



SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

DMSA 1.5 mg powder for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition of DMSA powder for injection

Component Active substance	Quantity per vial	Function
Dimercapto succinic acid (DMSA)	1.5 mg	Organ-specific chelating agent of ^{99m} Tc radioisotope

Composition of ^{99m}Tc-DMSA radioactive injection

Component Active substance	Quantity per vial	Function
^{99m} Tc-DMSA	1.0–1.8 GBq	Organ-specific diagnostic information

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Pharmaceutical form of DMSA kit: powder for injection (lyophilisate)
Pharmaceutical form of ^{99m}Tc-DMSA: injection
^{99m}Tc-DMSA injection can be prepared in situ at the site of the use ie. at isotope laboratories of clinics or hospitals by mixing DMSA powder for injection (lyophilisate in the vial) and [^{99m}Tc]pertechnetate eluate. Sterile, pyrogen free solution of [^{99m}Tc]pertechnetate can be obtained by using ^{99m}Tc/⁹⁹Mo generator.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

INDICATION FIELD: ISOTOPE DIAGNOSTICS

- Kidney scintigraphy, static kidney imaging, localisation of the kidneys with imaging
- Determination of the functional mass of the kidney
- Determination of the relative function ratio (percentage) of the left and right kidneys

4.2 Posology and method of administration

Administration of ^{99m}Tc-DMSA for children is contraindicated except if the necessity and importance of obtaining the diagnostic information outweighs the risk associated with the radiation exposure

Posology

111–185 MBq ^{99m}Tc-DMSA for intravenous administration

Method of administration

^{99m}Tc-DMSA obtained in one labelling reaction can be divided to 3 – 6 doses. Label content of one vial of DMSA kit by using 1.0 – 1.8 GBq of [^{99m}Tc]pertechnetate activity.

^{99m}Tc-pertechnetate activity for labelling must be chosen so that individual patient dose should be 111 – 185 MBq at the time of the investigation.

For paediatric examination (see Chapter 4.3.) use Webster's equation to determine the activity to be administered:

$$A_{child} = \frac{[(N + 1) \cdot A_{Adult}]}{N + 7}$$

where N: age of the child [year]

A_{child}: activity [MBq]

Method of examination

The patient receives ^{99m}Tc-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 person in designated clinical settings. Receipt, storage, use, 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 interaction

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.

Treatment of women of child bearing potential is recommended in the first 10 days after menstruation.

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 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) 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 ^{99m}Tc 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 µGy in case of intravenous administration of 1 MBq of ^{99m}Tc-DMSA. Multiply these specific absorbed radiation dose data by the effectively administered activity (in MBq) to obtain the required absorbed radiation dose data in µGy.

Quantity of ^{99m}Tc-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 1.5 mg of ^{99m}Tc-DMSA is introduced in the body.

Acute toxicity studies on mice showed no clinical symptoms if less than 0.43 mg/kg of bodyweight is administered. 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 [^{99m}Tc-(DMSA)₂], i.e. it is a biscomplex, of which 75% binds to the plasma proteins of the blood. Plasma-binding highly depends on the pH value of the product, at pH = 3 binding is 90 %, at pH = 7 it is 50 %.

[^{99m}Tc-(DMSA)₂] bounded 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 [^{99m}Tc-(DMSA)₂] biscomplex is substituted by a -SH group of the receptor while one DMSA is released and the [^{99m}Tc-(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 DMSA per kg of bodyweight.

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 3% in the liver. In case of patient with impaired kidney function this ratio decreases and the radioactivity of the liver increases significantly.

Finally, ^{99m}Tc-(DMSA) bound in the kidneys is excreted via urine.

5.2 Pharmacokinetic properties

After intravenous administration ^{99m}Tc-DMSA leaves the bloodstream in three parallel processes which can be described by three-compartmental 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}(I) = 40 min and T_{1/2}(II) 120 min).

1 hour after administration 25-35% of ^{99m}Tc-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 clinical symptoms up to 0.43 mg/kg of body weight. Quantity of ^{99m}Tc-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 radiochemical purity of the preparation is not affected by the activity of [^{99m}Tc]pertechnetate in the range

of 1.0 – 1.8 GBq. Quantity of radiochemical impurities is always less than 10 %, therefore the kit is safe from the point of view of labelling

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Component Excipients	Quantity per vial	Function
Stannous chloride dihydrate	0.6 mg	Reducing agent of [^{99m} Tc]pertechnetate
Ascorbic acid	0.5 mg	Stabiliser
Calcium-gluconate	30.0 mg	Filler

6.2 Incompatibilities

For preparation of ^{99m}Tc-DMSA only ^{99m}Tc-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.

^{99m}Tc-labelled DMSA must be used within 3 hours.

6.4 Special precautions for storage

Store in refrigerator (2 - 8°C).

Do not store ^{99m}Tc-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 BEKA type 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.

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8. MARKETING AUTHORISATION NUMBER(S)

OGYI-T-9245/01

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

09 February 1989 / 17 December 2009

10. DATE OF REVISION OF THE TEXT

17 December 2009

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

11. DOSIMETRY

Individual patient dose is 111 – 185 MBq. Estimated absorbed dose values of 1 MBq of the injection for an average body weight of 70 kg are given in the table below.

Organ	Absorbed dose [µGy / MBq]
Kidney cortex	205.0
Whole kidney	167.0
Urinary bladder	75.0
Liver	5.4
Ovaries	5.9
Whole body	4.3

Radiation physical properties

Physical half-life	6 hours
Energy and intensity of the emitted gamma photons	140 keV 100 %
Energy and intensity of the emitted beta particles	–

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Remove the protective foil and lift up the upper part of the paper box to access the vials.

DMSA kit can only be administered to patient after labelling with ^{99m}Tc.

Never administer DMSA kit without performing the labelling.

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

Labelling procedure

Place the vial containing the freeze-dried powder in a small lead container with a wall thickness of 3 mm. Under aseptic circumstances inject 1.0 – 1.8 GBq of sterile sodium pertechnetate into the vial through the rubber stopper with a sterile syringe. This solution can be used for intravenous administration.

pH of the labelled solution is in the range of pH = 3 – 4.

Utilize the labelled solution in 3 hours. Over this period the percentage of radiochemical impurities should not be more than 10%.

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



PACKAGE LEAFLET: INFORMATION FOR THE USER

DMSA 1.5 mg powder for injection
Dimercapto-succinic acid (DMSA)

Read all of this leaflet carefully before this medicine is used for your examination.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

In this leaflet:

1. What DMSA is and what it is used for
2. Before you use DMSA
3. How to use DMSA
4. Possible side effects
5. How to store DMSA
6. Further information

1. WHAT DMSA IS AND WHAT IT IS USED FOR

This medicine is for diagnostic use only.

^{99m}Tc-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.

^{99m}Tc-DMSA injection is administered intravenously. After intravenous administration, ^{99m}Tc- DMSA is transported to the kidneys via the blood circulation. As the medicine contains gamma-radiator radioactive isotope, it can be detected from outside the body using gamma cameras. The pictures taken by this camera show the distribution of the radioactive isotope in your body and organs. The pictures can give your doctor valuable information about the structure and working of the organ helping this way to choose the best treatment.

^{99m}Tc-DMSA is suitable for kidney scintigraphy, static imaging of kidney, determination of positions of the kidneys by means of imaging, determination of functional mass of kidney, determination of relative functions of right and left kidneys.

2. BEFORE YOU USE DMSA

Do not use DMSA

- if you are allergic (hypersensitive) to the active substance or any of the other ingredients of DMSA.
- If you are pregnant or breast feeding, except if your doctor decides otherwise
- If 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.

The radioactive isotope is excreted in the urine, faeces, sweat and other secretions temporarily contaminating the environment this way.

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

Using other medicines

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

No interactions with other medicines are known.

Using DMSA with food and drink

You can take DMSA with any food or drink.

Pregnancy and breast-feeding

It is important to tell your doctor if there is any possibility that you are pregnant or if you breast-feed.

In these cases your doctor will consider the necessity of the radioisotope diagnostics. The radioisotope can be dangerous to the foetus and the infant, and it is excreted in mother's milk. Therefore, it is possible that your doctor will choose other, non-radioactive method. Trust your doctor, because the decision will be made in accordance with strict regulations.

If you are breast-feeding and you will be examined with this product, you should stop breast-feeding for the period recommended by your doctor. During this time the radioactive isotope will be eliminated from your body. Use formula feed for your child. The breast milk should be expressed and collected and spilled out after dilution. You can restart breast-feeding when the radiation dose for the child is less than 1 mSv. Your doctor will decide about the restart of breast -feeding.

Paediatric use

The use of DMSA is generally not recommended for children and for adolescents under age of 18 years, but the decision about the necessity of the radioisotope diagnostic examination is up to the your Doctor.

Driving and using machines

^{99m}Tc-DMSA has no influence on the ability to drive and use machines.

Important information about some of the ingredients of DMSA

When you are given ^{99m}Tc-DMSA you receive a small amount of radiation. The adsorbed dose in this case is usually smaller than those of certain X-ray examinations (e.g. CT). Your doctor will always consider the possible risks and advantages.

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

3. HOW TO USE DMSA

^{99m}Tc-DMSA injection is prepared by mixing the content DMSA kit and radioactive ^{99m}Tc-pertechnate at the site of the use (hospitals, clinics). The injection is administered intravenously.

Amount of the administered activity, method and timing of imaging is decided by your doctor according to the type of examination and your state of health.

What should you do if you received overdose of the medicinal product?

There are strict rules and regulations on handling, use and disposal of radioactive materials. Therefore, ^{99m}Tc-DMSA can only be used in hospitals or institutes.

DMSA can be handled, used and administered only by people specialized for handling of radioactive materials and waste. These people give you instructions about the precautions and warnings. Comply with their instructions.

Since ^{99m}Tc-DMSA is given by a doctor under controlled conditions, the probability of overdose is low. 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.

^{99m}Tc-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 ^{99m}Tc-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 powder for injection should be store in refrigerator at 2-8 °C.

Radioactive ^{99m}Tc-DMSA is to be stored below 25°C, considering the regulations for radiation safety.

^{99m}Tc-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: ^{99m}Tc-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 komicap (aluminium and plastic).

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

Marketing Authorisation Holder and Manufacturer

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