POTASSIUM DIHYDROGEN PHOSPHATE 13.6%  
CONCENTRATED INJECTION

NAME OF THE MEDICINE

Potassium Dihydrogen Phosphate

Synonyms: potassium biphosphate, potassium acid phosphate, monopotassium phosphate, or monoibasic Potassium Phosphate)

The molecular weight of the compound is 136.1 and the CAS registry number is 7778-77-0. The molecular formula is KH$_2$PO$_4$.

DESCRIPTION

POTASSIUM DIHYDROGEN PHOSPHATE CONCENTRATED INJECTION contains 136.1 mg/mL potassium phosphate - monobasic in water for injections.

Each mL of solution contains 1.0 millimole (1.0 mEq) of potassium and 1.0 millimole (1.0 mEq) of phosphate. The pH of the solution is 4.0 - 5.0.

PHARMACOLOGY

Potassium:
Potassium ion is the principal intracellular ion of most body tissues. Potassium ions are involved in a number of essential physiological processes, including the maintenance of intracellular tonicity, the transmission of nerve impulses, the contraction of cardiac, skeletal, and smooth muscle and the maintenance of normal renal function. Excretion of potassium occurs via the kidneys and normally any amounts given in excess of intracellular requirements are rapidly eliminated.

Phosphate:
Phosphate is found mainly as calcium phosphate in the skeleton and soft tissues of the body. Phosphate is the principle anion of intracellular fluid. Apart from its essential role in bone structure, and as intracellular buffers, phosphate is also important in many metabolic and enzymatic pathways. Approximately two thirds of the ingested phosphate is absorbed from the gastrointestinal tract. Excess phosphate is primarily excreted in the urine with the remainder being excreted in the faeces. Parathyroid hormone decreases the tubular reabsorption of phosphate, thereby increasing urinary excretion. Calcium concentrations in the body are inversely proportional to the amount of phosphate, via the control of calcitrol.

INDICATIONS

POTASSIUM DIHYDROGEN PHOSPHATE CONCENTRATED INJECTION is indicated for:

• The treatment of severe hypophosphataemia (serum levels <0.3 mmol/L) and other degrees of hypophosphataemia when oral therapy is not possible.
• Lowering the pH of urine.
• The treatment of potassium depletion in patients with hypokalaemia; IV administration is indicated when the patient is unable to take potassium orally or if hypokalemia is severe.

CONTRAINDICATIONS

POTASSIUM DIHYDROGEN PHOSPHATE CONCENTRATED INJECTION is contraindicated in:

• Patients with severe renal function impairment (less than 30% normal) since there is an increased risk of hyperphosphataemia in these patients. The symptoms of hypophosphataemia include muscle weakness, paraesthesia, convulsions, cardiomyopathy, respiratory failure and haematological abnormalities. Prolonged hypophosphataemia may result in rickets or osteomalacia.
• Patients with hyperkalaemia.
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- Addison’s disease.
- Urolithiasis (magnesium ammonium phosphate type, infected) as it may exacerbate the condition.
- Renal impairment with oliguria or azotaemia.
- Ventricular fibrillation.
- Hyperadrenalism associated with adrenogenital syndrome.
- Extensive tissue breakdown as in severe burns.
- Acute dehydration.
- Heat cramps.
- Increased sensitivity to potassium administration as in adynamia episodica hereditaria or congenital paramyotonia.

PRECAUTIONS

Potassium

The use of potassium salts in patients with chronic renal disease, adrenal insufficiency or any other conditions which impairs potassium excretion, requires particularly careful monitoring of the serum potassium concentration and appropriate dosage adjustment.

Hypokalemia should not be treated by the concomitant administration of potassium salts and potassium-sparing diuretic (e.g. spironolactone or triamterene), since the simultaneous administration of these agents can produce severe hyperkalemia.

In patients on a low-salt diet particularly, hypokalaemic hypochloraemic alkalosis is a possibility that may require chloride as well as potassium supplementation.

The treatment of potassium depletion, particularly in the presence of cardiac disease, renal disease or acidosis, requires careful attention to acid-base balance and appropriate monitoring of serum electrolytes, the ECG and the patient’s clinical status.

Potassium should be used with caution in diseases associated with heart block since increased serum potassium may increase the degree of block.

Hyperkalemia: Potassium phosphates should be avoided in patients with hyperkalemia. Sodium phosphates may be substituted.

Phosphate

Phosphate should be administered with caution in conditions where high phosphate levels may be encountered, such as hypoparathyroidism, chronic renal disease, rhabdomyolysis, acute dehydration, pancreatitis, severe renal insufficiency and extensive tissue damage (such as severe burns).

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, rickets, myotonia congenita and heart disease (particularly in digitalised patients, see Interactions), since these conditions may be exacerbated by the potassium in the injection.

The cause of hypophosphataemia should be identified and treated. Caution should be used where patients may be hypocalcaemic.

Serum electrolyte and especially phosphate levels in the body and renal function should be monitored during treatment.

Use in Pregnancy

Animal reproduction studies have not been conducted with this product. It is not known whether this product can adversely affect the fetus when administered to a pregnant woman. Therefore, POTASSIUM DIHYDROGEN 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 CONCENTRATED INJECTION is not recommended for use during lactation.

Warnings

In patients with impaired mechanisms for excreting potassium, administration of potassium salts can produce hyperkalemia and cardiac arrest. This is an important concern in patients given IV potassium. Potentially fatal hyperkalemia can develop rapidly and be asymptomatic. In patients being given potassium especially by IV, monitoring of serum electrolytes, the ECG and the patient's clinical status is indicated.

INTERACTIONS WITH OTHER MEDICINES

Angiotensin converting enzyme (ACE) inhibitors: Concurrent use with Potassium dihydrogen phosphate may result in hyperkalaemia, especially in patients with renal impairment.

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

Digitalis glycosides: The administration of Potassium dihydrogen phosphate injection in digitalised patients with severe or complete heart block may result in hyperkalaemia.

Potassium sparing diuretics: Concurrent use with Potassium dihydrogen phosphate injection may result in hyperkalaemia, especially in patients with renal impairment.

Nonsteroidal anti-inflammatory agents (NSAIDs): Concurrent use with Potassium dihydrogen phosphate injection may result in hyperkalaemia, especially in patients with renal impairment.

Phosphate containing medicines: Concurrent use with Potassium dihydrogen phosphate injection may result in hyperphosphataemia, especially in patients with impaired renal function.

Potassium containing medicines: Concurrent use with Potassium dihydrogen phosphate injection may result in hyperkalaemia, especially in patients with renal impairment.

Salicylates: Concurrent use with Potassium dihydrogen phosphate 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 stabilised on salicylates.

Incompatibilities

Phosphates are incompatible with calcium, or magnesium containing solutions. Admixture will lead to precipitates being formed in the solution. Other solutions containing other cations such as iron and aluminium may also precipitate.

Effect on Laboratory tests:

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

Phosphates should not be administered to patients with severely impaired renal function. Aluminium, calcium, or magnesium salts should not be administered concomitantly with phosphates as they bind phosphate thus impairing its absorption from the gastro-intestinal tract.
ADVERSE EFFECTS

Adverse effects which may occur after parenteral administration also include hypocalcaemic tetany, hypotension, oedema, and acute renal failure. Adverse effects occur less frequently after oral administration due to poor absorption from the gastro-intestinal tract, but nausea, vomiting, diarrhoea, and abdominal pain have been reported.

Hyperphosphataemia, accompanied by hypocalcaemia or other severe electrolyte disturbances and resulting in tetany and even death, has been reported on a number of occasions following the use of phosphate enemas; infants or children have often been the subjects of these adverse effects. Rectal gangrene has been associated with the use of phosphate enemas in elderly patients and was believed to be due to a direct necrotising effect of the phosphate on the rectum.

Cardiovascular
Uncommon: hypotension.
Rare: myocardial infarction.

Endocrine
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.

The symptoms and signs of potassium intoxication include paraesthesias of the extremities, flaccid paralysis, listlessness, mental confusion, weakness and heaviness of the legs, fall in blood pressure, cardiac arrhythmias and heart block. Hyperkalemia may exhibit the following ECG abnormalities: disappearance of the P-wave, widening and slurring of QRS complex, changes of the S-T segment, tall-peaked T-waves. Nausea, vomiting, diarrhoea and abdominal discomfort have been reported.

Treatment of adverse effects involves withdrawal of phosphate, general supportive measures, and correction of serum-electrolyte concentrations, especially calcium.

DOSAGE AND ADMINISTRATION

POTASSIUM DIHYDROGEN PHOSPHATE CONCENTRATED INJECTION is administered by slow intravenous infusion. The injection must be diluted before use. 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 six hours. The dose may be repeated at six 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/hour.

For the treatment of hypokalaemia, the following doses are suggested. The dose and rate of injection are dependent upon the individual patient's condition. The usual maximum concentration is 40 mmol/L. In patients whose serum potassium concentration is above 2.5 mmol/L, the rate of infusion should not exceed 10 mmol/hour. The total dose should not exceed 200 mmol/24 hours.

If urgent treatment is required (serum potassium concentration less than 2 mmol/L with ECG changes or paralysis), infuse potassium in a suitable concentration at a rate of 40 mmol/hour, up to a rate of 400 mmol/24-hour period. In critical states,
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potassium may be infused in saline (unless saline is contra-indicated) rather than in glucose solutions, as the latter may decrease serum potassium concentrations.

Diluent’s Compatibility:

POTASSIUM DIHYDROGEN PHOSPHATE CONCENTRATED INJECTION has been reported to be compatible with the following IV infusion fluids:

Glucose-Ringers injection combinations, Glucose-lactated Ringers injection combinations, Glucose 5% in lactated Ringers injection, Glucose - saline combinations, Glucose 5% in sodium chloride 0.9%, Glucose 2.5% in water, Glucose 5% in water, Glucose 10% in water, Glucose 20% in water, Ringer's injection, Lactated Ringer's injection, Sodium chloride 0.45%, Sodium chloride 0.9%, Sodium chloride 3%.

OVERDOSE

Phosphate: Excessive administration of phosphate, particularly by the intravenous route, may cause hyperphosphataemia but this rarely occurs unless there is renal failure. Hyperphosphataemia may also occur in the presence of acidosis, acromegaly, haemolysis, hypoparathyroidism, tissue destruction, or vitamin D toxicity. Hyperphosphataemia leads in turn to hypocalcaemia, which may be severe, and to ectopic calcification. Secondary hyperparathyroidism may develop in the presence of renal failure.

Treatment of overdose involves the following measures: immediate cessation of phosphate therapy; correction of serum electrolyte concentrations, especially calcium; general supportive treatment.

Potassium Symptoms: If excretory mechanisms are impaired or if IV potassium is administered too rapidly, potentially fatal hyperkalemia can result (See Contra-indications and Precautions). However, hyperkalemia is usually asymptomatic and may be manifested only by an increased serum potassium concentration and characteristic ECG changes (peaking of T-waves, loss of P-wave, depression of S-T segment, and prolongation of the QT interval). Late manifestations include muscle paralysis and cardiovascular collapse from cardiac arrest. Should any of these manifestations occur, discontinue potassium administration immediately.

Treatment: If hyperkalemia develops, the following measures should be considered: elimination of foods and medications containing potassium and of potassium-sparing diuretics; IV administration of 300 to 500 mL/hour of 10% glucose solution containing 10 to 20 units of insulin/1000 mL; correction of acidosis, if present, with IV sodium bicarbonate, use of exchange resins, haemodialysis, or peritoneal dialysis, in presence of life-threatening cardiac arrhythmias, IV administration of 10 to 50 mL calcium gluconate 10% over 5 minutes. Continuous ECG monitoring is mandatory.

In treating hyperkalemia in digitalised patients, too rapid a lowering of the serum potassium concentration can produce digitalis toxicity.

In Australia, contact the Poisons Information Centre on 13 11 26 for further advice on overdose management.

PRESENTATION AND STORAGE CONDITIONS
POTASSIUM DIHYDROGEN PHOSPHATE INJECTION contains 136.1 mg/mL potassium phosphate monobasic in water for injections. Store below 25°C.

It is presented as a 10mL glass vial in a carton of 10.

AUST R 23183
Phebra Product Code - INJ089

NAME AND ADDRESS OF SPONSOR
Phebra Pty Ltd, 19 Orion Road, Lane Cove West, NSW 2066, Australia.
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POISON SCHEDULE OF THE MEDICINE

Unscheduled

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