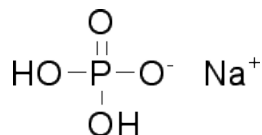


PHOSPHATE-SANDOZ® Tablets

(High dose phosphate supplement)

PHOSPHATE-SANDOZ

PHOSPHATE-SANDOZ® Tablets are a high dose phosphate supplement containing sodium phosphate monobasic. The CAS registry number is 7558-80-7. The empirical formula is $\text{Na H}_2\text{PO}_4$. The molecular weight is 119.98 and the structural formula is given below.



DESCRIPTION

Phosphate-Sandoz® effervescent tablets are large, white, flat, circular uncoated tablets with a slightly rough surface. The tablets effervesce when placed in water and dissolve to give a palatable orange-flavoured solution. The solution provides elemental phosphorus 500 mg (16.1 mmol phosphate). In addition each tablet provides sodium 469 mg (20.4 mmol Na^+), potassium 123 mg (3.1 mmol K^+), and citric acid - anhydrous 800 mg. The inactive excipients are sodium bicarbonate, potassium bicarbonate, macrogol 4000, sucrose 136 mg, orange flavour and sodium saccharin. Each tablet has a calorific value of 2.5 kcals.

PHARMACOLOGY

Pharmacodynamics

Phosphorous is one of the most abundant elements in the human body: nearly 85 % is present in the skeleton, with the balance in soft tissues and extracellular fluid. Most phosphorous is complexed as phosphate which is the body's major intercellular anion and an essential component of cell membrane phospholipids, DNA, and RNA. It is also critical to most biochemical processes, including ATP synthesis and metabolic and enzymatic pathways. Phosphorous, as phosphate, also assists in maintaining normal physiological pH balance.

Phosphorous balance is regulated by several hormones, including Parathyroid hormone (PTH), which controls the release of phosphate from bones and inhibits renal reabsorption. Serum phosphate levels are inversely proportional to serum calcium levels and their physiological requirements are the same.

Mechanism of Action. Oral administration of inorganic phosphates produces a fall in serum calcium in patients with hypercalcaemia. The sodium ions in Phosphate-Sandoz® effervescent tablets aid in the correction of the dehydration and sodium depletion which is seen in hypercalcaemia. In cases of hypercalcaemia associated with impaired renal function and hypophosphataemia, the main effect of oral phosphate is to bind calcium in the gut and thus reduce calcium absorption.

Pharmacokinetics

Absorption and Distribution

Phosphates are mainly absorbed from the jejunum and duodenum by passive and active transport. Approximately two thirds of ingested phosphate is absorbed from the gastrointestinal tract and most absorbed phosphate is filtered by the glomeruli and subsequently undergoes reabsorption. PTH and vitamin D stimulate absorption of phosphate from the small intestine and its reabsorption from the proximal tubule. Phosphorous absorption varies linearly with ingestion and diffusion is the primary method of absorption. The presence of large quantities of aluminium, calcium or magnesium may reduce the net absorption due to binding and formation of insoluble salts.

Metabolism and Excretion

Virtually all absorbed phosphate is excreted in the urine; the remainder being excreted in the faeces.

INDICATIONS

PHOSPHATE-SANDOZ® tablets are used as an oral phosphate supplement in the treatment of the following conditions:

1. Hypercalcaemia associated with such conditions as:
 - hyperparathyroidism
 - multiple myelomatosis, and
 - metastatic bone disease.
2. Hypophosphataemia associated with Vitamin D-resistant rickets.

CONTRAINDICATIONS

PHOSPHATE-SANDOZ® tablets are contraindicated in patients with a known hypersensitivity to sodium phosphate monobasic or any of the components of the tablets.

PRECAUTIONS

Consideration should be given to the sodium and potassium content of Phosphate-Sandoz® tablets (see "DESCRIPTION") before administration to patients suffering from conditions associated with significant electrolyte imbalance, or impaired renal function. In cases where restricted sodium intake is indicated, e.g. in the treatment of congestive cardiac failure, hypertension, pre-eclamptic toxemia, etc., the sodium and potassium content of PHOSPHATE-SANDOZ® tablets should be taken into consideration.

Soft tissue calcification and nephrocalcinosis have been reported in isolated cases following intravenous therapy with phosphate. This is thought to be a function of dosage and rapidity of phosphate administration. While such effects appear less likely to occur following treatment with oral phosphates, careful surveillance of patients is recommended. The effect of oral phosphate on serum phosphate is likely to be minimal, but close monitoring of serum levels is recommended.

Effects on fertility. The effects of PHOSPHATE SANDOZ® tablets in fertility have not been formally studied.

Use in Pregnancy. The safety of PHOSPHATE SANDOZ® tablets in human pregnancy has not been formally studied.

Use in Lactation. The safety of PHOSPHATE SANDOZ® tablets in breastfeeding mothers and their infants has not been formally studied however both sodium and phosphate are found in human milk.

Use in the elderly. As an excessive dosage has been reported to produce hypocalcaemia in isolated cases, particular care should be taken to ensure appropriate dosage in the elderly.

Interactions with other medicines. Concurrent administrations of PHOSPHATE SANDOZ® tablets with antacids, containing agents such as aluminium hydroxide, calcium or magnesium salts, may result in the displacement of calcium from binding to oral phosphate, thus reducing the efficacy of this medication.

Parathyroid hormone (PTH) increases the urinary excretion of phosphate by blocking tubular re-absorption.

The risk of ectopic calcification may be increased by concurrent use of calcium supplements.

Vitamin D increases the gastrointestinal absorption of phosphates and therefore increases the potential for hyperphosphataemia.

ADVERSE EFFECTS

Adverse drug reactions are listed according to system organ classes in MedDRA. Within each system organ class, the adverse drug reactions are ranked by frequency, with the most frequent reactions first. Within each frequency grouping, adverse drug reactions are presented in order of decreasing seriousness. In addition, the corresponding frequency category, using the following convention (CIOMS III) is also provided for each adverse drug reaction: Very common ($\geq 1/10$); common ($\geq 1/100$, $< 1/10$); uncommon ($\geq 1/1,000$, $< 1/100$); rare ($\geq 1/10,000$, $< 1/1,000$); very rare ($< 1/10,000$), not known (cannot be estimated from the available data), including isolated reports.

Table Adverse Drug Reactions

System Organ Class	Preferred Terms	Frequency
<i>Renal and urinary disorders</i>	Nephrocalcinosis (acute phosphate nephropathy) leading to acute renal failure	Not known
<i>Gastrointestinal disorders</i>	Abdominal pain, nausea, vomiting and diarrhoea	Not known
<i>Metabolism and nutrition disorders</i>	Hyperphosphataemia, hypocalcaemia, hypokalaemia and hypernatraemia	Not known

DOSAGE AND ADMINISTRATION

Phosphate-Sandoz® effervescent tablets should be dissolved in $\frac{1}{3}$ to $\frac{1}{2}$ glass of water and taken orally. The dosage should be adjusted to suit the requirements of individual patients.

Adults

Hypercalcaemia: up to 6 tablets daily (adjustment being made according to requirements).

Vitamin D-resistant rickets: 4-6 tablets daily.

Children

Hypercalcaemia: up to 3 tablets daily (adjustment being made according to requirements).

Vitamin D-resistant rickets: 2-3 tablets daily.

OVERDOSAGE

Contact the Poisons Information Centre on 131 126 for advice on management. Excessive dosage has been reported to produce hypocalcaemia in isolated cases. This has proved reversible when dosage has been adjusted.

CLINICAL STUDIES

Not applicable (NA).

PRESENTATION AND STORAGE CONDITIONS

Presentation

White, effervescent tablets available in cartons of 100 tablets. Each carton contains 5 tubes, each containing 20 tablets.

Storage

Store in the tightly closed original container below 25°C. Keep out of reach of children.

NAME AND ADDRESS OF THE SPONSOR

NOVARTIS Pharmaceuticals Australia Pty Limited

ABN 18 004 244 160

54 Waterloo Road

NORTH RYDE, NSW 2113

POISON SCHEDULE

Phosphate-Sandoz® tablets are unscheduled.

DATE OF APPROVAL

This amended document was last approved by the Therapeutic Goods Administration (TGA) on 01.07.98.

Date of most recent amendment: 17 March 2011
