SOREQ RADIOPHARMACEUTICALS

Tc-MDP

Kit for Tc-99m MDP

The format and content of this document have been approved by the Ministry of Health

TO BE USED IN DIAGNOSTIC INSTITUTES ONLY

DESCRIPTION

Diagnostic agent for intravenous injection.
Sterile, non-pyrogenic, lyophilized, one step kit.
Presentation - Box of 5 vials.
Mixture pH 6.0 - 7.0
Contains no preservatives.

COMPOSITION

Per vial:
Active substance:

MDP = Methylene diphosphonic acid	7.0 mg
Inactive substances:	
$SnCl_2 \times 2H_2O$	1.0 mg
Ascorbic Acid	2.0 mg

CLINICAL PHARMACOLOGY

Following its intravenous administration, **Tc-99m MDP**, about 50% of the dose is retained in the skeleton, and about 50% is renally excreted.
Post injection – only 4% of the injected dose can be detected in blood.
Tc-99m MDP is absorbed onto hydroxyapatite crystals at sites of new bone formation and amount of osseous uptake is proportional to the metabolic activity of the bone, and to skeletal blood flow.
Tc-99m MDP shows specific affinity for areas of altered osteogenesis.

INDICATIONS: Bone imaging

DOSAGE AND ADMINISTRATION

The recommended intravenous dose for the average adult patient (70 Kg) is: **10 - 20 mCi** per examination.
Prior to administration, the injection should be inspected visually for particulate matter and discoloration.
Optimal imaging results are obtained 1-4 hours after administration.
The preparation should be used within 8 hours, since it contains no bacterial preservatives.
Store in a cold place 2-8^{0}c before reconstitution.

CONTRAINDICATIONS

None known, however, hypersensitivity to any component of this product, should be considered.

ADVERSE REACTIONS

Adverse reactions have been reported following injection of MDP. Those appear to be allergic dermatological reaction that can be treated with non-sedative histamine H1 antagonist.
Other hypersensitivity reactions may include itching, various skin rashes, hypotension, chills, nausea, fever and vomiting.

PRECAUTIONS

The patients should be encouraged to increase fluid intake and to void when the examination is completed and as often thereafter as possible for the next 4 to 6 hours in order to minimize the radiation dose to the bladder.
Impaired renal function may adversely affect image quality.
Voiding is also recommended immediately prior to imaging procedures to reduce background interference that may result because of the accumulation of the agent in the bladder.

WARNINGS

This class of compounds 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).
Preliminary reports indicate impairment of brain scans using Sodium Pertechnetate Tc-99m Injection, which have been preceded by a bone scan using an agent containing stannous ions. The impairment may result in false-positive or false-negative brain scans. It is recommended, where feasible, that brain scans precede bone imaging procedures.

GENERAL

Radiopharmaceuticals should be used only by personnel 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.

The contents of the vial are intended only for use in the preparation of **Tc-99m MDP** and are not to be administered directly to the patient. The components of the kit are supplied sterile and non-pyrogenic. Aseptic procedures normally employed in making additions and withdrawals from sterile, non-pyrogenic containers should be used during the addition of the sodium pertechnetate Tc-99m solution and the withdrawal of doses for patient administration.

Tc-99m MDP injection, as other radioactive drugs, must be handled with care. Appropriate safety measures should be taken to minimize radiation exposure to both the clinical personnel and the patients.
Contents of the kit before preparation are not radioactive. However, after the sodium pertechnetate Tc-99m is added, adequate shielding of the final preparation must be maintained.

Technetium Tc-99m labeling reactions involved depend on maintaining the stannous ion in the reduced state. Hence, sodium pertechnetate Tc-99m injection containing oxidants should not be used.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY

No long term animal studies have been performed to evaluate carcinogenic potential or whether **Tc-99m MDP** injection affects fertility in males or females.

PREGNANCY CATEGORY C

Animal reproduction and teratogenicity studies have not been conducted with **Tc-99m MDP** injection. It is also not known whether **Tc-99m MDP** injection can cause fetal harms when administered to a pregnant woman or can affect reproductive capacity.

Tc-99m (as free pertechnetate) crosses the placenta, therefore, **Tc-99m MDP** 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 feedings.

PEDIATRIC USE
Safety and effectiveness in children before the age of 18 have not been established.

INTERACTIONS
Due to other medications
Antacids, aluminum-containing
(high blood concentrations of aluminum ion, which may occur in patients with gastrointestinal obstruction or impaired renal function, may cause localization of technetium Tc 99m medronate in the liver)
Diatrizoate sodium
(possible renal and hepatic uptake of technetium Tc 99m medronate if diatrizoate sodium is administered intravenously immediately after technetium Tc 99m medronate)
Etidronate
(etidronate may interfere with bone uptake of technetium Tc 99m medronate: a 2 week period after discontinuation of etidronate therapy is recommended before performance of a bone scan with technetium Tc 99m medronate)
Heparin calcium, subcutaneous or
Iron dextran, intramuscular
Meperidine, intramuscular
(possible accumulation of technetium Tc 99m medronate at site(s) of injection of these medications)
Iron supplements or preparations
(iron overload may cause a decrease in bone uptake of technetium Tc 99m medronate)
Potassium phosphates or
Potassium and sodium phosphates or
Sodium phosphates
(saturation of bone binding sites by phosphorus ions in these medications may cause decreased bone uptake of technetium Tc 99m medronate)
Due to medical problems or conditions
Bone demineralization, glucocorticoid - induced
(long - term therapy with these medications may induce bone mineral depletion thus causing decreased bone uptake of technetium Tc 99m medronate)
Gynecomastia, estrogen - induced
(possible localization of technetium Tc 99m medronate in breast)
Nephrotoxicity, drug - induced
(increased retention of technetium Tc 99m medronate in kidneys)
Obesity
(attenuation of photons coming from bone may decrease visualization)
Osteoporosis
(reduced mineral deposit in bone may result in images with lower target to non - target ratio)
Renal function impairment
(decreased clearance of technetium Tc 99m medronate from blood and soft tissues may decrease visualization because of a lower bone to background ratio resulting from the increased circulating activity; also, chronic renal function impairment may cause metastatic calcification and altered biodistribution of technetium Tc 99m medronate)
With results of other tests
Brain imaging
(brain scans using sodium pertechnetate Tc 99m may result in high blood background activity when performed after a bone scan using technetium Tc 99m medronate, which contains stannous ions; to avoid this potential diagnostic interference, brain scan may be performed prior to bone scan or with a brain imaging agent other than sodium pertechnetate Tc 99m [e.g., technetium Tc 99m pentetate])

ESTIMATED ABSORBED RADIATION DOSES

Organs	**Absorbed Dose rads / 20mCi**
Total Body	0.13
Bone Total	0.70
Red Marrow	0.56
Kidneys	0.80
Liver	0.06
Bladder Wall: 2 hr void	2.60
4.8 hr void	6.20
Ovaries: 2 hr void	0.24
4.8 hr void	0.34
Testes: 2 hr void	0.16
4.8 hr void	0.22

INSTRUCTIONS FOR PREPARATION OF TC-99M MDP
1. Waterproof gloves should be worn during the preparation procedure.
2. Remove the plastic disc from the flip-off seal of the reaction vial and swab the rubber septum with alcohol.
3. Place the reaction vial in a suitable radiation shield with fitted lead cap.
4. Using a sterile, shielded syringe, aseptically obtain 3-6 ml sterile, non-pyrogenic sodium pertechnetate Tc-99m, containing the wanted amount of radioactivity (50-500mCi) and aseptically inject into the reaction vial.
5. Place the lead cap on the vial shield, gently swirl the contents of the vial. To ensure maximal labeling yield, allow the preparation 15 minutes incubation at room temperature.
6. Calibrate the vial and record the information on the radiation label, together with volume, date and time.
7. Using proper shielding, the vial containing the reconstituted product should be visually inspected for foreign matter prior to injection.
   Do not use if foreign matter is observed.
8. Aseptically withdraw material using a sterile shielded syringe with a sterile needle.
9. The radiolabeled preparation should be stored, adequately shielded, at room temperature (15-25°C) and used within 8 h.

Manufacturer: Soreq Nuclear Research Center, Yavne 81800

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