

MDP Multidose**Kit for the Preparation of Technetium Tc99m Medronate Injection****DIAGNOSTIC - FOR INTRAVENOUS USE****DESCRIPTION**

Each kit contains 10 multidose reaction vials, each containing 10 mg of medronic acid, 0.17 mg (minimum) stannous chloride (maximum stannous and stannic chloride 0.29 mg), and 2 mg ascorbic acid. The contents of the vial are sterile, pyrogen-free, lyophilized and sealed under nitrogen. The pH has been adjusted to 4.0-7.8 with hydrochloric acid and sodium hydroxide.

Administration is by intravenous injection for diagnostic use, after reconstitution with oxidant-free sodium pertechnetate Tc99m injection. The product as supplied is sterile and pyrogen-free.

The precise structure of stannous technetium Tc99m medronate complex is unknown at this time.

Physical Characteristics

Technetium Tc99m decays by isomeric transition with a physical half-life of 6.02 hours.¹ The principal photon that is useful for detection and imaging studies is listed in Table 1.

Table 1. Principal Radiation Emission Data¹

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

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

External Radiation

The specific gamma ray constant for Tc99m is 0.78 R/hr-mCi at 1 cm. The first half-value layer is 0.017 cm of Pb. 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 a 0.25 cm thickness of Pb will attenuate the radiation emitted by a factor of 1,000.

Table 2. Radiation Attenuation of Lead (Pb) 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 shown in Table 3.

Table 3. Physical Decay Chart: Tc99m, half-life 6.02 hours

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

*Calibration Time

CLINICAL PHARMACOLOGY

During the initial 24 hours following intravenous injection of technetium Tc99m medronate about 50% of each dose is retained in the skeleton, and about 50% of each dose is excreted into the bladder.

Within 3 hours bone uptake is about 40-50% of each dose. Clearance of the complex from the blood is rapid and within the first 3-6 hours up to about 50% of each dose is cleared by urinary excretion.

Skeletal uptake of the complex occurs as a function of blood flow to bone and bone efficiency in extracting the complex. Bone mineral crystals are generally considered to be hydroxyapatite, and the complex appears to have an affinity for the hydroxyapatite crystals in bone.

INDICATIONS AND USAGE

Technetium Tc99m medronate injection may be used as a bone imaging agent to delineate areas of altered osteogenesis.

CONTRAINDICATIONS

Hypersensitivity to technetium Tc99m medronate or to any of the excipients.

WARNINGS

Anaphylactic/anaphylactoid reactions that may be life-threatening have occurred with the use of technetium Tc99m medronate. Manifestations include: shock, hypotension, loss of consciousness, dyspnea, cyanosis, wheezing, generalized rash, and pruritus. Advanced life support equipment and trained personnel should be readily available.

This class of compound is known to complex cations such as calcium. Particular caution should be used with patients who have, or who may be predisposed to, hypocalcemia (i.e., alkalosis). The clinical significance of this information is unknown as no cases of hypocalcemia have been reported.

Reports indicate impairment of brain scans using sodium pertechnetate Tc99m injection which have been preceded by a bone scan using an agent containing stannous ions. This

impairment may result in false-positive or false-negative brain scans. It is recommended that brain scans precede bone imaging procedures. Alternately, a brain-imaging agent such as technetium Tc99m pentetate injection may be employed.

PRECAUTIONS

General

The contents of the kit before preparation are not radioactive. However, after the sodium pertechnetate Tc99m injection is added, adequate shielding of the final preparation must be maintained.

Contents of the vial are intended only for use in the preparation of technetium Tc99m medronate injection and are NOT to be administered directly to the patient.

Technetium Tc99m medronate injection, as well as other radioactive drugs, must be handled with care. Once sodium pertechnetate Tc99m injection is added to the vial, appropriate safety measures should be used to minimize external radiation to clinical occupational personnel. Care should also be taken to minimize radiation exposure to patients in a manner consistent with proper patient management.

To minimize radiation dose to the bladder, the patient should be encouraged to drink fluids and to void immediately before the examination and as often thereafter as possible for the next 4-6 hours.

Technetium Tc99m medronate injection contains no bacteriostatic preservative. The preparation should be formulated within 6 hours prior to clinical use. Optimal imaging results are obtained 1 to 4 hours after administration. Technetium Tc99m medronate injection should be discarded 6 hours after reconstitution. The solution should not be used if cloudy. Image quality may be adversely affected by patient obesity, old age, and impaired renal function.

The finding of an abnormal concentration of radioactivity implies the existence of underlying pathology, but further study is required to distinguish benign from malignant lesions.

The components of the kit are sterile and pyrogen-free. It is essential to follow directions carefully and to adhere to strict aseptic procedures during preparation.

Technetium Tc99m labeling reactions involved depend on maintaining the stannous ion in the reduced state. Hence, sodium pertechnetate Tc99m containing oxidants should not be used.

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

Carcinogenesis, Mutagenesis, Impairment of Fertility

No long-term animal studies have been performed to evaluate carcinogenic potential, mutagenic potential, or whether technetium Tc99m medronate injection affects fertility in males or females.

Pregnancy Category C

Animal reproduction studies have not been conducted with technetium Tc99m medronate injection. It is also not known whether technetium Tc99m medronate injection can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Technetium Tc99m medronate 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 Tc99m is excreted in human milk during lactation. Therefore, formula feedings should be substituted for breast feedings.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

Several adverse reactions due to technetium Tc99m medronate have been reported. These were usually hypersensitivity reactions characterized by itching, various skin rashes, hypotension, chills, nausea and vomiting. There have also been rare cases of dizziness and asthenia associated with the use of technetium Tc99m medronate.

Postmarketing Experience

The following adverse reactions associated with the use of technetium Tc99m medronate have been identified during post-approval use:

Anaphylactic/anaphylactoid reactions that may be life-threatening and include shock, hypotension, loss of consciousness, dyspnea, cyanosis, and wheezing. Advanced life support equipment and trained personnel should be readily available.

Local or generalized rash with itching and dermal irritation, headache, malaise, edema of the extremities, and arthralgia have also been reported. The time to onset of these symptoms may occur within minutes or be delayed by several hours post-administration of technetium Tc99m medronate. Users are requested to report to GE Healthcare any instances of suspected adverse drug reactions associated with the use of technetium Tc99m medronate.

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.

DOSAGE AND ADMINISTRATION

After preparation with oxidant-free sodium pertechnetate Tc99m injection the suggested dose range of technetium Tc99m medronate injection in the average patient (70 kg) is 370-740 MBq (10-20 mCi) given intravenously. Imaging post injection is optimal at 1 to 4 hours.

The patient dose should be measured by a suitable radioactivity calibration system immediately prior to administration.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. Shielding should be utilized when preparing the technetium Tc99m medronate injection.

Slow administration of the drug over a period of 30 seconds is recommended.

Radiation Dosimetry

The effective half-life was assumed to be the physical half-life for all calculated values. The estimated radiation absorbed doses² to an average patient (70 kg) for an intravenous injection of a maximum dose of 740 MBq (20 mCi) of technetium Tc99m medronate injection are shown in Table 4.

Table 4. Absorbed Radiation Dose²

Organ	mGy/740 MBq	rads/20 mCi
Total Body	1.3	0.13
Bone Total	7.0	0.70
Red Marrow	5.6	0.56
Kidneys	8.0	0.80
Liver	0.6	0.06
Bladder Wall 2-hr. void	26.0	2.60
4.8-hr. void	62.0	6.20
Ovaries 2-hr. void	2.4	0.24
4.8-hr. void	3.4	0.34
Testes 2-hr. void	1.6	0.16
4.8-hr. void	2.2	0.22

²Method of Calculation: "S" Absorbed Dose per Unit Cumulated Activity Selected Radionuclides and Organs, MIRD Pamphlet No. 11, 1975.

The typical total body exposure to a person administering a maximum dose of 740 MBq (20 mCi) of technetium Tc99m to a patient is about 0.2 μ Sv, 0.02 mR.³

HOW SUPPLIED

Kit Contents

10 STERILE REACTION VIALS, each 10 mL vial contains, in lyophilized form and under nitrogen atmosphere, 10 mg of medronic acid, 0.17 mg (minimum) stannous chloride (maximum stannous and stannic chloride 0.29 mg), and 2 mg ascorbic acid. Hydrochloric acid and sodium hydroxide have been added for pH adjustment prior to lyophilization.

10 PRESSURE-SENSITIVE LABELS for final preparation of technetium Tc99m medronate injection.

1 PACKAGE INSERT

NDC 17156-438-04

Storage

Store kit contents and final preparation at or below 25°C (77°F).

³Barrall, R.C., Smith, S.J., Personnel Radiation Exposure and Protection from 99m Tc Radiations, In: Kereiakes, J. G., Corey, K. R., eds. Biophysical Aspects of the Medical Use of Technetium Tc99m, American Association of Physicists in Medicine Monograph No. 1, 1976: p. 77.

Preparation

The following directions must be carefully followed for optimum preparation of technetium Tc99m medronate injection.

Note: Use aseptic procedures throughout and take precautions to minimize radiation exposure by the use of suitable shielding. Waterproof gloves should be worn during the preparation procedure.

1. Remove the protective disc from the reaction vial and aseptically swab the rubber septum with alcohol.
2. Affix a pressure-sensitive label to a lead shield* and place the vial in the labeled lead shield.
3. Using a shielded, sterile syringe, aseptically add 2-8 mL of sterile, pyrogen-free, oxidant-free sodium pertechnetate Tc99m injection to the vial.
4. Place fitted cover onto the lead shield. Swirl the contents of the vial for one minute and let stand 1-2 minutes. Using proper shielding, visually inspect the vial. Discard if foreign matter is observed.
5. Record the time and date of preparation and the volume, activity and calibration of the sodium pertechnetate Tc99m injection added.
6. The technetium Tc99m medronate injection is ready for use.
7. Store the finished product in the capped lead shield at or below 25°C (77°F). Use within 6 hours after formulation.

Note: It is recommended that with proper shielding and equipment, the final formulation be tested for radiochemical purity. If radiochemical purity is not adequate, discard the finished drug.

*Use vial shield, Catalog No. 99-0520, or equivalent.

Disposal

The residual materials may be discarded in ordinary trash provided the vials and syringes read no greater than background with an appropriate low-range survey meter. All identifying labels should be destroyed before discarding.

This reagent kit is approved by the U.S. Nuclear Regulatory Commission for distribution to persons licensed to use by-product material identified in §35.200 of 10 CFR Part 35, to persons who have a similar authorization issued by an Agreement State, and, outside the United States, to persons authorized by the appropriate authority.

GE Healthcare



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