DBL™ MAGNESIUM CHLORIDE CONCENTRATED INJECTION

Name of Medicine
Magnesium chloride hexahydrate

Presentation
The molecular formula of magnesium chloride hexahydrate is MgCl₂·6H₂O. It has a molecular weight of 203.3. The CAS Registry number of magnesium chloride hexahydrate is 7791-18-6. Magnesium chloride hexahydrate exists as colourless, odourless, deliquescent or hygroscopic crystals or flakes. It is very soluble in water and freely soluble in alcohol.

DBL™ Magnesium Chloride Concentrated Injection is a clear, colourless, sterile solution. Each 5 mL solution contains magnesium chloride hexahydrate equivalent to 480 milligrams of magnesium chloride anhydrous and water for injection. The product contains no preservative. The pH of the solution ranges between 5.0 and 8.0. Each mL of injection contains 1 mmol (2 mEq) of magnesium ions and 2 mmol (2 mEq) of chloride ions.

Uses

Actions
Magnesium is the second most abundant cation of intracellular fluid. It is an essential cation in over 300 enzymatic processes, and is necessary for several steps in glycolysis, the Krebs cycle and in protein and nucleic acid synthesis. It is thus vital for normal energy storage and transfer. Magnesium plays an important role in neurochemical transmission, and is essential for proper neurochemical functioning.

Magnesium has an anticonvulsant effect. It possibly has antiarrhythmic effects and a role in calcium homeostasis and bone mineralisation. There is conflicting evidence that the routine use of intravenous magnesium in the setting of acute myocardial infarction is beneficial.

Deficiency of magnesium is closely associated with other electrolyte disturbances, particularly hypocalcaemia and hypokalaemia. The specific symptoms of hypomagnesaemia are therefore difficult to determine, but may include nausea, vomiting, muscle weakness, neuromuscular dysfunction such as paraesthesia, tremor and cramp, tachycardia and cardiac arrhythmias.

Pharmacokinetics
The 95% confidence intervals for magnesium levels in healthy Australian subjects are: neonate 0.6 to 0.9 mmol/L and adult 0.8 to 1.0 mmol/L.

Approximately 50% of magnesium in the body is found in bone, with the majority of the remainder stored in muscle and soft tissue. 1% or less is contained in the extracellular compartment, of which approximately 33% is protein bound, with a further 12% bound to anions.

After intravenous infusion the duration of action of magnesium is approximately 30 minutes. Magnesium is primarily excreted in the urine, with small amounts excreted in faeces, saliva and breast milk. Over 90% of magnesium filtered by the kidneys is reabsorbed, mainly in the ascending limb of the Loop of Henle, with significant amounts also absorbed in the proximal and distal tubules. The clearance is proportional to the plasma magnesium concentration and the glomerular filtration rate.

Indications
Parenteral administration of magnesium is indicated in the treatment of acute hypomagnesaemia.

Magnesium salts are also indicated to prevent hypomagnesaemia in patients receiving total parenteral nutrition.
Contraindications
Magnesium may form precipitates if mixed with other electrolyte solutions (see Interactions – Incompatibilities for important information).

Magnesium is contraindicated in patients with heart block, since magnesium may exacerbate this condition.

Magnesium is also contraindicated in patients with renal failure (creatinine clearance <20 mL/min), since there is an increased risk of hypermagnesaemia in these patients.

Magnesium chloride should not be given to a pregnant woman within two hours preceding delivery as there is a risk of respiratory depression due to hypermagnesaemia in the neonate.

Warnings and Precautions
Magnesium should be administered with caution in patients with impaired renal function, since the risk of hypermagnesaemia is increased in these patients.

Magnesium may precipitate an acute myasthenic crisis. Sensitivity to parenteral magnesium has been reported. An intravenous preparation of a calcium salt (e.g. calcium gluconate) should be readily available when magnesium chloride is given.

The patellar reflex should be tested prior to administering repeat doses of magnesium chloride. Suppression of the reflex is an indication of magnesium intoxication. Respiration rate should be determined and should be at least 16 per minute prior to each dose of magnesium as respiratory depression is the most critical side effect of the medication. Urine output should be monitored and should be at least 100 mL during the four hours preceding dosing to ensure adequate excretion of magnesium.

Laboratory Tests
Monitoring of serum magnesium levels is advised at periodic intervals during therapy to ensure that normal serum magnesium levels are not exceeded.

Pregnancy and Lactation
Use in pregnancy
Magnesium readily crosses the placenta. Foetal serum concentrations approximate those of the mother. Magnesium chloride should not be given to a pregnant woman within two hours preceding delivery as there is a risk of respiratory depression due to hypermagnesaemia in the neonate.

Bony abnormalities and congenital rickets have been reported in neonates born to mothers treated with parenteral magnesium for prolonged periods of time (4 to 13 weeks duration).

Use in lactation
After intravenous administration, magnesium is distributed into breast milk, and the concentration of magnesium in the breast milk is approximately twice that in the maternal serum. Magnesium chloride is therefore not recommended in lactating patients.

Interactions
Cardiac glycosides/Digitalis
Magnesium salts should be administered with caution in patients treated with cardiac glycosides, since heart block may occur if calcium salts are required to treat magnesium toxicity (see OVERDOSAGE).

CNS depressants
Concurrent use of magnesium salts and CNS depressant drugs may result in an enhanced CNS depressant effect.

Magnesium containing preparations (including antacids, laxatives)
Concurrent use of magnesium salts with other magnesium containing preparations may cause magnesium toxicity especially in patients with renal insufficiency.

**Neuromuscular blocking agents**
Concurrent use of magnesium salts with neuromuscular blocking agents may result in an excessive neuromuscular blockade.

**Antihypertensive agents**
Concurrent use of magnesium and nifedipine or other antihypertensive agents may result in an exaggerated hypotensive response.

**Incompatibilities**
As mixtures of the following products with DBL™ Magnesium Chloride Concentrated Injection may cause precipitates to form, products containing these anions should not be mixed or co-administered with DBL™ Magnesium Chloride Concentrated Injection.

Magnesium salts have been reported to be incompatible with alkali carbonates, bicarbonates and soluble phosphates. Magnesium salts may also react with arsenates, phosphates and tartrates.

**Adverse Effects**
Excessive administration of magnesium chloride may result in hypermagnesaemia. The signs of hypermagnesaemia may include: nausea, vomiting, flushing, hypotension, muscle weakness, muscle paralysis, blurred or double vision, CNS depression and loss of reflexes. More severe hypermagnesaemia may result in respiratory depression, respiratory paralysis, renal failure, coma, cardiac arrhythmias and cardiac arrest. Hypocalcaemia with tetany, secondary to hypermagnesaemia, has been reported.

**Dosage And Administration**
DBL™ Magnesium Chloride Concentrated Injection is administered intravenously, usually by slow intravenous infusion. Intravenous doses should be diluted in glucose 5%.

Maximum dose: 1.9 grams of magnesium chloride anhydrous (40 mEq of magnesium) may be diluted with 250 mL of 5% glucose and infused at a rate not to exceed 3 mL per minute (0.5 mEq/min).

The dose of magnesium should be adjusted according to the patient’s individual requirements and response. The total adult daily dose should not exceed 18.7 grams of magnesium chloride anhydrous per day.

Acute hypomagnesaemia:
**Adults:** It is suggested that a dose of 3.3 to 7.2 grams of magnesium chloride anhydrous (70 to 150 mEq of magnesium) be given by slow intravenous infusion on the first day, followed by 2.4 grams of magnesium chloride anhydrous (50 mEq of magnesium) daily until hypomagnesaemia is corrected. A total of 15.3 grams of magnesium chloride anhydrous (320 mEq of magnesium) may be required.

**Total Parenteral Nutrition:**
**Adults:** A dose of 0.2 to 1.2 grams magnesium chloride anhydrous (4 to 24 mEq of magnesium) daily may be administered.  
**Infants:** A dose of 0.1 to 0.5 grams magnesium chloride anhydrous (2 to 10 mEq of magnesium) daily may be administered.

**Compatibilities**
Magnesium salts are reported to be chemically stable and compatible with either sodium chloride 0.9%, glucose 5% in water or glucose 5% in sodium chloride 0.9%. Solutions diluted for infusion should be prepared and used immediately as they are not preserved.
Overdosage

Clinical features
Hypermagnesaemia may occur when large doses of magnesium are given, especially in patients with renal failure. Signs of hypermagnesaemia include: nausea, vomiting, flushing, hypotension, muscle weakness, muscle paralysis, blurred or double vision, CNS depression and loss of reflexes. More severe hypermagnesaemia may result in respiratory depression, respiratory paralysis, renal failure, coma, cardiac arrhythmias and cardiac arrest.

Treatment
In the treatment of hypermagnesaemia, the following measures may be required:

- blood pressure and respiratory support
- intravenous administration of 2.5 to 5.0 mmol calcium salts (such as calcium gluconate) reverses the effects of magnesium toxicity
- dialysis may be required, particularly if renal function is impaired
- if renal function is normal, adequate fluids should be given so that urine output is at least 60 mL/hour to assist removal of magnesium from the body
- physostigmine (0.5 to 1.0 milligrams subcutaneously) may be helpful, but routine use is not recommended due to the potential toxicity.

In case of overdose, immediately contact the Poisons Information Centre for advice on management. (In New Zealand call 0800 764 766.)

Pharmaceutical Precautions

Special Precautions for Storage
Store below 25°C. Protect from light

Incompatibilities
See Interactions section

Medicine classification
General Sale Medicine

Package Quantities
DBL™ Magnesium Chloride Concentrated Injection is available as follows:
Strength Magnesium chloride (anhydrous) 480 milligrams in 5 mL
Pack 10 x 5 mL ampoules

Name And Address
New Zealand Sponsor:
Pfizer New Zealand Limited,
PO Box 3998
Auckland, New Zealand, 1140

Toll Free Number: 0800 736 363

Date of preparation: 12th April 2017