AUSTRALIAN PRODUCT INFORMATION – DBL™ POTASSIUM DIHYDROGEN PHOSPHATE CONCENTRATED INJECTION (monobasic potassium phosphate)

1. NAME OF THE MEDICINE

Monobasic potassium phosphate

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 10 mL ampoule contains 1.361 g of monobasic potassium phosphate (KH_2PO_4) in Water for Injection. The pH of the solution is approximately 4.5. Each mL of injection contains 1 mmol of potassium ions, 1 mmol of phosphate ions and 2 mmol of hydrogen ions.

For the full list of excipients, see section 6.1 LIST OF EXCIPIENTS.

3. PHARMACEUTICAL FORM

Monobasic potassium phosphate is a white, odourless, granular or crystalline powder, or colourless crystals. It is freely soluble in water and practically insoluble in alcohol.

DBL™ Potassium Dihydrogen Phosphate Concentrated Injection is a clear, colorless, sterile solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Treatment of severe hypophosphataemia (serum levels less than 0.3 mmol/L) and other degrees of hypophosphataemia when oral therapy is not possible.

The cause of hypophosphataemia should be identified and treated.

4.2 Dose and Method of Administration

Dosage

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: 0.15-0.33 mmol/kg administered over 6 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/h.

Method of Administration

DBL™ Potassium Dihydrogen Phosphate Concentrated Injection is administered by slow intravenous infusion. The injection must be diluted before use.

Dilution: DBL™ Potassium Dihydrogen Phosphate Concentrated Injection must be diluted before use. The drug can be given in 0.9% sodium chloride or 5% glucose solution. It should be administered by slow infusion to avoid phosphate intoxication.

Monitoring: Serum sodium, potassium, phosphate and calcium concentrations and renal function should be monitored every 12 to 24 hours during therapy.

Conversion to oral phosphate therapy should occur as soon as possible.

Dosage Adjustments

Renal Impairment: dose should be reduced. Use of phosphates in severe renal impairment is contraindicated (see section 4.3 CONTRAINDICATIONS).

4.3 Contraindications

DBL™ 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.
- Patients with hyperphosphataemia, since phosphate therapy will exacerbate the condition.
- Patients with hypocalcaemia due to the close relationship between hypocalcaemia and hyperphosphataemia.
- Patients with hyperkalaemia, since the potassium in the injection may exacerbate the condition.
- Addison's disease since there is an increased risk of hyperkalaemia in these patients.
- Urolithiasis (magnesium ammonium phosphate type, infected) since it may exacerbate the condition.
- Renal impairment with oliguria and 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 paramytonia.

4.4 Special Warnings and Precautions for Use

Potassium

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

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

Hyperkalaemia: monobasic potassium phosphates should be avoided in patients with hyperkalaemia. Sodium phosphates may be substituted.

In patients with impaired mechanisms for excreting potassium, administration of potassium salts can produce hyperkalaemia and cardiac arrest. This is an important concern in patients given IV potassium. Potentially fatal hyperkalaemia 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.

Phosphate

Phosphate should be administered with caution in conditions where high phosphate levels may be encountered, such as hypoparathyroidism, chronic renal disease, acute dehydration, pancreatitis, rhabdomyolysis, 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 section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS) since these conditions may be exacerbated by the potassium in the injection.

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.

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.

Use in the elderly

No data available.

Paediatric use

No data available.

Effects on laboratory tests

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

4.5 Interactions with Other Medicines and Other Forms of Interactions

Angiotensin converting enzyme (ACE) inhibitors:

Concurrent use with DBL™ Potassium Dihydrogen Phosphate Concentrated Injection may result in hyperkalaemia, especially in patients with renal impairment.

Calcium containing medicines:

Concurrent use of DBL™ Potassium Dihydrogen Phosphate Concentrated Injection and calcium containing medicines may increase the risk of deposition of calcium in soft tissues.

Digitalis glycosides:

The administration of DBL™ Potassium Dihydrogen Phosphate Concentrated Injection in digitalised patients with severe or complete heart block may result in hyperkalaemia.

Potassium sparing diuretics:

Concurrent use with DBL™ Potassium Dihydrogen Phosphate Concentrated Injection may result in hyperkalaemia, especially in patients with renal impairment.

Non-steroidal antiinflammatory agents (NSAIDS):

Concurrent use with DBL™ Potassium Dihydrogen Phosphate Concentrated Injection may result in hyperkalaemia, especially in patients with renal impairment.

Phosphate containing medicines:

Concurrent use with DBL™ Potassium Dihydrogen Phosphate Concentrated Injection may result in hyperphosphataemia, especially in patients with impaired renal function.

Potassium containing medicines:

Concurrent use with DBL™ Potassium Dihydrogen Phosphate Concentrated Injection may result in hyperkalaemia, especially in patients with renal impairment.

Salicylates:

Concurrent use with DBL™ Potassium Dihydrogen Phosphate Concentrated 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 stabilized on salicylates.

4.6 Fertility, Pregnancy and Lactation

Effects on fertility

No data available.

Use in pregnancy

Animal reproduction studies have not been conducted with this product. It is not known whether this product can adversely effect the foetus when administered to a pregnant woman.

Therefore DBL™ 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 DBL™ Potassium Dihydrogen Phosphate Concentrated Injection is not recommended for use during lactation.

4.7 Effects on Ability to Drive and Use Machines

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 Adverse Effects (Undesirable Effects)

Cardiovascular

Uncommon: hypotension

Rare: myocardial infarction

Endocrine/Metabolic

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. Hyperkalaemia 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 (see section 4.9 OVERDOSE).

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

4.9 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. Symptoms associated with hyperphosphataemia include muscle weakness, paraesthesia, convulsions, cardiomyopathy, respiratory failure and haematological abnormalities.

Hyperphosphataemia leads in turn to hypocalcaemia, which may be severe, and to ectopic calcification. Secondary hyperparathyroidism may develop in the presence of renal failure.

Crystal deposition may occur in important structures including blood vessels of the eye, lung, heart and kidney. Fatal alveolar diffusion block has occurred, the risk being greater if the patient is alkalotic.

Treatment

Treatment of overdosage involves the following measures:

- Immediate cessation of phosphate therapy
- Correction of serum electrolyte concentrations, especially calcium
- General supportive treatment.

Potassium

If excretory mechanisms are impaired or if IV potassium is administered too rapidly, potentially fatal hyperkalaemia can result (see section 4.3 CONTRAINDICATIONS and section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE). However, hyperkalaemia 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 hyperkalaemia 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 hyperkalaemia in digitalised patients, too rapid a lowering of the serum potassium concentration can produce digitalis toxicity.

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of action

The majority (80%) of the body's phosphate is found as calcium phosphate in the skeleton, where it gives rigidity to the bone. The remainder is found in soft tissues. Phosphate is the principle anion of intracellular fluid. In body fluids, phosphate is present mainly as divalent hydrogen phosphate (HPO_4^{2-}) ions (approximately 80%) and monovalent dihydrogen phosphate ($H_2PO_4^-$) ions (approximately 20%).

Apart from its essential role in bone structure, phosphate is also important in many metabolic and enzymatic pathways. It is involved in energy storage and transfer, the utilization of B-complex vitamins, the buffering of body fluids, and in the renal excretion of hydrogen ions.

Hypophosphataemia may arise from a variety of causes including primary hyperparathyroidism, Vitamin D deficiency, X-linked familial hypophosphataemia, alcoholism, hepatic failure and septicaemia. The symptoms of hypophosphataemia include muscle weakness, paraesthesia, convulsions, cardiomyopathy, respiratory failure and haematological abnormalities. Prolonged hypophosphataemia may result in rickets or osteomalacia.

Clinical trials

No data available.

5.2 Pharmacokinetic Properties

The normal concentration range of phosphate in plasma is 0.8 to 1.5 mmol/L.

Phosphate is primarily excreted in the urine. Over 90% of plasma phosphate is filtered in the kidneys with the majority being reabsorbed in the proximal tubule. Parathyroid hormone decreases the tubular reabsorption of phosphate, thereby increasing urinary excretion. In addition, serum phosphate levels are inversely related to serum calcium levels and to renal metabolism of Vitamin D. A decrease in serum calcium concentration will result in increased serum phosphate levels.

5.3 Preclinical Safety Data

Genotoxicity

No data available.

Carcinogenicity

No data available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Water for injections

6.2 Incompatibilities

Phosphates are reported to be incompatible with calcium or magnesium containing solutions. Admixture will lead to precipitates being formed in the solution. Solutions containing other cations such as iron and aluminium may also form precipitates when added to the product.

6.3 Shelf life

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 Special Precautions for Storage

Store below 25^{o}C.

6.5 Nature and Contents of Container

	Strength
Potassium phosphate monobasic	136.1 milligrams/mL

6.6 Special Precautions for Disposal

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 Physicochemical Properties

Chemical structure

The molecular formula of potassium phosphate monobasic is KH_2PO_4, Its molecular weight is 136.1.

CAS number

7778-77-0

7. MEDICINE SCHEDULE (POISONS STANDARD)

Unscheduled

8. SPONSOR

Pfizer Australia Pty Ltd
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Sydney NSW 2000
Toll Free Number: 1800 675 229
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9. DATE OF FIRST APPROVAL

28 January 1998

10. DATE OF REVISION

3 November 2021

Summary Table of Changes

Section changed	Summary of new information
4.3	Additional information on contraindications: • Renal impairment with oliguria and 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 hereditarian or congenital paramytonia.
4.4	Additional special warnings and precautions for use: • Phosphate should be administered with caution in conditions such as acute dehydration, pancreatitis, severe renal insufficiency and extensive tissue damage (such as severe burns). • In patients with impaired mechanisms for excreting potassium, administration of potassium salts can produce hyperkalaemia and cardiac arrest. • 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.
4.8	Added symptoms and signs of potassium intoxication.
4.9	Additional information on overdose: • Hyperphosphataemia may also occur in the presence of acidosis, acromegaly, haemolysis, hypoparathyroidism, tissue destruction or vitamin D toxicity. • Potentially fatal hyperkalaemia if excretory mechanisms are impaired or administered too rapidly. • Treatment if hyperkalaemia develops.
6.2	Added information on precipitates.
8	Updated sponsor contact details to www.pfizermedinfo.com.au
All	Minor editorial changes.