranolol.
- Calcium channel blockers such as nifedipine, diltiazem or felodipine.
- Nitrates such as glyceryl trinitrate, isosorbide mononitrate or isosorbide dinitrate.
- Any medicines for your blood pressure, your heart or heart failure.

If you are not sure if any of the above applies to you, talk to your nuclear medicine doctor before having Myoview.

Having Myoview with food and drink

If you are having:

- A **heart scan** - you may be asked not to eat the night before. Or you may be asked to have only a light breakfast on the morning of the scan.
- A **breast scan** - you can eat and drink liquids normally.

Pregnancy and breast-feeding

You should not be given Myoview if you are pregnant or think you may be pregnant. This is because it may affect the baby.

Do not breast-feed if you are given Myoview. This is because small amounts of 'radioactivity' may pass into the mother's milk. If you are breast-feeding, your nuclear medicine doctor may wait until you have finished breast-feeding before using Myoview. If it is not possible to wait, your nuclear medicine doctor will ask you to:

- stop breast-feeding for 3 to 6 hours, and
- use formula feed for your child, and
- express (remove) breast milk and throw away the milk.

Your nuclear medicine doctor will let you know when you can start breast-feeding again.

Driving and using machines

It is considered unlikely that Myoview will affect your ability to drive or to use machines. Ask your nuclear medicine doctor if you can drive or use machines after you have been given Myoview.

Myoview contains sodium

This medicine contains 15 – 29 mg sodium (main component of cooking/table salt) per reconstituted vial. This is equivalent to 0.7 – 1.4% of the recommended maximum daily dietary intake of sodium for an adult.

When Myoview is used you are exposed to radioactivity.

- Your nuclear medicine doctor will always consider the possible risks and benefits before you are given the medicine.

Ask your nuclear medicine doctor if you have any questions.

3. How to use Myoview

There are strict laws on the use, handling and disposal of radiopharmaceutical products.

Myoview will be given to you by a specially trained and qualified person.

- Myoview will always be used in a hospital or clinic.
- They will tell you anything you need to know for its safe use.

The dose you are given depends on the type of scan you are having. Your nuclear medicine doctor will decide on the dose that is best for you. It will be the smallest dose necessary to get the desired information.

Administration of Myoview and conduct of the procedure

For a heart scan the usual dose is:

- One injection after you have rested.
- A second injection (after at least one hour), when your heart is working harder than normal. Such as during or just after exercise.

The order of the two injections may be the opposite way round for some people. Other people only need one injection. In some cases your nuclear medicine doctor may decide that it is best to give the two injections on separate days.

For a breast scan the usual dose is:

- One single injection.

If you are given more Myoview than you should

Myoview is given in a hospital or clinic by a specially trained and qualified person. It is unlikely that you will be given too much. However, in the case of an overdose, you will receive the appropriate treatment.

If you have any concerns talk to your nuclear medicine doctor.

Duration of the procedure

Your nuclear medicine doctor will inform you about the usual duration of the procedure.

PACKAGE LEAFLET: INFORMATION FOR HEALTHCARE PROFESSIONAL

1 NAME OF THE MEDICINAL PRODUCT

MYOVIEW 230 micrograms kit for radiopharmaceutical preparation.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains 230 micrograms of tetrofosmin.

Excipients with known effect:

The reconstituted vial contains 15-29 mg sodium.

For a full list of excipients, see section 6.1.

Myoview is reconstituted with Sodium Pertechnetate (^{99m}Tc) Injection Ph.Eur. (not included in this kit) to prepare technetium (^{99m}Tc) tetrofosmin injection.

3 PHARMACEUTICAL FORM

Kit for radiopharmaceutical preparation.

A white powdery solid.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

After reconstitution with Sodium Pertechnetate (^{99m}Tc) Injection the product is indicated in adults for:

Myocardial Imaging

Myoview is a myocardial perfusion agent indicated as an adjunct in the diagnosis and localization of myocardial ischaemia and/or infarction.

In patients undergoing myocardial perfusion scintigraphy, ECG-gated SPECT can be used for assessment of left ventricular function (left ventricular ejection fraction and wall motion).

Breast Tumour Imaging

Myoview is indicated as an adjunct to the initial assessments (e.g. palpation, mammography, or alternative imaging modalities and/or cytology) in the characterisation of malignancy of suspected breast lesions where all these other recommended tests were inconclusive.

4.2 Posology and method of administration

Posology

Paediatric population

Myoview is not recommended for use in children or adolescents as data are not available for these age groups.

Adults

Myocardial Imaging

Patients should be requested to fast overnight or to have only a light breakfast on the morning of the procedure.

For diagnosis and localization of myocardial ischaemia (using planar or SPECT techniques) and assessment of left ventricular function using ECG-gated SPECT, the usual procedure involves two intravenous injections of tetrofosmin (^{99m}Tc), one given at peak stress and one given at rest. The order of the two administrations can be either rest first and stress second or stress first and rest second.

When rest and stress injections are administered on the same day, the activity administered for the second dose should result in a myocardial count rate at least three times greater than that of the residual activity from the first dose. The recommended activity range for the first dose is 250-400 MBq; the recommended activity range for the second dose given at least 1 hour later, is 600-800 MBq. For studies employing ECG-gated SPECT, use of activities at the higher end of these ranges is warranted.

When rest and stress injections are administered on different days, the recommended activity range for each dose of tetrofosmin (^{99m}Tc) is 400-600 MBq. For studies on larger individuals (e.g. those with abdominal obesity or women with large breasts) and for those employing ECG-gated SPECT, use of activities at the higher end of this range is warranted.

The total activity administered for stress and rest myocardial imaging studies, whether performed on one or two days, should be restricted to 1200 MBq.

Based upon clinical trial data a minimum activity of 550 MBq has been shown to be adequate for ECG-gated SPECT. The activity administered for ECG-gated SPECT myocardial imaging should adhere to the guidelines specified in the previous paragraphs.

As an adjunct in the diagnosis and localization of myocardial infarction, one injection of tetrofosmin (^{99m}Tc) (250-400 MBq) at rest is sufficient.

Planar or preferably SPECT imaging should begin no earlier than 15 minutes post-injection.

There is no evidence for significant changes in myocardial concentration or redistribution of tetrofosmin (^{99m}Tc). Therefore, images may be acquired up to at least four hours postinjection.

For planar imaging the standard views (anterior, LAO 40°-45°, LAO 65°-70° and/or left lateral) should be acquired.

Breast Imaging

For the diagnosis and localization of suspected breast lesions, the recommended procedure involves a single intravenous injection of tetrofosmin (^{99m}Tc) between 500– 750 MBq. The injection should preferably be given in a foot vein or a site other than the arm on the side of the suspected breast lesion. The patient does not need to fast before the injection.

Breast imaging optimally initiated 5 – 10 minutes post injection with the patient in the prone position with the breast(s) freely pendant. A special imaging couch designed for nuclear medicine breast imaging is recommended. A lateral image of the breast suspected of containing lesions should be obtained with the camera face as close to the breast as is practicable.

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

Method of administration

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

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

For patient preparation, see section 4.4

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Must not be given during pregnancy (see section 4.6).

4.4 Special warnings and precautions for use

Potential for hypersensitivity or anaphylactic reactions

The possibility of hypersensitivity including anaphylactic/anaphylactoid reactions should always be considered. Advanced life support facilities should be readily available.

Paediatric population

Paediatric population, see section 4.2.

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 impairment and hepatic impairment

Careful consideration of the benefit risk ratio in these patients is required since an increased radiation exposure is possible.

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.

Breast lesions less than 1 cm in diameter may not all be detected with scintimammography as the sensitivity of Myoview for the detection of these lesions is 36% (n=5 of 14,95% CI 13% to 65%) relative to histological diagnosis. A negative examination does not exclude breast cancer especially in such a small lesion.

Efficacy in the identification of axillary lesions has not been proven, consequently scintimammography is not indicated for staging breast cancer.

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

Precautions with respect to environmental hazard see section 6.6

Specific warnings

This medicinal product contains 15 – 29 mg sodium per reconstituted vial, equivalent to 0.7 – 1.4% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

4.5 Interaction with other medicinal products and other forms of interaction

No formal studies on the interaction of Myoview with other drugs have been performed. However, no interactions were reported in clinical studies in which Myoview was administered to patients receiving comedication. Drugs which influence myocardial function and/or blood flow, e.g. beta blockers, calcium antagonists or nitrates, can lead to false negative results in diagnosis of coronary artery disease. The results of imaging studies should always, therefore, be considered in the light of current medication.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

When it is necessary to administer radioactive medicinal products 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

Myoview is contraindicated in pregnancy (see section 4.3). Radionuclide procedures carried out on pregnant women also involve radiation doses to the foetus. Administration of 250 MBq tetrofosmin (^{99m}Tc) at exercise, followed by 750 MBq at rest results in an absorbed dose to the uterus of 8.1 mGy. A radiation dose above 0.5 mGy (equivalent to the exposure from annual background radiation) would be regarded as a potential risk to the foetus.

Breast feeding

Before administering a radiopharmaceuticals to a mother who is breast feeding consideration should be given to the possibility of delaying the administration of radionuclide until the mother has ceased breast feeding and to what is the most appropriate choice of radiopharmaceuticals, bearing in mind the secretion of activity in breast milk. Tetrofosmin (^{99m}Tc) is present in human milk in small amounts (<1% of maternal dose), If the administration is considered necessary, breastfeeding should be interrupted for 3 to 6 hours and the expressed feeds discarded.

Fertility

Animal reproductive toxicity studies have not been performed with this product.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects

Summary of the safety profile

The listed frequencies are based on internal clinical documentation comprising approximately 3000 patients.

The frequencies of the undesirable effects are defined as follows:

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) and not known (cannot be determined with the data available).

Adverse drug reactions following administration of tetrofosmin (^{99m}Tc) are very rare (less than 1 in 10,000).

The following undesirable effects are recognised for Myoview:

Immune system disorders
Not known: Hypersensitivity reactions, including anaphylactoid or anaphylactic reactions and anaphylactic or anaphylactoid shock.

Nervous system disorders
Uncommon: Taste metallic
Rare: Disturbances of smell
Not known: Headache, dizziness

Eye disorders
Rare: Abnormal vision

Cardiac disorders
Not known: Tachycardia, chest pain

Vascular disorders
Uncommon: Flushing,
Not known: Hypotension

Respiratory, thoracic and mediastinal disorders
Not known: Dyspnoea, bronchospasm, throat tightness, cough

Gastrointestinal disorders
Uncommon: Vomiting
Rare: Abdominal pain, nausea, burning mouth

Skin and subcutaneous tissue disorder
Rare: Rash
Not known: Urticaria, pruritus, erythema, angioedema

General disorders and administration site conditions
Uncommon: Feeling of warmth
Not known: Local swelling, face oedema, fever

Investigations
Not known: White blood cell count increased.

Some reactions were delayed by several hours following administration of tetrofosmin (^{99m}Tc). Isolated cases of serious reactions have been reported, including anaphylactic reaction (less than 1 in 100,000) and severe allergic reaction (single report).

Since the administered substance quantity is very low, the major risk is caused by the radiation. Exposure to ionising radiation is linked with cancer induction and a potential for developing hereditary defects.

As the effective dose is 8.5 mSv when the maximal recommended activity of 1200 MBq 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 Yellow Card Scheme, at

Website: www.mhra.gov.uk/yellowcard.

4.9 Overdose

In cases of overdosage of radioactivity frequent micturition and defaecation should be encouraged in order to minimize radiation dosage to the patient.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: diagnostic radiopharmaceuticals, cardiovascular system, technetium (^{99m}Tc) tetrofosmin, ATC Code: V09GA02.

Pharmacological effects are not expected following intravenous administration of reconstituted Myoview at the recommended dosage. Studies in animals have shown that myocardial uptake of tetrofosmin (^{99m}Tc) is linearly related to coronary blood flow, confirming the effectiveness of the complex as a myocardial perfusion imaging agent.

Based upon clinical experience with ECG-gated myocardial perfusion scintigraphy, this method can be used to monitor for changes (or stability) in left ventricular function over time. Reliability of such serial assessment is expected to be similar to that of other commonly used measurement techniques (e.g. ECG-gated blood-pool scintigraphy).

Limited data in animals show uptake of tetrofosmin (^{99m}Tc) into breast tumour cells.

5.2 Pharmacokinetic properties

Organ uptake

Myocardial uptake: Uptake in the myocardium is rapid, reaching a maximum of about 1.2% of injected dose with sufficient retention to allow imaging of the myocardium by planar or SPECT techniques from 15 minutes up to 4 hours post-administration.

Elimination

Tetrofosmin (^{99m}Tc) is rapidly cleared from the blood after intravenous injection; less than 5% of the administered activity remains in whole blood at 10 minutes post-injection. Background tissue clearance is rapid from lung and liver and activity is reduced in these organs following exercise, with enhanced sequestration in skeletal muscle. Approximately 66% of the injected activity is excreted within 48 hours post-injection, with approximately 40% excreted in the urine and 26% in the faeces.

Half-life

Sodium Pertechnetate (^{99m}Tc) Injection Ph.Eur. is produced by a [^{99}Mo/^{99m}Tc] generator. Technetium (^{99m}Tc) disintegrates with the emission of gamma radiation (energy 141 keV) and a half-life of 6.02 hours.

Renal/hepatic impairment

The pharmacokinetics in patients with renal or hepatic impairment has not been characterised.

5.3 Preclinical safety data

Acute toxicity studies employing Myoview at dosage levels of approximately 1050 times the maximum human single dose failed to reveal mortality or any significant signs of toxicity in rats or rabbits. In repeated dose studies some evidence of toxicity was observed in rabbits, but only at cumulative doses exceeding 10,000 times the maximum human single dose. In rats receiving these doses there was no significant evidence of toxicity. Studies on reproductive toxicity have not been conducted. Tetrofosmin showed no evidence of mutagenic potential *in vitro* or *in vivo* mutagenicity studies. Studies to assess the carcinogenic potential of Myoview have not been performed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Stannous chloride dihydrate
Disodium sulphosalicylate
Sodium D-gluconate
Sodium hydrogen carbonate

6.2 Incompatibilities
In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products except those mentioned in section 12.

6.3 Shelf life
The shelf-life of the packaged product is 52 weeks.
Chemical and physical in-use stability of the reconstituted solution for injection has been demonstrated for 12 hours at 2°C-25°C.

Store the reconstituted product below 25°C. Do not freeze.

6.4 Special precautions for storage
Store in a refrigerator (2°C-8°C). Store in the original package in order to protect from light.

For storage conditions of the reconstituted medicinal product, see section 6.3.

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

6.5 Nature and contents of container
The product is supplied in a 10 ml clear glass vial sealed with a chlorobutyl rubber closure and flip off overseal.

Pack sizes: 2 or 5 vials.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling
The reconstituted product is a clear colourless solution.

General warning
Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings. Its 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 (^{99m}Tc) tetrofosmin injection and are not to be administered directly to the patient without first undergoing the preparative procedure.

For instructions on reconstitution 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 reconstitution is not radioactive. However, after sodium pertechnetate (^{99m}Tc), Ph. Eur. is added, adequate shielding of the final preparation must be maintained.
The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spill of urine, vomiting etc. Radiation protection precautions in accordance with national regulations must therefore be taken.

After use, all materials associated with the preparation and administration of radiopharmaceuticals, including any unused product and its container, should be decontaminated or treated as radioactive waste and disposed of in accordance with the conditions specified by the local competent authority. Contaminated material must be disposed of as radioactive waste via authorised route.

7 MARKETING AUTHORISATION HOLDER
GE Healthcare Limited, Pollards Wood, Nightingales Lane, Chalfont St Giles, Buckinghamshire, HP8 4SP

8 MARKETING AUTHORISATION NUMBER(S)
PL 00221/0142

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
Date of first authorisation: 02 August 2001
Date of last renewal: 02 August 2009

10 DATE OF REVISION OF THE TEXT
May 2024

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 a mean energy of 140keV and a half life of 6.02 hours to technetium (^{99}Tc) which, in view of its long half life of 2.13 x 10^5 years can be regarded as quasi stable.
The estimated absorbed radiation doses to an average adult patient (70kg) from intravenous injections of tetrofosmin (^{99m}Tc) are listed below. The values are calculated assuming urinary bladder emptying at 3.5 hour intervals.
Frequent bladder emptying should be encouraged after dosing to minimize radiation exposure.
The table below shows the dosimetry according to ICRP Publication 128 (International Commission of Radiological Protection, Radiation Dose to Patients from Radiopharmaceuticals: A Compendium of Current Information Related to Frequently Used Substances, Ann ICRP 2015).

	Absorbed dose per unit of activity administered (mGy/MBq)	
Organ	**Exercise**	**Rest**
Adrenals	4.40E-03	4.20E-03
Bone surfaces	6.3E-03	5.8E-03
Brain	2.7E-03	2.3E-03
Breast	2.20E-03	1.80E-03
Gallbladder wall	2.7E-02	3.6E-02
Gastrointestinal tract		
Stomach wall	4.6E-03	4.5E-03
Small intestine wall	1.1E-02	1.5E-02
Colon wall	1.8E-02	2.4E-02
(Upper large intestine wall	2.0E-02	2.7E-02)
(Lower large intestine wall	1.5E-02	2.0E-02)
Kidneys	1.0E-02	1.3E-02
Liver	3.3E-03	4.0E-03
Lungs	3.2E-03	2.8E-03
Muscles	3.5E-03	3.3E-03
Oesophagus	3.3E-03	2.8E-03
Ovaries	7.7E-03	8.8E-03
Pancreas	5.0E-03	4.9E-03
Red marrow	3.9E-03	3.8E-03
Skin	2.2E-03	2.0E-03
Spleen	4.1E-03	3.9E-03
Testes	3.4E-03	3.1E-03
Thymus	3.3E-03	2.8E-03
Thyroid	4.7E-03	5.5E-03
Urinary bladder wall	1.4E-02	1.7E-02
Uterus	7.0E-03	7.8E-03
Remaining organs	3.8E-03	3.8E-03
Effective Dose (mSv/MBq)	**6.9 E-03**	**8.0 E-03**

^{99m}Tc-tetrofosmin is administered as two intravenous injections either rest first and stress second or stress first and rest second. The recommended activity range for the first dose is 250-400 MBq; the recommended activity range for the second dose given at least 1 hour later, is 600-800 MBq.
Myocardial Imaging
The effective dose resulting from administration of 800 MBq for an adult weighing 70 kg at rest is about 6.4 mSv. After exercise, the same administered activity results in a dose of 5.5 mSv.
For an administered activity of 800 mBq, the absorbed radiation dose for the resting subject in the heart is 3.8 mGy and after exercise is 4.2 mGy. The absorbed radiation dose in the urinary bladder wall(3.5 hour voiding) is 13.6 mGy at rest or 11.2 mGy after exercise.
Breast imaging
The effective dose resulting from the administration of 750 MBq for an adult weighing 70 kg at rest is about 6.0 mSv.
For an administered activity of 750 MBq, the absorbed radiation dose to the breast is 1.7 mGy. The absorbed radiation dose in the urinary bladder wall (3.5 hours voiding) is 12.8 mGy.

12 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS
Withdrawals should be performed under aseptic conditions. The vials must not be opened before disinfecting the stopper, the solution should be withdrawn via the stopper using a single dose syringe fitted with suitable protective shielding and a disposable sterile needle or using an authorised automated application system.
If the integrity of this vial is compromised, the product should not be used

Method of preparation
The following steps as detailed are critical and should be followed to ensure adequate preparation of the product.
Use aseptic technique throughout.
(1) Place the vial in a suitable shielding container and sanitize the rubber septum with the swab provided.
(2) Insert a sterile needle (the venting needle, see Note a) through the rubber septum. Using a shielded, 10 ml sterile syringe, inject the required activity of Sodium Pertechnetate (^{99m}Tc) Injection Ph.Eur. (appropriately diluted with 0.9% Sodium Chloride Injection BP) into the shielded vial (see Notes b to d). Before removing the syringe from the vial, withdraw 5 ml of gas from above the solution (see Note e). Remove the venting needle. Shake the vial to ensure complete dissolution of the powder.
(3) Incubate at room temperature for 15 minutes.
(4) During this time assay the total activity, complete the user label provided and attach it to the vial.
(5) Store the reconstituted injection below 25°C and do not freeze. Use within 12 hours of preparation. Dispose of any unused material and its container via an authorised route.

Notes:
(a) A needle of size 19G to 26G may be used.
(b) The Sodium Pertechnetate (^{99m}Tc) Injection Ph.Eur. used for reconstitution should contain less than 5ppm aluminium.
(c) The volume of diluted Sodium Pertechnetate (^{99m}Tc) Injection Ph.Eur. added to the vial must be in the range 4-8 ml.
(d) The radioactive concentration of the diluted Sodium Pertechnetate (^{99m}Tc) Injection Ph.Eur. must not exceed 1.5 GBq/ml when it is added to the vial.
(e) For preparation volumes of more than 6 ml, the remaining vial headspace is less than the 5 ml added air volume. In these cases, the withdrawal of a 5 ml volume of gas ensures that all of the vial headspace is replaced by air.
(f) The pH of the prepared injection is in the range 7.5-9.0.

Quality control
Radiochemical Purity (RCP) by ascending chromatography on TLC-SA (method 1).
Equipment and eluent
(1) Glass Microfiber Chromatography Paper impregnated with Silicic Acid (GMCP-SA) TLC strip (2cm x 20cm) – Do not heat activate
(2) Ascending chromatography tank and cover
(3) 65:35% v/v acetone : dichloromethane mixture (prepared fresh daily)
(4) 1ml syringe with 22-25G needle
(5) Suitable counting equipment
Method
(1) Pour the 65:35% v/v acetone:dichloromethane mixture into the chromatography tank to a depth of 1cm and cover the tank to allow the solvent vapour to equilibrate.
(2) Mark a Glass Microfiber Chromatography Paper impregnated with Silicic Acid (GMCP-SA) TLC strip with a pencil line at 3cm from the bottom and, using an ink marker pen, at 15cm from the pencil line. The pencil line indicates the origin where the sample is to be applied and movement of colour from the ink line will indicate the position of the solvent front when upward elution should be stopped.
(3) Cutting positions at 3.75cm and 12cm above the origin (Rf's 0.25 and 0.8 respectively) should also be marked in pencil.
(4) Using a 1ml syringe and needle, apply a 10µl sample of the prepared injection at the origin of the strip. Do not allow the applied sample to come into contact with the pencil mark. Do not allow the spot to dry. Place the strip in the chromatography tank immediately and replace the cover. Ensure that the strip is not adhering to the walls of the tank.

Note: A 10µl sample will produce a spot with a diameter of approximately 10mm. Different sample volumes have been shown to give unreliable radiochemical purity values.
(5) When the solvent reaches the ink line, remove the strip from the tank and allow it to dry.
(6) Cut the strip into 3 pieces at the marked cutting positions and measure the activity on each using suitable counting equipment. Try to ensure similar counting geometry for each piece and minimize equipment dead time losses.
(7) Calculate the radiochemical purity from:-

$$\%\text{RCP } (^{99m}\text{Tc-tetrofosmin}) = \frac{\text{Activity of centre piece}}{\text{Total activity of all 3 pieces}} \times 100$$

Note: Free (^{99m}Tc) pertechnetate runs to the top piece of the strip. Tetrofosmin (^{99m}Tc) runs to the centre piece of the strip. Reduced hydrolysed-^{99m}Tc and any hydrophilic complex impurities remain at the origin in the bottom piece of the strip.

Do not use material if the radiochemical purity is less than 90%.
Simplified Chromatographic Procedure for Rapid Quality Control (method 2):
Equipment and eluent
(1) Solid Phase Extraction (SPE) C18 cartridge (360 mg Sorbent, 55 – 105 µm particle size), e.g. Waters Sep-Pak® or equivalent)
(2) 3 x 10ml vials and caps, Labelled "A", "B" and C
(3) Lead pots
(4) 0.9% Sodium chloride
(5) Ethanol
(6) Dose calibrator
Method
Note: all loading steps (sample and solvents) must be performed using a slow flow rate (i.e. drop by drop application of the mobile phase). If the flow is too high, components may not interact sufficiently with the stationary phase which will give an inaccurate result for radiochemical purity.
1. Place the cartridge in the correct orientation (short end facing upwards) in a clamp stand and place behind a suitable lead shield
2. Place the vial labelled 'A' under the cartridge as a collection vial.
3. Condition the stationary phase by flushing with 2ml 0.9% Sodium Chloride collecting in vial 'A'.
4. Carefully load 25 - 50µL of the preparation onto the cartridge.
5. Elute the cartridge with 2ml 0.9% Sodium chloride, collecting the eluate in vial 'A'.
6. Cap vial 'A' and place in a shielded container. Cap and retain for measurement.
7. Place vial 'B' under the cartridge as a collection vial.
8. Elute the cartridge with 5ml ethanol, collecting the eluate in vial 'B'.
9. Cap vial 'B' and place in a shielded container. Cap and retain for measurement.
10. Remove the SPE cartridge using tweezers and place into vial 'C' and place in a shielded container. Cap and retain for measurement.
11. Measure the activity of each of the vials labelled A to C using a dose calibrator. Under the test conditions employed:

- Free ^{99m}Tc O_4- (pertechnetate) is eluted from the cartridge with 2ml 0.9% Sodium Chloride (Vial A)
- ^{99m}Tc - tetrofosmin is retained on the stationary phase and is eluted with 5ml ethanol (Vial B)
- Reduced hydrolysed ^{99m}Tc (RHT) and hydrophilic impurities remain on the cartridge (Vial C)

12. Calculate the % ^{99m}Tc-tetrofosmin as follows:

$$\%\text{ RCP } (^{99m}\text{Tc-tetrofosmin}) = \frac{\text{Activity in vial B}}{\text{Sum of activity in vial A + B + C}} \times 100$$

13. Do not use material if the radiochemical purity is less than 90%.

13 FURTHER INFORMATION
Manufacturers
GE Healthcare AS
Nycoveien 1, NO-0485 Oslo, Norway

GE Healthcare

HEALTHCARE PROFESSIONAL INFORMATION

MYOVIEW ™

230 micrograms kit for radiopharmaceutical preparation

Tetrofosmin

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Document: 1206681 GBR Version: 2 Draft: 2