FITATO **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
phytic acid	20.0 mg
stannous chloride dihydrate	1.0 mg
water for injection	1.1 mL

Table 1 – Composition of the FITATO kit vials

1. INDICATIONS
FITATO-Tc-99m is recommended for diagnostic imaging of liver and spleen diseases, visualization of regional lymph channels and lymph nodes (lymphoscintigraphy) and the study of gastroesophageal reflux.

INTRAVENOUS ADMINISTRATION IN ADULTS AND CHILDREN

2. EFFICACY
Rats and rabbits tests showed the detection of sentinel lymph nodes on using the radiopharmaceutical (Alavi e Shesol, 1978; Strand e Persson , 1979). Moreover, Pereira (2010) proved that splenectomized rats had FITATO-Tc-99m biodistribution changes. An extensive review on FITATO-Tc-99m use in hepatic and spleen pathologies was carried out by Pereira (2010). The radiopharmaceutical efficacy for detection and sentinel lymph nodes in humans has been demonstrated in several studies (Coelho-Oliveira *et al.*, 2004; Freitas *et al.*, 2008;. Santos *et al.*, 2012;. Xavier *et al.*, 2005). The radiopharmaceutical is also used to imaging for pulmonary ventilation assessment (Peltier *et al.* 1991).

3. PHARMACOLOGICAL CHARACTERISTICS
When administered intravenously, the radiopharmaceutical FITATO-Tc-99m forms an insoluble colloid with endogenous calcium. Particle sizes formed are 1-30 µm (≥ 90%), 30-40 µm (8%) and 40-45 µm (2%). Uptake of the colloid is 85% by the liver, 7% by the spleen and 5% by bone marrow via sequestration by the reticuloendothelial cells in these organs, particularly Kupffer cells.
When injected interstitially, FITATO-Tc-99m migrates through the lymphatic channels and accumulates in regional lymph nodes. From there it can diffuse into the vascular system where it is eliminated by the excretory organs. The half-life of colloids in the bloodstream is less than 5 minutes.

4. CONTRAINDICATIONS
There are no reported contraindications.

5. WARNINGS AND PRECAUTIONS
During pregnancy 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. FITATO-Tc-99m interacts directly or indirectly with compounds containing androgens, estrogens, aluminum or magnesium compounds, cytarabine, methotrexate, nitrosoureas, halothane and other halogenated anesthetics, glucocorticoids, heparin, vitamin 12, immunosuppressants, atropine, bethanechol, analgesics , narcotics, and total parenteral nutrition, 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 FITATO 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 USE INSTRUCTIONS
Route of administration: intravenous.
The recommended activity for liver scintigraphy in adults is (70 kg) by intravenous administration is 185-555 MBq (5-15 mCi), for lymphoscintigraphy (intradermal) 37-74 MBq (1-2 mCi) and for gastroesophageal reflux (oral administration) 18.5-37 MBq (0.5-1 mCi). For pediatric patients the dose should be adjusted according to age, weight and body mass index.

8.1. INSTRUCTIONS FOR PREPARATION AND STORAGE AFTER COMPLEXATION
- Use 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 6 mL of 99mTcO$_4^-$ (if needed, top up with 0.9% NaCl) with maximum activity of 5920 MBq (160 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.

8.2. QUALITY CONTROL - RADIOCHEMICAL
Use a 3mm Whatman 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 plate in a chromatography tank containing butanone PA. Wait until the solvent has migrated to the top line of the plate. Remove the plate from the tank, cut it in alf and calculate labeling efficiency using the formula below:

Analyze the results of labeling efficiency in accordance with table 2.

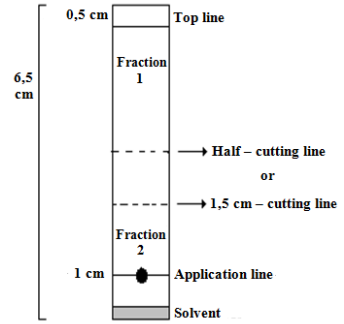

Figure 1 – Cutting the chromatography plates

PLATE: % 99mTcO$_4^-$:

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

Labeling efficiency/radiochemical purity should be = 95%.

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

Chromatography Analysis of FITATO-Tc-99m			
Chromatography System		**(99m Tc) Species**	
Stationary Phase	**Mobile Phase**	**Origin**	**Front**
Whatman Plate	Butanona PA	FITATO-Tc-99m 99mTcO$_2$	99mTcO$_4^-$

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

8.3. QUALITY CONTROL - pH
Apply a sample of the radiopharmaceutical on the pH indicator strip. Wait 30 seconds and compare the strip color with the parameters in this box.
The pH range for the radiopharmaceutical FITATO-Tc-99m should be between 5.0 and 7.0.

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	Organ	mGy/MBq
Adrenal glands	0.01	Liver	0.074
Bladder	0.000091	Lungs	0.0054
Bones	0.0079	Ovaries	0.0023
Breasts	0.0025	Pancreas	0.012
Stomach	0.006	Bone marrow	0.015
Small Intestine	0.0043	Spleen	0.077
Upper large intestine	0.0055	Testicles	0.00048
Lower large intestine	0.0018	Thyroid	0.00069
Kidneys	0.0097	Uterus	0.0018
Other tissue	0.0027	Effective dose (mSv/MBq)	0.014

Table 4 – Dosage for administering FITATO-Tc-99m. Source: ICRP, 1990.

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

No side effects were found for the colloidal form of FITATO in the sources consulted. In addition, there is no references to any experiments conducted through animal testing.

10. OVERDOSE

In case of a radiation overdose with FITATO-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
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