

MDP-10 KIT for the Preparation of Technetium-99m Medronate Radiodiagnostic Reagent

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Name

MDP-10 Kit for the Preparation of Tc-99m Medronate Injection

Description

MDP-21 Kit is a sterile, non-pyrogenic lyophilized powder containing 10 mg methylene diphosphonate, 0.92 mg stannous chloride, 0.125 mg ascorbic acid in a sealed vial. The pH is adjusted to 6.2 to 6.5 with hydrochloric acid and sodium hydroxide prior to lyophilization. MDP-10 Kit is used in the preparation of Technetium-99m Medronate 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

Technetium-99m Medronate prepared using MDP-10 Kit, upon intravenous injection, is relatively rapidly cleared from the blood by bone deposition and urinary excretion. In the normal patient, 30-70% of the administered dose is present in the bone two hours after administration with approximately 5% remaining in the blood. Increased localization in areas of abnormal osteogenesis is probably at least partially due to an increase in blood flow in these areas.

Indications

Technetium-99m Medronate Injection prepared using MDP-10 Kit is used for diagnostic skeletal imaging.

Contraindications

There are no known contraindications to the use of technetium-99m medronate.

Warnings

As with any radiopharmaceutical, technetium-99m medronate 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 medronate 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

This class of compounds is known to complex cations such as calcium. Particular caution should be used with patients who have, or may be predisposed to hypocalcemia.

Contents of the reaction vial are intended only for use in the preparation of Technetium Tc-99m Medronate Injection and are not to be administered directly to the patient.

Once radiolabeled with technetium-99m, adequate shielding of the product

must be maintained to minimize radiation exposure to personnel and patients.

The contents of MDP-10 Kit 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 technetium-99m medronate prepared from the product should be discarded 12 hours after reconstitution. To reduce radiation exposure to

the bladder, the patient should be encouraged to drink fluids and to void

frequently following administration of technetium-99m medronate. The biodistribution of technetium-99m medronate 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 medronate. 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

Hypersensitivity type reactions have been reported following the administration of technetium-99m medronate. This is most commonly manifested as skin rash with or without itch or nausea and vomiting. The incidence of reactions is hard to determine but may be in the order of 1 in 1,000. Symptoms normally disappear within a few hours without treatment.

Toxicology

The toxicity of stannous methylene diphosphonate (medronate) was investigated in the mouse. An intravenous injection at the level of 66

mg/kg (2 mg/0.2 ml/30 g) produced no immediate or delayed (up to 30 days)

gross effects. These results indicate a safety factor of at least 500. Subramanian et al (J. Nucl. Med. 16, 744, 1975) found the acute LD50 of methylene diphosphonate in mice and rabbits to be 45-50 mg/kg.

Variation

in toxicity results may be attributable to differences in formulation, dilution and rate of injection.

Radiation Dosimetry

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 Medronate Injection

Organ	uGy/MBq
Bone Surfaces	61.0
Red Marrow	9.3
Kidneys	8.4
Bladder wall	34.0
Ovaries	3.2
Testes	2.2
Remainder of body	2.8

The effective dose equivalent is 7.4 uSv/MBq for males and 7.6 uSv/MBq for females.

Dosage and Administration

The usual adult intravenous dose of technetium-99m medronate is 185 - 555

MBq. Optimum imaging time is 2 to 4 hours after administration. The patient dose should be measured in a suitable calibration system immediately before administration.

Instructions -

Preparation of Technetium-99m Medronate

- 1) Place MDP-10 Kit vial in adequate lead shielding.
- 2) Using aseptic technique, add 2.0 to 10.0 ml (4 to 20 GBq) of oxidant-free Tc-99m Sodium Pertechnetate U.S.P.
- 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 medronate. Other validated

procedures may be used to verify the radiochemical purity of the final preparation. Instant 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. Measure the radioactivity contained in each segment using a suitable detector. Technetium-99m medronate 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. Measure the radioactivity contained in each segment using a suitable detector. Technetium-99m colloidal impurity will remain at the origin (first two segments) while technetium-99m medronate 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:

Purity = 100 - ((percent Tc-99m sodium pertechnetate impurity) + (percent Tc-99m colloidal impurity)) If the purity is less than 90% the product should not be used.

How Supplied

Each reaction vial of MDP-10 Kit contains:

Methylene Diphosphonic Acid	10.0 mg
Stannous Chloride (Anhydrous)	0.92 mg
Ascorbic Acid	0.125 mg

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

Storage

MDP-10 Kit vials should be stored at 15o C to 30o C.

Technetium-99m Medronate should be stored at 15o C to 30o C.

Expiry

MDP-10 Kit - as indicated on label

Technetium-99m Medronate - 12 hours from preparation

References:

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