GE Healthcare

2020 Coding and Reimbursement Guide for Myoview™ (Kit for the Preparation of Technetium Tc99m Tetrofosmin for Injection)

Myoview is the only FDA-approved myocardial perfusion imaging agent that can begin gathering diagnostic information about a patient's heart in as soon as in 15 minutes.

PRODUCT INDICATIONS: Myoview™ 30 mL (Kit for the Preparation of Technetium Tc-99m Tetrofosmin for Injection) is indicated for myocardial perfusion imaging under rest and/or exercise or pharmacologic stress conditions to delineate regions of reversible myocardial ischemia or infarcted myocardium in patients with known or suspected coronary artery disease. Myoview is also indicated for the assessment of left ventricular function (left ventricular ejection fraction and wall motion) in patients with known or suspected heart disease.

Important Safety Information About Myoview

WARNINGS and PRECAUTIONS – Risks Associated with Exercise or Pharmacologic Stress: Patients evaluated with exercise or pharmacologic stress may experience serious adverse reactions such as myocardial infarction, arrhythmia, hypotension, and bronchoconstriction, as well as cerebrovascular reactions such as headache, paraesthesias, convulsions, somnolence and cerebrovascular accident, including hemorrhage. Perform stress testing in a setting where cardiac resuscitation equipment and trained staff are readily available. When pharmacologic stress is selected as an alternative to exercise, perform the procedure in accordance with the pharmacologic stress agent's prescribing information.

Please click here for additional Important Safety Information About Myoview and here for full Prescribing Information before use.

MYOVIEW™ 30mL
(Kit for the Preparation of Technetium Tc99m Tetrofosmin for Injection)

GE Healthcare

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2020 Coding and Reimbursement Guide

The 2020 Coding and Reimbursement Guide for Myoview is intended to provide available current reimbursement information. In this document, coding and payment for Myocardial Perfusion Imaging with Myoview are reviewed.

Basics of Reimbursement

Securing reimbursement for a medical procedure or service is dependent on having not only the appropriate coding to bill the procedure or service, but also the appropriate coverage and payment by the specific health plan.

Coding

Healthcare providers identify a patients' diagnosis, procedures, drugs and devices provided using various coding systems. The purposes of these systems are to provide a uniform language that describes medical, surgical, and diagnostic services.

Healthcare Common Procedure Coding System (HCPCS) is a standardized coding system developed by the Centers for Medicare and Medicaid Services (CMS) for reporting medical procedures, supplies, products and services to Medicare, Medicaid and third- party payers.

Level I or Current Procedural Terminology (CPT®) Codes are issued and maintained by the American Medical Association (AMA). These codes describe a medical service, and/or procedure. These are five-digit numeric codes.

Level II codes are used to describe non-physician services provided (eg. contrast agents, ambulance services, wheelchairs, and other durable medical equipment.) These codes are alphanumeric five-digit codes.

To receive appropriate reimbursement, physicians should report the appropriate HCPCS code for the product used along with the appropriate CPT® code describing the procedure performed.

Some payers may require reporting a product's National Drug Code (NDC). NDC codes are unique, 10-digit numeric codes used to identify drugs. The first segment of the code identifies the manufacturer, the second segment identifies the product, and the third identifies the packaging.

CPT is a registered trademark of the American Medical Association.

HCPCS, Healthcare Common Procedure Coding System.

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Coverage

The existence of codes that describe a product or procedure does not guarantee payment or coverage. Each payer has unique coverage policies and guidelines.

Medicare

For procedures and products covered by Medicare Part B, coverage decisions are typically made through local coverage determinations (LCDs). LCDs are specific to the jurisdiction of a Medicare Administrative Contractor (MAC). An LCD only applies to the specific issuing MAC.

Commercial/Private Payers

Commercial or private payers each determine their own coverage policy. Coverage may also vary based on a patient's benefits or on the negotiated contract between the providers and the payer.

Medicaid

Each Medicaid program is administered by its specific state. The state determines its own coverage policies or guidelines.

Payment

Payment is the amount that a payer renders to a healthcare entity or provider for covered services and products. The payment methodology and amount vary based on site of service.

CMS sets a reimbursement amount for procedures, drugs, and/or supplies to allow for a uniform method of payment. Their rates are set nationally, with adjustments made to reflect geographic differences in costs.

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MYOVIEW™ 30mL
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MYOVIEW

In the hospital outpatient setting, Medicare claims for use of Myoview are paid per the Ambulatory Payment Classification (APC). Under APCs hospitals are paid one amount per encounter. Both the procedure and the radiopharmaceutical should be indicated on the claim, but the radiopharmaceutical is not paid separately.

In the physician office or independent diagnostic testing facility (IDTF) setting, payment is based on each CPT and HCPCS code billed.

DISCLAIMER: All information included in this guide is for informational purposes only. It is intended to assist in the coding, and reimbursement process. It represents no statement of guarantee by GE Healthcare. The final decision or coding on any procedure must be made by the provider of care after considering the medical necessity of the services and supplies provided as well as considering any regulations and local, state or federal laws that may apply. All coding and reimbursement information is subject to change without notice, and specific payers may have their own coding and reimbursement requirements and policies. Please contact your local payer for interpretation of the appropriate codes to use for specific procedures.

HCPCS, Healthcare Common Procedure Coding System.

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MYOVIEW™ 30mL
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Cardiac Imaging

Code	Description
78451	Myocardial perfusion imaging, tomographic (SPECT) (including attenuation correction, qualitative or quantitative wall motion, ejection fraction by first pass or gated technique, additional quantification, when performed), single study, at rest or stress (exercise or pharmacologic)
78452	Myocardial perfusion imaging, tomographic (SPECT) (including attenuation correction, qualitative or quantitative wall motion, ejection fraction by first pass or gated technique, additional quantification, when performed), multiple studies, at rest and/or stress (exercise or pharmacologic) and/or redistribution and/or rest reinjection.

Myoview™ (Kit for the Preparation of Technetium Tc99m Tetrofosmin for injection)

For Medicare Part B

Code	Description	Payment	
		Hospital Outpatient	Physcian Office or IDTF
HCPCS: A9502	Technetium Tc-99m Tetrofosmin, diagnostic, per study dose	Packaged payment included in APC 5593	Payment based on Average Wholesale Price (AWP), Average Sale Price (ASP) or invoice

- Providers should ensure the number of units reported is consistent with the quantity of radiopharmaceutical administered to complete the study.

	National Drug Code (NDC)
Myoview, 30 mL	17156-026-30

Please click here for Important Safety Information About Myoview and here for full Prescribing Information before use.

MYOVIEW™ 30mL
(Kit for the Preparation of Technetium Tc99m Tetrofosmin for Injection)

GE Healthcare Customer Service

To place an order:
800 292 8514

GE Healthcare Medical Affairs for Clinical or Scientific Support

Please contact us at:
800 654 0118 (option 2, then option 3) or
medical.affairs@ge.com

GE Healthcare Reimbursement Hotline

GE Healthcare is pleased to offer toll-free customer support and documentation for coding and reimbursement related to our products. Please contact us at:
800 767 6664

GE Healthcare Website

For information regarding other GE Healthcare products, please visit our website at:
gehealthcare.com

Please click here for Important Safety Information About Myoview and here for full Prescribing Information before use.

MYOVIEW™ 30mL
(Kit for the Preparation of Technetium Tc99m Tetrofosmin for Injection)

PRODUCT INDICATIONS: Myoview™ 30 mL (Kit for the Preparation of Technetium Tc-99m Tetrofosmin for Injection) is indicated for myocardial perfusion imaging under rest and/or exercise or pharmacologic stress conditions to delineate regions of reversible myocardial ischemia or infarcted myocardium in patients with known or suspected coronary artery disease. Myoview is also indicated for the assessment of left ventricular function (left ventricular ejection fraction and wall motion) in patients with known or suspected heart disease.

Important Safety Information About Myoview

CONTRAINDICATIONS: None known. **WARNINGS and PRECAUTIONS — Risks Associated With Exercise or Pharmacologic Stress**: Patients evaluated with exercise or pharmacologic stress may experience serious adverse reactions such as myocardial infarction, arrhythmia, hypotension, and bronchoconstriction, as well as cerebrovascular reactions such as headache, paraesthesias, convulsions, somnolence and cerebrovascular accident, including hemorrhage. Perform stress testing in a setting where cardiac resuscitation equipment and trained staff are readily available. When pharmacologic stress is selected as an alternative to exercise, perform the procedure in accordance with the pharmacologic stress agent's prescribing information. **Radiation Risks:** Technetium Tc-99m contributes to a patient's overall long-term cumulative radiation exposure. Long-term cumulative radiation exposure is associated with an increased risk of cancer. Ensure safe handling and preparation reconstitution procedures to protect patients and healthcare workers from unintentional radiation exposure. Encourage adequate hydration; instruct patients to void when the examination is completed and as often thereafter as possible. **Hypersensitivity Reactions:** Hypersensitivity reactions, including anaphylaxis, dyspnea, bronchospasm, throat tightness, coughing, tachycardia, chest pain, hypotension, abdominal pain, and cutaneous reactions (rash, urticuria, pruritus, erythema, and swelling or angiodema) have been observed after the administration of Myoview. Always have cardiopulmonary resuscitation equipment and personnel available, and monitor all patients for hypersensitivity reactions. **Nursing Mothers:** Technetium Tc-99m tetrofosmin is present in human milk in small amounts (<1% of maternal dose). There are no data available regarding the effects of technetium Tc-99m tetrofosmin on the breastfed infant or on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Myoview and any other potential adverse effects on the breastfed child from Myoview or from the underlying maternal condition. **Pediatric Use:** Safety and effectiveness in pediatric patients have not been established. **Geriatric Use:** No overall differences in safety were observed between these subjects and younger subjects. Other reported clinical experience has not identified differences in responses between elderly and younger patients, but greater sensitivity regarding some older individuals cannot be ruled out. **ADVERSE REACTIONS:** Serious episodes of angina, ventricular tachycardia, and respiratory arrest were reported. Other events included angina, hypertension, torsades de pointes, vomiting, abdominal discomfort, cutaneous allergy, hypotension, dyspnea, metallic taste, burning of the mouth, and smell alteration. The following were reported when used with pharmacological stress: Angina, flushing, dyspnea, headache, abdominal pain, dizziness, palpitations, nausea, hypotension, pain, cough, arrhythmia, bronchospasm, ECG (electrocardiogram) abnormalities, hypertension, vomiting, and asthenia. Postmarketing adverse reactions included rash, urticaria, abnormal vision, hypersensitivity reactions, and fever.

Prior to DaTscan administration, please read the full Prescribing Information here.

To report SUSPECTED ADVERSE REACTIONS, contact GE Healthcare at 800 654 0118 (option 2, then option 1), or the FDA at 800 FDA 1088 or www.fda.gov/medwatch.

SOURCES

1. CPT 2020 Professional Edition, American Medical Association
2. HCPCS Level II Professional 2020, American Medical Association
3. Revisions to Payment Policies under the Medicare Physician Fee Schedule , Quality Payment Program and Other Revisions to Part B for CY 2020. https://ww.cms.gov/Medicare/Medicare-Fee-for Service-Payment/PhysicianFeeSched/PFS-Federal-Regulation-Notices-Items/CMS-1693-F.html.

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HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use MYOVIEW 30 mL safely and effectively. See full prescribing information for MYOVIEW 30 mL.

MYOVIEW 30 mL

(Kit for the preparation of technetium Tc99m tetrofosmin injection) for intravenous use Initial U.S. Approval: 1996

----------INDICATIONS AND USAGE----------

MYOVIEW 30 mL is a kit for the preparation of technetium Tc99m tetrofosmin for injection. Technetium Tc99m tetrofosmin injection is a radioactive diagnostic agent indicated for the following:

- Myocardial perfusion imaging under rest and/or exercise or pharmacologic stress conditions to delineate regions of reversible myocardial ischemia or infarcted myocardium in patients with known or suspected coronary artery disease (1.1)
- Assessment of left ventricular function (left ventricular ejection fraction and wall motion) in patients with known or suspected heart disease (1.2)

----------DOSAGE AND ADMINISTRATION----------

- Use appropriate radiation safety measures and aseptic technique during preparation and handling (2.1, 2.3)
- The recommended dose range for MYOVIEW for rest or stress imaging is 185-1221 megabecquerels (MBq) [5-33 millicuries (mCi)] by intravenous administration (2.2) When rest and stress injections are administered on the same day, the first dose should be 185-444 MBq (5-12 mCi) followed by the second dose of 555-1221 MBq (15-33 mCi) given approximately 1 to 4 hours later (2.2)
- The recommended dose range for MYOVIEW for ventricular function assessment is 185-1221 MBq (5-33 mCi) as an intravenous injection (2.2)
- See Full Prescribing Information for instructions for preparation and determination of radiochemical purity (2.4, 2.5)
- Imaging may begin 15 minutes following administration of the agent (2.6)

----------DOSAGE FORMS AND STRENGTHS----------

Kit for preparation injection: lyophilized powder containing 1.38 mg tetrofosmin in a multiple-dose vial after reconstitution with Tc99m eluate, clear solution not exceeding 2960 MBq/mL (80 mCi/mL). (3)

CONTRAINDICATIONS

- None (4)

----------WARNINGS AND PRECAUTIONS----------

- Risk with exercise or pharmacologic stress:
  - Continuous cardiac monitoring should be performed in studying patients with known or suspected coronary artery disease (5.1)
  - When pharmacologic stress is selected as an alternative to exercise, perform the procedure in accordance with the pharmacologic stress agent's prescribing information (5.1)
- Appropriate safety measures should be used to minimize radiation exposure to clinical personnel and to the patient consistent with proper patient management (2.1, 5.2)

----------ADVERSE REACTIONS----------

Most common adverse reactions (incidence < 1%) after MYOVIEW injection: Cardiovascular: angina, hypertension, torsades de pointes. Gastrointestinal: vomiting, abdominal discomfort. Hypersensitivity: cutaneous allergy, hypotension, dyspnea. Special Senses: metallic taste, burning of the mouth, smell alteration. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact GE Healthcare at 1-800-654-0118 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------USE IN SPECIFIC POPULATIONS----------

- Advise the pregnant woman of the potential risk to the fetus based on the radiation dose from technetium Tc99m and the gestational timing of exposure (8.1)
- Lactation - A lactating woman should pump and discard breastmilk for 60 hours after technetium Tc99m tetrofosmin administration (8.2)

See 17 for PATIENT COUNSELING INFORMATION **Revised: 4/2017**

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Myocardial Perfusion Imaging

Myocardial perfusion imaging under rest and/or exercise or pharmacologic stress conditions to delineate regions of reversible myocardial ischemia or infarcted myocardium in patients with known or suspected coronary artery disease.

1.2 Ventricular Function Imaging

MYOVIEW is indicated for assessment of left ventricular function (left ventricular ejection fraction and wall motion) in patients with known or suspected heart disease.

2 DOSAGE AND ADMINISTRATION

2.1 Radiation Safety – Drug Handling

Technetium Tc99m tetrofosmin is a radioactive drug and should be handled with appropriate safety measures to minimize radiation exposure during administration [see Warnings and Precautions (5.2)]. Use waterproof gloves and effective shielding, including syringe shields, when preparing and administering technetium Tc99m tetrofosmin injection.

2.2 Recommended Dosage

- The recommended dose range for MYOVIEW is 185-1221 MBq (5-33 mCi) by intravenous administration for rest and stress imaging.
- When rest and stress intravenous injections are administered on the same day, the first dose should be 185-444 MBq (5-12 mCi) and followed by the second dose of 555-1221 MBq (15-33 mCi) given approximately 1 to 4 hours later.
- The recommended dose range for MYOVIEW is 185-1221 MBq (5-33 mCi) by intravenous administration as an intravenous injection for ventricular function assessment.

2.3 Administration Instructions

- Use aseptic technique for all drug preparation and handling.
- Measure the dose in a suitable radioactivity calibration system immediately prior to intravenous administration.
- Visually inspect the drug for particulate matter and discoloration prior to administration. Do not use or administer the drug if there is evidence of particulate matter or discoloration.
- Instruct patients to remain hydrated and void frequently following administration to decrease radiation exposure [see Warnings and Precautions (5.2)].

2.4 Instructions for Preparation

1. The technetium Tc99m labeling reaction involved in the preparation of MYOVIEW Injection depends on maintaining tin in the divalent (reduced) state. Any oxidant present in the sodium pertechnetate Tc99m used may adversely affect the quality of the preparation. Sodium pertechnetate Tc99m containing oxidants should not be used for the preparation of the labeled product.
2. Elute the technetium generator with sodium chloride injection, USP.
3. Insert a venting needle (standard 18-26 gauge needle, not provided) through the rubber septum of the shielded vial containing the lyophilized powder.
4. Inject no more than 89 GBq (2.4 Ci) of technetium Tc99m generator eluate into the shielded vial.
5. Use sodium chloride injection, USP as a diluent. Inject 10-30 mL to achieve a radioactive concentration no greater than 2.96 GBq/mL (80 mCi/mL) in the vial.
6. If a venting needle is not used, before removing the syringe from the vial, withdraw an adequate volume of gas from above the solution to avoid over-pressurizing the vial.
7. Remove the venting needle.
8. Mix gently for 10 seconds to ensure complete dissolution of the powder.
9. Incubate at room temperature for 15 minutes.
10. Assay the total activity using a suitably calibrated instrument; complete the user radiation label and attach it to the vial.
11. Measure the pH of the prepared injection and verify it is between 7.5-9.0.
12. Store the reconstituted MYOVIEW 30 mL vial and withdrawals for injection at 2°-25°C (36°- 77°F) and use within 12 hours of preparation.

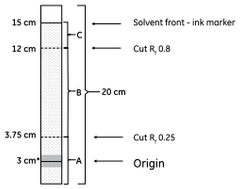
2.5 Determination of Radiochemical Purity

<u>Obtain the following materials:</u>

1. Varian SA TLC strip (2 cm • 20 cm), do not heat activate
2. Ascending chromatography tank and cover
3. Mixture of acetone and dichloromethane (65:35% v/v), prepare freshly
4. Syringe (1 mL) with needle (22-25 gauge)
5. Suitable counting equipment

<u>Perform the following:</u>

1. Pour the 65:35% v/v acetone:dichloromethane mixture into the chromatography tank to a depth of 1 cm and cover the tank to allow the solvent vapor to equilibrate.
2. Mark a Varian SA TLC strip with a pencil line at 3 cm from the bottom and, using an ink marker pen, at 15 cm from the pencil line. The pencil line indicates the origin where the sample is to be applied and movement of color from the ink line will indicate the position of the solvent front when upward elution should be stopped.
3. Mark cutting positions at 3.75 cm and 12 cm above the origin [retention value (Rf) 0.25 and 0.8 respectively] in pencil.
4. Using a 1 mL syringe and needle, apply a 10 microliter 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 microliter sample will produce a spot with a diameter of approximately 10 mm. 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. Ensure similar counting geometry for each piece and minimize equipment dead time losses. Note: Free Tc99m pertechnetate runs to the top piece of the strip. MYOVIEW runs to the center piece of the strip. Reduced hydrolyzed Tc99m and any hydrophilic complex impurities remain at the origin in the bottom piece of the strip.



*Measured from plate edge; all other measurements are from origin.
Count radioactivty in sections A, B, and C separately.
Percent radiochemical purity = 100% x B / (A + B + C).

7. Calculate the radiochemical purity from:

$$\% \text{ Tc99m tetrofosmin} = \frac{\text{Activity of center piece}}{\text{Total activity of all 3 pieces}} \times 100$$

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

2.6 Imaging Instructions

- Imaging may begin 15 minutes after injection.
- The recommended imaging duration of the scan may vary depending on dose, imaging acquisition, and reconstruction parameters.

2.7 Radiation Dosimetry

Radiation absorbed dose per unit activity of the agent injected intravenously in an adult of average weight (74 kg) is estimated in Table 1 for exercise and resting conditions. The values listed correspond to a 3.5-hour voiding period for excretion from the urinary bladder.

Table 1 Estimated Radiation Absorbed Dose (Technetium Tc99m Tetrofosmin Injection)

Radiation absorbed dose per unit activity injected intravenously				
	Exercise		Rest	
Target organ	**rad/mCi**	**microGy/MBq**	**rad/mCi**	**microGy/MBq**
Gall bladder wall	0.10	27	0.13	36
Upper large intestine	0.074	20	0.10	27
Lower large intestine	0.055	15	0.074	20
Bladder wall	0.052	14	0.063	17
Small intestine	0.041	11	0.056	15
Kidney	0.037	10	0.048	13
Salivary glands	0.030	8.0	0.043	12
Ovaries	0.029	7.7	0.033	8.8
Uterus	0.026	7.0	0.029	7.8
Bone surface	0.023	6.3	0.021	5.8
Thyroid	0.017	4.7	0.020	5.5
Pancreas	0.019	5.0	0.018	4.9
Heart wall	0.019	5.2	0.017	4.7
Stomach	0.017	4.6	0.017	4.5
Adrenals	0.016	4.4	0.016	4.2
Liver	0.012	3.3	0.015	4.0
Spleen	0.015	4.1	0.014	3.9
Red marrow	0.014	3.9	0.014	3.8
Muscle	0.013	3.5	0.012	3.3
Testes	0.013	3.4	0.011	3.1
Thymus	0.012	3.3	0.010	2.8
Esophagus	0.012	3.3	0.010	2.8
Lungs	0.012	3.2	0.010	2.8
Brain	0.010	2.7	0.0085	2.3
Skin	0.0081	2.2	0.0074	2.0
Breasts	0.0085	2.3	0.0074	2.0
Remaining organs	0.014	3.8	0.014	3.8
Effective dose per unit activity	**0.026 rem/mCi**	**6.9 microSv/MBq**	**0.030 rem/mCi**	**8.0 microSv/MBq**

3 DOSAGE FORMS AND STRENGTHS

Kit for the preparation of technetium Tc99m tetrofosmin injection: 30 mL multiple-dose, clear, glass vial with a white sterile, non-pyrogenic, lyophilized powder of 1.38 mg tetrofosmin, 0.09 mg stannous chloride dihydrate, 1.92 mg disodium sulphosalicylate, 3 mg sodium D-gluconate, 11 mg sodium hydrogen carbonate, and 3 mg ascorbic acid.

Following reconstitution with the Tc99m eluate, MYOVIEW is a clear solution not exceeding 2960 MBq/mL (80 mCi/mL) of Tc99m.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Risks Associated with Exercise or Pharmacologic Stress

Patients evaluated with exercise or pharmacologic stress may experience serious adverse reactions such as myocardial infarction, arrhythmia, hypotension, bronchoconstriction, and cerebrovascular reactions such as headache, paraesthesias convulsions, somnolence and cerebrovascular accident, including hemorrhage. Perform stress testing in the setting where cardiac resuscitation equipment and trained staff are readily available. When pharmacologic stress is selected as an alternative to exercise, perform the procedure in accordance with the pharmacologic stress agent's prescribing information.

5.2 Radiation Risks

Technetium Tc99m contributes to a patient's overall long-term cumulative radiation exposure. Long-term cumulative radiation exposure is associated with an increased risk of cancer. Ensure safe handling and preparation reconstitution procedures to protect patients and health care workers from unintentional radiation exposure. Encourage adequate hydration; instruct patients to void when the examination is completed and as often thereafter as possible [see Dosage and Administration (2.1) and (2.3)].

5.3 Hypersensitivity Reactions

Hypersensitivity reactions including anaphylaxis, dyspnea, bronchospasm, throat tightness, coughing, tachycardia, chest pain, hypotension, abdominal pain, and cutaneous reactions (rash, urticaria, pruritus, erythema, and swelling or angioedema) have been observed after the administration of MYOVIEW. Always have cardiopulmonary resuscitation equipment and personnel available and monitor all patients for hypersensitivity reactions.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Hypersensitivity Reactions [see Warnings and Precautions (5.3)].

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of MYOVIEW cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Adverse reactions were evaluated in clinical studies (using an exercise/rest protocol) of 764 adults (511 men) with a mean age of 58.7 years (range 29-94 years). The subjects received a mean dose of 285 MBq (7.7 mCi) on the first injection and 829 MBq (22.4 mCi) on the second injection of MYOVIEW.

After MYOVIEW injection, angina occurred in 4 subjects, ventricular tachycardia in 1 subject, and respiratory arrest in 1 subject.

The following reactions were noted in less than 1% of subjects:
Cardiovascular: angina, hypertension, torsades de pointes.
Gastrointestinal: vomiting, abdominal discomfort.
Hypersensitivity: cutaneous allergy, hypotension, dyspnea.
Special Senses: metallic taste, burning of the mouth, smell alteration.

In four studies, 438 adults (232 men and 205 women: gender was not recorded for one subject) with a mean age of 65 years (range 27-97 years) received a single pharmacologic stress agent. The subjects received a mean dose of 7-8 mCi on the rest/first injection and 22-34 mCi on the stress/second injection. Among the 438 subjects, 319 subjects (73%) experienced an adverse reaction. Reactions occurring in ≥1% of the subjects included angina (39%), flushing (36%), dyspnea (28%), headache (14%), abdominal pain (11%), dizziness (7%), palpitations (2%), nausea (2%), hypotension (1%) and pain (1%). Events occurring in <1% include cough, arrhythmia, bronchospasm, ECG abnormalities, hypertension, vomiting and asthenia.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post approval use of MYOVIEW. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

The most common adverse reactions reported included: rash, urticaria, abnormal vision, hypersensitivity reactions, and fever.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no data with technetium Tc99m tetrafosmin use in pregnant women to inform any drug associated risks. Animal reproduction studies with technetium Tc99m tetrofosmin have not been conducted. However, all radiopharmaceuticals have the potential to cause fetal harm depending on the fetal stage of development and the magnitude of the radiation dose. If considering technetium Tc99m tetrafosmin administration to a pregnant woman advise the pregnant woman of risk to the fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

8.2 Lactation

Risk Summary

Technetium Tc99m tetrofosmin is present in human milk in small amounts (<1% of maternal dose). There are no data available regarding the effects of technetium Tc99m tetrofosmin on the breastfed infant or on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for MYOVIEW and any potential adverse effects on the breastfed child from MYOVIEW or from the underlying maternal condition.

Clinical Considerations

To decrease radiation exposure to the breastfed infant, advise a lactating woman to pump and discard breast milk for 60 hours (10 half-lives) after technetium Tc99m tetrofosmin administration.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

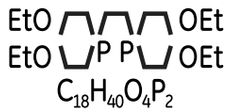
Of 2300 subjects in clinical studies of MYOVIEW, 1053 (46%) were 65 or older and 270 (12%) were 75 or older. No overall differences in safety were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

11 DESCRIPTION

11.1 Chemical Characteristics

MYOVIEW 30 mL is a kit for the preparation of technetium Tc99m tetrofosmin injection for intravenous use. Technetium Tc99m tetrofosmin is a radioactive diagnostic agent. Each multiple-dose 30 mL glass vial contains a sterile, non-pyrogenic, lyophilized powder of 1.38 mg tetrofosmin [6,9-bis(2-ethoxyethyl)-3,12-dioxa-6,9-diphosphatetradecane], 0.09 mg stannous chloride dihydrate, (minimum stannous tin 0.015 mg; total stannous and stannic tin 0.0522 mg) 1.92 mg disodium sulphosalicylate, 3 mg sodium D-gluconate, and 11 mg sodium hydrogen carbonate, and 3 mg ascorbic acid. The lyophilized powder is sealed under a nitrogen atmosphere with a rubber closure.

The product contains no antimicrobial preservative. The chemical formula of tetrofosmin is $C_{18}H_{40}O_4P_2$ with the following structural formula:



$C_{18}H_{40}O_4P_2$

When sterile, pyrogen-free sodium pertechnetate Tc99m in isotonic saline is added to the vial, a Tc99m complex of tetrofosmin is formed. The reconstituted product is a clear solution and the pH is in the range of 7.5-9.0.

11.2 Physical Characteristics

Technetium Tc99m decays by isomeric transition with a physical half-life of 6 hours. Photons that are useful for imaging studies are listed in Table 2.

Table 2 Principal radiation emission data - technetium Tc99m

Radiation	Mean % disintegration	Mean energy (keV)
Gamma 2	88.5	140.5

11.3 External Radiation

The air-kerma-rate (exposure-rate) constant for technetium Tc99m is 5.23 $m^2 \cdot pGy \cdot (MBq)^{-1} \cdot s^{-1}$ [0.795 $cm^2 \cdot R \cdot (mCi)^{-1} \cdot h^{-1}$].

A range of values for the relative radiation attenuation by various thicknesses of Pb shielding is shown in Table 3. For example, the use of 3mm thick Pb will decrease the external radiation exposure by a factor of approximately 1000.

Table 3 Radiation attenuation by lead shielding

Shield thickness (Pb) mm	Factor of attenuation
0.25	0.5
1	10^{-1}
2	10^{-2}
3	10^{-3}
4	10^{-4}
5	10^{-5}

To correct for physical decay of this radionuclide, the fractions that remain at selected intervals relative to the time of calibration are shown in Table 4.

Table 4 Physical decay chart - Tc99m half-life 6 hours

Hours	Fraction Remaining	Hours	Fraction Remaining
*Calibration time (time of preparation)			
0*	1.000	7	0.446
1	0.891	8	0.397
2	0.794	9	0.354
3	0.707	10	0.315
4	0.630	11	0.281
5	0.562	12	0.250
6	0.500	24	0.063

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Technetium (99mTc) tetrofosmin is a lipophilic, cationic complex which diffuses passively through the cell membrane and is locally retained actively due to the presence of intact mitochondria reflecting the presence of viable cells. After intravenous injection, it is distributed within the myocardium according to myocardial perfusion and viability.

12.2 Pharmacodynamics

The relationship between Tc99m tetrofosmin plasma concentrations and successful imaging has not been explored in clinical trials.

12.3 Pharmacokinetics

Uptake in the myocardium is dependent on coronary flow and reaches a maximum of 1.2% of the injected dose (i.d.) at 5 minutes and 1% of the i.d. at 2 hours, respectively. Background activities in the blood, liver and lung were less than 5% of the administered activity in whole blood at 10 minutes post-injection, less than 4.5% i.d., after 60 minutes, and less than 2% i.d. after 30 minutes.

Elimination

Approximately 66% of the injected activity is excreted within 48 hours post-injection, with approximately 40% excreted in the urine and 26% in the feces.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies have not been conducted to evaluate carcinogenic potential or effects on fertility. Tetrofosmin sulphosalicylate was not mutagenic in vitro in the Ames test, mouse lymphoma, or human lymphocyte tests, nor was it clastogenic in vivo in the mouse micronucleus test.

14 CLINICAL STUDIES

14.1 Exercise/Resting Myocardial Perfusion Imaging Studies

A total of 252 subjects with ischemic heart disease or atypical chest pain were studied in two open-label, multi-center, clinical studies (study a and study b). Of these 252 subjects there were 212 (84%) males and 40 (16%) females with a mean age of 60.5 years (range 33.7 to 82.4 years).

All subjects had exercise and rest planar imaging with MYOVIEW and thallium-201; 191 (76%) subjects also had single photon emission computed tomography (SPECT) imaging. At peak exercise, maximum heart rate achieved and peak systolic blood pressure were comparable after MYOVIEW and thallium-201 exercise studies. The MYOVIEW and thallium-201 images were separated by a mean of 5.1 days (1-14 days before or 2-14 days after MYOVIEW). For MYOVIEW imaging, each subject received 185-296 MBq (5-8 mCi) Tc99m tetrofosmin at peak exercise and 555-888 MBq (15-24 mCi) Tc99m tetrofosmin at rest approximately 4 hours later. For thallium-201 imaging, subjects received thallium-201 55.5-74 MBq (1.5-2 mCi) at peak exercise.

The images were evaluated for the quality of the image (excellent, good or poor) and the diagnosis (with scores of 0 = normal, 1 = ischemia, 2 = infarct, 3 = mixed infarct and ischemia). The primary outcome variable was the percentage of correct diagnoses in comparison to the final clinical diagnosis. All planar images were blindly read; SPECT images were evaluated by the unblinded investigator. The results for each blinded reader are noted in Table 5.

Table 5 Overall Diagnostic Outcome

		Thallium 201		MYOVIEW	
		Reader 1	Reader 2	Reader 1	Reader 2
Diagnosis	Study	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
Ischemia	a	77.7 (68.8, 85.0)	75.0 (65.9, 82.7)	66.3 (56.7, 75.1)	63.6 (53.9, 72.6)
	b	75.6 (66.9, 83.0)	68.9 (59.8, 77.1)	66.4 (57.2, 74.8)	66.4 (57.2, 74.8)
Infarct	a	75.9 (66.9, 83.5)	75.0 (65.9, 82.7)	74.5 (65.4, 82.4)	75.5 (66.3, 83.2)
	b	70.6 (61.5, 78.6)	69.7 (60.7, 77.8)	73.1 (64.2, 80.8)	68.1 (58.9, 76.3)

14.2 Pharmacological Stress Myocardial Perfusion Imaging Studies

MYOVIEW imaging after pharmacologic stress was evaluated in two studies in subjects with known or suspected coronary artery disease (CAD). Three blinded reads were obtained for 57 subjects (45 male [79%], 12 female [21%]; mean age 60.1 years) all of whom had angiography. Subject level analyses were based on the finding of SPECT myocardial perfusion abnormalities in patients with angiographically confirmed disease. Subject level sensitivities for MYOVIEW ranged from 68-83% and subject level specificities ranged from 45-82% across readers and studies.

14.3 Ventricular Function Stress Myocardial Perfusion Imaging Studies

Two open-label, multicenter, identically designed, blinded image read studies were conducted to assess left ventricular function using MYOVIEW ECG gated SPECT (GSPECT) myocardial perfusion imaging. A total of 329 subjects (216 male [65.7%], 113 female [34.3%]); mean age of 60.4 years) with known or suspected heart disease or requiring ventricular function assessments were dosed with MYOVIEW. Of these, 297 were considered evaluable. MYOVIEW was administered at rest and at peak stress using either a one-day or a 2-day dosing protocol.

For both studies, all subjects' stress GSPECT exams were compared to the reference exam of radionuclide ventriculography with Tc99m labeled RBCs (multiple gated acquisition [MUGA]), performed 1 to 5 days after the second MYOVIEW injection. All subjects' GSPECT exams were assessed by 3 independent blinded readers per study. The MUGA exams were evaluated by an independent consensus panel composed of 3 blinded readers. Subject level assessments were based upon discrimination between normal and abnormal values for LVEF (LVEF ≥50% was considered normal) and normal and abnormal wall motion as judged visually. Sensitivity and specificity of LVEF determinations ranged from 81%-88% and 76%-85% respectively across studies and readers. Sensitivity and specificity of wall motion determinations ranged from 80%-92% and 68%-86% respectively across studies and readers.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How supplied

Five (5) multiple-dose kits, each containing a 30 mL glass vial with a sterile, non-pyrogenic, lyophilized powder containing 1.38 mg tetrofosmin, 0.09 stannous chloride dihydrate, 1.92 mg disodium sulphosalicylate, 3 mg sodium D-gluconate, 11 mg sodium hydrogen carbonate and 3 mg ascorbic acid.

NDC 17156-026-30

The radionuclide is not part of the kit. Before reconstitution and radiolabeling with Tc99m, the contents of the kit are not radioactive.

16.2 Storage and Handling

Store the kit at 2°-8°C (36°-46°F). Protect the kit from light.

This reagent kit is approved for use by persons under license by the Nuclear Regulatory Commission or the relevant regulatory authority of an Agreement State; store and dispose of technetium Tc99m tetrofosmin in accordance with these regulations.

17 PATIENT COUNSELING INFORMATION

- Instruct patients to remain hydrated and void frequently following administration to decrease radiation exposure.
- Advise a lactating woman to pump and discard breast milk for 60 hours (10 half-lives) after technetium Tc99m tetrofosmin administration to decrease radiation exposure to the breastfed infant.

Manufactured by:
GE Healthcare AS
Oslo, Norway
Patent No. 5,045,302

Distributed by:
GE Healthcare
Medi-Physics, Inc.
Arlington Heights, IL 60004

GE Healthcare

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