PACKAGE LEAFLET: INFORMATION FOR THE USER

MON.MDP KIT 10 mg
Lyophilized powder for I.V. injection in a vial
5 vials/box
Administered intravenously.

Active ingredient:
Methylenediphosphonic acid (MDP): 10 mg.

Excipients:
Stannous (II) chloride, gentisic acid, sodium chloride (0.9%), sodium hydroxide, hydrochloric acid.

Read all of this LEAFLET carefully before you start using this medicine because it contains important information for you.
- *Keep this leaflet. You may need to read it again.*
- *If you have any further questions, ask your doctor or pharmacist.*
- *Please strictly follow the instructions given in this leaflet. Do not ever use **higher or lower** dose than the dosage prescribed for and recommended to you.*

In this leaflet:

1. What is MON.MDP KIT and what it is used for?

MON.MDP KIT is sterile, and lyophilized powder in 10 ml glass vial.

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It is manufactured to administer intravenously after labelling with Tc-99m radionuclide.
Kit content is not radioactive prior to adding Tc-99m.

The solution Tc-99m-MDP obtained with the addition of Tc-99m is radioactive and used by the nuclear medicine physicians as an imaging agent for examination of the bone diseases in order to help disease diagnosis.

It is administered before scanning and it helps imaging of the body region to be examined with a special camera.

2. Before MON.MDP KIT is administered

MON.MDP KIT must never be used
- If you are hypersensitive to the technetium Tc-99m medronate or any of the excipients.
- Consult your doctor for administration of MON.MDP KIT if you are pregnant.
- Consult your doctor for administration of MON.MDP KIT if you are a breast-feeding mother.

Take special care with MON.MDP KIT
If you think any of the following applies to you, you should inform your doctor;
- Phosphonate compounds complex with the cations such as calcium. Therefore, if you have or are prone to hypocalcaemia (alkalosis), your doctor would carefully consider your disease.
- Tc-99m crosses the placenta barrier when it is free pertechnetate. Therefore, in the case of suspected pregnancy, take a test before using the medicine.

"Please consult your doctor if any of these warnings applies to you even in a period in the past"

Taking MON.MDP KIT with foods and drinks
In terms of administration method, it does not interact with any food or drink.

Pregnancy
Ask your doctor or pharmacist before taking any medicine.

As with all radiopharmaceutical drugs, your doctor would administer this medicine to you if the expected benefit of Tc99m-MDP is higher than its potential damage.

Ask your doctor or pharmacist before using this medicine if you are pregnant or might be pregnant.

Breast-feeding
Ask your doctor or pharmacist before taking any medicine.

The Tc-99m pertechnetate passes to the breast milk. Therefore, if this medicine is necessary during the breast-feeding period, do not breastfeed for 12 hours after using the medicine; and express and dispose of the milk during this period and feed the baby using any other feeding method (baby formula, etc.). In addition, avoid contact with the baby during this period.

Driving and using machines
Administration of Tc-99m-MDP has no negative effect on driving and using machines.

Important information about some of the ingredients of MON.MDP KIT

If you are not hypersensitive to the ingredients of MON.MDP KIT or technetium-99m, no negative effect is expected due to such substances.

Using other medicines
- Antacids (stomach medicines) containing aluminium causes involvement in the liver.
- Estrogens cause involvement in the breast tissue.
- Sodium diatrizoate causes increase in renal and hepatic involvement.
- Iron salts causes increase in intravascular activity.
- E-amino caproic acid causes involvement of the radiopharmaceutical in the muscle tissue.
- Dextrose, cortisone and nifedipine decrease the involvement of the radiopharmaceutical in the bone tissue and affect the examination in the Tc-99m-MDP scintigraphy.
- Cytotoxic cancer chemotherapy causes "Sickle Sign" finding (increased activity distribution around the calvarium) in the scintigraphy.

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

3. How MON.MDP KIT will be used?

RADIOPHARMACEUTICALS SHOULD BE ADMINISTERED ONLY BY NUCLEAR MEDICINE CENTERS.

Instructions for appropriate administration and dose /administration frequency
Your doctor will determine the dose and administer the medicine based on your disease.

Method and route of administration
The solution Tc-99m-MDP obtained by combining the lyophilized powder with the solution Tc-99m is administered intravenously.

Different age groups

Use in children
The doctor will determine the dose and administer the medicine to the children.

Use in elderly
Image quality might be affected in the elderly.

Special patient populations

Renal /Hepatic impairment
Image quality might be affected in the patients with kidney function disorder.

If you think that the effect of Tc-99m-MDP is too high or low, please ask your doctor or pharmacist.

If more Tc-99m-MDP is given to you than necessary
It is considered that there is no overdose risk since the administration will be performed by the nuclear medicine physicians. However, in the case of overdose, the risk of damage due to the radioactivity would increase. In such cases, plenty of liquid should be consumed in order to decrease the radiation dose of the bladder, and the patient should frequently urinate for 4-6 hours following completion of the administration.

4. Possible side effects

Like all medicines, MON.MDP KIT can cause side effects for the patients hypersensitive to any of the ingredients.

Please tell your doctor immediately or consult to the emergency of the nearest hospital, if you notice any of the following cases;

- Shivering
- Hypotension
- Nausea/vomiting
- Intracutaneous reactivities such as local or generalized itching or skin eruption
- Loss of consciousness, respiratory distress, hepatization or stertorous respiration
- Edema and/or arthralgia in hands or feet

All of the aforementioned are serious side effects. Immediate medical response might be necessary. Serious side effects are rare.

Please tell your doctor, if you notice any of the following cases;
- Fatigue
- Dizziness

These are the mild side effects of MON.MDP KIT.

If you notice any side effect not listed in this leaflet, please tell your doctor or pharmacist.

Reporting of side effects
If you get any side effects, talk to your doctor or Nuclear Medicine doctor who supervises the procedure. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system. By reporting side effects you can help to provide more information on the safety of this medicine.

5. How to store MON.MDP KIT?

Keep out of the reach and sight of children.

MON.MDP KIT should be stored at 2-8 °C and protected from light in its original package.

The kit labelled with Tc-99m (radiopharmaceutical product Tc-99m-MDP) should be kept in a lead shield at the room temperature under 25 °C with protection from light.

Use it in compliance with its expiry date.

Do not use MON.MDP KIT after the expiry date stated on the package.

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THE FOLLOWING INFORMATION IS PROVIDED FOR THE MEDICINAL PERSONNEL THAT WILL ADMINISTER THIS MEDICINE

MON.MDP KIT is sterile, lyophilized powder. The content of MON.MDP KIT is not radioactive before addition of the Tc-99m sodium pertechnetate solution. Content of the vial should not be directly administered to the patient before marked with the Technetium Tc-99m sodium pertechnetate.

The kit vials should be checked before the operation. Broken or cracked vials or vials with broken cap seal must not be used.

Labelling with the Tc-99m sodium pertechnetate solution must be carried out under aseptic conditions and behind a lead shield. Solution prepared upon addition of Tc-99m sodium pertechnetate solution, is radioactive and it must be kept in an appropriate lead shield and at room temperature below 25°C.

The bonding reaction between the kit content and Tc-99m radionuclide is depending on the amount of the +2-valency stannous ion in the kit. Therefore, no sodium pertechnetate solutions containing any oxidizing agent must be used in the marking operation.

As with the other radioactive products, appropriate safety precautions must be taken in order to prevent unnecessary exposure of the clinic staff and other persons to the radiation.

Any unused product or waste material should be disposed of in accordance with local requirements.

Preparation of ^{99m}Tc-MDP
Preparation of ^{99m}Tc-MDP solution via labelling of MON.MDP KIT with Tc-99m sodium pertechnetate solution should be performed as described below under aseptic conditions and behind an appropriate lead shield, in order to protect from radiation.

- Plastic sterile gloves should be worn during the operations.
- Kit sample stored at 2 - 8°C is taken and allowed to come to room temperature.
- Remove the plastic flip-off cap of the vial and mop the rubber stopper with the alcohol swabs included in the container, and then, place the vial in the protective lead shield.
- Adhere the solution label within the cardboard box to the lead shield.
- Since the product vial is sealed under the nitrogen gas, stick a sterile needle to the vial cap in order to equilibrate pressure in the vial.
- Add 2-5 ml of sterile, Tc-99m-sodium pertechnetate solution to the vial using the lead-shielded, sterile injector. Maximum recommended Tc-99m activity is 500 mCi.
- Before removing injector needle, in order to equilibrate pressure in the vial, air is withdrawn in an equal volume to the volume of solution added to the vial.
- Kit vial in the lead shield closed with a cap is shaked up and down strongly approx. for 1 minute, in order to ensure that the lyophilized powder is completely dissolved.
- Check if the solution visually behind a lead shield, if it contains any particulate matter and if the solution is clear. If the solution is blurred or discoloured, it should not be used.
- Prepared solution is ready to use after 15 minutes of incubation period.
- Write the preparation date and time, volume, activity of the solution, and name of the preparer on the solution label on the lead shield.
- Shelf life of 99mTc-MDP solution is 9 hours. Until the expiration time it should be stored at room temperature below 25 °C. Dispose of the remaining part which is not used after.
- Before using 99mTc-MDP solution, take a measurement in the dose calibrator and determine the radioactivity amount.

The kit vial contains nitrogen in order to prevent oxidation. It should be taken care not to give air in the kit vial while drawing the patient administration dose.

Determination of radiochemical purity
Warning: The study should be carried out under the radiation safety working condition!
Radiochemical impurity determination is performed 15 minutes after kit labelling procedure.

1. Determination of impurity of Tc-99m in colloidal form
Stationary phase: Silica-gel impregnated TLC layer (ITLC-SG)

Mobile phase: Sodium acetate solution (136 g/l)

Procedure steps:
- The ITLC-SG layer is activated by heating at 120°C for 20 minutes.
- The chromatography tank is prepared using the aforementioned solvent system.
- 1 µL sample is dropped to the starting point. TLC layer is placed to the chromatography tank before the drop is dried.
- Allow mobile phase to run 10 - 15 cm from the dropping point.
- Then TLC layer is removed from the tank and allowed to dry in the air.
- The Rf values and activity distribution are determined using the TLC scanner.

For Hydrolyzed technetium and colloidal form, Rf= 0- 0,1
For Tc-99m-medronate and Sodium pertechnetate, Rf=0.9-1,0

2. Determination of the impurity of sodium pertechnetate
Stationary phase: Silica-gel impregnated TLC plate (ITLC-SG)
Mobile phase: Methyl-Ethyl Ketone
1. The chromatography tank and plate is prepared as explained above.
2. 1 µL sample is dropped to the starting point and after the drop is dried, TLC layer is placed in the chromatography tank
3. Allow mobile phase to run 10 - 15 cm from the dropping point and remove the layer from the tank, allow it to dry in the air.
4. The Rf values and activity distribution are determined using the TLC scanner.
   For Sodium pertechnetate, Rf=0.9-1,0
   For Tc-99m-medronate and colloidal form, Rf= 0-0,1

CONCLUSION: The purity value % is calculated from the peak areas. The impurity of pertechnetate should not be more than 2,0%, and total impurity from both chromatograms should not be more than 5,0 %.

CAUTION: After MON.MDP KIT is labelled with Tc-99m sodium pertechnetate, please stick specially prepared labels included in the cardboard box preferably onto the lead container after completing the information or onto the vial before labelling in order to identify 99mTc-MDP.

The box includes swab for the disinfection of the rubber stoppers of the vial. Please use this swab when preparing the vial for use. The swabs contain 70% isopropyl alcohol. Please do not use an antiseptic agent except for the antiseptic used in the swab.

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