DBL™ POTASSIUM DIHYDROGEN PHOSPHATE AND DIPOTASSIUM HYDROGEN PHOSPHATE CONCENTRATED INJECTION

NAME OF THE MEDICINE

Potassium phosphate dibasic (dipotassium hydrogen phosphate)
Potassium phosphate monobasic (potassium dihydrogen phosphate)

The molecular formula of potassium phosphate dibasic is K_2HPO_4, and of potassium phosphate monobasic is KH_2PO_4. The molecular weight of potassium phosphate dibasic is 174.2, and of potassium phosphate monobasic is 136.1. The CAS Registry number of potassium phosphate dibasic is 7758-11-4, and of potassium phosphate monobasic is 7778-77-0.

DESCRIPTION

Potassium phosphate dibasic is a colourless or white, hygroscopic granular powder. It is freely or very soluble in water and very slightly soluble in alcohol. Potassium phosphate monobasic is a white, odourless, granular or crystalline powder, or colourless crystals. It is freely soluble in water and practically insoluble in alcohol.

DBL™ Potassium Dihydrogen Phosphate and Dipotassium Hydrogen Phosphate Concentrated Injection is a clear, colorless, sterile solution. Each 10 mL ampoule contains 540 milligrams of potassium phosphate monobasic (KH_2PO_4) and 1.83 g of potassium phosphate dibasic (K_2HPO_4) in Water for Injection. The pH of the solution is approximately 7.5. Each mL of injection contains 2.5 mmol of potassium ions, 1.45 mmol of phosphate ions and 1.84 mmol of hydrogen ions.

PHARMACOLOGY

The majority (80%) of the body's phosphate is found as calcium phosphate in the skeleton, where it gives rigidity to the bone. The remainder is found in soft tissues. Phosphate is the principle anion of intracellular fluid. In body fluids, phosphate is present mainly as divalent hydrogen phosphate (HPO_4^{2-}) ions (approximately 80%) and monovalent dihydrogen phosphate ($H_2PO_4^-$) ions (approximately 20%).

Apart from its essential role in bone structure, phosphate is also important in many metabolic and enzymatic pathways. It is involved in energy storage and transfer, the utilization of B-complex vitamins, the buffering of body fluids, and in the renal excretion of hydrogen ions.

Hypophosphataemia may arise from a variety of causes including primary hyperparathyroidism, Vitamin D deficiency, X-linked familial hypophosphataemia, alcoholism, hepatic failure and septicaemia. The symptoms of hypophosphataemia include muscle weakness, paraesthesia, convulsions, cardiomyopathy, respiratory failure and haematological abnormalities. Prolonged hypophosphataemia may result in rickets or osteomalacia.

Pharmacokinetics

The normal concentration range of phosphate in plasma is 0.8 to 1.5 mmol/L

Phosphate is primarily excreted in the urine. Over 90% of plasma phosphate is filtered in the kidneys with the majority being reabsorbed in the proximal tubule. Parathyroid hormone decreases the tubular reabsorption of phosphate, thereby increasing urinary excretion. In addition, serum phosphate levels are inversely related to serum calcium levels and to renal

metabolism of Vitamin D. A decrease in serum calcium concentration will result in increased serum phosphate levels.

INDICATIONS

Treatment of severe hypophosphataemia (serum levels less than 0.3 mmol/L) and other degrees of hypophosphataemia when oral therapy is not possible.

The cause of hypophosphataemia should be identified and treated.

CONTRAINDICATIONS

Phosphate administration is contraindicated in patients with severe renal function impairment (less than 30% normal) since there is an increased risk of hyperphosphataemia in these patients.

Phosphate administration is contraindicated in patients with hyperphosphataemia, since phosphate therapy will exacerbate the condition.

Phosphate administration is contraindicated in patients with hypocalcaemia due to the close relationship between hypocalcaemia and hyperphosphataemia.

Potassium dihydrogen phosphate and dipotassium hydrogen phosphate concentrated injection is contraindicated in patients with hyperkalaemia, since the potassium in the injection may exacerbate the condition.

Potassium dihydrogen phosphate and dipotassium hydrogen phosphate concentrated injection is contraindicated in Addison's disease since there is an increased risk of hyperkalaemia in these patients.

Phosphate administration is contraindicated in urolithiasis (magnesium ammonium phosphate type, infected) since it may exacerbate the condition.

PRECAUTIONS

Phosphate should be administered with caution in conditions where high phosphate levels may be encountered, such as hypoparathyroidism, chronic renal disease, and rhabdomyolysis.

Phosphate should be administered with caution in conditions where low calcium levels may be encountered, such as hypoparathyroidism, osteomalacia, chronic renal disease, acute pancreatitis, rhabdomyolysis and rickets.

Potassium dihydrogen phosphate and dipotassium hydrogen phosphate concentrated injection should be administered with caution in conditions where high potassium levels may be encountered, such as acute dehydration, pancreatitis, rhabdomyolysis, severe renal insufficiency and extensive tissue damage (such as severe burns).

Potassium dihydrogen phosphate and dipotassium hydrogen phosphate concentrated injection should be administered with caution in patients with myotonia congenita, and heart disease (particularly in digitalised patients) (see **Interactions with other medicines**) since these conditions may be exacerbated by the potassium in the injection.

Effects on laboratory tests

Saturation of bone binding sites by phosphate ions may cause decreased bone uptake of tecnetium Tc^{99m} labelled contrast agents in bone imaging.

Use in pregnancy
Animal reproduction studies have not been conducted with this product. It is not known whether this product can adversely effect the foetus when administered to a pregnant woman. Therefore potassium dihydrogen phosphate and dipotassium hydrogen phosphate concentrated injection is not recommended for use during pregnancy.

Use in lactation
It is not known whether phosphates are excreted into breast milk, therefore potassium dihydrogen phosphate and dipotassium hydrogen phosphate concentrated injection is not recommended for use during lactation.

Interactions with other medicines
Angiotensin converting enzyme (ACE) inhibitors
Concurrent use with potassium dihydrogen phosphate and dipotassium hydrogen phosphate concentrated injection may result in hyperkalaemia, especially in patients with renal impairment.

Calcium containing medicines
Concurrent use of phosphate and calcium containing medicines may increase the risk of deposition of calcium in soft tissues.

Digitalis Glycosides
The administration of potassium dihydrogen phosphate and dipotassium hydrogen phosphate concentrated injection in digitalised patients with severe or complete heart block may result in hyperkalaemia.

Diuretics, potassium sparing
Concurrent use with potassium dihydrogen phosphate and dipotassium hydrogen phosphate concentrated injection may result in hyperkalaemia, especially in patients with renal impairment.

Non-steroidal anti-inflammatory agents (NSAIDS)
Concurrent use with potassium dihydrogen phosphate and dipotassium hydrogen phosphate concentrated injection may result in hyperkalaemia, especially in patients with renal impairment.

Other phosphate containing medicines
Concurrent use with potassium dihydrogen phosphate and dipotassium hydrogen phosphate concentrated injection may result in hyperphosphataemia, especially in patients with impaired renal function.

Potassium containing medicines
Concurrent use with potassium dihydrogen phosphate and dipotassium hydrogen phosphate concentrated injection may result in hyperkalaemia, especially in patients with renal impairment.

Salicylates
Concurrent use with potassium dihydrogen phosphate and dipotassium hydrogen phosphate concentrated injection may increase the serum concentration of salicylates, since salicylate excretion is decreased in acidified urine. This may result in toxic salicylate concentrations when phosphate is administered to patients already stabilized on salicylates.

Incompatibilities
Phosphates are reported to be incompatible with calcium or magnesium containing solutions.

ADVERSE EFFECTS

Cardiovascular:

Uncommon: hypotension
Rare: myocardial infarction

Endocrine/Metabolic:

The following events have been reported but are uncommon:

Fluid retention as indicated by swelling of feet or lower legs or weight gain.

Hyperkalaemia leading to confusion, tiredness or weakness, irregular or slow heart rate, numbness or tingling around lips, hands or feet, unexplained anxiety, weakness or heaviness of legs, shortness of breath or troubled breathing.

Hypernatraemia leading to confusion, tiredness or weakness, convulsions, oliguria or decreased frequency of micturition, tachycardia, headache or dizziness, increased thirst.

Hyperphosphataemia, hypocalcaemia or hypomagnesaemia leading to convulsions, muscle cramps, numbness, tingling, pain or weakness in hands or feet, shortness of breath or troubled breathing, tremor.

Extraskeletal calcification as nephrocalcinosis has been reported in children with hypophosphataemic rickets treated with phosphate supplements.

Genitourinary:

Rare: acute renal failure

DOSAGE AND ADMINISTRATION

DBL™ Potassium Dihydrogen Phosphate and Dipotassium Hydrogen Phosphate Concentrated Injection is administered by slow intravenous infusion. For the treatment of severe hypophosphataemia, the following doses are suggested:

Adults: up to 10 mmol phosphate administered over 12 hours. The dose may be repeated at 12 hour intervals until serum phosphate exceeds 0.3 mmol/L.

Children: 0.15 to 0.33 mmol/kg administered over 6 hours. The dose may be repeated at 6 hour intervals until serum phosphate exceeds 0.6 mmol/L. The dose should not exceed the maximum recommended adult dose. The rate of infusion should not exceed 0.2 mmol/kg/h.

Renal Impairment: dose should be reduced. Use of posphates in severe renal impairment is contraindicated (see **CONTRAINDICATIONS**).

Dilution: DBL™ Potassium Dihydrogen Phosphate and Dipotassium Hydrogen Phosphate Concentrated Injection must be diluted before use. The drug can be given in 0.9% sodium chloride or 5% glucose solution. It should be administered by slow infusion to avoid phosphate intoxication.

Monitoring: Serum sodium, potassium, phosphate and calcium concentrations and renal function should be monitored every 12 to 24 hours during therapy.

Conversion to oral phosphate therapy should occur as soon as possible.

OVERDOSAGE

Clinical features:

Hyperphosphataemia may occur when large doses of phosphate are given, especially in patients with renal failure. Symptoms associated with hyperphosphataemia include muscle weakness, paraesthesia, muscle cramps, convulsions, cardiomyopathy, respiratory failure and haematological abnormalities.

Hyperphosphataemia may in turn lead to hypocalcaemia and to ectopic calcification, which may be severe.

Crystal deposition may occur in important structures including blood vessels of the eye, lung, heart and kidney. Fatal alveolar diffusion block has occurred, the risk being greater if the patient is alkalotic.

Treatment:

Treatment of overdosage involves the following measures:

- immediate cessation of phosphate therapy
- correction of serum electrolyte concentrations, especially calcium
- general supportive treatment

In case of overdose, immediately contact the Poisons Information Centre for advice. (In Australia, call 13 11 26. In New Zealand, call 0800 764 766.)

PRESENTATION AND STORAGE CONDITIONS

Strength		**Pack**	**AUST R**
Potassium phosphate dibasic	183 milligrams/mL		
Potassium phosphate monobasic	54 milligrams/mL	10 x 10 mL	16268

Store below 25°C

NAME AND ADDRESS OF THE SPONSOR

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