Magnesium Sulfate INJECTION, USP

Pharmacokinetics
With IV administration the onset of anticonvulsant action is immediately hastened about 30 minutes. Following IM administration, the onset of action occurs in about one hour and lasts for two to four hours. Effective anticonvulsant serum levels range from 2.5 to 7.5 mEq/L. Magnesium is excreted slowly 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 situations where profound magnesium deficiency may be accompanied by signs of tetany similar to those observed in hypocalcemia. In such cases, the serum magnesium level is usually below the lower limit of normal (1.5 to 2.5 mEq/L) and the serum calcium level is normal (4.3 to 4.7 mEq/L) 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 is also indicated for the prevention and control of seizures in pre-eclampsia, respectively.

CONTRAINDICATIONS:
Parenteral administration of the drug is contraindicated in patients with heart block or myocardial damage.

WARTINGS:
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. Bone abnormalities include skeletal demineralization and osteopenia. In addition, calcium and magnesium withdrawal syndrome has been reported. The shortest duration of treatment that can lead to fetal harm is not known. Magnesium sulfate should be used only if clear need is evident. If magnesium sulfate is given for treatment of preterm labor, the patient 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 cause anemia. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly at risk. Patients may be iron deficient and require large amounts of aluminum and phosphorus 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 aluminum toxicity. IV use in eclampsia should be reserved for immediate control of life-threatening convulsions.

PRECAUTIONS:
General
Administer with caution if flushing and sweating occur. When magnesium or other hypnotics (or systemic anesthetics) are to be given in conjunction with magnesium, their dosage should be adjusted with regard to the 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/min). 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/L). If serum magnesium levels of 10 mEq/L are increased, stop administering magnesium.

As plasma magnesium rises above 4 mEq/L, the deep tendon reflexes are first decreased and then disappear as the plasma level approaches 10 mEq/L. At this level respiratory paralysis may occur. Heart block also may occur at this or lower plasma levels of magnesium. Serum magnesium concentrations exceeding 12 mEq/L may be fatal. Magnesium acts peripherally to produce vasodilation. With low doses only flushing and sweating occur. With larger doses cause lowering of blood pressure. The central and peripheral effects of magnesium poisoning are thought to be caused to some extent by IV administration of calcium.

Laboratory Tests
Magnesium sulfate injection should not be given unless hypomagnesemia has been confirmed and the serum concentration of magnesium is monitored. A 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 concurrently with caution.

Cardiac Glycosides—Magnesium sulfate should be administered with extreme caution in digitalized patients, because serious changes in cardiac conduc-
tivity can result. Furthermore, if magnesium or calcium administration if calcium is required to treat magnes-
inium toxicity.

Pregnancy
Teratogenic Effects:

Pharmacology Category D (see WARNINGS and PRECAUTIONS).

See WARNINGS and PRECAUTIONS.

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, and increased fractures in newborns of mothers who received magnesium sulfate for more than 5 to 7 days.3 10 Magnesium sulfate injection should be used during pregnancy only if clearly needed and if maternal magnesium sulfate is required. During pregnancy, the woman should be apprised of the potential hazard to the fetus.

Nonteratogenic Effects:
When administered by continuous IV infusion (espe-
cially for more than 24 hours or when delivering to control convulsions in a toxiemic woman, the newborn may show signs of magnesium toxicity, including neuromuscular or respiratory depression (see OVERDOSAGE).

Laboratory Tests
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 sul-
fate 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 par-
ental 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 of renal function, serum magnesium levels 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/L). If serum magnesium levels of 10 mEq/L are increased, stop administering magnesium.

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, respiratory collapse, cardiac and CNS 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. In addition, the cessation of the patient’s breathing may occur. In the absence of an effective artificial respirator, the clinical sign to detect the onset of magnesium intoxication. In the event of overdosage, artificial ventilation and/or sodium hydroxide may have been added to neutralize the effect of the drug. Any solution containing magnesium sulfate injection should be discarded as soon as the desired effect is obtained.

In Pre-eclampsia or Eclampsia
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 only if clear need is evident. 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.

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WARTINGS:
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**MAGNESIUM SULFATE**

**DESCRIPTION:**
Magnesium sulfate injection should be used during pregnancy only if clearly needed. If this drug is used during pregnancy, the mother should be warned of the hazards of magnesium intoxication in eclampsia.

**CONTRAINDICATIONS:**
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**PRECAUTIONS:**
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**CLINICAL PHARMACOLOGY:**
Magnesium sulfate injection should be used during pregnancy only if clearly needed. If this drug is used during pregnancy, the mother should be warned of the hazards of magnesium intoxication in eclampsia.

**INDICATIONS AND USAGE:**
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**Dosage and Administration:**
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**INCOMPATIBILITIES:**
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**REFERENCES:**
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