Method of examination
The patient receives 99mTc-DMSA as intravenous injection. In case of static imaging and kidney scintigraphy it is recommended to take images 1-3 hours after administration. In case of functional test the time-dependence of accumulation after administration can be measured.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients.
- Pregnancy and lactation (See section 4.6) except if the necessity and importance of obtaining the diagnostic information outweighs the risk associated with the radiation exposure.
- Under 18 years of age (See section 4.2) except if the necessity and importance of obtaining the diagnostic information outweighs the risk associated with the radiation exposure.

4.4 Special warnings and precautions for use

Radioactive medicinal products should be received, used and administered only by authorised persons in designated clinical settings. Receipt, storage, transfer and disposal of the radioactive medicinal products are subject to the regulations and appropriate licences of the competent authorities.

Use of the product is contraindicated for patients under 18 years of age (See section 4.2) except if the necessity and importance of obtaining the diagnostic information outweighs the risk associated with the radiation exposure. In this case use lower activity, see 4.2.

Use of the product is contraindicated in case of pregnancy and lactation (See section 4.6) except if the necessity and importance of obtaining the diagnostic information outweighs the risk associated with the radiation exposure.

4.5 Interaction with other medicinal products and other forms of information

No interactions are known.

4.6 Pregnancy and lactation

Use of the product is contraindicated in case of pregnancy and lactation except if the necessity and importance of obtaining the diagnostic information outweighs the risk associated with the radiation exposure.

When it is necessary to administer radioactive medicinal products to women of childbearing potential, information should always be sought about pregnancy. Any woman who has missed a period should be assumed pregnant until proven otherwise. Alternative techniques which do not involve ionising radiation should be considered.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

In occurrence of unexpected adverse reactions driving and/or working with machines should be reconsidered.

4.8 Undesirable effects

Exposure to ionising radiation is linked with cancer induction and a potential for hereditary defects. However these effects are hardly expected regarding the applied amount of activity.

Adverse event and reactions have not been reported ever since the authorization of the product (1989) nor registered in the literature. Considering the number of the examinations carried out since, no adverse reactions are expected (frequency lower than 1/10000).

4.9 Overdose

No case of overdose has been reported.

Administration of higher activities than prescribed is unnecessary and must be avoided in order to avoid the excess absorbed radiation dose of the patient and his/her environment.

In case of incidental overdose, the effectively administered activity of 99mTc must be determined (in MBq) and the actual absorbed radiation dose must be calculated by using the data of the dosimetric table of Chapter 11. Necessity and method of further treatment should be concluded based on these results.

The Table of Chapter 11 contains absorbed radiation dose data in MBq in case of intravenous administration of 1 MBq of 99mTc-DMSA. Multiply these specific absorbed radiation dose data by the effectively administered activity (in MBq) to get the required absorbed radiation dose data in MBq.

Quantity of 99mTc-DMSA administered to one patient is not less than 0.25 mg and not more than 0.50 mg if administration is complying with the recommendations. If the whole content of the vial containing the labelled substance is administered to one patient by mistake, it represents 0.0214 mg/kg of bodyweight level (calculated on 70 kg average bodyweight). This is equivalent to 5% of the no observed effect level. Thus, no toxic effects are expected in case of overdose.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Diagnostic radiopharmaceutical, ATC code: V09CA02

The structure of DMSA-complex administered to the body is [99mTc-(DMSA)], i.e. it is a bischelate, in which 99mTc binds to the plasma proteins. Blood plasma-binding depends on the pH value of the product, at pH=3 binding is 90%, at pH=7 it is 50%.

[99mTc-(DMSA)] bound to plasma proteins is taken up by the kidneys, it binds to receptors containing free -SH groups of the tubules, especially the proximal tubules. One DMSA ligand of [99mTc-(DMSA)] bischelate is substituted on a group of the receptor while one DMSA is released and the [99mTc-(DMSA)-receptor] complex is formed. The released DMSA is excreted via the urine. This mechanism allows the binding of not more than 0.1 mg of the administered activity.

With this mechanism maximum 0.1 mg DMSA can be bound per kg bodyweight.

Since the proximal tubules are situated in the cortex of the kidneys imaging is performed by visualising the cortex itself. 40-50% of the injected activity appears in the kidney cortex and approximately 1% is in the liver. In case of patient with impaired kidney function this ratio decreases and the radioactivity of the liver increases significantly.

Finally, [99mTc-(DMSA)] bound in the kidneys is excreted via urine.

5.2 Pharmacokinetic properties

After intravenous administration [99mTc-DMSA] leaves the bloodstream in three parallel processes which can be illustrated by three-compartamental exponential curve.

The effective half-life is approximately 1 hour. Most of the activity leaves the bloodstream during the first two phases (T 1/2=40 min and T 1/2=20 min).

1 hour after administration 25-35% of 99mTc-DMSA activity is localised in the kidneys, while after 3 hours 40-50%. Simultaneously, 25% of the administered activity is excreted via the urine during the first hour. After 6 hours the excretion via urine increases.

5.3 Preclinical safety data

Acute toxicity study on mice showed no clinically significant effects up to 0.43 mg/kg of body weight. Quantity of 99mTc-DMSA, if administration is complying with the recommendations, is not less than 0.25 mg and not more than 0.5 mg. Calculated on an average 70 kg of bodyweight the smallest and the greatest quantities are equivalent to 0.8 and 1.6 % of the no observed effect level, respectively. Thus, the use of the product is considered safe.

Further advantage of the product is that radioclinical impurities is always less than 10%, therefore the kit is safe from the point of view of labeling.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Component | Quantity per vial | Function
--- | --- | ---
DMSA | 1.0-1.8 GBq | Organ-specific diagnostic information
Stannous chloride | 0.6 mg | Reducing agent of 99mTc-pertechnetate
Ascorbic acid | 0.5 mg | Stabiliser
Calcium-gluconate | 30.0 mg | Filler

6.2 Incompatibilities

For preparation of 99mTc-DMSA only 99mTc-pertechnetate- and physiological saline solution can be used (See chapter 12). The DMSA kit is incompatible with other materials.

Stannous chloride component of DMSA kit is a reducing agent. It reduces free pertechnetate from +7 oxidation state to +4 oxidation state, in which technetium readily forms complex with DMSA. It is important to keep away the content of the vials from moisture and oxidising agents, for example chemical oxidation agents or oxygen of the air.

Alkaline media facilitate the oxidation of Sn(II) before the labelling reaction this is why the product is incompatible with bases. As a result of these incompatibilities it is recommended to remove the closure of the closed injection vials just before the labelling reaction. Perform the labelling by observing the instructions detailed in Chapter 12.

6.3 Shelf life

Shelf life of DMSA kit (lyophilised, non-radioactive components in injection vials closed with rubber stopper and aluminium cap) is 12 month from the date of the manufacture.

One paper box contains 6 of injection vials, which can be labelled at different times within the expiry time.

99mTc-labelled DMSA must be used within 3 hours.

6.4 Special precautions for storage

Store in refrigerator (2-8°C).

Do not store 99mTc-DMSA injection above 25°C. Comply with the regulations for radiation safety.

6.5 Nature and contents of container

The injection vials of DMSA kit contain the sterile, pyrogen-free and freeze-dried components. The labelled 6 ml injection vials are closed with rubber stopper and tear-off aluminium cap. One box contains six vials, one Summary Of Product Characteristic and Patient Information Leaflet and six labels with radioactive material sign.

6.6 Special precautions for disposal and other handling

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

7. MARKETING AUTHORISATION HOLDER

Institute Of Isotopes Co. Ltd.
1121 Budapest, Kossuth Thége Miklós str. 29-33.
1535 Budapest, P.O.B. 851.
Tel.: 36 1 392 2577, 395 9081
Fax: 36 1 395 9247, 392 2575
E-mail: commerce@izotop.hu
1. **What DMSA is and what it is used for**

This medicine is for diagnostic use only.

**99mTc-DMSA** injection prepared from DMSA kit is a colourless solution that contains radioactive isotope. Use of **DMSA** is permitted only in departments of nuclear medicines.

2. **Before you use DMSA**

- Do not use **DMSA** if:
  - you are allergic (hypersensitive) to the active substance or any of the other ingredients;
  - you are pregnant or breast feeding, except if your doctor decides otherwise;
  - you are under 18 years of age, except if your doctor decides otherwise.

Make sure you carry out the doctor's instructions both before and after the examination in order to avoid radioactive exposure of other people and the radioactive contamination of the environment.

Make sure that your location is suitable for the examination. Use of **DMSA** injection is only carried out in hospitals and institutes.

3. **How to use DMSA**

- **99mTc-DMSA** injection is prepared by mixing the content DMSA kit and radioactive **99mTc**-pertechnetate at the site of the use (hospitals, clinics). The labelling will be carried out immediately following the mixing procedure. Labelling will be done by an experienced medical staff. You will be provided with a study sheet for the examination. In the unlikely event of overdose your doctor will advise you to drink lots of liquid which will accelerate the elimination of the drug from your body. You should take all necessary precautions against the contamination of your environment with radioactivity. Comply with the instructions given by your doctor.

- **99mTc-DMSA** which is temporarily present in your body and the excreted material loose their radioactivity in a natural way.

If you have any further questions on the use of this medicine, ask your doctor.

4. **Possible side effects**

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. However these effects are hardly expected regarding the applied amount of activity.

Adverse event and reactions have not been reported ever since the authorization of the product (1989). Considering the number of the examinations carried out since, no adverse reactions are expected.

The amount of radioactivity in the body from **99mTc-DMSA** is small. It will be passed out of the body in a few days without any intervention. If you have any further questions on the use of this medicine, ask your doctor.

5. **How to store DMSA**

Keep out of the reach and sight of children and people who are not authorized to handle, use or transport this product!

Hospital staff will ensure that the product is stored correctly and not used after expiry date stated on the label.

**DMSA** should be stored in refrigerator at 2-8 °C.

Radioactive **99mTc**-**DMSA** is to be stored below 25°C, considering the regulations for radiation safety.

**99mTc**-labelled **DMSA** must be used within 3 hours.

6. **Further information**

**What DMSA contains**

- The active substance is 1.5 mg dimercapto succinic acid (DMSA) per vial.
- Other ingredients are: stannous chloride dihydrate, ascorbic acid, calcium gluconate.
- The active substance of the labelled, radioactive **DMSA**: **99mTc**-**DMSA**.

**What DMSA looks like and contents of the pack**

The injection vials (BEKA type, 6 ml) containing the sterile, pyrogen-free freeze-dried product are closed with rubber stopper and tear-off kombicap (aluminium and plastic).

Six vials of **DMSA** kit are packed into one paper box, with six labels with radioactive symbol.

Marketing Authorisation Holder and Manufacturer
Institute Of Isotopes Co. Ltd.
Address: 1121 Budapest, Konkoly Thege Miklós str. 29-33.
Tel.: 36 1 395 9070; 36 1 391 0860
Fax: 36 1 395 9070
E-mail: raygo@isotop.hu

This leaflet was last approved in: 17/12/2009.

This leaflet was translated by the manufacturer based on the original Hungarian document, authorized by the Hungarian National Institute of Pharmacy on 17.12.2009.

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**1. Dose and administration**

**DMSA** powder for injection should be store in refrigerator at 2-8 °C.

**DMSA** should be used after expiry date stated on the label.

**DMSA** is an intravenous injection.

**DMSA** is used after expiry date stated on the label.

**DMSA** injection is administered intravenously.

**DMSA** is a colourless solution that contains radioactive isotope. Use of **DMSA** is permitted only in departments of nuclear medicines.

**99mTc-DMSA** injection contains radioactive isotope. For handling, shipping and storage of this product the rules and regulations referring to radioactive materials should be observed.

99mTc-DMSA injection contains radioactive isotope. For handling, shipping and storage of this product the rules and regulations referring to radioactive materials should be observed.

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