HAUTE AUTORITÉ DE SANTÉ

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TRANSPARENCY COMMITTEE

OPINION

20 September 2006

TECHNESCAN PYP, powder for an injectable solution.
Red blood cell labelling kit with Technetium Tc 99m

Box of 5 vials containing 15.26 mg of powder (CIP: 556 546.8)

Applicant : **MALLINCKRODT FRANCE**

Sodium pyrophosphate, stannous chloride

List I
Medicinal product reserved for hospital use

Radiopharmaceutical products must only be used by qualified persons. They may only be supplied to practitioners who have obtained the special authorisation provided for under Article R 1333-24 of the Public Health Code.

Marketing Authorisation date: 30 April 1992

Reason for request: Inclusion on the list of medicines approved for use by hospitals

Health Technology Assessment Division

1. CHARACTERISTICS OF THE MEDICINAL PRODUCT

1.1. Active ingredient

Sodium pyrophosphate, stannous chloride

1.2. Indications

This medicinal product is used for diagnostic purposes only.

TechneScan PYP is used to label in vivo, in vitro or in vivo/vitro red blood cells for the scintigraphic exploration of the blood pool.

The main indications are:

a) Angiography with the aim of:

- evaluating the ventricular ejection fraction
- analysing the global and segmental wall motion of the myocardium

b) Perfusion scintigraphy of vascular organs and abnormalities

c) Determination of the total red cell volume

d) Splenic scintigraphy

1.3. Dosage

TechneScan PYP is only administered intravenously.

Red blood cell labelling method

Stannous pyrophosphate in lyophilised form is first reconstituted with a sterile solution of 0.9% sodium chloride (NaCl 0.9%).

In vivo method

The reconstituted stannous pyrophosphate solution is administered to the patient intravenously, 30 minutes later, the sodium pertechnetate Tc 99m solution is administered.

In vitro method

Take between 6 and 10 mL of blood from the patient, then incubate in vitro the reconstituted solution with the total blood sample taken or the red blood cell (erythrocyte) fraction. Add the sodium pertechnetate Tc 99m solution 15 minutes later and reinject the labelled red blood cells.

In vivo/vitro method

Administer the reconstituted solution of stannous pyrophosphate intravenously to saturate the red blood cells in vivo.

Take a blood sample from the patient to label the red blood cells in vitro, saturated by sodium pertechnetate Tc 99m.

Reinject the labelled red blood cells.

Method for labelling denatured red blood cells

The red blood cells saturated by stannous pyrophosphate using the in vivo/in vitro method or in vitro method are denatured by heat at 49.5° C fo r 20 minutes and are then labelled using

sodium pertechnetate Tc 99m. After a final wash, the labelled denatured blood cells are injected into the patient.

Adult dosage

a) Total blood pool imaging: the mean activity administered by a single intravenous injection, after labelling in vivo or in vitro, is 500 MBq (300 to 1000 MBq).

b) Determining blood volume: the mean activity administered by a single intravenous injection, after labelling in vitro, is 3 MBq (1 to 5 MBq).

c) Splenic scintigraphy: the mean activity administered by a single intravenous injection, after labelling in vitro denatured red blood cells, is 50 MBq (20 to 70 MBq). The images may be taken immediately after the tracer has been injected.

The optimum quantity of tin for labelling the red blood cells, whether in vivo or in vitro, is 10 to 20 µg/kg for adults. This tin concentration must not exceed the recommended dose, especially in the case of the in vitro labelling method.

Paediatric dosage

When this type of examination is justified, the administered activity must be a fraction of the activity recommended for adults, calculated according to the child's mass or body surface area. In practice, the guidelines specified by the Paediatric Task Group of the European Association of Nuclear Medicine may be followed.

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 under the age of 1 year, a minimum dose of 100 MBq is required to be able to obtain images of adequate quality. Due to the long-term binding of tin salts to red blood cells, it is recommended to wait for at least 3 months before repeating the examination.

2. SIMILAR MEDICINAL PRODUCTS

2.1. ATC Classification (2005)

V: Various
V09: Diagnostic radiopharmaceuticals
V09B: Skeleton
V09BA: Technetium (^{99m}Tc) compounds
V09BA03: Technetium (^{99m}Tc) pyrophosphate

2.2. Medicines in the same therapeutic category

ANGIOCIS Kit for the preparation of stannous pyrophosphate used for in vivo labelling of red blood cells with technetium [Tc 99m].

AMERSCAN STANNOUS TIN, powder for injection.

3. ANALYSIS OF AVAILABLE DATA

Based on the clinical data supplied by the company, it is not possible to evaluate TECHNESCAN PYP in specific detail as this data relates to the diagnostic efficacy of the examinations carried out using Tc PYP, without differentiating the role of this medicinal product and comparing it to other Tc PYP-based medicinal products available.

The quantitative effect of TECHNESCAN PYP cannot be evaluated by the Transparency Committee.

4. TRANSPARENCY COMMITTEE CONCLUSIONS

4.1. Actual benefit

TECHNESCAN PYP is a radiopharmaceutical product used for diagnostic purposes.
The nature of the condition's severity is determined based on the results of the exploration.
The efficacy/adverse effects ratio for this medicinal product is high.
There are alternative diagnostic methods available.

Public health benefit
In view of the lack of data concerning the diagnostic value of TECHNESCAN PYP and its expected impact on the population's health and given the availability of other stannous pyrophosphate-based contrast products, TECHNESCAN PYP has no expected public health benefit.

The actual benefit of TECHNESCAN PYP is substantial.

4.2. Improvement in actual benefit

TECHNESCAN PYP does not provide any improvement in the actual benefit (IAB V) as part of the usual diagnostic strategy in relation to the other medicinal products available.

4.3. Therapeutic use

Stannous pyrophosphate is a reducing agent which supports the pre-treatment of red blood cells with a view to labelling them with pertechnetate [Tc-99m0_4]. In the absence of stannous tin, pertechnetate [Tc-99m0_4^-] diffuses freely through the red blood cell's membrane. Only its reduced form remains trapped within the red blood cell.

The indications for TECHNESCAN PYP are:

- Angiography with the aim of:
    - examining the ventricular ejection fraction
    - and analysing the global and segmental wall motion of the myocardium

Radioisotopic angiocardiography is based on the peripheral intravenous injection of a small quantity of radioactive tracer and recording precordial radioactivity using a scintillation camera connected to a computer. In its most complete form, the examination comprises two phases: a first transit study during the first minute after the injection and an equilibrium study a few minutes later when the tracer has been diluted evenly in the blood pool.

The most commonly used isotope is Tc 99m.

If it is sufficient to limit the isotopic angiocardiography to the first passage of the tracer through the cardiac cavities, Tc 99m may be injected directly in the form of pertechnetate as it hardly has time to leave the blood pool during the few seconds required to record the images. On the other hand, if it is desirable to carry out the equilibrium study several minutes after the intravenous injection, the elements which are certain to remain within the vascular space for the time required to record the images must be labelled. In practice, albumin or red blood cells are used for this.

Several methods have been proposed for labelling red blood cells. The most awkward in terms of manipulation is the *in vitro* method for labelling the patient's red blood cells. This involves isolating a red blood cell unit from a blood sample and labelling the red blood cells with technetium in vitro, before reinjecting them into the patient. A simpler labelling method, known as *in vivo*, has since been developed.

- Perfusion scintigraphy of vascular organs and abnormalities

After a negative endoscopy, scintigraphy using technetium-labelled red blood cells makes it possible to highlight acute gastrointestinal bleeding (haematemesis, melaena). It can also be useful for exploring unexplained lower bleeding.

Similarly, scintigraphy using technetium-labelled red blood cells is useful for detecting intermittent bleeding after a negative endoscopy. It can detect tiny amounts of bleeding in the order of 0.1 ml/min.

This examination is also used to highlight hepatic haemangioma.

- Determination of the total red cell volume

The purpose of the isotopic study of the total red blood cell volume is to quantify the volume occupied by red blood cells within the total volume of blood.

This involves dilution using the patient's red blood cells, labelled in vitro using a radioactive isotope. This fraction of labelled red blood cells is reinjected into the patient and is diluted in the patient's general circulation. When a blood sample is taken later on, it is possible to establish from this the radioactivity of a given volume and to calculate the total volume of red blood cells.

- Splenic scintigraphy

Injecting red blood cells that have been labelled with Tc 99m and denatured by heat provides the basis for splenic scintigraphy. In fact, the red blood cells made fragile by the heat are selectively captured by the functional spleen tissue.

According to the experts, the major practical indication for TECHNESCAN PYP is isotopic ventriculography for determining the global ejection fraction, as well as the contraction phase and amplitude of the various segments of the myocardium.

The other indications are less widespread in practice.

4.4. Target population

There is no reliable epidemiological data available making it possible to quantify the target population for TECHNESCAN PYP in France.

4.5. Transparency Committee recommendations

The Transparency Committee recommends inclusion on the list of medicines approved for use by hospitals and various public services in the marketing authorisation.