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Drug Name Phosphocol P-32 Item Code # A470K0
Size Sticker Label Date 10/23/08
Vendor _____ Country US
Plant Site Maryland Heights Vendor Item # _____
Colors: BLACK  Part # _____
Prepared by VI



| | WIDTH | HEIGHT | CORNER RADIUS |
|-------------------|---------------------|--------|-----------------------|
| SIZE / DIMENSIONS | 1.5 x 1.5 INCHES | | Circle INCHES |
| | MM | | NONE SPECIAL SHAPE |



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Phosphocol® P 32
Chromic Phosphate P 32 Suspension

Rx Only.

Therapeutic – intraperitoneal or intracavitary injection only for treatment of peritoneal or pleural effusions caused by metastatic disease.

DESCRIPTION

Phosphocol® P 32 is supplied as a sterile, nonpyrogenic aqueous suspension in a 30% dextrose solution with 2% benzyl alcohol added as preservative. Each milliliter contains 1 mg sodium acetate. Sodium hydroxide or hydrochloric acid may be present for pH adjustment.

ACTIONS

Local irradiation by beta emission.

INDICATIONS

Phosphocol P 32 is employed by intracavitary instillation for the treatment of peritoneal or pleural effusions caused by metastatic disease, and may be injected interstitially for the treatment of cancer.

CONTRAINDICATIONS

Chromic phosphate P 32 therapy should not be used in the presence of ulcerative tumors.

Administration should not be made in exposed cavities or where there is evidence of loculation unless the extent of loculation is determined.

WARNINGS

Not for intravascular use.

This radiopharmaceutical should not be administered to patients who are pregnant or during lactation unless the therapeutic benefits outweigh the potential hazards.

Radiopharmaceuticals should be used only by physicians who are qualified by specific training in the safe use and handling of radionuclides produced by nuclear reactor or particle accelerator and whose experience and training have been approved by the appropriate government agency authorized to license the use of radionuclides.

Leukemia

Phosphocol P 32 may increase the risk for leukemia in certain situations. Two children (ages 9 and 14) with hemophilia developed acute lymphocytic leukemia approximately 10 months after intra-articular injections of Phosphocol P 32 (0.6 and 1.5 mCi total dose). Phosphocol P 32 is not indicated in the intra-articular treatment of hemarthroses.

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PRECAUTIONS

General

As in the use of any other radioactive material care should be taken to insure minimum radiation exposure to the patient, consistent with proper patient management, and to insure minimum radiation exposure to occupational workers.

Careful intracavitary instillation is required to avoid placing the dose of chromic phosphate P 32 into intrapleural or intraperitoneal loculations, bowel lumen or into the body wall. Intestinal fibrosis or necrosis and chronic fibrosis of the body wall have been reported to result from unrecognized misplacement of the therapeutic agent.

The presence of large tumor masses indicates the need for other forms of treatment. However, when other forms of treatment fail to control the effusion, chromic phosphate P 32 may be useful. In bloody effusion, treatment may be less effective.

Pediatric Use

Safety and effectiveness in pediatric patients has not been established.

Risk of Malignancy

Acute lymphocytic leukemia has been reported in children following the intra-articular administration of Phosphocol P 32 (*see* **WARNINGS**).

ADVERSE REACTIONS

Untoward effects may be associated with use of chromic phosphate P 32. These include transitory radiation sickness, bone marrow depression, pleuritis, peritonitis, nausea and abdominal cramping. Radiation damage may occur if accidentally injected interstitially or into a loculation.

Post-marketing Experience

The following adverse reactions associated with the use of Phosphocol P 32 have been identified during post approval use:

Leukemia in Children (*see* **WARNINGS**)

Radiation injury (necrosis and fibrosis) to the small bowel, cecum, and bladder following administration of P 32 into the peritoneal cavity.

Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

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DOSAGE AND ADMINISTRATION

The suggested dose range employed in the average patient (70 kg) is:

Intraperitoneal instillation: 370 to 740 megabecquerels (10 to 20 millicuries)

Intrapleural instillation: 222 to 444 megabecquerels (6 to 12 millicuries)

Doses for interstitial use should be based on estimated gram weight of tumor, about 3.7 to 18.5 MBq/gm (0.1 to 0.5 mCi/gm).

The patient dose should be measured by a suitable radioactivity calibration system immediately prior to administration.

PHYSICAL CHARACTERISTICS

Phosphorus P 32 decays by beta emission with a physical half-life of 14.3 days.¹ The mean energy of the beta particle is 695 keV.

Table 1. Principal Radiation Emission Data

| Radiation | Mean Percent/ Disintegration | Mean Energy (keV) |
|-----------|------------------------------|-------------------|
| Beta-1 | 100.0 | 694.9 |

The range of the phosphorus P 32 beta particle, which has a maximum energy of 1.71 MeV, is 2.9 mm of aluminum.

To correct for physical decay of this radionuclide, the percentages that remain at selected time intervals before and after the day of calibration are shown in Table 2.

¹ Stabin MG, da Luz CQPL. New Decay Data for Internal and External Dose Assessment, Health Phys. 83(4):471-475, 2002.

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Table 2. Physical Decay Chart; Phosphorus P 32, Half-life 14.3 days

| Days | Fraction Remaining | Days | Fraction Remaining | Days | Fraction Remaining |
|------|--------------------|------|--------------------|------|--------------------|
| -15 | 2.07 | 2 | 0.908 | 35 | 0.183 |
| -10 | 1.62 | 5 | 0.785 | 40 | 0.144 |
| -5 | 1.27 | 10 | 0.616 | 45 | 0.113 |
| -2 | 1.10 | 15 | 0.483 | 50 | 0.089 |
| -1 | 1.05 | 20 | 0.379 | 55 | 0.070 |
| 0* | 1.00 | 25 | 0.298 | 60 | 0.055 |
| 1 | 0.953 | 30 | 0.234 | 65 | 0.043 |

*Calibration Day

RADIATION DOSIMETRY

The effective half-life of phosphorus P 32 is considered to be equal to its physical half-life, with a residence time of 495 hours.

The radiation dose from a uniformly distributed concentration of 37 kilobecquerels (1 microcurie) per gram within a 16-gram prostate is estimated to be equivalent to about 7.3 grays (730 rads)². Table 3 shows the estimated radiation doses to the prostate and the pleural or peritoneal surfaces³ of an average patient (70 kg) from a dose of 740 megabecquerels (20 millicuries) of phosphorus P 32.

In comparison to the distribution in the prostate, the distribution of phosphorus P 32 on the pleural and peritoneal surfaces is non-uniform, with great extremes in local doses. To obtain an estimate of the average dose, the surface area of the pleural and peritoneal cavities can be assumed to amount to 4,000 and 5,000 cm², respectively. The estimated radiation doses to an average patient (70 kg) with 90% retention of a dose of 740 megabecquerels (20 millicuries) of phosphorus P 32 distributed uniformly over these areas are shown in Table 3. The decreases of the averaged radiation doses at various tissue depths away from the surfaces of the pleural and peritoneal cavities are also tabulated.

² Stabin MG. A Model of the Prostate Gland for Use in Internal Dosimetry. J Nucl Med 35(3):516-520, 1994.

³ Watson EE, Stabin MG, Davis JL and Eckerman KF. A Model of the Peritoneal Cavity for Use in Internal Dosimetry. J Nucl Med 30:2002-2011, 1989.

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Table 3. Estimated Radiation Doses

| Surface/Organ | | Pleural | | Peritoneal | | Prostate | | |
|----------------------|------------------------------|------------------------------|--------------------------------|----------------------------|-------|--------------|-------|--------|
| % Retention Area/wt | | 90 4000 cm ² | | 90 5000 cm ² | | 100 16 gm | | |
| Depth in tissue (cm) | Dose Rate | | Tissue Dose / 740 MBq (20 mCi) | | | | | |
| | mGy-cm ² MBq-s | rad-cm ² μCi-h | grays | rads | grays | rads | grays | rads |
| 0.006 | 0.75 | 10 | 178 | 17800 | 134 | 13400 | 9180 | 918000 |
| 0.018 | 0.53 | 7 | 125 | 12500 | 94 | 9360 | | |
| 0.03 | 0.42 | 5.6 | 100 | 10000 | 74.9 | 7490 | | |
| 0.12 | 0.15 | 2 | 36 | 3570 | 26.7 | 2670 | | |
| 0.21 | 0.064 | 0.85 | 15 | 1520 | 11.4 | 1140 | | |
| 0.3 | 0.023 | 0.31 | 5.5 | 550 | 4.1 | 410 | | |
| 0.4 | 0.0047 | 0.062 | 1 | 110 | 0.83 | 83 | | |

HOW SUPPLIED

Catalog Number 470

Phosphocol P 32 - Chromic Phosphate P 32 Suspension (NDC No. 0019-N470-P0) is available in 10 milliliter vials containing 555 megabecquerels (15 millicuries) with a concentration of 185 megabecquerels (5 millicuries) per milliliter. The radiopharmaceutical is manufactured with a specific activity of 122 megabecquerels (3.3 millicuries) per milligram Chromic Phosphate at the time of standardization.

The U.S. Nuclear Regulatory Commission has approved distribution of this radiopharmaceutical to persons licensed to use byproduct material listed in Section 35.300, and to persons who hold an equivalent license issued by an Agreement State.

STORAGE AND HANDLING

Store at controlled room temperature 20 to 25°C (68 to 77°F).

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Mallinckrodt Inc.
Hazelwood, MO 63042 U.S.A.

