MAGNESIUM SULFATE INJECTION, USP

R_x only

An intravenous nutritional supplement to prevent or treat hypomagnesemia and a means for parenteral control of seizures in toxemia of pregnancy and acute nephritis in children.

Ampul
Fliptop Vial

DESCRIPTION

Magnesium Sulfate Injection, USP is a sterile solution of magnesium sulfate heptahydrate in Water for Injection, USP administered by the intravenous or intramuscular routes as an electrolyte replenisher or anticonvulsant. It is available in 50% concentration. May contain sulfuric acid and/or sodium hydroxide for pH adjustment. The pH is 6.0 (5.5 to 7.0). The 50% concentration has an osmolarity of 4.06 mOsmol/mL (calc.).

The solution contains no bacteriostat, antimicrobial agent or added buffer (except for pH adjustment). Any unused portion remaining in container should be discarded within 24 hours of initial use.

See HOW SUPPLIED section for the content and characteristics of available dosage forms and sizes.

Magnesium Sulfate, USP heptahydrate is chemically designated $MgSO_4 \bullet 7H_2O$, colorless crystals or white powder freely soluble in water.

CLINICAL PHARMACOLOGY

Magnesium (Mg^{++}) is an important cofactor for enzymatic reactions and plays an important role in neurochemical transmission and muscular excitability.

As a nutritional adjunct in hyperalimentation, the precise mechanism of action for magnesium is uncertain. Early symptoms of hypomagnesemia (less than 1.5 mEq/liter) may develop as early as three to four days or within weeks. Predominant deficiency effects are neurological, e.g., muscle irritability, clonic twitching and tremors. Hypocalcemia and hypokalemia often follow low serum levels of magnesium. While there are large stores of magnesium present intracellularly and in the bones of adults, these stores often are not mobilized sufficiently to maintain plasma levels. Parenteral magnesium therapy repairs the plasma deficit and causes deficiency symptoms and signs to cease.

Magnesium prevents or controls convulsions by blocking neuromuscular transmission and decreasing the amount of acetylcholine liberated at the end plate by the motor nerve impulse. Magnesium is said to have a depressant effect on the central nervous system, but it does not adversely affect the mother, fetus or neonate when used as directed in eclampsia or pre-eclampsia. Normal plasma magnesium levels range from 1.5 to 2.5 or 3.0 mEq/liter.

As plasma magnesium rises above 4 mEq/liter, the deep tendon reflexes are first decreased and then disappear as the plasma level approaches 10 mEq/liter. At this level respiratory paralysis may occur. Heart block also may occur at this or lower plasma levels of magnesium.

Magnesium acts peripherally to produce vasodilation. With low doses only flushing and sweating occur, but larger doses cause lowering of blood pressure. The central and peripheral effects of magnesium poisoning are antagonized to some extent by intravenous administration of calcium.

With intravenous administration the onset of anticonvulsant action is immediate and lasts about 30 minutes. Following intramuscular administration the onset of action occurs in about one hour and persists for three to four hours. Effective anticonvulsant serum levels range from 2.5 or 3.0 to 7.5 mEq/liter. Magnesium is excreted solely by the kidney at a rate proportional to the plasma concentration and glomerular filtration.

INDICATIONS AND USAGE

Magnesium Sulfate Injection, USP is suitable for replacement therapy in magnesium deficiency, especially in acute hypomagnesemia accompanied by signs of tetany similar to those observed in hypocalcemia. In such cases, the serum magnesium (Mg^{++}) level is usually below the lower limit of normal (1.5 to 2.5 or 3.0 mEq/liter) and the serum calcium (Ca^{++}) level is normal (4.3 to 5.3 mEq/liter) or elevated.

In total parenteral nutrition, magnesium sulfate may be added to the nutrient admixture to correct or prevent hypomagnesemia which can arise during the course of therapy.

Magnesium Sulfate Injection, USP is also indicated as a parenteral anticonvulsant for the prevention and control of seizures (convulsions) in severe toxemia of pregnancy. When used judiciously it effectively prevents and controls the convulsions of eclampsia without producing deleterious depression of the central nervous system of the mother or infant. However, other effective drugs are available for this purpose.

Magnesium Sulfate Injection, USP may be used to control hypertension, encephalopathy and convulsions associated with acute nephritis in children. However, other drugs such as barbiturates, reserpine or hydralazine should be tried first.

CONTRAINDICATIONS

Intravenous magnesium should not be given to mothers with toxemia of pregnancy during the two hours preceding delivery.

WARNINGS

Intravenous use in eclampsia should be reserved for immediate control of life-threatening convulsions.

Parenteral use in the presence of renal insufficiency may lead to magnesium intoxication.

WARNING: This product contains aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly at risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which contain aluminum.

Research indicates that patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum at greater than 4 to 5 mcg/kg/day accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.

PRECAUTIONS

Because magnesium is removed from the body solely by the kidneys, the drug should be used with caution in patients with renal impairment. Urine output should be maintained at a level of 100 mL every four hours. Monitoring serum magnesium levels and the patient's clinical status is essential to avoid the consequences of overdosage in toxemia. Clinical indications of a safe dosage regimen include the presence of the patellar reflex (knee jerk) and absence of respiratory depression

(approximately 16 breaths or more/minute). Serum magnesium levels usually sufficient to control convulsions range from 3 to 6 mg/100 mL (2.5 to 5.0 mEq/liter). The strength of the deep tendon reflexes begins to diminish when magnesium levels exceed 4 mEq/liter. Reflexes may be absent at 10 mEq magnesium/liter, where respiratory paralysis is a potential hazard. An injectable calcium salt should be immediately available to counteract the potential hazards of magnesium intoxication in eclampsia.

50% Magnesium Sulfate Injection, USP must be diluted to a concentration of 20% or less prior to I.V. infusion. Rate of administration should be slow and cautious, to avoid producing hypermagnesemia. The 50% solution also should be diluted to 20% or less for intramuscular injection in infants and children.

Pregnancy Category A. Studies in pregnant women have not shown that magnesium sulfate injection increases the risk of fetal abnormalities if administered during all trimesters of pregnancy. If this drug is used during pregnancy, the possibility of fetal harm appears remote. However, because studies cannot rule out the possibility of harm, magnesium sulfate injection should be used during pregnancy only if clearly needed.

When administered by continuous intravenous infusion (especially for more than 24 hours preceding delivery) to control convulsions in toxemic mothers, the newborn may show signs of magnesium toxicity, including neuromuscular or respiratory depression. See OVERDOSAGE.

ADVERSE REACTIONS

The adverse effects of parenterally administered magnesium usually are the result of magnesium intoxication. These include flushing, sweating, hypotension, depressed reflexes, flaccid paralysis, hypothermia, circulatory collapse, cardiac and central nervous system depression proceeding to respiratory paralysis. Hypocalcemia with signs of tetany secondary to magnesium sulfate therapy for eclampsia has been reported.

OVERDOSAGE

Magnesium intoxication is manifested by a sharp drop in blood pressure and respiratory paralysis. Disappearance of the patellar reflex is a useful clinical sign to detect the onset of magnesium intoxication. In the event of overdosage artificial ventilation must be provided until a calcium salt can be injected intravenously to antagonize the effects of magnesium.

In adults intravenous administration of 5 to 10 mEq of 10% calcium gluconate will usually reverse respiratory depression or heart block due to magnesium intoxication. In extreme cases, peritoneal or hemodialysis may be required.

Hypermagnesemia in the newborn may require resuscitation and assisted ventilation via endotracheal intubation or intermittent positive pressure ventilation as well as intravenous calcium.

DOSAGE AND ADMINISTRATION

Both intravenous and intramuscular administration are appropriate. Intramuscular administration of the undiluted 50% solution results in therapeutic plasma levels in 60 minutes, whereas I.V. doses will provide a therapeutic level almost immediately. The rate of I.V. injection should generally not exceed 1.5 mL of a 10% concentration (or its equivalent) per minute, except in severe eclampsia with seizures (see below).

Solutions for intravenous infusion must be diluted to a concentration of 20% or less prior to administration. The diluents commonly used are 5% Dextrose Injection, USP and 0.9% Sodium Chloride Injection, USP. Deep intramuscular injection of the undiluted (50%) solution is appropriate for adults, but the solution should be diluted to a 20% concentration prior to such injection in children.

In Magnesium Deficiency

In the treatment of mild magnesium deficiency, the usual adult dose is 1 g, equivalent to 8.12 mEq of magnesium (2 mL of the 50% solution) injected intramuscularly every six hours for four doses (equivalent to a total of 32.5 mEq of magnesium per 24 hours). For severe hypomagnesemia, as much as 2 mEq (0.5 mL of the 50% solution) per kg of body weight may be given intramuscularly within a period of four hours if necessary. Alternatively, 5 g, (approximately 40 mEq) can be added to one liter of 5% Dextrose Injection, USP or 0.9% Sodium Chloride Injection, USP for slow intravenous infusion over a three-hour period.

In Hyperalimentation

In total parenteral nutrition, maintenance requirements for magnesium are not precisely known. The maintenance dose recommended for adults is 5 to 8 mEq magnesium/liter of TPN solution; typical daily adult intake ranges from 10 to 24 mEq. For infants, the recommended intake ranges from 0.25 to 0.6 mEq/kg/day.

In Eclampsia

In severe pre-eclampsia or eclampsia, the total initial dose is 10 to 14 g of magnesium sulfate. Intravenously, a dose of 4 to 5 g in 250 mL of 5% Dextrose Injection, USP or 0.9% Sodium Chloride Injection, USP may be infused. Simultaneously, intramuscular doses of up to 10 g (10 mL of the undiluted 50% solution in each buttock) are given. Alternatively, the initial intravenous dose of 4 g may be given by diluting the 50% solution to a 10 or 20% concentration; the diluted fluid (40 mL of a 10% solution or 20 mL of a 20% solution) may then be injected intravenously over a period of three to four minutes. Subsequently, 4 to 5 g (8 to 10 mL of the 50% solution) are injected intramuscularly into alternate buttocks every four hours, depending on the continuing presence of the patellar reflex and adequate respiratory function. Therapy should continue until paroxysms cease. A serum magnesium level of 6 mg/100 mL is considered optimal for control of seizures. A total daily (24 hr) dose of 30 to 40 g should not be exceeded and less should be used if the patient is anuric.

In Nephritic Seizures

In children with nephritic seizures, the 50% concentration should be diluted to a 20% solution for intramuscular injection. The dose for children is 20 to 40 mg (0.1 to 0.2 mL of a 20% solution) per kg of body weight administered intramuscularly as needed to control seizures.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Do not administer unless solution is clear and container is undamaged. Discard unused portion.

To prevent needle-stick injuries, needles should not be recapped, purposely bent, or broken by hand.

HOW SUPPLIED

Magnesium Sulfate Injection, USP is supplied in single-dose containers as follows:

List No.	Container	Total Amount	Concentration	mEq Mg^{++}/mL
4075	Ampul	1 g/2 mL	50%	4 mEq/mL
2168	Fliptop Vial	5 g/10 mL	50%	4 mEq/mL
2168	Fliptop Vial	10 g/20 mL	50%	4 mEq/mL

Store at 20 to 25ºC (68 to 77ºF). [See USP Controlled Room Temperature.]

Revised: January, 2005

 EN-0823 Printed in USA

HOSPIRA, INC., LAKE FOREST, IL 60045 USA