MAGNESIUM SULFATE- magnesium sulfate heptahydrate injection, solution
Henry Schein, Inc.

50% Magnesium Sulfate 5 g/mL Injection, USP 10 mL PreFilled Syringe

Ansyr Plastic Syringe
Rx Only

Description

Ansyr™ Plastic Syringe

Rx Only

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. Must be diluted before intravenous use. May contain sulfuric acid and/or sodium hydroxide for pH adjustment. The pH is 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) and is intended only for use as a single-dose injection. When smaller doses are required the unused portion should be discarded with the entire unit.

Magnesium Sulfate, USP heptahydrate is chemically designated $mgSO_4 \bullet 7H_2O$ with molecular weight of 246.48 and occurs as colorless crystals or white powder freely soluble in water.

The plastic syringe is molded from a specially formulated polypropylene. Water permeates from inside the container at an extremely slow rate which will have an insignificant effect on solution concentration over the expected shelf life. Solutions in contact with the plastic container may leach out certain chemical components from the plastic in very small amounts; however, biological testing was supportive of the safety of the syringe material.

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 are often 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 (CNS), but it does not adversely affect the woman, fetus or neonate when used as directed in eclampsia or pre-eclampsia. Normal plasma magnesium levels range from 1.5 to 2.5 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 may also occur at this or lower plasma levels of magnesium. Serum magnesium concentrations in excess of 12 mEq/L may be fatal.

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.

Pharmacokinetics

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 to 7.5 mEq/liter. Magnesium is excreted solely by the kidneys 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 mEq/liter) and the serum calcium (Ca++) level is normal (4.3 to 5.3 mEq/liter) or elevated.

In total parenteral nutrition (TPN), 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 for the prevention and control of seizures (convulsions) in pre-eclampsia and eclampsia, respectively.

Contraindications

Parenteral administration of the drug is contraindicated in patients with heart block and myocardial damage.

Warnings

FETAL HARM: Continuous administration of magnesium sulfate beyond 5 to 7 days to pregnant women can lead to hypocalcemia and bone abnormalities in the developing fetus. These bone abnormalities include skeletal demineralization and osteopenia. In addition, cases of neonatal fracture have been reported. The shortest duration of treatment that can lead to fetal harm is not known. Magnesium sulfate should be used

during pregnancy only if clearly needed. If magnesium sulfate is given for treatment of preterm labor, the woman should be informed that the efficacy and safety of such use have not been established and that use of magnesium sulfate beyond 5 to 7 days may cause fetal abnormalities.

ALUMINUM TOXICITY: 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.

Parenteral use in the presence of renal insufficiency may lead to magnesium intoxication. Intravenous use in the eclampsia should be reserved for immediate control of life-threatening convulsions.

Precautions

General

Administer with caution if flushing and sweating occurs. When barbiturates, narcotics or other hypnotics (or systemic anesthetics) are to be given in conjunction with magnesium, their dosage should be adjusted with caution because of additive CNS depressant effects of magnesium.

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 or more during the four hours preceding each dose. 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). When repeated doses of the drug are given parenterally, knee jerk reflexes should be tested before each dose and if they are absent, no additional magnesium should be given until they return. Serum magnesium levels usually sufficient to control convulsions range from 3 to 6 mg/100 mL (2.5 to 5 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 intravenous 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.

Laboratory Tests

Magnesium sulfate injection should not be given unless hypomagnesemia has been

confirmed and the serum concentration of magnesium is monitored. The normal serum level is 1.5 to 2.5 mEq/L.

Drug Interactions

CNS Depressants — When barbiturates, narcotics or other hypnotics (or systemic anesthetics), or other CNS depressants are to be given in conjunction with magnesium, their dosage should be adjusted with caution because of additive CNS depressant effects of magnesium. CNS depression and peripheral transmission defects produced by magnesium may be antagonized by calcium.

Neuromuscular Blocking Agents — Excessive neuromuscular block has occurred in patients receiving parenteral magnesium sulfate and a neuromuscular blocking agent; these drugs should be administered concomitantly with caution.

Cardiac Glycosides — Magnesium sulfate should be administered with extreme caution in digitalized patients, because serious changes in cardiac conduction which can result in heart block may occur if administration of calcium is required to treat magnesium toxicity.

Pregnancy (See WARNINGS and PRECAUTIONS)

Teratogenic Effects

Magnesium sulfate can cause fetal abnormalities when administered beyond 5 to 7 days to pregnant women. There are retrospective epidemiological studies and case reports documenting fetal abnormalities such as hypocalcemia, skeletal demineralization, osteopenia and other skeletal abnormalities with continuous maternal administration of magnesium sulfate for more than 5 to 7 days.1-10 Magnesium sulfate injection should be used during pregnancy only if clearly needed. If this drug is used during pregnancy, the woman should be apprised of the potential harm to the fetus.

Nonteratogenic Effects

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

Labor and Delivery

Continuous administration of magnesium sulfate is an unapproved treatment for preterm labor. The safety and efficacy of such use have not been established. The administration of magnesium sulfate outside of its approved indication in pregnant women should be by trained obstetrical personnel in a hospital setting with appropriate obstetrical care facilities.

Nursing Mothers

Since magnesium is distributed into milk during parenteral magnesium sulfate administration, the drug should be used with caution in nursing women.

Geriatrics

Geriatric patients often require reduced dosage because of impaired renal function. In patients with severe impairment, dosage should not exceed 20 grams in 48 hours. Serum magnesium should be monitored in such patients.

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 reflect 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.

For Treatment of Overdose

Artificial respiration is often required. Intravenous calcium, 10 to 20 mL of a 5% solution (diluted if desirable with isotonic sodium chloride for injection) is used to counteract effects of hypermagnesemia. Subcutaneous physostigmine, 0.5 to 1 mg may be helpful.

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

Dosage of magnesium sulfate must be carefully adjusted according to individual requirements and response, and administration of the drug should be discontinued as soon as the desired effect is obtained.

Both intravenous and intramuscular administration are appropriate. Intramuscular administration of the undiluted 50% solution results in therapeutic plasma levels in 60 minutes, whereas intravenous doses will provide a therapeutic level almost immediately. The rate of intravenous injection should generally not exceed 150 mg/minute (1.5 mL of a 10% concentration or its equivalent), except in severe eclampsia with seizures (see below). Continuous maternal administration of magnesium sulfate in pregnancy beyond 5 to 7 days can cause fetal abnormalities.

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% or less concentration prior to such injection in children.

In Magnesium Deficiency

In the treatment of mild magnesium deficiency, the usual adult dose is 1 gram, 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 32.5 mEq of magnesium per 24 hours). For severe hypomagnesemia, as much as 250 mg

(approximately 2 mEq) per kg of body weight (0.5 mL of the 50% solution) may be given intramuscularly within a period of four hours if necessary. Alternatively, 5 grams, (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 the treatment of deficiency states, caution must be observed to prevent exceeding the renal excretory capacity.

In Hyperalimentation

In total parenteral nutrition, maintenance requirements for magnesium are not precisely known. The maintenance dose used in adults ranges from 8 to 24 mEq (1 gram to 3 grams) daily; for infants, the range is 2 to 10 mEq (0.25 gram to 1.25 grams) daily.

In Pre-eclampsia or Eclampsia

In severe pre-eclampsia or eclampsia, the total initial dose is 10 grams to 14 grams of magnesium sulfate. Intravenously, a dose of 4 grams to 5 grams 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 gram (5 grams to 10 mL of the undiluted 50% solution in each buttock) are given. Alternatively, the initial intravenous dose of 4 grams 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 grams to 5 grams (8 to 10 mL of the 50% solution) are injected intramuscularly into alternate buttocks every four hours as needed, depending on the continuing presence of the patellar reflex and adequate respiratory function. Alternatively, after the initial intravenous dose, some clinicians administer 1 gram to 2 grams/hour by constant intravenous infusion. 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 grams to 40 grams should not be exceeded. In the presence of severe renal insufficiency, the maximum dosage of magnesium sulfate is 20 grams/48 hours and frequent serum magnesium concentrations must be obtained. Continuous use of magnesium sulfate in pregnancy beyond 5 to 7 days can cause fetal abnormalities.

Other Uses

In counteracting the muscle-stimulating effects of barium poisoning, the usual dose of magnesium sulfate is 1 gram to 2 grams given intravenously.

For controlling seizures associated with epilepsy, glomerulonephritis or hypothyroidism, the usual adult dose is 1 gram administered intramuscularly or intravenously.

In paroxysmal atrial tachycardia, magnesium should be used only if simpler measures have failed and there is no evidence of myocardial damage. The usual dose is 3 grams to 4 grams (30 to 40 mL of a 10% solution) administered intravenously over 30 seconds with *extreme caution*.

For reduction of cerebral edema, 2.5 grams (25 mL of a 10% solution) is given intravenously.

Incompatibilities

Magnesium sulfate in solution may result in a precipitate formation when mixed with solutions containing:

Alcohol (in high concentrations)	Heavy Metals
Alkali carbonates and bicarbonates	Hydrocortisone sodium succinate
Alkali hydroxides	Phosphates
Arsenates	Polymixin B sulfate
Barium	Procaine hydrochloride
Calcium	Salicylates
Clindamycin phosphate	Strontium
	Tartrates

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The potential incompatibility will often be influenced by the changes in the concentration of reactants and the pH of the solutions.

It has been reported that magnesium may reduce the antibiotic activity of streptomycin, tetracycline and tobramycin when given together.

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

How Supplied

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

NDC No.	Container	Total Amount	Concentration	mEq Mg^{++}/mL
0409-1754-10	Ansyr™ Plastic Syringe	5 g/10 mL	50%	4 mEq/mL

Do not administer unless solution is clear and container is undamaged. Discard unused portion. Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.]

Product repackaged by: Henry Schein, Inc., Bastian, VA 24314

From Original Manufacturer/Distributor's NDC and Unit of Sale	To Henry Schein Repackaged Product NDC and Unit of Sale	Total Strength/Total Volume (Concentration) per unit
NDC 0409-1754-10 10 Ansyr™ Plastic Syringes in a Package	NDC 0404-9903-10 1 single-dose Ansyr™ Plastic Syringe in a bag (Syringe bears NDC 0409-1754-15)	50% 5 g/10 mL 4 mEq/mL

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3. Nassar AH, Sakhel K, Maarouf H, et al. Adverse maternal and neonatal outcome of prolonged course of magnesium sulfate tocolysis. *Acta Obstet Gynecol Scan.* 2006;85(9):1099-103.
4. Malaeb SN, Rassi A, Haddad MC. Bone mineralization in newborns whose mothers received magnesium sulphate for tocolysis of premature labor. *Pediatr Radiol.* 2004;34(5):384-6. Epub 2004 Feb 18.
5. Matsuda Y, Maeda Y, Ito M, et al. Effect of magnesium sulfate treatment on neonatal bone abnormalities. *Gynecol Obstet Invest.* 1997;44(2):82-8.
6. Schanler RJ, Smith LG, Burns PA. Effects of long-term maternal intravenous magnesium sulfate therapy on neonatal calcium metabolism and bone mineral content. *Gynecol Obstet Invest.* 1997;43(4):236-41.
7. Santi MD, Henry GW, Douglas GL. Magnesium sulfate treatment of preterm labor as a cause of abnormal neonatal bone mineralization. *J Pediatr Orthrop.* 1994;14(2):249-53.
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12. Riaz M, Porat R, Brodsky NL, et al. The effects of maternal magnesium sulfate treatment on newborns: a prospective controlled study. *J. Perinatol.* 1998;18(6 pt 1):449-54.

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SAMPLE PACKAGE LABEL

MAGNESIUM SULFATE

magnesium sulfate heptahydrate injection, solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0404-9903(NDC:0409-1754)
Route of Administration	INTRAMUSCULAR, INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
Magnesium Sulfate Heptahydrate (UNII: SK47B8698T) (Magnesium Cation - UNII:T6V3LHY838)	Magnesium Sulfate Heptahydrate	500 mg in 1 mL

Inactive Ingredients	
Ingredient Name	**Strength**
SULFURIC ACID (UNII: O40UQP6WCF)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
WATER (UNII: 059QF0KO0R)	

Packaging				
#	Item	Package Description	Marketing	Marketing

#	Code	Package Description	Start Date	End Date
1	NDC:0404-9903-10	1 in 1 BAG	01/12/2022	
1		10 mL in 1 SYRINGE, PLASTIC; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA075151	01/12/2022	

Labeler - Henry Schein, Inc. (012430880)

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