PRODUCT INFORMATION

Sodium Dihydrogen Phosphate 15.6% Injection

This product is an unapproved therapeutic good in Australia. It is manufactured in a TGA approved pharmaceutical manufacturing facility in Australia and is provided under Schedule 5A – subregulation 12(1A) of the Therapeutic Goods Act and Regulations. The product is supplied under contract between a public or private hospital or public institution and the licensed manufacturer in Australia in accordance with a specified formulation.

Approval for use is required from the hospital pharmacist and / or drug committee as appropriate. Informed consent should be obtained in accordance with good medical practice where applicable and practicable. Records of the use of the product should be fully detailed and include dose, route of administration, duration of treatment, clinical, biochemical, haematological and immunological monitoring as appropriate. Adverse events and reactions must be reported to Phebra Pty Ltd and the TGA.

The responsibility for the use of this product remains with the prescriber and the institution. The following product information has not been evaluated or approved by the Therapeutic Goods Administration. Physicians should consult the medical literature for the most recent advice concerning the appropriate dose, route of administration, warnings and adverse effects.

NAME OF THE MEDICINE

Sodium dihydrogen phosphate dihydrate

The molecular weight of the compound is 156.01 and the molecular formula is NaH\(_2\)PO\(_4\),\(\cdot\)2H\(_2\)O.

The CAS registry number is 13472-35-0.

DESCRIPTION

Each 10 mL vial contains 1.56 g of sodium dihydrogen phosphate dihydrate in water for injections to 10 mL.

This is equivalent to 10 millimoles of sodium dihydrogen phosphate dihydrate per 10 mL
- and 10 millimoles of sodium ion per 10 mL
- and 10 millimoles of phosphate ion per 10 mL

Hydrochloric acid and sodium hydroxide may also be added for pH adjustment. The pH of the sterile injection is 4.0 - 5.0.

PHARMACOLOGY

Sodium is the principal cation in the extracellular fluid, comprising more than 90% of total cations at its normal plasma concentration (between 135 to 145 millimol/L). Potassium ions predominate in the intracellular fluid. A membrane-bound enzyme, sodium-potassium-activated adenosine triphosphatase (Na\(^+\)-K\(^+\)-ATPase), actively transports or pumps sodium out of, and potassium into, cells to maintain this concentration gradient.

Sodium has a primary role in regulating extracellular fluid volume. It controls water distribution, fluid and electrolyte balance and the osmotic pressure of body fluids. Sodium is also involved in nerve conduction, muscle contraction, acid-base balance and cell nutrient uptake.

Sodium homeostasis is complex, and is closely associated with fluid balance. Small changes in plasma sodium concentrations are corrected by alterations to the extracellular fluid volume. The secretion or suppression of anti-diuretic hormone (ADH) primarily controls water excretion by the kidney. Lower plasma sodium levels suppress ADH secretion and promote renal water loss, while an increase in ADH secretion increases water reabsorption by the renal distal tubules. Changes in extracellular volume will also affect ADH release, independently of osmolality. In addition, changes in extracellular volume modulate renal sodium excretion.

Total body sodium content is regulated by renal sodium excretion. Mechanisms involved include the renin-angiotensin system, glomerular filtration rate and natriuretic factors. A reduction in extracellular fluid volume leads to the production of angiotensin II, which stimulates aldosterone secretion. Aldosterone promotes sodium ion reabsorption by the distal tubules. Adrenal insufficiency or mineralocorticoid excess may disturb this mechanism.

Sodium acetate is metabolised in the liver to the bicarbonate. This has been shown to proceed readily, even in the presence of severe liver disease.
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.

Pharmacokinetics

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 the hormone, calcitrol.

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Both the sodium and phosphate ions are excreted mainly in the urine. Some sodium is excreted in the faeces, and small amounts may also be excreted in saliva, sweat, bile and pancreatic secretions.

INDICATIONS

Sodium Dihydrogen Phosphate 15.6% Injection is indicated for inclusion in total parenteral nutrition (TPN) solutions as an electrolyte source.

It may also be used for the treatment of:
- hyponatraemia (sodium depletion) states, in cases where oral sodium therapy is contraindicated or not tolerated.
- Severe hypophosphataemia (serum levels <0.3 mmol/L) and other degrees of hypophosphataemia when oral therapy is not possible.

CONTRAINDICATIONS

Sodium Dihydrogen Phosphate 15.6% Injection is contraindicated in patients who are hypersensitive to sodium. It should not be administered to patients with hypernatraemia, fluid retention or severe renal impairment. It should not be administered to patients suffering from conditions, which are likely to lead to dehydration (e.g. severe burns, severe or prolonged diarrhoea or vomiting, or uncontrolled diabetes mellitus).

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. The symptoms of hyperphosphataemia include muscle weakness, paraesthesia, convulsions, cardiomyopathy, respiratory failure and haematological abnormalities. Prolonged hypophosphataemia may result in rickets or osteomalacia. Phosphates should not be administered to patients with severely impaired renal function.

PRECAUTIONS

Sodium Dihydrogen Phosphate 15.6% Injection is administered by slow intravenous (IV) infusion.

Solutions of Sodium Dihydrogen Phosphate 15.6% Injection must be administered slowly, as rapid intravenous injection of sodium may lead to hypernatraemia and fluid overload. Hypernatraemia is more likely to occur if Sodium Dihydrogen Phosphate 15.6% Injection is administered intravenously to patients with impaired mechanisms for excreting sodium (e.g. chronic renal disease). Potentially fatal hypernatraemia can develop rapidly and asymptptomatically. Therefore, careful monitoring of serum sodium concentration and appropriate dosage adjustment is recommended.

Elevated plasma sodium concentration may cause dehydration of the brain, which can result in somnolence and confusion, progressing to convulsions, coma, respiratory failure and death.

Sodium phosphate should be used with extreme caution in patients with congestive heart failure, other oedematous states, renal function impairment, cirrhosis, eclampsia, hypertension or aldosteronism. It should also be used with caution in patients with oliguria or anuria.

Solutions containing sodium ions should be administered cautiously to patients receiving corticosteroids or corticotropin.

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 supplementation may lead to hypocalcaemia and thus serum electrolyte levels should always be monitored.

Effects on Fertility
There is no information available on whether the administration of sodium phosphate would affect fertility.

Carcinogenicity
No information is available.

Mutagenicity
No information is available.

Use in Pregnancy
Sodium and phosphates are a natural constituent of human tissues and fluids. Since high levels of sodium may lead to dehydration, serum levels should be closely monitored in pregnant women being treated with sodium salts.

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 Sodium Dihydrogen Phosphate 15.6% Injection should only be used in pregnant women if the expected benefits outweigh the possible risks to the mother or fetus.

Use in Lactation
Sodium and phosphate are likely to be excreted into breast milk. Sodium Dihydrogen Phosphate 15.6% Injection should only be used in women who are breast-feeding if the expected benefits to the mother outweigh the possible risks to the infant.

Effect on Laboratory Tests
Saturation of bone binding sites by phosphate ions may cause decreased bone uptake of technetium Tc99m labelled contrast agents in bone imaging.

Interactions with Other Medicines
Concurrent use in patients taking potassium supplements may reduce serum potassium levels by promoting an intracellular ion shift.

Solutions containing sodium ions should be administered with caution to patients receiving corticosteroids or corticotropin.

ADVERSE EFFECTS

1. Sodium
Excessive doses of sodium salts may lead to hypernatraemia. The most serious effect of hypernatraemia is dehydration of the brain, which causes somnolence and confusion, progressing to convulsions, coma, respiratory failure and death. Other symptoms include thirst, reduced salivation and lachrymation, fever, tachycardia, hypertension, headache, dizziness, restlessness, irritability and weakness.

2. Phosphates
The adverse effects of phosphates which may occur after parenteral administration include hypocalcaemic tetany, hypotension, oedema, and acute renal failure. Adverse effects occurs 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; 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.
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Treatment of adverse effects involves withdrawal of phosphate, general supportive measures, and correction of serum-electrolyte concentrations, especially calcium.

DOSAGE AND ADMINISTRATION

Each mL of Sodium Dihydrogen Phosphate 15.6% Injection contains 1.0 mEq (1.0 mmol) of sodium ions and 1.0 mEq (1.0 mmol) of phosphate ions.

For Hyponatraemia

1. Use in total parenteral nutrition (TPN) solutions or other parenteral solutions: The desired quantity of Sodium Dihydrogen Phosphate 15.6% Injection should be added to the TPN or other solution. Serum sodium levels should be monitored as a guide to dosage.

2. Treatment of hyponatraemia (sodium depletion): Administration by slow intravenous infusion is preferred. The concentration and dosage of sodium solutions for intravenous use is determined by several factors including the age, weight and clinical condition of the patient and in particular the patient’s hydration state. Serum electrolyte concentrations and total body water should be carefully monitored throughout. Hyponatraemia should not be allowed to develop.

Therapy should be guided by the rate and degree of development of hyponatraemia. Volume depletion should also be corrected where necessary.

For Hypophosphataemia

Administration by slow intravenous infusion is preferred. 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 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/hour.

Incompatibilities

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

OVERDOSAGE

Sodium Overdosage

Symptoms: Excessive administration or impaired excretion of sodium leads to the development of potentially fatal hyponatraemia, while excessive administration of the phosphate may lead to hypokalaemia and metabolic alkalosis (see Adverse Effects).

Treatment: Serum sodium concentrations should be measured, and if severe hyponatraemia is present, this should be treated. Treatment of hyponatraemia usually requires water replacement. In some cases, oral administration of water and restriction of sodium intake may be sufficient. In more severe cases, glucose 5% may be administered by slow intravenous infusion.

If the total body sodium content is too high, loop diuretics may be used to increase sodium excretion, with fluid losses being replaced by an infusion of glucose 5% and potassium chloride. Dialysis may be necessary if there is significant renal impairment, if the patient is moribund, or if the serum sodium concentration is greater than 200 mmol/L.

Phosphate Overdosage

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.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).
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PRESENTATION AND STORAGE CONDITIONS

Sodium Dihydrogen Phosphate 15.6% Injection is a clear, colourless solution in a 10 mL clear glass vial sealed with a rubber stopper and aluminium seal with a plastic flip off cap. It is supplied in a carton containing 10 vials. Store below 25°C.

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- and 10 millimoles of sodium ion per 10 mL
- and 10 millimoles of phosphate ion per 10 mL

Hydrochloric acid and sodium hydroxide may also be added for pH adjustment.

Phebra product code- INJ082

NAME AND ADDRESS OF THE SPONSOR

Phebra Pty Ltd, 19 Orion Road, Lane Cove West, NSW 2066, Australia.
Telephone: 1800 720 020

POISON SCHEDULE OF THE MEDICINE

Not scheduled.

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