SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Braun Monopotassium Phosphate 136.13 mg/ml solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ampoule (=20 ml) of solution for injection contains
Monopotassium phosphate 2.723 g

1 ampoule (=10 ml) of solution for injection contains
Monopotassium phosphate 1.361 g

Electrolyte concentration:

Potassium	1 mmol/ml
Phosphate	1 mmol/ml

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection
Colourless, clear, aqueous solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Phosphate replacement in patients in intensive care, when there is a simultaneous deficiency in potassium and phosphate, with close monitoring of serum concentrations of potassium and phosphate.

4.2 Posology and method of administration

Recommended dose
The dose is adjusted according to actual basic values or correction requirements, in accordance with analytical values of serum electrolyte concentrations.

Adults
In defining a scheme for application of parenteral nutrition, basic phosphate requirements for an adult are 0.2 – 0.5 mmol/kg of body weight/day, which corresponds to 0.2 – 0.5 ml/kg of body weight.

Effective

In the treatment of severe hypophosphataemia, the dose should be adjusted according to the serum phosphate concentration. In these cases, it may be necessary to administer doses higher than the dose mentioned above.
1 mmol of potassium should be administered for each 1 mmol of phosphate.
The maximum daily dose of potassium is 2 – 3 mmol/kg of body weight.

Paediatric population
The dose should be carefully adjusted according to existing serum concentrations of potassium and phosphate.
In children, it is recommended that ingestion of potassium during parenteral nutrition should not exceed 1 – 3 mmol/kg of body weight/day.
Parenteral phosphate requirements in children are normally 0.2 mmol/kg of body weight/day.

The elderly
There are no special adjustments; the posology is the same as that for adults.

Maximum infusion rate
The infusion rate is limited by the potassium concentration of the solution. The maximum infusion rate is 20 mmol potassium per hour, that is, 0.3 mmol potassium per kg of body weight/hour.

Method of administration
Intravenous use.

It should only be administered diluted as an additive to other solutions for infusion. The potassium concentration in the solution for infusion should not exceed 40 mmol/l (corresponding to 40 mmol/l phosphate). For further information on dilution and diluents, see section 6.6.
The infusion should be continuous. The use of infusion pumps is recommended.

Particular care should be taken to ensure that the infusion is entirely intravenous, due to the risk of tissue necrosis, indurations and calcium deposits in the subcutaneous tissues if administration were to be paravenous.

4.3 Contraindications

Braun Monopotassium Phosphate should not be administered in cases of:
Hyperphosphataemia
Hyperkalaemia
Renal failure
Disorders frequently associated with hyperkalaemia, such as:
- dehydration
- diabetes mellitus
- limited renal excretion

- Addison's disease
- Familial periodic paralysis (hereditary episodic adynamy, Gamstorp's syndrome
- tumour lysis syndrome
- sickle-cell anaemia

Treatment with potassium-sparing diuretics
Hypocalcaemia
Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Braun Monopotassium Phosphate should be administered with particular care in the case of cardiac decompensation.
Administration should be discontinued if there are signs of renal failure.
Sudden interruption of potassium administration may be followed by marked hypokalaemia, which may cause an increase in the toxicity of cardiac glycosides when administered concomitantly.
Disorders of the potassium balance, that is, hyper- or hypokalaemia, lead to typical changes on the ECG. However, there is no linear relationship between ECG changes and the serum potassium concentration.

Since the administration of high levels of phosphate may cause metastatic calcifications and hypocalcaemia, ionised calcium and phosphate should be closely monitored if daily phosphate replacement exceeds 50 mmol.
Clinical monitoring should include regular testing of the serum electrolyte balance.
During phosphate replacement, the serum phosphate concentration and 24-hour urinary phosphate excretion should be monitored weekly.
When high doses of phosphate are administered, it may be necessary to administer calcium at the same time. Calcium should be administered by a separate route.
Since the solution contains 1 mmol of potassium for 1 mmol of phosphate, the potassium concentration should be taken into account in calculating the electrolyte balance.
When providing phosphate replacement as part of parenteral nutrition, the fact that several solutions which already contain phosphate (including lipid emulsions) are used for parenteral nutrition should be taken into consideration.

4.5 Interaction with other medicinal products and other forms of interaction

Influence of Braun Monopotassium Phosphate on other medicines:
Cardiac glycosides:
Increase in the intracellular concentration of potassium reduces the effect of cardiac glycosides, and reduction in the intracellular concentration of potassium increases the arrhythmogenic effect of cardiac glycosides.
Suxamethonium:
Marked hyperkalaemia may also result from the simultaneous administration of potassium and suxamethonium.
Other phosphate-containing medicines:

Other phosphate-containing medicines administered with monopotassium phosphate may cause elevated serum phosphate levels and increase the risk of hyperphosphataemia, especially in patients with renal disease.

Influence of other medicines on Braun Monopotassium Phosphate:
Potassium-sparing diuretics, aldosterone antagonists, ACE inhibitors, tacrolimus, cyclosporines, non-steroidal anti-inflammatory drugs, peripheral analgesics and heparin used for extended periods:
These medicines reduce renal excretion of potassium. Simultaneous administration of potassium with these medicines may result in severe hyperkalaemia.
Salicylates:
The concomitant use of salicylates and monopotassium phosphate may increase plasma concentrations of salicylates, since excretion of salicylates is reduced in acidified urine.

4.6 Fertility, pregnancy and lactation

Pregnancy:
No data are available from clinical studies on pregnancies exposed to Braun Monopotassium Phosphate. Nor are there any available animal studies relating to pregnancy, development of the embryo/foetus, delivery or post-natal development. However, there are no known direct or indirect harmful effects in this respect.
Caution is recommended when prescribing this medicine to pregnant women.
Braun Monopotassium Phosphate should only be administered during pregnancy if the benefits outweigh the possible risks.

Breastfeeding:
It is unknown whether phosphates are excreted in human milk. However, there are no known problems in breastfeeding infants who ingest the recommended normal daily amounts.
Braun Monopotassium Phosphate should only be administered during lactation if the benefits outweigh the possible risks.

Fertility:
No data are available.

4.7 Effects on ability to drive and use machines

Braun Monopotassium Phosphate has no influence on the ability to drive and use machines.

4.8 Undesirable effects

The majority of undesirable effects associated with monopotassium phosphate solution for injection are dose-dependent and occur particularly as a result of overdose or a high infusion rate (see symptoms in section 4.9). However, if the medicine has been administered in accordance with the instructions, the following undesirable effect may be detected:

Definition of frequency terms used in this section:
Rare (≥1/10,000, <1/1,000) patients treated

Gastrointestinal disorders
Rare: Nausea

Particular situations such as drug interactions, sudden onset of acidosis and acute renal failure and other conditions may cause sudden hyperkalaemia. See section 4.9 for symptoms of hyperkalaemia.

4.9 Overdose

Overdose may lead to hyperkalaemia and hyperphosphataemia.

Symptoms:
Symptoms associated with hyperkalaemia:
Circulatory changes are hypotension and centralisation.
Neuromuscular symptoms include fatigue, confusional states, unexplained anxiety, weakness or a feeling of heaviness in the limbs, muscle spasms, paraesthesia, respiratory problems and ascending paralysis.
Cardiac arrhythmia may occur as a result of hyperkalaemia or very rapid infusion. Serum concentrations of potassium of 6.5 mmol/l or more are dangerous, and concentrations above 8 mmol/l may be fatal.
Symptoms associated with hyperphosphataemia:
Hyperphosphataemia may lead to renal damage as a result of calcium phosphate precipitation (nephrocalcinosis), precipitation of calcium phosphate into other tissues (for example, skin, cornea, lung) and hypocalcaemia (symptoms: convulsions, muscle spasms, tremors, numbness, tingling, pain or weakness in the hands and feet, breathlessness or difficulty in breathing), to hypocalcaemic tetany and metastatic calcifications (see section 4.4).
Treatment
Immediate discontinuation of the perfusion, slow intravenous administration of 10% w/v calcium gluconate, glucose solutions with insulin, increased diuresis or oral or rectal administration of ion exchangers, correction of acidosis if necessary.
Haemodialysis may be required in cases of massive overdose.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: 12.2.2 – Correction of blood volume and hydroelectrolytic alterations. Correction of hydroelectrolytic alterations. Phosphorus, ATC code: B05BB01

Pharmacodynamic properties of phosphate:
The total quantity of inorganic phosphate in an adult is approximately 0.7 kg. The greater proportion of this is present in the form of inorganic phosphate compounds. Ionised inorganic phosphate is present in plasma in the form NaH2PO4. Ionised phosphate acts as a buffer in the intracellular space and in blood and urine.
Phosphate deficiency syndrome may occur during parenteral nutrition if the phosphate administered is insufficient. In particular, when large quantities of carbohydrates are administered there is high absorption of phosphate by the cells, leading to a reduction in serum phosphate concentrations.
The pharmacodynamic effects of phosphate in Braun Monopotassium Phosphate are basically the same as in normal physiology. When it is specifically administered, therefore, no additional pharmacodynamic effects are expected.

Pharmacodynamic properties of potassium:
As a principal intracellular cation, potassium has two major physiological functions: the maintenance of intracellular tonicity and transmembranous potential. It is essential for the transmission of nerve impulses and contraction of the cardiac, skeletal and smooth muscle. Potassium also participates in the utilisation of carbohydrates and in protein synthesis. Daily potassium requirements are around 1 – 1.5 mmol per kg of body weight. Hypokalaemia is accompanied by muscle weakness, atony of the smooth gastrointestinal muscles (from constipation to paralytic ileus), loss of the ability of the kidneys to concentrate urine, ECG changes and cardiac arrhythmia. The pharmacodynamic effects of potassium in Braun Monopotassium Phosphate are basically the same as in normal physiology. When it is specifically administered, therefore, no additional pharmacodynamic effects are expected.

5.2 Pharmacokinetic properties

Phosphate
Absorption:
As the solution is intended for intravenous administration, its bioavailability is 100%.
Distribution:
Phosphate is the form of phosphorus present in the human body. Approximately 85 per cent of the total phosphorus in the body is stored in the bones. Of the remainder, 14 per cent is in the soft tissues and 1 per cent is found in the blood.
Biotransformation:
In the strict sense, phosphate does not undergo metabolism.
Elimination:
Phosphate is predominantly excreted by the kidneys. Parathormone, administration of calcium, oestrogens, thyroxin and acidosis increase renal excretion of phosphate; cholecalciferol, the growth hormone, insulin and cortisol reduce renal excretion of phosphate.

Potassium
Absorption:

As the solution is intended for intravenous administration, its bioavailability is 100%.
Distribution:
Potassium is the most important cation in the intracellular space; approximately 98 per cent of the total potassium in the body is stored in the intracellular space. The concentration of intracellular potassium is approximately 140 – 150 mmol/l. The normal plasma concentration of potassium is between 3.5 and 5 mmol/l.
Biotransformation:
In the strict sense, phosphate does not undergo metabolism.
Elimination:
Potassium is excreted chiefly in the urine (around 90 per cent) and around 10 per cent is excreted through the gastrointestinal tract. Even in situations of potassium deficit, 10 – 50 mmol of potassium are excreted daily by the kidneys. Potassium deficiency may be caused by increased renal excretion, increased gastrointestinal losses, for example through vomiting or diarrhoea, through fistulas, increased intracellular uptake, for example during treatment of acidosis or treatments with glucose or insulin, or by insufficient ingestion of potassium.

5.3 Preclinical safety data

Non-clinical data, based on conventional studies of pharmacological safety, repeated dose toxicity, genotoxicity, carcinogenic potential and reproductive and developmental toxicity, have revealed no special risks for humans.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injectable preparations.

6.2 Incompatibilities

Braun Monopotassium Phosphate is incompatible with solutions containing calcium and magnesium.

6.3 Shelf life

Packaging dated:
3 years.

After dilution:
From a microbiological point of view, the medicinal product should be administered immediately after dilution. If it is not administered immediately, storage times and the conditions which precede use are the responsibility of the user and should not normally exceed 24 hours at 2 – 8°C, unless the dilution has been performed under duly controlled and validated aseptic conditions.

6.4 Special precautions for storage

Store below 25°C.
Storage conditions for the product after reconstitution or dilution, see section 6.3.

6.5 Nature and contents of container

Braun Monopotassium Phosphate is packaged in 10 ml and 20 ml polyethylene ampoules, presented individually or in boxes of 100 units, respectively.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Containers are for single use only. Dispose of any unused contents after opening the container.
Only clear, colourless solutions from intact packaging should be used.
The electrolyte concentrate is to be added to the vehicle solution, under strictly aseptic conditions and immediately before preparing the infusion. The container should be gently shaken.
Vehicle solutions should be free from calcium and magnesium. Suitable solutions are, for example, a 5% glucose solution or isotonic sodium chloride solution. If sodium consumption must be limited, only sodium-free vehicle solutions may be used.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

B. Braun Medical, Lda.
Estrada Consiglieri Pedroso, 80
Queluz de Baixo
2730-053 Barcarena
Portugal

8. MARKETING AUTHORISATION NUMBERS

Registration No: 2300481 - 1 x 10 ml ampoule, solution for injection, 136.13 mg/ml
Registration No: 2300580 - 1 x 20 ml ampoule, solution for injection, 136.13 mg/ml
Registration No: 4089587 - 1 x 10 ml ampoule, solution for injection, 136.13 mg/ml
Registration No: 4089686 - 1 x 20 ml ampoule, solution for injection, 136.13 mg/ml

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22 November 1994.
Date of last renewal: 11 July 2005

Effective

10. DATE OF REVISION OF THE TEXT

11/2012

Effective

Title: 0335-SmPC-SOL. FOSFATO MONOPOTASICO (I M) BRAUN-PT-en Initiator: Marcus ? Thielemann

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