

STANNOUS PYROPHOSPHATE Kit for the Preparation of Technetium-99m Pyrophosphate Injection and Stannous Pyrophosphate Injection

RADIODIAGNOSTIC AGENT

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Edmonton, Alberta
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Name

Stannous Pyrophosphate Kit for the Preparation of Technetium-99m Pyrophosphate Injection and Stannous Pyrophosphate Injection.

Description

Stannous Pyrophosphate Kit is a sterile, non-pyrogenic lyophilized powder containing 11.9 mg sodium pyrophosphate and 3.4 mg stannous chloride in a sealed vial. The pH is adjusted to 6.2 to 6.5 with hydrochloric acid and sodium hydroxide prior to lyophilization. Stannous Pyrophosphate Kit is used in the preparation of Tc-99m Pyrophosphate Injection and in the preparation of Stannous Pyrophosphate Injection.

Physical Characteristics

Technetium-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 per Disintegration	Energy (keV)
Gamma-2	89.07	140.5

The specific gamma ray constant for technetium-99m is 5.4 microcoulombs/kg-MBq-hr (0.78 R/mCi) at 1 cm. The first half value thickness for lead (Pb) for technetium-99m is 0.017 cm. A range of values for the relative attenuation of the radiation emitted by this radionuclide resulting from the interposition of various thicknesses of lead (Pb) is

presented in Table 2. For example, the use of 0.25 cm of lead 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 intervals, after the time of calibration, are presented in Table 3.

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

Hours	Fraction	Hours	Fraction
1	0.891	7	0.446
2	0.794	8	0.397
3	0.707	9	0.354
4	0.630	10	0.315
5	0.561	11	0.281
6	0.500	12	0.250

Action

Tc-99m Pyrophosphate Injection: When administered intravenously, Tc-99m pyrophosphate is cleared relatively rapidly from the blood by bone deposition and urinary excretion. In the normal patient, 30-70% of the administered dose is present in the bone four hours after administration.

Tc-99m pyrophosphate has also been found to localize at sites of myocardial infarction.

Stannous Pyrophosphate Injection: Stannous pyrophosphate has an affinity

for red blood cells. When administered 30 minutes prior to the intravenous

administration of Tc-99m Sodium Pertechnetate Injection, approximately 75-80% of the administered radioactivity remains in the blood.

Indications

Tc-99m Pyrophosphate Injection may be used for diagnostic skeletal imaging

or for the detection of myocardial infarction.

Stannous Pyrophosphate Injection may be used in conjunction with Tc-99m Sodium Pertechnetate Injection for cardiac blood pool imaging.

Contraindications

There are no known contraindications to the use of Tc-99m Pyrophosphate Injection or Stannous Pyrophosphate Injection.

Warnings

As with any radiopharmaceutical, this product should not be administered to pregnant patients unless it is considered that the potential information outweighs the potential risks. If possible, examinations of women of child bearing capacity with this agent should be limited to the first few (10) days following menses. Since technetium-99m pyrophosphate or technetium-99m sodium pertechnetate may be excreted in the milk, the substitution of formula feeding for several days should be recommended to nursing mothers. This product should only be used by qualified physicians who have been licenced by the appropriate government agency to use and administer radiopharmaceuticals.

Precautions

To reduce radiation exposure to the bladder, the patient should be encouraged to drink fluids and to void frequently following administration of technetium-99m pyrophosphate. Once radiolabeled with technetium-99m, adequate shielding of the product must be maintained to minimize radiation exposure to personnel and patients. The contents of Stannous Pyrophosphate Kit vials are sterile and pyrogen-free. Aseptic technique must be maintained throughout the radiolabeling procedure to ensure that sterility is maintained. The preparation contains no bacteriostatic preservative. The biodistribution of technetium-99m pyrophosphate may be affected by various pathophysiological conditions which may be broadly categorized as hormonal, neoplastic, traumatic, inflammatory, ischemic, excretory and artifactual. In addition, concomitant medications, including iron containing compounds, therapeutic diphosphonates, and some antibiotics and chemotherapeutic agents, as well as other drugs, may change the biodistribution of technetium-99m pyrophosphate. Clinicians evaluating diagnostic studies with this agent should be familiar with the potential for altered biodistributions.

Carcinogenesis, Mutagenesis, Impairment of Fertility:

No long term studies have been done to evaluate the carcinogenic or mutagenic potential of this drug. There have been no studies done to determine if there is any effect of this drug on fertility in males or females.

Adverse Reactions

No adverse reactions specifically attributable to Tc-99m Pyrophosphate Injection or Stannous Pyrophosphate Injection have been noted.

Radiation Dosimetry

A. Tc-99m Pyrophosphate Injection:

The following radiation dose estimates are from Weber et al (J.

Nucl. Med. 30, 1117, 1989):

Table 4.
Absorbed Radiation Dose Estimates for
Technetium Tc-99m Pyrophosphate Injection

Organ	uGy/MBq
Bone Surfaces	68.0
Red Marrow	11.0
Kidneys	6.3
Bladder wall	25.0
Ovaries	3.7
Testes	2.6
Remainder of body	3.5

The Effective Dose is 7.6 uSv/MBq for males and 7.9 uSv/MBq for females.

B. Tc-99m Red Blood Cells labeled using Stannous Pyrophosphate Injection and Tc-99m Sodium Pertechnetate Injection

The following radiation dose estimates are from Atkins et al (J. Nucl. Med. 31, 378, 1990) (In Vivo labeling technique):

Table 5.
Absorbed Radiation Dose Estimates for
Technetium Tc-99m Red Blood Cells Injection

Organ	uGy/MBq
Heart Wall	15.0
Bladder Wall	17.0
Spleen	12.0
Lungs	12.0
Blood	10.0
Liver	7.6
Kidneys	7.3
Red Marrow	5.4
Thyroid	5.1
Ovaries	5.1
Testes	2.2
Total Body	4.3

The Effective Dose is 7.3 uSv/MBq for males and 8.0 uSv/MBq for females.

Dosage and Administration

Tc-99m Pyrophosphate Injection

Bone Imaging - The usual adult intravenous dose is 400-500 MBq with optimum imaging obtained 2 to 5 hours after administration.

Cardiac Infarct Imaging - The usual adult intravenous dose is 400-500 MBq

with optimum imaging 60 to 90 minutes after administration. Acute myocardial infarcts can be visualized from 1 to 9 days following onset of symptoms with maximum localization at 48 to 72 hours.

Stannous Pyrophosphate Blood Pool Imaging

A vial of Stannous Pyrophosphate Kit should be dissolved in 3.0 ml of Saline for Injection U.S.P. (without bacteriostatic agent) - see preparation instructions. The usual adult dose is one-third to two-thirds of the contents of one Stannous Pyrophosphate Kit vial by direct intravenous injection. Avoid administration by catheter, especially by heparinized catheter. Thirty minutes after administration of stannous pyrophosphate administer Tc-99m Sodium Pertechnetate Injection intravenously (usual adult dose 550-750 MBq)

Instructions -

A. Preparation of Technetium-99m Pyrophosphate Injection

- 1) Place Stannous Pyrophosphate Kit vial in adequate lead shielding.
- 2) Add 2.0 to 6.0 ml (1 to 6 GBq) of oxidant-free Tc-99m Sodium Pertechnetate U.S.P. Invert several times to dissolve contents. Using adequate shielding inspect solution for the presence of undissolved material. If solution is not clear, colorless and without any evidence of particulate material, do not use.
- 3) Label as to contents.
- 4) Allow to incubate at room temperature for 5 minutes before use.

Quality Control

The radiochemical purity of the finished radiopharmaceutical must be checked prior to patient administration. The following are suggested quality control procedures for technetium-99m pyrophosphate. Other validated procedures may be used to verify the quality of the final preparation.

Thin layer chromatography is used to determine the levels of technetium-99m sodium pertechnetate and technetium-99m colloidal impurities in the product.

a) Technetium-99m sodium pertechnetate impurity

- 1) Approximately 1 cm from the bottom of a 1 cm x 7 cm strip of Gelman ITLC-SG chromatography medium, spot a small drop of product using a 1 ml syringe with a 25 G needle.
- 2) Allow spot to dry in air without heat.
- 3) Develop strip with normal butanol. Allow solvent to run to within 1 cm of the top of the strip.
- 4) Cut strip into 1 cm segments. Count segments using a suitable detector.

Technetium-99m pyrophosphate and technetium-99m labeled colloidal impurity

will remain at the origin (first two segments) while technetium-99m sodium pertechnetate will migrate close to the solvent front.
5) Calculate the percent technetium-99m sodium pertechnetate impurity using the formula:

$$100 \times (\text{total counts in last 5 segments}) / (\text{total counts in all 7 segments})$$

b) Technetium-99m labeled colloidal impurity

1) Approximately 1 cm from the bottom of a 1 cm x 7 cm strip of Gelman ITLC-SG chromatography medium, spot a small drop of product using a 1 ml

syringe with a 25 G needle.

2) Without allowing the spot to dry develop the strip in 0.9% sodium chloride in water (normal saline).

3) Cut strip into 1 cm segments. Count segments using a suitable detector.

Technetium-99m colloidal impurity will remain at the origin (first two segments) while technetium-99m pyrophosphate and technetium-99m sodium pertechnetate will migrate close to the solvent front.

4) Calculate the percent technetium-99m colloidal impurity using the formula:

$$100 \times (\text{total counts in first 2 segments}) / (\text{total counts in all 7 segments})$$

Calculate the net percent purity using the formula:

$$\text{Purity} = 100 - ((\text{percent Tc-99m sodium pertechnetate impurity}) + (\text{percent Tc-99m colloidal impurity}))$$

If the purity is less than 90% the product should not be used.

B. Stannous Pyrophosphate Injection

1) Add 3.0 ml Saline for Injection U.S.P. (without bacteriostatic agent)

to Stannous Pyrophosphate Kit vial. Invert several times to dissolve contents.

2) Visually inspect contents of vial. If solution is not clear and colorless and without any evidence of particulate material, do not use.

How Supplied

Each vial Kit contains:

Sodium Pyrophosphate	11.9 mg
Stannous Chloride (Anhydrous)	3.4 mg

The pH is adjusted to 6.2 to 6.5 with hydrochloric acid and sodium hydroxide prior to lyophilization.

Storage

Stannous Pyrophosphate Kit vials should be stored at 15o C to 30o C.
Technetium-99m Pyrophosphate Injection should be stored at 15o C to 30o C.

Stannous Pyrophosphate Injection should be stored at 15o C to 30o C.

Expiry

Stannous Pyrophosphate Kit - as indicated on label

Tc-99m Pyrophosphate Injection - 8 hours from preparation

Stannous Pyrophosphate Injection - 3 hours from preparation

References:

1. Kocher, David, "Radioactive Decay Data Tables", DOE/TIC 11026, 108 (1981)

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