PIRO 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
sodium pyrophosphate decahydrate	20.12 mg
stannous chloride dihydrate	4.05 mg
water for injection	1.0 mL

Table 1 – Composition of the PIRO kit vials.

1. INDICATIONS
The radiopharmaceutical PIRO-Tc-99m is used primarily in myocardial scintigraphy to assess acute infarction and the extent of necrosis process. It can be used as a skeletal imaging agent to demonstrate areas of altered osteogenesis, as well as for blood pool images, ventriculography and occult blood tests, when administered 20 to 30 minutes prior to labeling the blood.

INTRAVENOUS ADMINISTRATION. ADULT AND PEDIATRIC USE.

2. EFFICACY
The efficacy of this radiopharmaceutical PIRO-Tc-99m for imaging after acute myocardial infarction was proved (Kelly et al., 1979; Zolle, 2007). Authors also evaluated its efficacy on bone imaging (Eckelman et al., 1973; Rudd et al., 1977; Zolle, 2007) and erythrocytes labeling for angiography (Zolle, 2007).

3. PHARMACOLOGICAL CHARACTERISTICS
When administered intravenously, the radiopharmaceutical PIRO-Tc-99m shows an affinity for areas of altered osteogenesis. One to two hours after intravenous injection of PIRO-Tc-99m, 40 to 50% of the injected dosed is concentrated in the skeleton. It is also taken up by the damaged myocardium, primarily in areas with irreversibly damaged myocardial cells, from 0.01 to 0.02% per gram of the radiopharmaceutical is concentrated in areas of acute myocardial infarction. Within an hour, 10 to 11% of activity remains in the vascular system, falling to about 2 to 3% 24 hours after injection. The radiopharmaceutical is predominantly excreted in the urine and around 40% of the administered dose is eliminated after 24 hours. PIRO-Tc-99m can also be used for labeling red blood cells. When administered 20 to 30 minutes before red blood cell labeling, approximately 75% of injected activity remains in the blood pool.

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
Coadministration with glucocorticoids, antacids, cytostatics, drugs containing iron, sodium phosphates, gentamicin, calcium gluconate and estrogens could reduce bone uptake and increase renal and extra-skeletal uptake.

7. STORAGE PRECAUTIONS
This medication 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 PIRO 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 10 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 medication that has expired.
All medication 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 dose for bone scintigraphy in adults weighing 70 Kg is 740 MBq (20 mCi) to 1110MBq (30 mCi). The recommended dose for myocardial scintigraphy in adults weighing 70 Kg is 555 MBq (15 mCi) to 1110MBq (30 mCi). For pediatric patients the dose should be adjusted according to age, weight and body mass index.
In the case of labeled red blood cells, 0.02 mg/kg to 0.05 mg/Kg of tin should be administered to adult patients. 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 3 mL of 99mTcO_4^- (if needed, top up with 0.9% NaCl) with maximum activity of 3700 MBq (100 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 30 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 two 3mm 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 PLATE 1 in a chromatography tank containing butanone PA and 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.

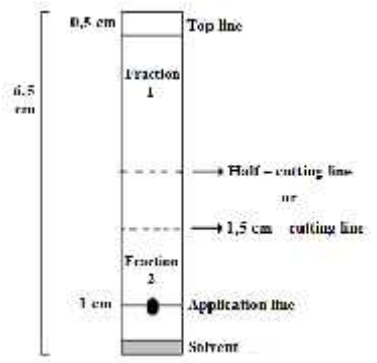

Figure 1 – Cutting the chromatography plates

Labeling efficiency (%)

100−(% **99mTcO4** + % **99mTcO2**) ≥ **90%, where**

PLATE 1: % 99mTcO_4^-:

$$\frac{\text{activity fraction 1}}{\text{activity fraction 1} + 2} \times 100$$

PLATE 2: % 99mTcO_2:

$$\frac{\text{activity fraction 2}}{\text{activity fraction 1} + 2} \times 100$$

Labeling efficiency should be greater than or equal to 90%.

CHROMATOGRAPHY ANALYSIS OF PIRO-Tc-99m			
Chromatography System		**(99m Tc) Species**	
Stationary Phase	**Mobile Phase**	**Origin**	**Front**
Plate 1 (Whatman 3mm)	Butanone PA	PIRO-Tc-99m 99mTcO_2	99mTcO_4^-
Plate 2 (Whatman 3mm)	0.9% NaCl	99mTcO_2	PIRO-Tc-99m 99mTcO_4^-

Table 2 – Chromatography systems for radiochemical control of PIRO-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 PIRO-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 (%)	AVERAGE ENERGY (keV)
Gama -2	89.07	140.5

Table 3 – Data on the main radiation emitted
'Kocher, David C., "Radioactive Decay Data Tables," DOE/ TIC-11026. 108(1981).

8.7. DOSAGE
The dose absorbed by a 70 Kg patient on administration of PIRO-Tc-99m is shown in table 3:

ORGAN	mSv/MBq
Adrenal glands	0.0087
Bladder walls	0.0092
Bone surfaces	0.0092
Breasts	0.0043
Stomach	0.0048
Heart	0.0230
Kidneys	0.0100
Ovaries	0.0042
Testicles	0.0027
Lungs	0.0140
Spleen	0.0150
Bone marrow	0.0073
Liver	0.0075
Uterus	0.0047
Other tissue	0.0037
Effective dose	**0.0085**

Table 4 – Dosage for administering PIRO-Tc-99m.
Source: González-Vázquez et al., 2006.

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
There are no reports of side effects.

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