DTPA

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
pentetic acid	10.0 mg
ascorbic acid	1.0 mg
calcium chloride dihydrate	1.44 mg
stannous chloride dihydrate	0.50 mg
water for injection	1.0 mL

Table 1 – Composition of the DTPA kit vials

1. INDICATIONS
The radiopharmaceutical DTPA-Tc-99m is used both for diagnostic image purposes and to obtain *in vivo* quantitative data of glomerular filtration. DTPA-Tc-99m is a versatile renal radiotracer that assesses renal blood flow, the function of the parenchyma and the permeability of the intra- and extra-renal collecting system. This radioactive tracer can assess the existence of renal artery stenosis, renovascular hypertension, and certain complications of kidney transplants, particular the clinical kind. It is also used for direct and indirect radioisotope cystography; brain scintigraphy to assess changes in the permeability of the blood-brain barrier; to confirm the diagnosis of brain death; to detect tumors of the central nervous system; for aerosol ventilation scintigraphy; to detect gastrointestinal bleeding and evaluate CSF flow through radionuclide cisternography.

INTRAVENOUS ADMINISTRATION. ADULT AND PEDIATRIC USE.

2. EFFICACY
In an animal model of nephrotoxicity by cisplatin in rats, the study using DTPA-Tc-99m radiopharmaceutical proved very effective process in discern normal and abnormal kidney function (McAfee *et al*., 1989).

3. PHARMACOLOGICAL CHARACTERISTICS
After administration, the vascular phase allows access renal perfusion at capillary level. First-order filtering is 10 to 20% in patients with normal kidney function and is lower in those with low-functioning kidneys. Cortical uptake peaks within 3 to 5 minutes of administering the radioactive tracer. Excretion depends on the glomerular filtration rate, whose normal value is 120 mL/minute. The biological half-life of DTPA-Tc-99m is approximately 2.5 hours, with around 95% of the administered dose eliminated within 24 hours in normal individuals.

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. The DTPA-Tc-99m complex interacts directly or indirectly with compounds containing alumina, acetazolamide, cyclosporine, mitomycin, oral contraceptives, tetracycline, anesthetics, furosemide and amiodarone, 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 DTPA without the presence of air, the sterile pyrogen-free solution of sodium pertechnetate ($Na99mTcO_4$) produces rapid labeling that remains stable *in vitro* for 8 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 USE INSTRUCTIONS
Route of administration: intravenous.
All the activities indicated are based on patients weighting 70 Kg. For pediatric patients the dose should be adjusted according to the child's weight. The recommended dose for renal scintigraphy is 185 - 555 MBq (5-15 mCi). In the case of brain scintigraphy, recommended activity is 1110 MBq (30 mCi). For scintigraphy to diagnose renovascular hypertension, recommended activity is 185-370 MBq (5-10 mCi). Recommended activity to locate gastrointestinal bleeding is 740-925 MBq (20-25 mCi) and 185 MBq (5 mCi) to study cerebrospinal fluid leaks. Recommended activity to study possible kidney transplant complications is 370 MBq (10 mCi) and 1110-1480 MBq (30-40 mCi) for pulmonary ventilation. When used for direct radionuclide cystography, recommended activity is 74 to 92.5 MBq (2-2.5 mCi), and 74 MBq (2 mCimCi) for indirect radionuclide cystography.

8.1. INSTRUCTIONS FOR PREPARATION AND STORAGE AFTER COMPLEXATION
- Follow aseptic procedures and take 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.
- Aseptically add 1 to 5 mL of $99mTcO_4^-$ (if needed, top up with 0.9% NaCl) with maximum activity of 5550 MBq (150 mCi) to the vial.
- Without removing the needle, aspirate an equal volume of air to maintain atmospheric pressure within the bottle.
- Use a fitted cover for the lead shield.
- 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 10 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 and needles.
- In case of intrathecal administration for cisternography, it is recommended that the radiopharmaceutical be filtered beforehand using a 0.22um. A new vial should be used for filtration.

8.2. QUALITY CONTROL - RADIOCHEMICAL
Use two Whatman plates 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 one of the plates in a chromatographic tank containing Butanone PA (PLATE 1) and the other into a chromatographic tank containing a solution of 0.9% NaCl (PLATE 2). 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.

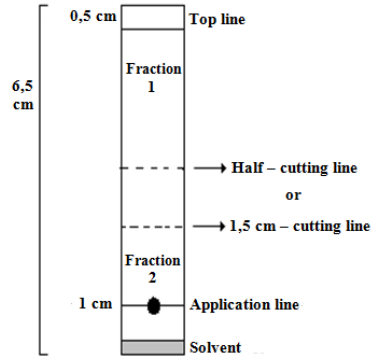

Figure 1 – Cutting chromatography plates

PLATE 1: % $99mTcO_4^-$:

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

PLATE 2: % $99mTcO_{2:}$

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

Labeling efficiency/radiochemical purity should be ≥ 85%.

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

CHROMATOGRAPHIC ANALYSIS OF DTPA-Tc-99m			
Chromatography System		**(99m Tc) Species**	
Stationary Phase	**Mobile Phase**	**Origin**	**Front**
PLATE 1	Butanone PA	DTPA-Tc-99m $99mTcO_2$	$99mTcO_4^-$
PLATE 2	0.9% NaCl	$99mTcO_2$	DTPA-Tc-99m $99mTcO_4^-$

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

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 DTPA-Tc-99m should be between 3.8 and 7.5.

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 THE 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 CHARACTRERISTICS 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 doses for the total body and selected organs are listed in table 4.

Organ	mGy/MBq	rad/mCi
Kidneys	0.017	0.069
Bladder	0.019	0.07
Spleen	0.013	0.048
Adrenal glands	0.013	0.048
Liver	0.01	0.037
Pancreas	0.009	0.033
Red marrow	0.0014	0.005
Stomach walls	0.005	0.018
Small Intestine	0.005	0.018
Uterus	0.005	0.018
Ovaries	0.004	0.015
Bone surfaces	0.003	0.011
Lungs	0.002	0.007
Testicles	0.002	0.007

Table 4 – Dosage for administering DTPA-99mTc

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
DTPA can cause shivering, nausea, erythema, flushing, diffuse rash, itching, hives, hypertension, hypotension, respiratory reaction, tachycardia, syncope, fainting, headache, cyanosis, anaphylaxis, arthralgia, pain, burning at the injection site, cough; if administered intrathecally, it can cause neurological disorders.

10. OVERDOSE
In case of a radiation overdose with DTPA-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
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