Technescan™ PYP™

Kit for the Preparation of Technetium Tc 99m Pyrophosphate Injection

Rx only

Diagnostic—For Intravenous Use

DESCRIPTION

Technescan™ PYP™ (Kit for the Preparation of Technetium Tc 99m Pyrophosphate Injection) is a sterile, non-pyrogenic, diagnostic radiopharmaceutical suitable for intravenous administration after reconstitution with sterile sodium pertechnetate Tc 99m injection or sterile 0.9% sodium chloride injection.

Each 10 milliliter reaction vial contains 11.9 milligrams sodium pyrophosphate, 3.2 milligrams (minimum) stannous chloride ($SnCl_2 \cdot 2H_2O$) and 4.4 milligrams (maximum) total tin expressed as stannous chloride ($SnCl_2 \cdot 2H_2O$) in lyophilized form under an atmosphere of nitrogen. Prior to lyophilization the pH is adjusted with hydrochloric acid. The pH of the reconstituted drug is between 4.5 and 7.5. No bacteriostatic preservative is present.

The precise structures of the stannous-pyrophosphate and technetium-stannous-pyrophosphate complexes are not known at this time.

PHYSICAL CHARACTERISTICS

Technetium Tc 99m decays by isomeric transition with a physical half-life of 6.02 hours.[1] The principal photon that is useful for detection and imaging is listed in Table 1.

Table 1. Principal Radiation Emission Data[1]

Radiation	Mean Percent/ Disintegration	Energy (keV)
Gamma-2	89.07	140.5

The specific gamma ray constant for technetium Tc 99m is 0.78 R/mCi-hr at 1 cm. The first half-value thickness of lead (Pb) for technetium Tc 99m is 0.017 cm. A range of values for the relative attenuation of the radiation emitted by this radionuclide that results from interposition of various thicknesses of Pb is shown in Table 2. For example, the use of 0.25 cm of Pb will decrease the external radiation exposure by a factor of about 1000.

Table 2. Radiation Attenuation by Lead Shielding

Shield Thickness (Pb) cm	Coefficient of Attenuation
0.017	0.5
0.08	10^{-1}
0.16	10^{-2}
0.25	10^{-3}
0.33	10^{-4}

To correct for physical decay of this radionuclide, the fractions that remain at selected time intervals after the time of calibration are shown in Table 3.

Table 3. Physical Decay Chart; Technetium Tc 99m, Half-Life 6.02 Hours

Hours	Fraction Remaining	Hours	Fraction Remaining
0*	1.000	7	0.447
1	0.891	8	0.398
2	0.794	9	0.355
3	0.708	10	0.316
4	0.631	11	0.282
5	0.562	12	0.251
6	0.501		

*Calibration Time

CLINICAL PHARMACOLOGY

When injected intravenously, Technetium Tc 99m Pyrophosphate has a specific affinity for areas of altered osteogenesis. It is also concentrated in the injured myocardium, primarily in areas of irreversibly damaged myocardial cells.

[1]Kocher, David C., Radioactive Decay Data Tables, DOE/TIC-11026, 108 (1981).

One to two hours after intravenous injection of Technetium Tc 99m Pyrophosphate, an estimated 40 to 50% of the injected dose had been taken up by the skeleton, and approximately 0.01 to 0.02% per gram of acutely infarcted myocardium. Within a period of one hour, 10 to 11% remains in the vascular system, declining to approximately 2 to 3% twenty-four hours post injection. The average urinary excretion was observed to be about 40% of the administered dose after 24 hours.

Technescan PYP also has an affinity for red blood cells. When administered 15 to 30 minutes prior to the intravenous administration of sodium pertechnetate Tc 99m (in vivo red blood cell labeling), approximately 75% of the injected radioactivity remains in the blood pool providing excellent images of the cardiac chambers. When the modified in vivo/in vitro red blood cell labeling method is used, comparable percentages of the injected radioactivity are obtained.

Toxicology data are available upon request.

INDICATIONS AND USAGE

Technetium Tc 99m Pyrophosphate Injection is a skeletal imaging agent used to demonstrate areas of altered osteogenesis, and a cardiac imaging agent used as an adjunct in the diagnosis of acute myocardial infarction.

As an adjunct in the diagnosis of confirmed myocardial infarction (ECG and serum enzymes positive), the incidence of false negative images has been found to be 6%. False negative images can also occur if made too early in the evolutionary phase of the infarct or too late in the resolution phase. In a limited study involving 22 patients in whom the ECG was positive and serum enzymes questionable or negative, but in whom the final diagnosis of acute myocardial infarction was made, the incidence of false negative images was 23%. The incidence of false positive images has been found to be 7 to 9%. False positive images have been reported following coronary by-pass graft surgery, in unstable angina pectoris, old myocardial infarcts and in cardiac contusions.

Technescan PYP is a blood pool imaging agent which may be used for gated blood pool imaging and for the detection of sites of gastrointestinal bleeding. When administered intravenously 15 to 30 minutes prior to intravenous administration of sodium pertechnetate Tc 99m for in vivo red blood cell labeling, approximately 75% of the injected activity remains in the blood pool. The modified in vivo/in vitro red blood cell labeling method may also be used for blood pool imaging.

CONTRAINDICATIONS

None known.

WARNINGS

Reports indicate impairment of brain images using sodium pertechnetate Tc 99m, which have been preceded by a bone image. The impairment may result in false positives or false negatives. It is recommended, where feasible, that brain imaging precede bone imaging procedures.

Preliminary reports indicate impairment of blood pool images in patients receiving sodium heparin for anticoagulant therapy. This is characterized by a reduction in the amount of injected radioactivity remaining in the blood pool.

Technescan PYP should be injected by direct venipuncture. Heparinized catheter systems should be avoided.

PRECAUTIONS

General

Technescan PYP should not be used more than six hours after preparation.

The components of the kit are sterile and non-pyrogenic. It is essential that the user follow the directions carefully and adhere to strict aseptic procedures during preparation.

The contents of this kit are not radioactive. However, after sodium pertechnetate Tc 99m is added, adequate shielding of the final preparation must be maintained.

The imaging of gastrointestinal bleeding is dependent on such factors as the region of imaging, rate and volume of the bleed, efficacy of labeling of the red blood cells and timeliness of imaging. Due to these factors, images should be taken sequentially over a period of time until a positive image is obtained or clinical conditions warrant the discontinuance of the procedure. The period of time for collecting the images may range up to thirty-six hours.

Any sodium pertechnetate Tc 99m solution which contains an oxidizing agent is not suitable for use in the preparation of Technetium Tc 99m Pyrophosphate Injection.

The contents of the Technescan PYP reaction vial may be used for the preparation of Technetium Tc 99m Pyrophosphate Injection. Technescan PYP may also be reconstituted with sterile, non-pyrogenic normal saline containing no preservatives and injected intravenously prior to labeling of red blood cells with sodium pertechnetate Tc 99m using either the in vivo or modified in vivo/in vitro method.

As in the use of any other radioactive material, care should be taken to ensure minimum radiation exposure to the patient, consistent with proper patient management, and to ensure minimum radiation exposure to occupational workers.

Radiopharmaceuticals should be used only by physicians who are qualified by specific training in the safe use and handling of radionuclides produced by nuclear reactor or particle accelerator and whose experience and training have been approved by the appropriate government agency authorized to license the use of radionuclides.

Overdosage

In case of overdose of Technetium Tc 99m Pyrophosphate, encourage patients to maintain hydration and to void frequently to minimize radiation exposure.

Bone Imaging

Both prior to and following administration of Technetium Tc 99m Pyrophosphate Injection, patients should be encouraged to drink fluids. Patients should void as often as possible after administration of Technetium Tc 99m Pyrophosphate Injection to minimize background interference from its accumulation in the bladder and to reduce unnecessary exposure to radiation.

Cardiac Imaging

The patient's cardiac condition should be stable before beginning the cardiac imaging procedure.

If not contraindicated by the cardiac status, patients should be encouraged to ingest fluids and to void frequently in order to reduce unnecessary radiation exposure.

Interference from chest wall lesions such as breast tumors and healing rib fractures can be minimized by employing the three recommended projections.

Carcinogenesis, Mutagenesis, Impairment of Fertility

No long term animal studies have been performed to evaluate carcinogenic or mutagenic potential, or whether this drug affects fertility in males or females.

Pregnancy Category C

Animal reproduction studies have not been conducted with Technetium Tc 99m Pyrophosphate Injection. It is also not known whether this drug can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Technetium Tc 99m Pyrophosphate Injection should be given to a pregnant woman only if clearly needed.

Ideally, examinations using radiopharmaceuticals, especially those elective in nature, of a woman of childbearing capability should be performed during the first few (approximately 10) days following the onset of menses.

Nursing Mothers

Technetium Tc 99m is excreted in human milk during lactation, therefore, formula feedings should be substituted for breast feeding.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

Several adverse reactions due to the use of Technetium Tc 99m Pyrophosphate Injection have

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been reported. These were usually flushing, hypotension, fever, chills, nausea, vomiting and dizziness, as well as hypersensitivity reactions such as itching and various skin rashes.

DOSAGE AND ADMINISTRATION

Bone and Cardiac Imaging

The recommended adult doses of Technetium Tc 99m Pyrophosphate Injection are:

Indication	Doses as Technetium Tc 99	Fraction of Vial Contents Required
Skeletal Imaging	185 to 555 megabecquerels (5 to 15 mCi)	0.07 to 0.91
Cardiac Imaging	370 to 555 megabecquerels (10 to 15 mCi)	0.26 to 0.45

Technetium Tc 99m Pyrophosphate Injection is injected intravenously over a 10- to 20-second period. For optimal results, bone imaging should be done one to six hours following administration. Cardiac imaging should be done 60 to 90 minutes following administration. The acute myocardial infarct can be visualized from 24 hours to nine days following onset of symptoms, with maximum localization at 48 to 72 hours. Cardiac imaging should be done with a gamma scintillation camera. It is recommended that images be made of the anterior, left anterior oblique and left lateral projections.

The patient dose should be measured by a suitable radioactivity calibration system immediately prior to administration. It is also recommended that the radiochemical purity be checked prior to administration.

Blood Pool Imaging

The recommended adult dose of Technescan PYP is one-third (0.33) to the entire vial contents, followed by 555 to 740 megabecquerels (15 to 20 millicuries) of sodium pertechnetate Tc 99m. Cardiac imaging should be done 10 minutes following the administration of sodium pertechnetate Tc 99m (in vivo method) or Tc 99m labeled red blood cells (modified in vivo/in vitro method) utilizing a scintillation camera interfaced to an electrocardiographic gating device.

In Vivo Method: Technescan PYP is reconstituted with sterile, non-pyrogenic normal saline containing no preservatives. The patient dose is administered intravenously 15 to 30 minutes prior to the intravenous administration of 555 to 740 megabecquerels (15 to 20 millicuries) of sodium pertechnetate Tc 99m. Technescan PYP should be injected by direct venipuncture. **Heparinized catheter systems should be avoided.**

Modified In Vivo/In Vitro Method Using Acid-Citrate-Dextrose (ACD): Technescan PYP is reconstituted with sterile, non-pyrogenic normal saline containing no preservatives, and the patient dose is administered intravenously. An intravenous line containing a 3-way stopcock is inserted in a large peripheral vein and kept patent with a continuous drip of sterile, non-pyrogenic normal saline containing no preservatives. Thirty minutes after Technescan PYP injection, the infusion line and stopcock are cleared by withdrawing and discarding approximately 5 milliliters of whole blood. Immediately following, approximately 5 milliliters of whole blood are withdrawn into a syringe containing 1 milliliter preservative-free acid-citrate-dextrose (ACD) and 555 to 740 megabecquerels (15 to 20 millicuries) of sodium pertechnetate Tc 99m. The stopcock is then turned, residual blood is flushed from the intravenous line, and the normal saline flow is readjusted. The syringe is gently rotated to mix and allowed to incubate at room temperature for 10 minutes prior to injection via the 3-way stopcock.

Modified In Vivo/In Vitro Method Using Heparin: Technescan PYP is reconstituted with sterile, non-pyrogenic normal saline containing no preservatives, and the patient dose is administered intravenously. An infusion set fitted with a 3-way stopcock is placed in a large peripheral vein, and the intravenous line is heparinized with a saline solution containing 5 to 10 units preservative-free heparin per milliliter. Thirty minutes after Technescan PYP injection, 3 milliliters of blood are withdrawn into a syringe containing 555 to 740 megabecquerels (15 to 20 millicuries) of sodium pertechnetate Tc 99m. Anticoagulation of the blood is provided by residual heparin in the intravenous line. The syringe is gently rotated to mix and allowed to incubate at room temperature for 10 minutes prior to injection via the 3-way stopcock.

Parenteral drug products should be visually inspected for particulate matter and discoloration prior to administration whenever solution and container permit. Do not use if contents are turbid.

RADIATION DOSIMETRY

Method of Calculation: The following radiation absorbed dose values were obtained using the Medical Internal Radiation Dose Committee (MIRD) Schema.

Bone and Cardiac Imaging

Maximum Dose: 555 megabecquerels (15 millicuries) administered intravenously. The effective half-life was assumed to be the physical half-life for all calculated values. About 50% of each dose of Technetium Tc 99m Pyrophosphate Injection is retained in skeleton, and about 50% is excreted into the bladder. The estimated absorbed radiation doses to an average patient (70 kg) from an intravenous injection of a maximum dose of 555 megabecquerels (15 millicuries) of Technetium Tc 99m Pyrophosphate Injection are shown in Table 4.

Table 4. Absorbed Radiation Doses (Bone and Cardiac Imaging)

Tissue	Technetium Tc 99m Pyrophosphate Injection	
	mGy/555 MBq	rads/15 mCi
Skeleton*	5.9	0.59
Bone Marrow	4.2	0.42
Kidneys	21.0	2.10
Total Body	1.3	0.13
Bladder		
2-hr. void	14.6	1.46
4.8-hr. void	34.5	3.45
Testes		
2-hr. void	1.5	0.15
4.8-hr. void	2.3	0.23
Ovaries		
2-hr. void	1.4	0.14
4.8-hr. void	2.3	0.23
Heart		
Normal	1.1	0.11
Impaired	2.2	0.22

*Dose at point of highest uptake may be a factor of 10 higher.

Blood Pool Imaging

The estimated absorbed radiation doses to an average patient (70 kg) from administration of 740 megabecquerels (20 millicuries) of sodium pertechnetate Tc 99m, 30 minutes after the intravenous administration of Technescan PYP are shown in Table 5.

*Table 5. Absorbed Radiation Doses[2] (Blood Pool Imaging)**

Tissue	Sodium Pertechnetate Tc 99m 30 min. Post Technescan PYP Administration	
	mGy/740 MBq	rads/20 mCi
Bladder Wall	6.8	0.68
Ovaries	4.6	0.46
Testes	2.6	0.26
Red Marrow	3.8	0.38
Spleen**	3.0	0.30
Blood	10.2	1.02
Total Body	3.0	0.30

*Assumes non-resting state, with 75% of the sodium pertechnetate Tc 99m labeling red blood cells and the other 25% remaining as pertechnetate.

** Assumes no initial uptake in spleen.

[2] Data supplied by Oak Ridge Associated Universities, Radiopharmaceutical Internal Dose Information Center, 1986.

HOW SUPPLIED

Catalog Number 094.

Technescan PYP is supplied as a lyophilized powder packaged in vials. Each vial contains 11.9 mg sodium pyrophosphate, 3.2 mg (minimum) stannous chloride ($SnCl_2 \cdot 2H_2O$) and 4.4 milligrams (maximum) total tin expressed as stannous chloride ($SnCl_2 \cdot 2H_2O$), sealed under an atmosphere of nitrogen. Prior to lyophilization the pH is adjusted with hydrochloric acid. The pH of the reconstituted drug is between 4.5 and 7.5.

Kit containing 5 vials is available.

Storage

The Technescan PYP Kit must be maintained in a refrigerator, 2° to 8°C (36° to 46°F) until use. The reconstituted vial should be stored at controlled room temperature, 20° to 25°C (68° to 77°F).

INSTRUCTIONS FOR PREPARING THE DRUG

Procedural Precautions

All transfer and vial stopper entries must be done using aseptic techniques.

Procedure

Bone and Cardiac Imaging

Note 1: Wear waterproof gloves during the entire preparation procedure and during subsequent patient dose withdrawals from the reaction vial.

Note 2: Make all transfers of sodium pertechnetate Tc 99m solution during the preparation procedure with an adequately shielded syringe.

Note 3: Keep the **Radioactive Preparation** in the lead shield described below (with cap in place) during the useful life of the **Radioactive Preparation**. Make all withdrawals and injections of the **Radioactive Preparation** with an adequately shielded syringe.

1. A **Technescan PYP** reaction vial is removed from the refrigerator and approximately five (5) minutes are allowed for the contents to come to room temperature.
2. Attach radioassay information label with radiation warning symbol to the reaction vial and place the vial in a lead Dispensing Shield fitted with a lead cap and having a minimum wall thickness of 1/8 inch. Do not remove reaction vial from the Dispensing Shield except, temporarily, for Step 5 below.
3. Sodium pertechnetate Tc 99m solution (1 to 10 milliliters) is added to the reaction vial. In choosing the amount of technetium Tc 99m radioactivity to be used in the preparation of the Technetium Tc 99m Pyrophosphate Injection, the labeling efficiency, number of patients, administered radioactive dose, and radioactive decay must be taken into account. The recommended **maximum amount** of technetium Tc 99m to be added to the reaction vial is **3.7 gigabecquerels (100 millicuries)**.
4. With the reaction vial in the Dispensing Shield (with cap in place), shake sufficiently to bring the lyophilized material into solution. Allow to stand for five (5) minutes at room temperature.
5. Using proper shielding, the reaction vial should be visually inspected. The resulting solution should be clear and free of particulate matter. If not, the reaction vial should not be used.
6. Assay the product in a suitable calibrator and record the time, date of preparation and the activity of the Technetium Tc 99m Pyrophosphate Injection onto the radioassay information label. Store the reaction vial in the Dispensing Shield at 20° to 25°C (68° to 77°F) when not in use and **discard after six (6) hours from the time of preparation.**

Blood Pool Imaging

1. A **Technescan PYP** reaction vial is removed from the refrigerator and approximately five (5) minutes are allowed for the contents to come to room temperature.
2. Reconstitute the reaction vial with 3 milliliters of sterile, non-pyrogenic normal saline containing no preservatives.
3. Shake the reaction vial sufficiently to bring the lyophilized material into solution. Allow to stand for five (5) minutes at room temperature.
4. The reaction vial should be visually inspected. The resulting solution should be clear and free of particulate matter. If not, the reaction vial should not be used.
5. Store reconstituted reaction vial at 20° to 25°C (68° to 77°F) when not in use and **discard after six (6) hours from time of preparation**.

This reagent kit is approved for distribution to persons licensed by the U.S. Nuclear Regulatory Commission to use byproduct material identified in Section 35.200 or under an equivalent license of an Agreement State.

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Made in USA

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