Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Potassium Phosphate 1mmol/ml + 0.6mmol/ml Concentrate for Solution for Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One ampoule (=20 ml) of concentrate for solution for infusion contains

Dipotassium phosphate 1.394 g
Potassium dihydrogen phosphate 0.544 g

Electrolyte concentrations
Potassium 1 mmol/ml
Phosphate 0.6 mmol/ml

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Concentrate for solution for infusion (sterile concentrate)
Clear, colourless aqueous solution

Theoretical osmolarity 1600 mOsm/l
pH 6.8 – 7.2

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Phosphate substitution in intensive-care patients, with co-existing potassium deficiency, in whom close monitoring of serum potassium and phosphate concentrations can be performed.

4.2 Posology and method of administration

Posology

The dose is adjusted according to the actual basic or correction requirements, according to the analytical values of the serum electrolyte concentrations.

Adults

In the setting of parenteral nutrition the basic phosphate requirement in adults is 0.3 – 0.5 mmol per kg body weight (BW) per day, corresponding to 0.5 – 0.8 ml per kg BW per day.

In therapy of severe hypophosphataemia the dose is adjusted according to the serum phosphate concentration. Then higher amounts than those stated above may be needed.

Per 0.6 mmol phosphate 1 mmol of potassium is administered.

The maximum daily dose of potassium is 2 – 3 mmol per kg BW

Paediatric patients

The dose should be adjusted strictly according to the prevailing serum potassium and phosphate concentrations which may be affected by fluid retention, dehydration or excessive water losses.

In children potassium intake during parenteral nutrition is recommended not to exceed 1 – 3 mmol/kg body weight per day.

Parenteral phosphate requirements in children above 1 year are adequately met with 0.2 mmol/kg body weight per day. Children below 1 year of age require in total up to 0.5 mmol/ kg body weight per day.

Elderly patients

As for adults.

Other special patient groups

See section 4.4.

Maximum infusion rate
The infusion rate is limited by the potassium content of the solution. The maximum infusion rate is 20 mmol of potassium per hour, corresponding to 0.3 mmol of potassium per kg BW per hour.

Method of administration

Intravenous use.

Only to be administered diluted as an additive to infusion solutions. The concentration of potassium in the infusion solution must not exceed 40 mmol/l (corresponding to 24 mmol/l of phosphate). For further details regarding dilution and suitable diluents see section 6.6.

Infusion should be carried out continuously. Use of infusion pumps is advisable.

Particular care should be taken to ensure that infusion is strictly intravenous, because paravenous administration can lead to tissue necrosis and to indurations and chalky deposits in the subcutaneous tissue.

4.3 Contraindications

Potassium Phosphate 1mmol/ml + 0.6mmol/ml must not be administered in cases of:

-Hyperphosphataemia
-Hyperkalaemia
-Hypocalcaemia
-Renal insufficiency
-Disorders that are frequently associated with hyperkalaemia such as dehydration, diabetic ketoacidosis, limited renal excretion, Addison's disease, Familial periodic paralysis (*Adynamia episodica hereditaria*, Gamstorp's syndrome), tumour lysis syndrome (TLS), sickle cell anaemia,
-Therapy with potassium sparing diuretics.

4.4 Special warnings and precautions for use

Potassium Phosphate 1mmol/ml +0.6mmol/ml should only be administered with particular caution in cases of cardiac decompensation.

Administration should be discontinued if there are signs of renal insufficiency.

Sudden discontinuation of potassium administration may be followed by marked hypokalaemia, which may lead to increased toxicity of cardiac glycosides taken concomitantly.

Disturbances of the potassium balance, i.e. hyper- or hypokalaemia, lead to typical alterations in the ECG. There is, however, no linear relationship between the ECG alterations and the potassium concentration in serum.

Since high levels of phosphate administration can cause hypocalcaemia and metastatic calcifications, the ionized calcium and phosphate should be monitored regularly if daily phosphate substitution exceeds 50 mmol.

Clinical monitoring should include regular checks of the serum electrolyte concentrations.

During phosphate substitution the plasma phosphate concentration and the amount of phosphate excreted in 24 hour urine should be monitored once weekly.
When high doses of phosphate are administered it can be necessary to administer calcium simultaneously. The calcium must be administered by a separate route.

Since per 0.6 mmol phosphate the solution contains 1 mmol of potassium, the potassium concentration should be taken into account when calculating the electrolyte balance.

When carrying out phosphate substitution as a part of parenteral nutrition, account should be taken of the fact that various solutions used for parenteral nutrition (including lipid emulsions) already contain phosphate.

4.5 Interaction with other medicinal products and other forms of interactions

- **Cardiac glycosides**

An increase of the intracellular potassium concentration weakens the effect of cardiac glycosides, a decrease of the intracellular potassium concentration increases the arrhythmogenic effect of cardiac glycosides.

- **Suxamethonium**

Marked hyperkalaemia may also result from simultaneous administration of potassium and suxamethonium.

- **Other phosphate-containing medicinal products**

Other phosphate-containing medications used with potassium phosphates may cause high blood levels of phosphate and may increase the risk of hyperphosphataemia, especially in patients with renal disease.
Potassium sparing diuretics, aldosterone antagonists, Angiotensin Converting Enzyme (ACE) inhibitors, **tacrolimus**, **ciclosporin**, non-steroid anti-inflammatory drugs, peripheral analgesics **and long-term heparin use**
These reduce the renal potassium excretion. Potassium administration simultaneously with those drugs may result in severe hyperkalaemia.

- **Salicylates**

Concurrent use of salicylates with potassium phosphates may increase plasma concentrations of salicylates since salicylate excretion is decreased in acidified urine.

Interaction with food or beverages

None.

4.6 Fertility, pregnancy and lactation

Pregnancy

For Potassium Phosphate 1mmol/ml +0.6mmol/ml no data from clinical studies on exposed pregnancies are available. Animal studies with respect to pregnancy, embryonal/foetal development, parturition or postnatal development are not available either. However no findings are known indicating direct or indirect harmful effects in that respect.

Caution should be exercised when prescribing the product to pregnant women.

Potassium Phosphate 1mmol/ml +0.6mmol/ml should only be administered during pregnancy if its benefits outweigh its possible risks.

Breastfeeding

It is not known if phosphates are secreted into breast milk. However, no problems in the breast-feeding of infants have been documented with intake of normal daily recommended amounts.

Potassium Phosphate 1mmol/ml +0.6mmol/ml should only be administered during breastfeeding if its benefits outweigh its possible risks.

Fertility

No data available.

4.7 Effects on ability to drive and use machines

Potassium Phosphate 1mmol/ml +0.6mmol/ml has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Normally adverse effects are dose-dependent and are likely to occur only if an overdose of Potassium Phosphate 1mmol/ml +0.6mmol/ml is administered or if the administration rate is too high (symptoms see section 4.9). Nevertheless, if the product is administered in accordance to the instructions given, the following adverse effect has been detected.

Definition of frequency terms used in this section:

Rare (≥1/10,000 to <1/1,000)

Gastrointestinal disorders

Rare: Nausea

Information on particular undesirable effects

Drug interactions (see above) or suddenly occurring acidosis, acute impairment of renal function and other conditions may lead to sudden hyperkalaemia. Symptoms of hyperkalaemia see section 4.9.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Overdose can lead to hyperkalaemia and hyperphosphataemia.

Symptoms associated with hyperkalaemia

The neuromuscular symptoms encompass fatigue, states of confusion, unexplained anxiety, weakness or heaviness of limbs, muscle twitching, paraesthesia, breathing problems, ascending paralysis.

Cardiac arrhythmia may occur due to hyperkalaemia or too rapid infusion.
Plasma potassium concentrations of 6.5 mmol/l or more are dangerous, concentrations above 8 mmol/l often lethal.

Symptoms associated with hyperphosphataemia

Hyperphosphataemia may lead to

- renal damage as a result of the precipitation of calcium phosphate (nephrocalcinosis)
- the precipitation of calcium phosphate in other tissues (e.g. skin, cornea, lungs)
- and to hypocalcaemia (symptoms: convulsions, muscle cramps, tremor, numbness, tingling, pain or weakness in hands or feet; shortness of breath, or troubled breathing), up to hypocalcaemic tetany and metastatic calcification (see also section 4.4).

Treatment

Immediate discontinuation of infusion, slow intravenous administration of 10% w/v calcium gluconate, glucose infusions together with insulin, increase of diuresis or ion exchangers administered orally or rectally, correction of acidosis if necessary.

In cases of massive overdose haemodialysis may be necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: IV solution additives, potassium phosphate, incl. combinations with other potassium salts

ATC code: B05XA06

Pharmacodynamic properties of phosphate

Mechanism of action, therapeutic effect

The total quantity of inorganic phosphate in an adult is approx. 0.7 kg. The major proportion of this is present in the form of inorganic phosphate compounds in the bones and teeth. Ionised inorganic phosphate is present in the plasma in the form of NaH_2PO_4. Ionised phosphate acts as a buffer in the intracellular space, in the blood and in the urine.

Phosphate deficiency syndrome can occur if insufficient phosphate is administered during parenteral nutrition. Particularly when large quantities of carbohydrate are administered there is a large uptake of phosphate by the cells thus leading to a diminution of the blood phosphate concentration.

Other pharmacological effects

The pharmacodynamic effects of phosphate in Potassium Phosphate 1mmol/ml + 0.6mmol/ml are essentially the same as in normal physiology. Thus, when administered as specified, no further pharmacodynamic effects have to be expected.

Pharmacodynamic properties of potassium

Mechanism of action, therapeutic effect

As principal intracellular cation, potassium has two major physiological functions: maintenance of intracellular tonicity and transmembrane potential.

It is essential for transmission of nerve impulses, and contraction of cardiac, skeletal and smooth muscle. Potassium further participates in carbohydrate utilisation and protein synthesis.

The daily requirements for potassium are about 1 – 1.5 mmol per kg body weight.

Hypokalaemia is accompanied by muscle weakness, atony of gastro-intestinal smooth muscles (constipation up to paralytic ileus), loss of capability of kidneys to concentrate urine, ECG alterations and cardiac arrhythmia.

Other pharmacological effects

The pharmacodynamic effects of potassium in Potassium Phosphate 1mmol/ml + 0.6mmol/ml are essentially the same as in normal physiology. Thus, when administered as specified, no further pharmacodynamic effects have to be expected.

5.2 Pharmacokinetic properties

Phosphate

Absorption

As the solution is intended for intravenous use its bio-availability is 100%.

Distribution

Phosphate is the relevant form of phosphorus in the human body. Approx. 85 per cent of the total body phosphorus is stored in bone. Of the remainder, 14 per cent occurs in soft tissues and 1 per cent is found in the blood.

Biotransformation

Phosphate underlies no metabolism in the strict sense.

Elimination

Phosphate is predominantly excreted via the kidneys. Parathormone, calcium administration, oestrogen, thyroxine and acidosis increase the renal excretion of phosphate; cholecalciferol, growth hormone, insulin and cortisol have the effect of reducing it. The phosphate and calcium balances are closely linked to each other.

Potassium

Absorption

As the solution is intended for intravenous use its bio-availability is 100%.

Distribution

Potassium is the most important cation of the intracellular space, approx. 98 per cent of the organism's total potassium being located there. The intracellular potassium concentration is approx. 140 – 150 mmol/l. The normal potassium concentration in plasma is between 3.5 and 5 mmol/l.

Biotransformation

Potassium underlies no metabolism in the strict sense.

Potassium is mainly excreted in urine (about 90 per cent) and about 10 per cent are excreted via the gastro-intestinal tract.

Even in situations of potassium deficiency 10 - 50 mmol of potassium are renally excreted per day. Potassium deficiency may be caused by increased renal excretion, increased gastro-intestinal losses, e.g. by vomiting or diarrhoea, or through fistulae, by increased intracellular uptake, e.g. during therapy of acidosis or therapy with glucose and insulin, or by insufficient potassium intake.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections

6.2 Incompatibilities

Potassium Phosphate 1mmol/ml +0.6mmol/ml is incompatible with solutions containing calcium and magnesium.

6.3 Shelf life

- unopened 3 years

- after first opening the container
- Use immediately. Any unused contents should be discarded after dilution

Chemical and physical in-use stability has been demonstrated for 24 hours at a temperature below 25°C.
From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

6.4 Special precautions for storage

Do not store above 25°C.

For storage conditions of the reconstituted or diluted medicinal product, see section 6.3.

6.5 Nature and contents of container

Round or oval colourless low-density polyethylene ampoules Mini-Plasco®, contents: 20 ml available in packs of 20 x 20 ml

Outer packing: cardboard box containing 20 ampoules.

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

Before administration, Potassium Phosphate 1mmol/ml + 0.6mmol/ml must be diluted by addition to a suitable infusion solution.
The containers are for single use only. After use discard container and any remaining contents.

Only to be used if solution is clear and colourless and if the ampoule is undamaged.

The electrolyte concentrate is to be added to the infusion solution under strictly aseptic conditions, immediately before setting up the infusion. The container should then be shaken gently.

Infusion solutions should be free of calcium and magnesium. Suitable solutions are e.g. 5% glucose solution or isotonic sodium chloride solution.

The volume of the infusion solution should be chosen so that concentrations of 40 mmol/l of potassium and 24 mmol/l of phosphate in the infusion solution are not exceeded.

7 MARKETING AUTHORISATION HOLDER

B. Braun Medical Limited
3 Naas Road Industrial Park
Dublin 12
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0179/005/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 24 February 1993

Date of last renewal: 24 February 2008

10 DATE OF REVISION OF THE TEXT

May 2017