

## SUMMARY OF PRODUCT CHARACTERISTICS

### 1 NAME OF THE MEDICINAL PRODUCT

**MYOVIEW™**

### 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One vial contains : Tetrofosmin 0.23mg.

For reconstitution with Sodium Pertechnetate [<sup>99m</sup>Tc] Injection (not included in this kit).

For excipients see 6.1.

### 3 PHARMACEUTICAL FORM

Powder for solution for injection – Radiopharmaceutical Kit.

### 4 CLINICAL PARTICULARS

#### 4.1 Indications

This medicinal product is for diagnostic use only.

##### **Myocardial Imaging**

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

##### **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

Lyophilisate for injection, intended for reconstitution with 4-8ml of sterile Sodium Pertechnetate [<sup>99m</sup>Tc] Injection Ph. Eur. at a radioactive concentration not exceeding 1.5 GBq/ml.

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

Instructions for use and handling are given in section 6.6.

##### **Myocardial Imaging**

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

For the diagnosis and localization of myocardial ischaemia the recommended procedure involves two intravenous injections of <sup>99m</sup>Tc-tetrofosmin. For adults and the elderly 185-250MBq is given at peak exercise, followed by 500-750MBq given at rest approximately 4 hours later. The activity administered should be restricted to 1000MBq in any one day.

As an adjunct in the diagnosis and localization of myocardial infarction, one injection of  $^{99m}\text{Tc}$ -tetrofosmin (185-250MBq) 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  $^{99m}\text{Tc}$ -tetrofosmin, therefore, images may be acquired up to at least four hours post-injection. 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  $^{99m}\text{Tc}$ -tetrofosmin 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.

### **4.3 Contra-indications**

Myoview is contraindicated in pregnancy (see Section 4.6) and in patients with known hypersensitivity to tetrofosmin or any of the excipients.

### **4.4 Special warnings and precautions for use**

Breast lesions less than 1cm 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.

Radiopharmaceutical agents should only be used by qualified personnel with the appropriate government authorisation for the use and manipulation of radionuclides. They may 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 local competent official organisations.

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.

### **4.5 Interaction with other medicinal products and other forms of interaction**

The interaction of Myoview with other drugs has not been systematically investigated, 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 Pregnancy and lactation**

Myoview is contraindicated in pregnancy. Animal reproductive toxicity studies have not been performed with this product. Radionuclide procedures carried out on pregnant women also involve radiation doses to the foetus. Administration of  $^{99m}\text{Tc}$ -tetrofosmin at doses of 250MBq at exercise, followed by 750MBq at rest results in an absorbed dose to the uterus of 8.1mGy. A radiation dose above 0.5mGy (equivalent to the exposure from annual background radiation) would be regarded as a potential risk to the foetus.

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.

Before administering a radioactive medicinal product to a mother who is breast feeding consideration should be given as to whether the investigation could be reasonably delayed until the mother has ceased breast feeding and as to whether the most appropriate choice of radiopharmaceutical has been made, bearing in mind the secretion of activity in breast milk. It is not known whether  $^{99m}\text{Tc}$ -tetrofosmin is secreted in human milk, therefore if administration is considered necessary, formula feeding should be substituted for breast feeding for at least 12 hours.

#### **4.7 Effects on ability to drive and use machines**

Myoview has no influence on the ability to drive or use machines.

#### **4.8 Undesirable Effects**

Adverse drug reactions following administration of  $^{99m}\text{Tc}$ -tetrofosmin are very rare (<0.01%). A few patients have experienced a feeling of bodily warmth, vomiting (12-24 hours post-injection), headache, dizziness, a transient metallic taste, disturbance of smell or a mild burning sensation in the mouth after injection. In addition, hypersensitivity reactions have occurred including flushing, itching, urticarial or erythematous rash, facial oedema, hypotension and dyspnoea. Some reactions were delayed by several hours following administration of  $^{99m}\text{Tc}$ -tetrofosmin. Transient rises in white blood cell counts have also been reported in a small number of patients. Isolated cases of serious reactions have been reported, including anaphylactic reaction (<0.001%) and severe allergic reaction (single report).

For each patient, exposure to ionising radiation must be justifiable 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 result. Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. For diagnostic nuclear medicine investigations the current evidence suggests that these adverse events will occur with negligible frequency because of the low radiation dose incurred.

For most diagnostic investigations using a nuclear medicine procedure the radiation dose (ED) delivered is less than 20mSv. Higher doses may be justified in some clinical circumstances.

#### **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 PARTICULARS**

#### **5.1 Pharmacodynamic properties**

Pharmacotherapeutic group : Diagnostic radiopharmaceutical for cardiovascular system imaging, ATC Code : V09G A 02.

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

Limited data in animals show uptake of  $^{99m}\text{Tc}$ -tetrofosmin into breast tumour cells.

#### **5.2 Pharmacokinetic properties**

$^{99m}\text{Tc}$ -tetrofosmin 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.

### 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.

### 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 *in vitro* or *in vivo* mutagenicity studies. Studies to assess the carcinogenic potential of Myoview have not been performed.

#### Radiation dosimetry data

The estimated absorbed radiation dose to an average adult patient (70kg) from intravenous injections of <sup>99m</sup>Tc-tetrofosmin 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.

Organ	Absorbed radiation dose ( Gy/MBq)	
	Exercise	Rest
Gallbladder wall	33.2	48.6
Upper large intestine	20.1	30.4
Lower large intestine	15.3	22.2
Urinary bladder wall	15.6	19.3
Small intestine	12.1	17.0
Kidney	10.4	12.5
Salivary glands	8.0	11.6
Ovaries	7.9	9.6
Uterus	7.3	8.4
Bone surface	6.2	5.6
Thyroid	4.3	5.8
Pancreas	5.0	5.0
Stomach	4.6	4.6
Adrenals	4.3	4.1
Red Marrow	4.1	4.0
Heart wall	4.1	4.0
Spleen	4.1	3.8
Muscle	3.5	3.3
Testes	3.4	3.1
Liver	3.2	4.2
Thymus	3.1	2.5
Brain	2.7	2.2
Lungs	2.3	2.1
Skin	2.2	1.9
Breasts	2.2	1.8
Total body	3.8	3.7

The effective dose (ED) resulting from the administration of doses of reconstituted Myoview of 250MBq after exercise and 750MBq at rest is 1.50mSv after exercise and 5.36mSv at rest (per 70kg individual).

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

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Stannous chloride dihydrate, disodium sulphosalicylate, sodium D-gluconate, sodium hydrogen carbonate.

### 6.2 Incompatibilities

None known, however <sup>99m</sup>Tc-tetrofosmin should not be mixed or diluted with any substance other than those recommended for reconstitution.

### 6.3 Shelf-life

The shelf-life of the packaged product is 35 weeks.

Chemical and physical in-use stability of the reconstituted solution for injection has been demonstrated for 12 hours at 2 - 8°C.

### 6.4 Special precautions for storage

Store at 2-8 °C before and after reconstitution.

### 6.5 Nature and contents of the container

The product is supplied in a 10ml clear glass vial sealed with a chlorobutyl rubber closure and metal overseal in pack sizes of 2 or 5 vials.

### 6.6 Instructions for use/handling and disposal.

Normal safety precautions for the handling of radioactive materials should be observed in addition to the use of aseptic technique to maintain sterility of the vial contents.

Procedure for the preparation of  $^{99m}\text{Tc}$ -tetrofosmin:

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 1) through the rubber septum. Using a shielded, 10ml sterile syringe, inject the required activity of Sodium Pertechnetate [ $^{99m}\text{Tc}$ ] Injection Ph. Eur. (appropriately diluted with 0.9% Sodium Chloride Injection BP) into the shielded vial (see Notes 2 to 4). Before removing the syringe from the vial, withdraw 5 ml of gas from above the solution (see Note 5). 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 at 2-8 °C and use within 12 hours of preparation. Dispose of any unused material and its container via an authorised route.

#### Notes:

1. A needle of size 19G to 26G may be used.
2. The Sodium Pertechnetate [ $^{99m}\text{Tc}$ ] Injection Ph. Eur. used for reconstitution should contain less than 5ppm aluminium.
3. The volume of diluted Sodium Pertechnetate [ $^{99m}\text{Tc}$ ] Injection Ph. Eur. added to the vial must be in the range 4-8ml.
4. The radioactive concentration of the diluted Sodium Pertechnetate [ $^{99m}\text{Tc}$ ] Injection Ph. Eur. must not exceed 1.5GBq/ml when it is added to the vial.
5. 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.
6. The pH of the prepared injection is in the range 7.5-9.0.

#### Radiochemical purity measurement

Radiochemical purity may be checked according to the following procedure:

## Equipment and eluent

1. Gelman ITLC/SG strip (2cm x 20cm)
2. Ascending chromatography tank and cover
3. 35:65 v/v mixture of acetone and dichloromethane
4. 1ml syringe with 22-25G needle
5. Suitable counting equipment

## Method

1. Pour the 35:65 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 an ITLC/SG 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 3cm and 12cm above the origin (Rf's 0.2 and 0.8 respectively) should also be marked in pencil.
4. Using a 1ml syringe and needle, apply a 10-20  $\mu$ l sample of the prepared injection at the origin of the strip. 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 10-20  $\mu$ l sample will produce a spot with a diameter of 7-10mm. Smaller 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:-

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

**Note:** Free [ $^{99m}\text{Tc}$ ] pertechnetate runs to the top piece of the strip.  $^{99m}\text{Tc}$ -tetrofosmin runs to the centre piece of the strip. Reduced hydrolysed- $^{99m}\text{Tc}$  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%.

## 7 MARKETING AUTHORISATION HOLDER

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IMPORTER:

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