SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF MEDICINAL PRODUCT

TechneScan® PYP
(Curium Netherlands catalogue number: DRN 4342)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Sodium pyrophosphate 11.93 mg

3 PHARMACEUTICAL FORM

Powder for injection.

4 CLINICAL PARTICULARS

4.1 Diagnostic indications

A In-vivo or in-vivo/in-vitro red blood cell labelling for blood pool scintigraphy. Major indications are:
- angiocardioscintigraphy for:
  - evaluation of ventricular ejection fraction,
  - evaluation of global and regional cardiac wall motion,
  - myocardial phase imaging.
- organ perfusion and vascular abnormalities imaging.
- diagnosis and localization of occult gastro-intestinal bleeding.

B Determination of blood volume.

C Spleen scintigraphy.

4.2 Posology and method of administration

Administration is by intravenous injection.

Red blood cell (RBC) labelling methods
The stannous pyrophosphate lyophilisate (non radioactive substance) is first reconstituted with isotonic sodium chloride solution for injection.

In-vivo method
Injection of the reconstituted solution of the stannous pyrophosphate complex and consecutive injection of sodium ^{99m}Tc pertechnetate 30 minutes later.

In-vitro method
- Sampling of 10 ml of the patient's blood.
- In-vitro incubation of the reconstituted solution with the sampled whole blood or separated red blood cells, followed 30 minutes by the addition of sodium (^{99m}Tc) pertechnetate and reinjection of the labelled red blood cells.

Modified in-vivo method (in-vivo/in-vitro)

- Injection of the reconstituted solution of the stannous pyrophosphate complex for in-vivo "stannous loading" of RBC.
- In-vitro RBC labelling with sodium (^{99m}Tc) pertechnetate after withdrawal of a blood sample.
- Reinjection of the labelled red blood cells.

Denatured red blood cell labelling

- In-vitro red blood cell labelling followed by denaturation of the erythrocytes e.g. heating 49-50°C for 25 minutes.
- Reinjection of the labelled denaturated red blood cells.

Posology

A Blood pool scintigraphy

The average activity administered by single injection after in-vivo or in-vitro labelling is 890 MBq (740-925 MBq).

B Determination of blood volume

The average activity administered by single injection after in-vitro labelling is 3 MBq (1-5 MBq).

C Spleen scintigraphy

The average activity administered by single injection for in-vitro labelling of denaturated erythrocytes is 50 MBq (20-70 MBq). The optimal amount of nonradioactive stannous tin for preparation of red blood cells in-vivo or in-vitro is 0.05 μg to 1.25 μg per ml of the total blood volume of the patient (near 5000 ml in a man of 70 kg weight). Especially in cases of in-vitro labelling this dose of stannous tin should not be exceeded. Sodium (^{99m}Tc) pertechnetate should be injected (in-vivo) or added to the incubation mixture (in-vitro) after 30 minutes. Scanning can be started immediately after injection of the tracer.

Paediatric doses

The activity for children may be calculated from the recommended range of adult activity and adjusted according to body weight or surface area. However, the Paediatric Task Group of EANM recommends to calculate the administered activity from the body weight according to the following table.

Fraction of adult dose:

3 kg = 0.1	4 kg = 0.14	6 kg = 0.19	8 kg = 0.23	10 kg = 0.27
12 kg = 0.32	14 kg = 0.36	16 kg = 0.40	18 kg = 0.44	20 kg = 0.46
22 kg = 0.50	24 kg = 0.53	26 kg = 0.56	28 kg = 0.58	30 kg = 0.62
32 kg = 0.65	34 kg = 0.68	36 kg = 0.71	38 kg = 0.73	40 kg = 0.76
42 kg = 0.78	44 kg = 0.80	46 kg = 0.82	48 kg = 0.85	50 kg = 0.88
52-54 kg = 0.90	56-58 kg = 0.92	60-62 kg = 0.96	64-66 kg = 0.98	68 kg = 0.99

In very young children (up to 1 year) a minimum dose of 80 MBq is necessary in order to obtain images of sufficient quality. For spleen scintigraphy a minimum dose of 20 MBq is necessary. Because of the long lasting fixation of stannous salts on red blood cells, it is recommended not to repeat the procedure before 3 months.

4.3 Contra-indications

None.

4.4 Special warning and precautions for use

4.4.1 Special warning

It is recommended that in-vivo (^{99m}Tc) RBC labelling be performed prior to administration of iodinated contrast media. Otherwise, labelling efficiency will be adversely affected.

4.4.2 Special precautions for use

Radiopharmaceutical agents should only be used by qualified personnel with appropriate government authorization for the use and manipulation of radionuclides. This radiopharmaceutical may be received, used and administered only by authorized persons in hospitals. Its receipt, storage, transfer and disposal are subject to the regulations and the appropriate licenses of the local competent official organizations. Radiopharmaceutical intended for administration to patients should be prepared by the user in a manner which satisfies both radiological safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken, complying with the requirements of Good Pharmaceutical Manufacturing Practice. In infants and children, a particularly careful assessment must be made of the diagnostic value, necessity for and risks of the procedure.

4.5 Interactions with other medicaments and other forms of interactions

Reduction in red blood cell labelling yield has been reported with heparin, tin overload, aluminum prazosin methyldopa, hydralazin, digitalic related compounds, quinidine, β-adrenergic blockers (e.g. propanolol), calcium channel blockers (e.g. verapamil, nifedipine), nitrates (e.g. nitroglycerin), anthracycline antibiotic, iodinated contrast agents and teflon catheter (the SN^{++} can react with the catheter).

4.6 Pregnancy and lactation

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 to be pregnant until proven otherwise. Where uncertainty exists, it is important that radiation exposure should be the minimum consistent with achieving the desired clinical information. Alternative techniques which do not involve ionizing radiation should be considered. Radionuclide procedures carried out on pregnant women also involve radiation doses to the foetus. Only imperative investigations should be carried out during pregnancy, when the likely benefit exceeds the risk incurred by mother and foetus. Administration of 925 MBq results in an absorbed dose to the uterus of 4.3 mGy. Doses above 0.5 mGy should be regarded as a potential risk to the foetus.

Before administering a radioactive medicinal product to a mother who is breast-feeding consideration should be given as to whether the investigation could be reasonably delayed until the mother has ceased breast-feeding and as to whether the most appropriate choice of radiopharmaceutical has been

made. If the administration is considered necessary, breast-feeding should be interrupted and the expressed feeds discarded. Breast-feeding can be restarted about 12 hours post injection or when the level in milk will not result in a radiation dose to the child greater than 1 mSv.

4.7 Effects on ability to drive and use machines

Effects on ability to drive and use machines have not been described.

4.8 Undesirable effects

For each patient exposure to ionising radiation must be justifiable on the basis of likely benefit. The activity administered must be such that the resulting radiation dose is as low as reasonably achievable bearing in mind the need to obtain the intended diagnostic result. Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. For diagnostic nuclear medicine investigations the current evidence suggests that these adverse effects will occur with low frequency because of the low radiation doses incurred. For most diagnostic investigations using a nuclear medicine procedure radiation dose delivered (EDE) is less than 20 mSv. Higher doses may be justified in some clinical circumstances.

Adverse reactions after the intravenous administration of both the unlabelled and the technetium-99m complexes have been reported in isolated cases (1-5 per 100,000 uses). The following effects have been described: flush, headache, vasodilatation, nausea, dizziness, swelling of the arm, erythema and itching at the injection site, diaphoresis and tinnitus, urticaria, generalized pruritus. Cardiac arrhythmia, facial edema and coma have been reported.

4.9 Overdose

In the event of the accidental administration of an overdose of the radiopharmaceutical very little supportive treatment can be undertaken since its elimination is entirely dependent on the normal haemolytic process. Forced diuresis and frequent bladder voiding are recommended in the case of overdosage with ^{99m}Tc pertechnetate.

5 PHARMACOLOGICAL PARTICULARS

5.1 Pharmacodynamic properties

At doses used for diagnostic procedures, neither stannous pyrophosphate, sodium (^{99m}Tc) pertechnetate nor stannous pyrophosphate (^{99m}Tc), nor labelled Red BIood Cells appear to exert any pharmacodynamic effects.

5.2 Pharmacokinetic properties

Intravenous injection of stannous salts induces a “stannous loading” of erythrocytes. Subsequent sodium (^{99m}Tc) pertechnetate injection results in an accumulation and a retention of sodium (^{99m}Tc) pertechnetate in the choroid plexus and red blood cells. Intravenous administration of 10-20 μg stannous ion/kg body weight (in form of stannous pyrophosphate) followed 30 minutes later by 370-740 MBq pertechnetate injection results in efficient labelling of blood pool. Under normal circumstances intravenously injected pertechnetate freely diffuses into and out from the erythrocytes. However, when the erythrocytes have been preloaded with stannous ion, the sodium (^{99m}Tc) pertechnetate is reduced within the cells and becomes bound to the chains of

globin. The mechanisms by which sodium (^{99m}Tc) pertechnetate becomes attached to tin primed red blood cells are not clearly understood. However, 20% of injected pertechnetate enters the red cell and binds to a beta chain of globin. While the remaining 70-80% of pertechnetate is believed to be located in the cytoplasm or on the red cell membrane. On the other hand reducing the surface charge of the erythrocytes decreases the efficiency of labelling down to 20%.

The most beneficial time for the injection of (^{99m}Tc) pertechnetate for the in-vivo labelling is 20-30 min after the administration of pyrophosphate. At 10 and 100 minutes post injection, 77 ± 15% and 71 ± 14% respectively, of the injected activity is found in the blood. This value remains constant for about 2 hours after injection with only about 6% decrease in total blood radioactivity during this period.

Up to eight days after the examination, labelling of erythrocytes with (^{99m}Tc) pertechnetate may still be observed. There is no appreciable effect with doses of up to 0.02 mg of tin/kg. The heat-denatured erythrocytes are sequestrated by splenic pulp.

5.3 Preclinical safety data

There are no preclinical safety data specific to technetium labelled erythrocytes. The toxicity of pertechnetate ion and stannous salts has been studied and reported in the literature. Systemic toxical effects are only observed at relatively high parenteral doses, giving a safety ratio of at least 150. Repeated dose toxicity studies in rats with 50-100 times human dose do not cause macroscopic or microscopic alterations. Stannous salts are reported to have a weak potential for mutagenicity. There are no studies describing possible effects on reproduction or tumour incidence.

5.4 Dosimetry

Technetium (^{99m}Tc) decays with the emission of gamma radiation with an energy of 140 keV and a half-life of 6 hours to technetium (^{99}Tc) which can be regarded as quasi stable. The radiation doses absorbed by a patient weighing 70 kg, after intravenous injection of ^{99m}Tc-labelled erythrocytes and ^{99m}Tc-labelled denatured erythrocytes, are reported hereafter (ICRP 53 -1988).

^{99m}Tc-labelled erythrocytes:
Absorbed dose per unit activity administered (mGy/MBq)

Organ	Adult	15 years	10 years	5 years	1 year
*Adrenals	8.7E-03	1.1E-02	1.7E-02	2.7E-02	4.9E-02
*Bladder wall	9.2E-03	1.2E-02	1.7E-02	2.5E-02	4.6E-02
Bone Surfaces	9.2E-03	1.3E-02	2.3E-02	3.9E-02	7.8E-02
Breast	4.3E-03	4.5E-03	7.2E-03	1.1E-02	1.9E-02
GI-tract					
Stomach wall	4.8E-03	6.1E-03	9.5E-03	1.4E-02	2.4E-02
Small intestine	4.4E-03	5.3E-03	8.1E-03	1.2E-02	2.2E-02
Upper large intest.	4.3E-03	5.5E-03	7.9E-03	1.3E-02	2.1E-02
Lower large intest.	3.9E-03	5.3E-03	8.0E-03	1.1E-02	2.1E-02
*Heart	2.3E-02	2.8E-02	4.1E-02	6.2E-02	1.1E-01
*Kidneys	1.0E-02	1.2E-02	1.9E-02	3.0E-02	5.5E-02
Liver	7.5E-03	8.8E-03	1.4E-02	2.1E-02	3.8E-02

Lungs	1.4E-02	1.8E-02	2.9E-02	4.5E-02	8.5E-02
Ovaries	4.2E-03	5.4E-03	7.9E-03	1.2E-02	2.1E-02
Pancreas	6.2E-03	7.5E-03	1.1E-02	1.7E-02	2.9E-02
Red marrow	7.3E-03	8.8E-03	1.3E-02	2.0E-02	3.5E-02
*Spleen	1.5E-02	1.8E-02	2.8E-02	4.4E-02	8.4E-02
Testes	2.7E-03	3.7E-03	5.4E-03	8.3E-03	1.5E-02
Thyroid	4.9E-03	7.1E-03	1.2E-02	1.9E-02	3.5E-02
Uterus	4.7E-03	5.7E-03	8.5E-03	1.3E-02	2.2E-02
Other tissue	3.7E-03	4.4E-03	6.4E-03	9.8E-03	1.8E-02
Effective Dose Equivalent (mSv/MBq)	**8.5E-03**	**1.1E-02**	**1.6E-02**	**2.5E-02**	**4.6E-02**

For blood pool scintigraphy the effective dose equivalent resulting of an administered dose of 925 MBq is 7.9 mSv (per 70 kg individual) and the typical radiation dose to the critical organ (heart) is 21 mGy.

For blood volume determination the effective dose equivalent resulting from an administered activity of 5 MBq is 0.05 mSv (per 70 kg individual).
^{99m}Tc-labelled denatured erythrocytes:

Absorbed dose per unit activity administered (mGy/MBq)

Organ	**Adult**	**15 years**	**10 years**	**5 years**	**1 year**
Adrenals	1.3E-02	1.8E-02	2.7E-02	3.8E-02	6.3E-02
Bladder wall	7.5E-04	1.1E-03	2.1E-03	3.8E-03	7.3E-03
Bone Surfaces	3.1E-03	4.1E-03	6.1E-03	9.5E-03	1.9E-02
Breast	2.1E-03	2.1E-03	4.1E-03	6.8E-03	1.0E-02
GI-tract					
*Stomach wall	1.9E-02	2.1E-02	3.0E-02	4.0E-02	5.8E-02
Small intestine	3.7E-03	4.6E-03	7.7E-03	1.3E-02	2.2E-02
Upper large intest					
	4.0E-03	4.9E-03	8.5E-03	1.4E-02	2.3E-02
Lower large intest					
	1.7E-03	2.3E-03	4.3E-03	6.9E-03	1.3E-02
Heart	6.0E-03	7.3E-03	1.1E-02	1.6E-02	2.6E-02
*Kidneys	1.8E-02	2.2E-02	3.2E-02	4.6E-02	7.0E-02
*Liver	1.8E-02	2.3E-02	3.4E-02	4.9E-02	8.7E-02
Lungs	5.7E-03	7.5E-03	1.1E-02	1.7E-02	2.8E-02
Ovaries	1.4E-03	2.2E-03	3.9E-03	7.0E-03	1.2E-02
*Pancreas	3.6E-02	4.0E-02	5.7E-02	7.8E-02	1.2E-01
Red marrow	4.3E-03	6.0E-03	8.4E-03	1.1E-02	1.7E-02
*Spleen	5.6E-01	7.8E-01	1.2E+00	1.8E+00	3.2E+00
Testes	4.7E-04	5.9E-04	1.1E-03	1.7E-03	4.1E-03
Thyroid	6.3E-04	1.0E-03	1.8E-03	3.2E-03	6.6E-03
Uterus	1.4E-03	1.8E-03	3.6E-03	5.9E-03	1.1E-02
Other tissue	3.3E-03	4.1E-03	5.8E-03	8.7E-03	1.5E-02
Effective Dose equivalent (mSv/MBq)	**4.1E-02**	**5.6E-02**	**8.4E-02**	**1.3E-01**	**2.2E-01**

For spleen scintigraphy the effective dose equivalent resulting from an administered activity of 70 MBq is 2.9 mSv (per 70 kg individual) and the typical radiation dose to the critical organ (spleen) is 39 mGy.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tin(II) chloride: 3.36 mg and nitrogen.

6.2 Incompatibilities

None known to date.

6.3 Shelf life

The expiry date for this product is 6 month from the day of manufacture. The labelled product should be used within 4 hours after labelling.

6.4 Special precautions for storage

The product is to be stored at 2-8°C. The labelled product is to be stored at 2-8°C. Storage should be in accordance with national regulations for radioactive material.

6.5 Nature and contents of container

10 ml glass vial (Type 1 Ph.Eur) closed with a bromobutyl rubber stopper sealed with an aluminium crimp cap. TechneScan® PYP is supplied as five vials in a carton.

6.6 Instructions for use/handling

Allow a vial to come to room temperature for 5 minutes, add aseptically the required amount of Sodium Pertechnetate (^{99m}Tc) Injection (Ph.Eur.), (maximum 3.7 GBq, 100 mCi) in a volume of 1-10 ml and shake until the contents have been dissolved. After 5 minutes at room temperature the preparation is ready for injection. For blood cell labelling the agent is to be reconstituted with 6 ml of isotonic sodium chloride 0.9% (Ph.Eur.). In a patient of average weight (70 kg), 2 ml of the volume is to be administered intravenously.

6.6.1 Instructions for quality control

Examine by TLC on silica gel coated glass-fibre sheets according Ph.Eur. Monograph 129.

A Apply 5 to 10 μl and develop 10-15 cm in 13.6% m/V solution of sodium acetate R. The technetium-99m tin pyrophosphate complex and pertechnetate ion migrate with an R_f of 0.9-1.0, whereas impurities in colloidal form remain at the start.

B Apply 5 to 10 μl and dry in a stream of nitrogen. Develop (10-15 cm) with methyl ethyl ketone R; pertechnetate ion migrates with an R_f 0f 0.95-1.0, whereas technetium-99m tin pyrophosphate complex remain at the start.

Sum of percentages radioactivity corresponding to impurities in test a) and in test b) (including pertechnetate ion): ≤ 10.0 %. The disposal of waste should be in accordance with national and international regulation for radioactive materials.

6.7 Manufactured and released by

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7 Information of product registration holder

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8 MARKETING AUTHORIZATION NUMBER

MAL19984355AZ

9 DATE OF APPROVAL/REVISION OF SPC

1st April 2024