SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Phosphates solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Monopotassium phosphate Cryst BPC 1949 (KH2PO4)	1.295 g/l
Sodium phosphate dibasic anhyd AR (Na2HPO4)	5.75 g/l
(equivalent to sodium phosphate BP)	14.5 g/l
Na+	162 mmol/l
K+	19 mmol/l
PO43-	100 mmol/l
pH-value	7.0-7.7
Theor. osmolarity	281 mosmol/l

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of moderate to severe hypophosphataemia

4.2 Posology and method of administration

Posology

The dosage must be adjusted to the conditions of the patient, the fluid, electrolyte and acid-base-balance.

Adults and Children over 12 years of age

The volume of phosphates infusion given intravenously will depend upon the requirements of the patient. The infusion must be given slowly (over 6-12 hours).

Moderate hypophosphataemia (serum inorganic phosphate 0.5-0.7 mmol/L) is treated with 0.1-0.2mmol phosphate/kg of bodyweight (equivalent to 1-2 ml Polyfusor Phosphates/kg bodyweight) over 6-12 hours. Severe hypophosphataemia (serum inorganic phosphate < 0.5 mmol/L) is treated with 0.2-0.5mmol phosphate/kg of bodyweight (equivalent to 2-5 ml Polyfusor Phosphates/kg bodyweight) over 6-12 hours. A total maximum dose of 50mmol per infusion should not be exceeded. Repeat doses may be required over subsequent days, dependant on serum phosphate determinations to correct any underlying deficiency state.

Not more than 15 mmol phosphate/hour should be given.

Elderly

The dosage of phosphates solution may need to be reduced in the elderly, particularly in patients with impaired renal function.

Method of administration

For intravenous infusion.

4.3 Contraindications

- Hypersensitivity to the active substance or any of the excipients listed in section 6.1.
- Hyperphosphataemia
- Hyperkalaemia
- Hypernatraemia
- Hypocalcaemia
- Hyperhydration
- Disturbance of renal function (renal insufficiency)

4.4 Special warnings and precautions for use

When administering Polyfusor Phosphates, serum electrolytes and renal function should be carefully monitored during therapy as well as ECG, fluid and acid-base-balance. In patients with renal impairment, its use must be carefully controlled by frequent determinations of plasma electrolyte concentrations.

Due to the potassium content the solution should be administered with considerable care to patients with cardiac disease or conditions predisposing to hyperkalaemia such as renal or adrenocortical insufficiency, acute dehydration, or extensive tissue destruction as occurs with severe burns. Care should be exercised if potassium salts are given concomitantly with potassium-sparing diuretics. Potassium supplements should generally not be administered to patients receiving potassium-sparing drugs such as amiloride, spironolactone and triamterene.

Intravenous injections of potassium containing solutions should be given slowly as high blood concentrations may affect cardiac function. Potassium should generally not be given in the immediate postoperative period until urine flow is established.

Due to the sodium content the solution should be administered with caution to patients with hypertension, cardiac failure, peripheral or pulmonary oedema, impaired renal function and pre-eclampsia.

The label states: Rapid infusion may be harmful

Do not use unless the solution is clear and free from particles.

4.5 Interaction with other medicinal products and other forms of interaction

No clinically significant interactions.

4.6 Fertility, pregnancy and lactation

The safety of the solution during pregnancy and lactation has not been assessed, but its use during these periods is not considered to constitute a hazard.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Prolonged infusion of phosphates solution, especially in patients with renal failure, may result in hyperphosphataemia. This may lead in turn to hypocalcaemia, which may be severe, with tetany and convulsions/neuro-excitability and to extraskeletal calcification, particularly in patients with initial hypercalcaemia. Tissue calcification (metastatic calcium-phosphate precipitation in soft tissue) may cause hypotension and organ damage and result in acute renal failure.

If the phosphate solution is administered excessively, hyperkalaemia may occur. Symptoms include paraesthesia of the extremities, muscle weakness, cardiac arrhythmias, heart block, cardiac arrest, mental confusion, listlessness, paralysis and hypotension.

In cases of excessive intake also hypernatraemia may occur with symptoms as dehydration of the brain which causes somnolence and confusion progressing to convulsions, coma and respiratory failure. Other symptoms of hypernatraemia are thirst, reduced salivation and lachrymation, fever, tachycardia, hypertension, headache, dizziness, restlessness, irritability and weakness.

Pain and phlebitis at the injection site may occur during intravenous administration.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal

product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Although overdosage with polyfusor phosphates is unlikely, excessive dosage may give rise to hypocalcaemia and tetany. Treatment consists of discontinuing the infusion and giving appropriate supportive treatment depending on electrolyte determination.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Polyfusor Phosphates is a balanced formulation of inorganic phosphate (as its sodium and potassium salts) used in the management of moderate to severe hypophosphataemia (low serum levels of inorganic phosphate).

There are three main causes of hypophosphataemia observed in the critically ill patient. The first results from inadequate intake (secondary to chronic malnutrition) as a result of pre-admission state of health. If the individual is then re-fed, i.e. Total Parenteral Nutrition (TPN) or Enteral Nutrition (EN), induced hypophosphataemia may result, due to low provision of phosphate. In addition, inadequate intake may results where gut absorption of phosphate is reduced due to chemical binding reactions with certain elements such as aluminium and magnesium (found in most antacids).

Secondly, low serum phosphate levels may occur due to redistribution of phosphate into cells. Individuals receiving TPN or EN are often suffering from a total body depletion of phosphate. The chronically malnourished patient is frequently in a catabolic state, which is linked to muscle breakdown and loss therefore of intracellular phosphate. The serum phosphate level appears normal but this is against a background of increased urinary losses, resulting ultimately in total body depletion. When TPN/EN is commenced the individual receives a high glucose load, which promotes an anabolic state in part due to insulin release. The net result is an increase in intracellular phosphate requirements due to rapid acceleration of glucose phosphorylation and this can result in serum hypophosphataemia. Drug therapy is also thought to play a role in the distribution of phosphate. Catecholamines have been reported to produce an intracellular shift of phosphate, thought to be linked to beta-adrenergic receptor mediated stimulation of phosphate uptake. For example, adrenaline infusions in therapeutic ranges frequently used appear to produce dose dependant reductions in serum phosphate.

The development of either metabolic or respiratory alkalosis can also result in hypophosphataemia, thought to be due to an intracellular shift in phosphate.

Thirdly, hypophosphataemia may be caused by direct phosphate loss from the body. Increased renal clearance occurs as in primary hyperparathyroidism, vitamin D

deficiency, or X linked familial hypophosphataemia. Several drugs are linked to phosphate urinary excretion, e.g. acetazolamide. Urinary losses of phosphate and a reduction in the renal threshold are seen in patients on theophylline. Acute paracetamol overdosed produces severe hypophosphataemia in ~40% of patients. Individuals with glycosuria, ketonuria and polyuria also can be subject to increased losses.

Usually hypophosphataemia is asymptomatic, but clinical symptoms are apparent in severe deficiency states. Effects may include respiratory failure requiring mechanical ventilation or failure to wean individuals from mechanical ventilation, cardiomyopathy, neuromuscular dysfunction such as muscle weakness and paraesthesias, convulsions and haematological abnormalities.

Polyfusor Phosphates is administered intravenously to directly replace lost phosphate levels and to raise inorganic serum phosphate levels to within normal ranges.

5.2 Pharmacokinetic properties
No data available.

5.3 Preclinical safety data
No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Water for injections in bulk BP

Hydrochloric acid BP

Sodium hydroxide BP

6.2 Incompatibilities
Polyfusor phosphates infusion may be incompatible with metal ions such as magnesium and calcium, due to possible formation of insoluble calcium or magnesium phosphate precipitates.

6.3 Shelf life
500ml Polyethylene container - 36 months

500ml Polyolefin Bags - 36 months.

6.4 Special precautions for storage
Store between 2°- 25°C

6.5 Nature and contents of container
Sealed semi-rigid, cylindrical, neutral polythene 500ml container with a 'Twist-off' seal: at one end and a ring tab at the opposite end

or

A flexible 500ml polyolefine bag sealed in a polyolefine overwrap.

Not all pack sizes are marketed.

6.6 Special precautions for disposal and other handling

Do not dilute before use. Use standard sterile peritoneal dialysis equipment.

Opening the overwrap

Locate the corner tabs at the end of the bag. Grip the two tabs and pull the two halves of the overwrap apart, releasing the bag onto a clean surface.

Setting up the solution:

Position the roller clamp of the giving set to just below the drip chamber and close.

Hold the base of the giving set port firmly and grip the wings of the twist of tab. Twist to remove the protective cover.

Still holding the base of the giving set port push the set spike fully into the port to ensure a leak proof connection. Prime the set in accordance with the manufacturer's instructions.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

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10 DATE OF REVISION OF THE TEXT

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