DMSA RPHPHARMA

PLEASE READ CAREFULLY BEFORE USING THE PRODUCT.

DRUG FOR DIAGNOSTIC USE IN NUCLEAR MEDICINE.

This product is only for use in specialized clinics and hospitals.

PHARMACEUTICAL FORM AND PRESENTATION
Kit containing 5 vials of lyophilized, sterile and pyrogen-free reagents, sealed under nitrogen atmosphere.

COMPOSITION
Each vial contains:

COMPOSITION	AMOUNT
succimer	1.0 mg
ascorbic acid	0.7 mg
inositol	50 mg
stannous chloride dihydrate	0.42 mg
water for injection QS	1.0 mL

Table 1 – Composition of the DMSA kit vials

1. INDICATIONS
The radiopharmaceutical DMSA-Tc-99m is used only for diagnostic purposes, making it possible to obtain qualitative data using planar or SPECT imaging or quantitative data on the relative or absolute renal function of each kidney individually. It is used also to evaluate the anatomy of the renal cortex and can estimate renal functional mass. It enables the detection of brain lesions such as tumors, cysts, hematomas and renal abscesses, as well as infarction and renal scarring after infection. DMSA scintigraphy is currently considered the gold standard for the diagnosis of acute pyelonephritis. Its use also allows the detection of congenital malformations, such as: ectopic kidney, multicystic dysplastic kidney, renal fusion, among others.

INTRAVENOUS ADMINISTRATION. ADULT AND PEDIATRIC USE.

2. EFFICACY
The use of DMSA-Tc-99m on kidneys imaging and pyelonephritis diagnostic was performed in rats and rabbits. DMSA-Tc-99m efficacy in predicting the risk of scarring after pyelonephritis was verified by several authors and has also demonstrated the ability of DMSA- Tc-99m to quantify the absolute renal function in children.
A study with 115 children (under 5 years) showed that SPECT with DMSA-Tc-99m is better than other imaging tests (intravenous urography, ultrasound voiding cystourethrography) to detect kidney defects (Verber *et al*., 1988).

3. PHARMACOLOGICAL CHARACTERISTICS
Studies in animals show that within one hour of intravenous administration, DMSA-Tc-99m accumulates preferentially in the proximal and distal renal tubules. The cortex/medulla uptake ratio is 22:1. Regarding the bonding of DMSA-Tc-99m to large amounts of plasma proteins (75-90%), glomular filtration is insignificant when compared to tubular excretion. DMSA-Tc-99m has slow renal clearance, with 37% of the injected dose excreted within 24 hours. Although the ideal time for renal imaging is within 4 to 6 hours of injection, low urinary excretion means images can be taken after longer periods.

4. CONTRAINDICATIONS
There are no reported contraindications.

5. WARNINGS AND PRECAUTIONS
During pregnancy or breastfeeding, this radiopharmaceutical should only be used in cases of extreme necessity, when the risk of exposure of the fetus or newborn to radiation is justified by the importance of diagnosis.
The administration of a radiopharmaceutical during pregnancy can cause mutagenic changes in the fetus.
During lactation, technetium-99m (99m Tc) is excreted in breast milk. Breastfeeding should be suspended for at least 12 hours after injection and the milk produced during this period discarded.
Avoid close contact between mother and baby for the 12 hours following administration of the radiopharmaceutical.

6. DRUG INTERACTIONS
Several drugs and conditions interfere in the biodistribution of radiopharmaceuticals used in bone studies. The DMSA-Tc-99m complex interacts directly or indirectly with compounds containing aluminum chloride, sodium bicarbonate, ammonium chloride, mitomycin, captopril and other inhibitors of the angiotensin converting enzyme, potentially compromising image quality.

7. STORAGE PRECAUTIONS
This drug is valid for 12 months from the date of manufacture. Transport at room temperature and store in a cool dark place at temperatures between 2 and 8° C.
When added to the vial of DMSA without the presence of air, the sterile pyrogen-free solution of sodium pertechnetate (Na 99mTcO_4) produces rapid labeling that remains stable *in vitro* for 4 hours.
After complexation with technetium-99m (99m Tc) store in the dark between 2° and 30° C.

Lot number, manufacture and expiration dates: see packaging.
Do not take medicine that has expired.
All medicines should be kept out of reach of children.
Before administering to the patient, take note of the appearance of the product, which should be clear and colorless.

8. DOSAGE AND INSTRUCTIONS FOR USE
Route of administration: intravenous.
The recommended dose for renal scintigraphy is 37-185 MBq (1-5 mCi).

8.1. INSTRUCTIONS FOR PREPARATION AND STORAGE AFTER COMPLEXATION
- Follow aseptic standards and precautions to prevent exposure to radiation.
- Place the vial, previously disinfected with 70% ethyl alcohol, in a lead shield.
- Keep air from entering the vial and remove air bubbles from the syringe before adding the sodium pertechnetate solution.
- To quantify relative renal function: Aseptically add 4 mL of 99mTcO4- (if needed, top up with 0.9% NaCl) with maximum activity of 3700 MBq (100 mCi) to the vial.
- To quantify absolute renal function: Aseptically add 4 mL of 99mTcO4- (if needed, top up with 0.9% NaCl) with maximum activity of 1480 MBq (40 mCi) to the vial.
- Without removing the needle, aspirate an equal volume of air to maintain atmospheric pressure within the bottle.
- Use a lead cap for shielding purposes.
- Swirl the vial gently for 30 seconds until the lyophilisate has completely dissolved. The solution should be clear and free of particles.
- Let stand at room temperature for 20 minutes to allow a complete labeling reaction.
- Carry out quality control.
- Following quality control procedures, extract doses in accordance with the patient's body weight, taking care to avoid the entry of air when handling the flask. Use sterile, disposable syringes.

8.2. QUALITY CONTROL - RADIOCHEMICAL
Use a 3mm Whatman plate and a silica gel 60 plate measuring 6.5 cm long and 1 cm wide, as shown in figure 1. Once the complexation incubation time has elapsed, add a drop of the material on the application line of each of the plates. Place the Whatman plate (1) in a chromatography tank containing butanone PA, and the silica gel 60 plate (2) in a chromatography tank containing 0.9% NaCl. Wait until the solvents migrate to the top lines of the plates, which can happen at different times. Remove the plates from the chromatography tanks. Cut PLATE 1 in half and PLATE 2 1.5 cm from the application point. Calculate labeling efficiency using the formula below. Analyze the results of labeling efficiency in accordance with table 2.

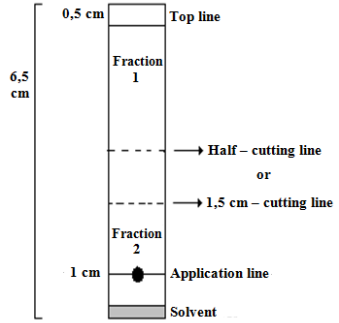

Figure 1 – Cutting the chromatography plates

PLATE 1: % 99mTcO_4-:

$$\frac{\text{activity fraction 1}}{\text{activity fraction 1} + 2}$$

PLATE 2: % 99mTcO_2:

$$\frac{\text{activity fraction 2}}{\text{activity fraction 1} + 2} \times 100 = 5\% \leq 99\text{mTcO} \leq 10\%$$

Labeling efficiency/radiochemical purity should be between 80% and 95%.

$$\mathbf{100 - (impurity\ plate\ 1 + impurity\ plate\ 2)} = \mathbf{80\% \leq PRQ \leq 95\%}$$

CHROMATOGRAPHY ANALYSIS OF DMSA-Tc-99m			
Chromatography System		(99m Tc) Species	
Stationary Phase	Mobile Phase	Origin	Front

PLATE 1	Butanone PA	DMSA-Tc-99m $99mTcO_2$	$99mTcO_4^-$
PLATE 2	0.9% NaCl	$99mTcO_2$	DMSA-Tc-99m $99mTcO_4^-$

Table 2 – Chromatography systems for radiochemical control of DMSA-Tc-99m.

To quantify absolute renal function marking efficiency/radiochemical purity should be between 85% and 95%.

100 – (impurity plate 1 + impurity plate 2) = 85% ≤ PRQ ≤ 95%.

To quantify relative renal function, marking efficiency/radiochemical purity should be ≥ 85%.

100 – (impurity plate 1 + impurity plate 2) = ≥ 85%.

8.3. QUALITY CONTROL - pH

Apply a sample of the radiopharmaceutical on the pH indicator strip. Wait 30 seconds and compare the color of the strip against the parameters in this box. The pH range for the radiopharmaceutical DMSA-Tc-99m should be between 2.0 and 3.0.

8.4. PRECAUTIONS ON ADMINISTRATION

This drug becomes radioactive after adding sodium pertechnetate solution. The use of lead shielding, suitable gloves and goggles should be mandatory.
The components of the kits are sterile and pyrogen-free. In order to preserve the sterility of the product, it should be handled in accordance with the Good Practices on Handling Sterile Products (intravenous products).
Precautions should be taken when using ionizing radiation. As such, radioactive waste (used materials, recipients and other waste) should be correctly disposed of in compliance with radiation protection guidelines.

DOSES ADMINISTERED TO CHILDREN AND ELDERLY SHOULD BE CALCULATED ACCORDING TO THE BODY SURFACE AREA

8.5. TOXICITY TESTS

Toxicity is not an issue when considering the design and development of radiopharmaceuticals due to the small amount used, which does not produce a pharmacological response.

8.6. PHYSICAL CHARACTERISTICS OF METASTABLE TECHNETIUM-99m

Tecnetium-99m (99m Tc) has the ideal physical properties for studying scintigraphic images.
(99m Tc) decreases into technetium-99 through isomeric transition and has a physical half-life of 6.02 hours.

RADIATION	AVERAGE/DECAY (5)	AVERAGE ENERGY (keV)
Gama -2	89.07	140.5

Table 3 – Data on the main radiation emitted

8.7. DOSAGE

Estimated absorbed radiation doses for the total body and selected organs are listed in table 4.

Organ	mGy/MBq	rad/mCi
Kidneys	0.17	0.63
Bladder	0.019	0.07
Adrenal glands	0.013	0.05
Liver	0.013	0.05
Ovaries	0.0037	0.014
Testicles	0.0018	0.007
Uterus	0.0046	0.017

Table 4 – Dosage for administering DMSA-Tc-99m.

8.8. EXTERNAL RADIATION

The constant dose for technetium-99m (99m Tc) is 0.78 R/mCi*h at 1 cm. The first half-value layer is 0.017 cm of lead (Pb). Attenuation resulting from various thicknesses of lead is described in table 5.

SHIELD THICKNESS (Pb) cm	COEFFICIENT OF ATTENUATION
0.017	0.5
0.08	0.1
0.15	0.01
0.25	0.001
0.33	0.0001

Table 5 – Radiation attenuation by lead shielding.

Table 6 shows the correction for the physical decline of technetium-99m, after calibration time.

HOUR	REMAINING FRACTION	HOUR	REMAINING FRACTION
1	0.891	7	0.447
2	0.794	8	0.398
3	0.708	9	0.355
4	0.631	10	0.316
5	0.562	11	0.282
6	0.501	12	0.251

Table 6 – Physical decline; half-life of technetium-99m (99m Tc): 6.02 hours.

9. SIDE EFFECTS

DMSA can cause erythema, nausea, flushing, syncope, fainting and abdominal pain. (Hesslewood, S. European system for reporting adverse reactions to and defects in radiopharmaceuticals: annual report. 2001).

10. OVERDOSE

In case of a radiation overdose with DMSA-Tc-99m the patient's absorbed dose should be lowered as much as possible by ingesting more liquids to eliminate the radionuclide from the body through an increase of urination.

In case of poisoning call 0800 722 6001 for instructions of how to proceed.

RESPONSIBLE PHARMACIST
Manoela Michelon Grazziotin
CRF/RS: 10225

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