Summary of Product Characteristics
^{32}P-Sodium orto-phosphate inj.

1. NAME OF THE MEDICINAL PRODUCT: ^{32}P-Sodium orto-phosphate inj.

2. QUALITATIVE AND QUANTITITATIVE COMPOSITION:

^{32}P Acidum phosphoricum		37 - 370	MBq
Natrii hydrophosphas		12	mg
Natrii chloridum 0.9mg/ml	ad	1	ml

The product does not contain any antimicrobial additives.

3. PHARMACEUTICAL FORM: Radiopharamceuticals - solution for injection.

4. CLINICAL PARTICULARS

4.1. Indication

Therapy of polycythemia vera and polythrombocytemia and related disorders, leukemia and other neoplastic haematological disorders. Palliative treatment of painful bone metastasis from prostate, breast, lung and other carcinomas is reported but its myelotoxicity should be considered.

4.2.Posology and method of administration

The preparation is destined for direct oral or intravenous administration to the patient in aliquots varying in activity depending on therapeutic application.

4.2.1. In the treatment of polycythemia vera recommended dose is 74 - 111 MBq (2 - 3 mCi) on 1 m^2 of body surface but not more than 185 MBq (5 mCi), another method recommends first application of 111 MBq (3 mCi) and if after 3 months the symptoms of polycythemia are still present the second, higher of 25% dose is administered. Single dose should not be higher than 250 MBq (7 mCi). In leukemia approximately 37 -74 MBq (1 to 2 mCi) is given weekly until the white blood cell count is sufficiently decreased.

4.2.2. In the treatment of of bone metastases the doses of 370 do 555 MBq (10 – 15 mCi) can be administered for pain palliation in terminally ill patients who have not responded to conventional therapies (hormones, wide or narrow beam radiotherpay, cytotoxicosis etc.) who present with widespread painful bone matestases from assorted primaries and who may be requiring or are likely to require increasing quantities of strong analgesics. Reduction of bone pain may take several weeks to occur and may be associated with improved morale as well as decreased analgesic requirements.

4.3. Contra indications

This agent is contraindicated in children, during pregnancy or females wishing to continue breast feeding. If the patient's platelet count is less than 15,000 it is suggested not to administer the preparation.

4.4. Special precautions

The administration of ^{32}P is usually not recommended in patients under 50 years of age. It should be noted that polycythemia rubra vera may also be palliated by repeated venesections, thioureas or regular courses of oral chlorambucil. More appropriate radiopharmaceuticals may be available for the treatment of painful bone metastases secondary to prostatic cancer.
Because of the relatively long effective half life ^{32}P-Sodium orto-phosphate it should not be administered to patients with a very short life expectancy.
Radiopharmaceutical agents should be used only by qualified personnel with the appropriate government authorisation for the use and manipulation of radionuclides.
This radiopharmaceutical may be received, used and administered only by authorised personnel in designated clinical settings. Its receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licenses of the local competent official organisations.
Because of the risk of serious, delayed bone marrow depression, cytotoxic agents should not be prescribed until aperiod of four months has elapsed from treatment with ^{32}P.

4.5. Interactions
The use of oestrogen and androgen preparations may affect the metabolism and retention of labelled phosphorus ^{32}P.
Interactions with other drugs are not known; with respect to the adverse effect on bone marrow, the product should not be administered simultaneously with chemotherapy and radiation therapy (or within a short interval after them), if the therapeutic effect does not outbalance the risk.

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.
Breast feeding should be discontinued after administration because of the potential hazard to the suckling; breast -feeding can only be restarted when the radiation dose obtained by the child due to the consuming of this milk and contact with the mother is lower than limits given by regulations on ionising radiation protection.
Pregnancy: There are no available data in animals or man but, at the activities proposed, this radiopharmaceutical is likely to both mutagenic and teratogenic. The administration of ^{32}P is therefore contraindicated in pregnancy.
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 ionising radiation should always be considered.

4.7. Effects on ability to drive and use machines
The product is safe.

4.8. Undesirable effects

Therapy with ^{32}P-Sodium orto-phosphate inj. gives the risk of leukemia in 2 - 15% of patients during 10 years (similar to chemotherapy).

4.9. Overdose

^{32}P-Sodium orto-phosphate should be administered by qualified personnel in designated clinical settings. The preparation is delivered in portions prepared on request with a patient activity dose. The possibility of overdosing is therefore markedly reduced. In the event of this occuring, however, overdose would be limited to excessive body irradiation rather than the remote possibility of chemical overdose. Excessive radiation effects all rapidly developing dividing tissues but those on haemopoietic tissues could be delayed for several months. In the event of overdosage an appropriate increase in fluid intake is advised to promote diuresis and excretion of the label (forced diuresis). Frequent bladder emptying is also advised. In addition, the administration of unlabelled phosphate salts can reduce the incorporation of the radionuclide in body tissues thereby reducing exposure.

5. PHARMACOLOGICAL PROPERTIES

5.1., 5.2. Pharmacodynamic and pharmacokinetic properties

Polycythemia vera is a disease characterized by an increased red blood cell mass, frequently associated with bone marrow hyperactivity. Therapy results from radiation injury to the cell precursors and the bone marrow due to bone accumulation of ^{32}P. A fraction of 0.30 of intravenously administered activity is assumed to go to mineral bone and to be permanently retained, and 0.70 is assumed to be distributed in soft tissues.

After injection the soluble radiophosphate is concentrated by rapidly proliferating tissue. The blood cells precursors in the bone marrow divide and proliferate rapidly in health and even more so in these diseases. The radionuclide ^{32}P present in sodium ortophosphate-^{32}P selectively concentrates in the mitotically active cells of the bone marrow and in trabecular and cortical bone. Selective uptake of ^{32}P by haemopoietic tissue provides a continuous irradiation of dividing cells which significantly interferes with their viability. Its uptake by the different tissues depends on several factors including exchangeable tissue phosphate in the tissue, the rate of new tissue formation and tissue vascularity.

5.3. Preclinical safety data

^{32}P-Sodium orto-phosphate has not been subjected to acute toxicity studies in any animal species. Likewise, its carcinogenicity or reproductive toxicity have not been evaluated.

5.4. Radiation dosimetry

Phosphorus [^{32}P] is a beta emitter (E_{max} 1.71 MeV) with a physical half-life of 14.29 days. It gives off Bremsstrahlung. According to ICRP model, a fraction of 0.30 of intravenously administered activity is assumed to go to mineral bone and to be permanently retained, and 0.70 is assumed to be distributed in soft tissues. Phosphorus metabolism is complex. Activity deposited in soft tissues is assumed to be rapidly eliminated from the body (30%) and about

40% of activity possesses a 19-day biological half-life, the remaining 30% is reduced by radioactive decay. The high-energy beta emissions can present a substantial skin dose hazard. The effective dose equivalent at adult patient (70 kg) after administration of ^{32}P-Sodium orto-phosphate is 2.20 mSv/MBq.The radiation dose absorbed in breast is about 0.92 mGy/MBq, in the bone marrow 11.0 mGy/MBq and in bone surfaces about 11.0 mGy/MBq. In the other organs, the absorbed radiation doses are lower (0.74 mGy/MBq).
The radiation dose to patients from the administered with ^{32}P-Sodium orto-phosphate inj. located in different organs and tissues. This distribution is presented in the ICRP 53: Annals of the ICRP, Radiation dose to Patients from Radiopharmaceuticals. Vol.18 No. 1-4 1987 p.83-84.

Organ	**Absorber dose per unit activity administrered (mGy/MBq)**				
	Adult	15 year	10 year	5 year	1 year
Adrenals	0,740	0,920	1,600	2,600	5,400
Bladder wall	0,740	0,920	1,600	2,600	5,400
Bone surface	1,100	1,400	23,00	40,00	96,00
Breast	0,920	0,920	1,600	2,600	5,400
GI-tract					
Stomach wall	0,740	0,920	1,600	2,600	5,400
Small intest	0,740	0,920	1,600	2,600	5,400
ULI wall	0,740	0,920	1,600	2,600	5,400
LLI wall	0,740	0,920	1,600	2,600	5,400
Kidneys	0,740	0,920	1,600	2,600	5,400
Liver	0,740	0,920	1,600	2,600	5,400
Lungs	0,740	0,920	1,600	2,600	5,400
Ovaries	0,740	0,920	1,600	2,600	5,400
Pancreas	0,740	0,920	1,600	2,600	5,400
Red marrow	1,100	1,500	26,00	58,00	120,0
Spleen	0,740	0,920	1,600	2,600	5,400
Testes	0,740	0,920	1,600	2,600	5,400
Thyroid	0,740	0,920	1,600	2,600	5,400
Uterus	0,740	0,920	1,600	2,600	5,400
Other tissue	0,740	0,920	1,600	2,600	5,400
Effective dose equvalent (mSv/MBq)	**2,200**	**3,000**	**5,100**	**10,00**	**22,00**

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Summary of Product Characteristics
^{32}P-Sodium orto-phosphate inj.

Sodium chloride
Sodium hydrophosphate
Water for injections

6.2. Incompatibilities
Not reported

6.3. Lifetime
14 days from the reference day

6.4. Storage
Store at room temperature, 5 -25°C, in accordance with regulations pertaining to health safety from ionising radiation.

6.5. Type of package
Glass vial 10 ml for multiple dosing closed with rubber stopper and aluminium cap.
Lead container, polystyrene case, tin.

6.6. Instructions for use
Radiopharmaceutical is delivered in portions containing required activity (certified on 12^{00}CET of the reference day) and volume, as ordered by the attending physician.
During handling and administration, the measures for radiation protection of the personnel must be strictly observed.

7. REGISTRATION DECISION HOLDER

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8. REGISTRATION DECISION NUMBER: R/3264, before 674/S

9. DATE OF REGISTRATION: June 28, 1999, before 28 September, 1976

10. DATE OF THE LATEST REVISION OF THE TEXT: **January, 2004**