

MAGNESIUM SULFATE IN DEXTROSE- magnesium sulfate heptahydrate injection, solution

Mylan Institutional LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use MAGNESIUM SULFATE IN 5% DEXTROSE INJECTION safely and effectively. See full prescribing information for MAGNESIUM SULFATE IN 5% DEXTROSE INJECTION.

MAGNESIUM SULFATE IN DEXTROSE injection, for intravenous use

Initial U.S. Approval: 1941

INDICATIONS AND USAGE

Magnesium Sulfate in 5% Dextrose Injection is indicated for (1):

- Prevention of eclampsia in patients with preeclampsia (1)
- Treatment of seizures and prevention of recurrent seizures in patients with eclampsia (1)

DOSAGE AND ADMINISTRATION

- Administer via intravenous infusion pump (2.1)
- Recommended loading dosage is 4 grams to 6 grams over 15 minutes followed by a recommended maintenance dosage of 1 gram to 2 grams every hour; maximum recommended dosage is 30 grams to 40 grams over 24 hours (2.2)
- Obtain serum magnesium concentrations and assess clinical status to adjust the dose (2.2)
- Administration beyond 5 to 7 days is not recommended (2.2, 5.1)
- In patients with severe renal impairment and/or urine output less than 0.5 mL/kg/hour, administer a 4 gram loading dose followed by a maintenance dosage of 1 gram every hour; do not exceed the maximum recommended dosage of 20 grams over 48 hours (2.3)
- Do not administer Magnesium Sulfate in 5% Dextrose Injection with incompatible drugs through the same intravenous line, specifically with salicylates and alkali carbonates (2.4)

DOSAGE FORMS AND STRENGTHS

Supplied in premixed single-dose bags: (3)

- 0.01 grams/mL (1%) in 100 mL bag containing 1 gram of Magnesium Sulfate in 5% Dextrose Injection, USP

CONTRAINDICATIONS

- Heart block or myocardial damage (4)
- Diabetic coma (4)
- Myasthenia gravis (4, 5.6)

WARNINGS AND PRECAUTIONS

- Fetal-neonatal toxicity with prolonged use: Administration beyond 5 to 7 days is not recommended and can lead to hypocalcemia and bone abnormalities (2.2, 5.1)
- Risk of magnesium toxicity: Monitor magnesium concentrations and clinical signs of magnesium toxicity including respiratory depression, an injectable calcium salt should be immediately available to counteract hazards, for significant toxicity stop Magnesium Sulfate in 5% Dextrose Injection (5.2)
- Risk of elevated blood glucose: Solutions containing dextrose should be used with caution in patients with known prediabetes or diabetes mellitus (5.3)
- Co-administration with unapproved tocolytics: Do not use concomitantly with beta adrenergic agents such as terbutaline and calcium channel blockers such as nifedipine (5.4)
- Aluminum toxicity: Aluminum may reach toxic concentrations with prolonged parenteral administration in patients with renal impairment (5.5)
- Exacerbation of Myasthenia Gravis: Use is contraindicated because use in patients with underlying myasthenia gravis can precipitate a myasthenic crisis (5.6)

----- **ADVERSE REACTIONS** -----

The most common adverse reactions are flushing, sweating, hypotension, depressed reflexes, flaccid paralysis, hypothermia, circulatory collapse, cardiac and central nervous system (CNS) depression proceeding to respiratory paralysis and hypocalcemia. Bradycardia, pulmonary edema, decreased respiratory rate, lethargy, sedation, somnolence, visual disturbances, and hypermagnesemia are also reported (6)

To report SUSPECTED ADVERSE REACTIONS, contact Mylan at 1-877-446-3679 (1-877-4-INFO-RX) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----- **DRUG INTERACTIONS** -----

- Neuromuscular blocking agents: Potentiation and prolongation of neuromuscular blockade is possible with the concomitant use of Magnesium Sulfate in 5% Dextrose Injection (7)
- Narcotics and/or propofol: Potentiation and prolongation of analgesia and CNS depression is possible with the concomitant use of Magnesium Sulfate in 5% Dextrose Injection (7)
- Dihydropyridine calcium channel blockers: An exaggerated hypotensive response is possible with the concomitant use of Magnesium Sulfate in 5% Dextrose Injection (7)
- Drugs that may induce magnesium loss with concomitant use of Magnesium Sulfate in 5% Dextrose Injection: Alcohol, aminoglycosides, amphotericin B, cisplatin, cyclosporine, digitalis, loop diuretics, and thiazide diuretics (7)

----- **USE IN SPECIFIC POPULATIONS** -----

Patients with severe renal impairment and/or a urine output less than 100 mL every 4 hours are at greater risk for increased magnesium concentrations that may lead to toxicity (8.6)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 6/2019

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Magnesium Sulfate in 5% Dextrose Injection is indicated for:

- Prevention of eclampsia in patients with preeclampsia
- Treatment of seizures and prevention of recurrent seizures in patients with eclampsia

2 DOSAGE AND ADMINISTRATION

2.1 Important Administration Instructions

Magnesium Sulfate in 5% Dextrose Injection is:

- A clear solution. Visually inspect Magnesium Sulfate in 5% Dextrose Injection for particulate matter and discoloration prior to administration. Do not administer unless solution is clear and colorless.
- For intravenous use only
- Administered via intravenous infusion pump

Magnesium Sulfate in 5% Dextrose Injection does not require dilution prior to intravenous administration.

After removing the overwrap, check for minute leaks by squeezing the container fully. Do not administer Magnesium Sulfate in 5% Dextrose Injection if there is a leak or there is greater than 2 mL of water in the overwrap [see Description (11)].

Do not administer Magnesium Sulfate in 5% Dextrose Injection with incompatible drugs through the same intravenous line [see Dosage and Administration (2.4)]. Do not use Magnesium Sulfate in 5% Dextrose Injection in series connections.

2.2 Recommended Dosage

- The recommended loading dosage of Magnesium Sulfate in 5% Dextrose Injection in patients with eclampsia or preeclampsia is 4 grams to 6 grams over 15 minutes followed by a recommended maintenance dosage of 1 grams to 2 grams every hour.
- Obtain serum magnesium concentrations and assess clinical status to adjust the dosage.
- In patients with eclampsia, consider targeting the maintenance dosage to achieve serum magnesium concentrations of 3 mg to 6 mg per 100 mL (2.5 to 5 mEq per liter). For patients with recurrent eclampsia, consider giving an additional 2 gram intravenous bolus.
- For patients with eclampsia, therapy should continue until seizures cease.
- The maximum recommended dosage is 30 grams to 40 grams of magnesium sulfate over 24 hours.
- Administration of Magnesium Sulfate in 5% Dextrose Injection beyond 5 to 7 days is not

recommended [see *Warnings and Precautions (5.1)*].

2.3 Dosage in Patients with Severe Renal Impairment and/or Oliguria

- In patients with severe renal impairment and/or a urine output less than 0.5 mL/kg/hour, initiate Magnesium Sulfate in 5% Dextrose Injection with a 4 gram loading dose followed by a maintenance dosage of 1 gram every hour.
- Titrate the magnesium sulfate maintenance dosage to maintain concentrations in the target range through frequent monitoring of magnesium concentrations and observation for clinical signs of magnesium toxicity (e.g., facial edema, diminished strength of deep tendon reflexes, respiratory depression). A lower maintenance dosage requirement is likely in these patients.
- Do not exceed the maximum recommended dosage of 20 grams of Magnesium Sulfate in 5% Dextrose Injection over 48 hours.

2.4 Drug Incompatibilities

Magnesium Sulfate in 5% Dextrose Injection is not compatible with administration of a variety of solutions and forms precipitates of magnesium salts. Before using Magnesium Sulfate in 5% Dextrose Injection with another parenteral product, investigate potential incompatibilities. Incompatible products that should not be coadministered include salicylates and alkali carbonates.

3 DOSAGE FORMS AND STRENGTHS

Magnesium Sulfate in 5% Dextrose Injection, USP is a clear and colorless solution supplied in single-dose bags:

- 0.01 grams per mL (1%):
 - 100 mL bag containing 1 gram of Magnesium Sulfate in 5% Dextrose Injection

Each 100 mL contains 5 grams of dextrose monohydrate in Water for Injection.

4 CONTRAINDICATIONS

Magnesium Sulfate in 5% Dextrose Injection is contraindicated in patients:

- with heart block or myocardial damage
- in diabetic coma
- with myasthenia gravis [see *Warnings and Precautions (5.6)*]

5 WARNINGS AND PRECAUTIONS

5.1 Fetal-Neonatal Toxicity with Prolonged Use

Continuous administration of magnesium sulfate beyond 5 to 7 days in pregnant women can lead to hypocalcemia and bone abnormalities in the developing fetus, including skeletal demineralization and osteopenia. In addition, cases of neonatal fracture have been reported.

Neonates of women receiving Magnesium Sulfate in 5% Dextrose Injection (especially with prolonged maternal use) are at risk for magnesium toxicity including hyporeflexia, hypotonia, and respiratory depression. There is one reported case of neonatal death as the result of magnesium toxicity after transplacental exposure.

The shortest duration of magnesium sulfate treatment that can lead to fetal harm is not known.

Administration of Magnesium Sulfate in 5% Dextrose Injection beyond 5 to 7 days is not recommended.

5.2 Risk of Magnesium Toxicity

Patients receiving Magnesium Sulfate in 5% Dextrose Injection are at risk for magnesium toxicity including respiratory depression, acute renal failure and rarely, pulmonary edema.

Monitor clinical signs of magnesium toxicity (for example, facial edema, diminished strength of deep tendon reflexes, respiratory depression) and magnesium concentrations during infusions of Magnesium Sulfate in 5% Dextrose Injection. 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 per minute). Serum magnesium concentrations usually sufficient to control convulsions range from 3 to 6 mg per 100 mL (2.5 to 5 mEq per liter). The strength of the deep tendon reflexes begins to diminish when serum magnesium concentrations exceed 4 mEq per liter. Reflexes may be absent at concentration of 10 mEq per liter, at which point respiratory paralysis is a potential hazard. An injectable calcium salt should be immediately available to counteract the potential hazards of magnesium toxicity in patients with preeclampsia and eclampsia. If there is significant magnesium toxicity, stop the Magnesium Sulfate in 5% Dextrose Injection infusion and recheck serum magnesium concentration.

Patients with renal impairment are at greater risk of magnesium toxicity because magnesium is excreted by the body solely by the kidneys [see *Use in Specific Populations (8.6)*]. Urine output should be maintained at a level of 100 mL per 4 hours. Monitoring serum magnesium levels and the patient's clinical status is essential to avoid the consequences of overdosage in patients with preeclampsia. Discontinuation of the magnesium infusion is recommended when urine output is less than 100 mL every 4 hours to avoid magnesium toxicity, especially if serum creatinine is increasing progressively.

5.3 Risk of Elevated Blood Glucose

Solutions containing dextrose should be used with caution in patients with known prediabetes or diabetes mellitus given the risk of elevated blood glucose.

5.4 Co-administration with Unapproved Tocolytics

Do not use Magnesium Sulfate in 5% Dextrose Injection with unapproved tocolytics (e.g., beta adrenergic agents such as terbutaline, or with calcium channel blockers such as nifedipine). Serious adverse events including pulmonary edema and hypotension have occurred [see *Drug Interactions (7)*].

5.5 Aluminum Toxicity

Magnesium Sulfate in 5% Dextrose Injection contains aluminum that may be toxic (Magnesium Sulfate in 5% Dextrose Injection contains less than 25 mcg/L of aluminum). Aluminum may reach toxic concentrations with prolonged parenteral administration in patients with renal impairment.

Patients with renal impairment who receive parenteral concentrations of aluminum at greater than 4 to 5 mcg/kg/day, accumulate aluminum at concentrations associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.

5.6 Exacerbation of Myasthenia Gravis

Magnesium Sulfate in 5% Dextrose Injection is contraindicated in patients with known myasthenia gravis.

Use of magnesium sulfate in patients with underlying myasthenia gravis can precipitate a myasthenic crisis. Myasthenic crisis is a life-threatening condition characterized by neuromuscular respiratory failure. Symptoms of myasthenic crisis may include difficulty swallowing, ptosis, facial droop, weakness and/or difficulty breathing that may require intubation.

If myasthenic crisis is suspected, discontinue use of Magnesium Sulfate in 5% Dextrose Injection immediately. Secure the patient's airway. Consider intensive care unit admission and elective intubation,

if respiratory failure is anticipated. Once the airway is secure, confirm the diagnosis. Therapies include plasmapheresis and plasma exchange or intravenous immunoglobulin (IVIG) and immunomodulating therapy in addition to high-dose glucocorticoids.

6 ADVERSE REACTIONS

The following adverse reactions have been identified in clinical studies or postmarketing reports. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Cardiovascular:	hypotension, circulatory collapse, cardiac depression including bradycardia
Central Nervous System:	central nervous system depression leading to respiratory paralysis, visual disturbances, flushing, sweating, hypothermia
Metabolic:	hypocalcemia with signs of tetany, hypermagnesemia
Neurologic:	lethargy, sedation, somnolence, myasthenic crisis
Neuromuscular:	depressed deep tendon reflexes, flaccid paralysis
Pulmonary:	decreased respiratory rate, pulmonary edema

7 DRUG INTERACTIONS

Table 1 presents the potential clinical impact of medications that may be commonly administered concomitantly with Magnesium Sulfate in 5% Dextrose Injection in the clinical setting.

Table 1: Potential Clinically Significant Drug Interactions with Magnesium Sulfate in 5% Dextrose Injection*

Neuromuscular Blocking Agents	
<i>Clinical Impact:</i>	<ul style="list-style-type: none"> Potential and prolongation of neuromuscular blockade is possible with the concomitant use of magnesium sulfate and neuromuscular blocking agents [see <i>Clinical Pharmacology (12.2)</i>]. The underlying mechanism of this interaction may involve suppression of peripheral neuromuscular function by decreasing acetylcholine release, reduction of endplate sensitivity, and decreased muscle fiber excitability with magnesium sulfate therapy.
<i>Intervention:</i>	<ul style="list-style-type: none"> Monitor respiration and the depth of neuromuscular blockade frequently (e.g., train-of-four monitoring) when a neuromuscular blocking agent is used concomitantly with Magnesium Sulfate in 5% Dextrose Injection. Adjust the dosage of the neuromuscular blocking agent accordingly to maintain the desired level of musculoskeletal activity. The amount of reversal agent(s) required to achieve adequate reversal of the neuromuscular blocking agent(s) may also be increased.
<i>Examples:</i>	<ul style="list-style-type: none"> Depolarizing neuromuscular blockers: succinylcholine Non-depolarizing neuromuscular blockers: atracurium, cisatracurium, pancuronium, rocuronium, vecuronium

Narcotics and/or Propofol	
<i>Clinical Impact:</i>	<ul style="list-style-type: none"> • Potentiation and prolongation of analgesia and CNS depression is possible with the concomitant use of Magnesium Sulfate in 5% Dextrose Injection with narcotics and/or propofol. The potential for magnesium sulfate to affect other CNS depressants is unknown [see <i>Clinical Pharmacology (12.2)</i>]. • The underlying mechanism of this interaction may involve antagonism of N-methyl-D-aspartate (NMDA) by magnesium sulfate therapy.
<i>Intervention:</i>	<ul style="list-style-type: none"> • Monitor the depth of CNS depression frequently using a reliable instrument. • Adjust the narcotic and/or propofol dosage accordingly to maintain the desired level of analgesia and sedation.
<i>Examples:</i>	<ul style="list-style-type: none"> • Narcotics and propofol
Dihydropyridine Calcium Channel Blockers	
<i>Clinical Impact:</i>	<ul style="list-style-type: none"> • An exaggerated hypotensive response is possible with the concomitant use of Magnesium Sulfate in 5% Dextrose Injection with dihydropyridine calcium channel blockers. The potential for magnesium sulfate to affect other calcium channel blockers (e.g., diltiazem and verapamil) is unknown [see <i>Clinical Pharmacology (12.2)</i>].
<i>Intervention:</i>	<ul style="list-style-type: none"> • Monitor vital signs (heart rate, blood pressure, respiration) frequently. • Supportive care and/or discontinuation of the calcium channel blocker may be required.
<i>Examples:</i>	<ul style="list-style-type: none"> • Amlodipine, clevidipine, felodipine, isradipine, nifedipine, nimodipine, and nisoldipine
Drugs that May Induce Magnesium Loss	
<i>Clinical Impact:</i>	<ul style="list-style-type: none"> • Reduced magnesium concentrations may impact efficacy
<i>Intervention:</i>	<ul style="list-style-type: none"> • Monitor magnesium concentrations frequently and adjust the Magnesium Sulfate in 5% Dextrose Injection dosage to maintain concentrations in the target range [see <i>Dosage and Administration (2)</i>].
<i>Examples:</i>	<ul style="list-style-type: none"> • Alcohol, aminoglycosides, amphotericin B, cisplatin, cyclosporine, digitalis, loop diuretics, thiazide diuretics

*For drug incompatibility information [see *Dosage and Administration (2.4)*].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Magnesium Sulfate in 5% Dextrose Injection is indicated in pregnant women for the prevention of eclampsia in women with preeclampsia and the treatment of seizures and prevention of recurrent seizures in women with eclampsia. Fetal, neonatal, and maternal risks are discussed throughout the labeling.

Clinical Considerations

Labor or Delivery:

Magnesium Sulfate in 5% Dextrose Injection is not approved for the treatment of pre-term labor.

Administration of Magnesium Sulfate in 5% Dextrose Injection to pregnant women longer than 5 to 7 days may lead to hypocalcemia and bone abnormalities in the developing fetus, including skeletal demineralization and osteopenia [see *Warnings and Precautions (5.1)*].

8.2 Lactation

The use of intravenous magnesium in pregnant women increases human milk magnesium concentrations only slightly and oral absorption of magnesium by the infant is poor. The effect of intravenous magnesium on milk production is unknown. The developmental and health benefits to the neonate of breastfeeding should be considered along with the mother's clinical need for Magnesium Sulfate in 5% Dextrose Injection and any potential adverse effects on the breastfed infant from Magnesium Sulfate in 5% Dextrose Injection or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of Magnesium Sulfate in 5% Dextrose Injection have been established for the prevention of eclampsia in adolescents with preeclampsia and the treatment of seizures and prevention of recurrent seizures in adolescents with eclampsia. Dosing recommendation in pregnant adolescent patients are the same as for pregnant adult patients [see *Dosage and Administration (2.2)*].

8.6 Renal Impairment

Magnesium is excreted solely by the kidneys. Patients with severe renal impairment (urine output less than 100 mL per 4 hours) are at greater risk for increased magnesium concentrations that may lead to magnesium toxicity [see *Warnings and Precautions (5.2)* and *Clinical Pharmacology (12.3)*]. In patients with severe renal impairment, dosage reduction is recommended and the maximum recommended dosage is lower than patients with normal renal function [see *Dosage and Administration (2.3)*].

10 OVERDOSAGE

Manifestations of magnesium toxicity include a drop in blood pressure, difficulty breathing, and disappearance of the patellar reflex. As serum magnesium rises above 4 mEq per liter, the deep tendon reflexes decrease. As the serum magnesium level approaches 10 mEq per liter, the tendon reflexes disappear and respiratory paralysis may occur [see *Warnings and Precautions (5.2)*]. Other signs and symptoms of magnesium overdosage include flushing, sweating, hypotension, weakness, hypothermia, circulatory collapse, cardiac and central nervous system depression proceeding to respiratory paralysis, cardiac arrest, and prolongation of PR and QRS intervals. Patients with renal impairment and underlying neuromuscular diseases such as myasthenia gravis may experience magnesium intoxication at lower magnesium concentrations (Magnesium Sulfate in 5% Dextrose Injection is contraindicated in patients with myasthenia gravis).

If patient is experiencing magnesium toxicity, immediately discontinue Magnesium Sulfate in 5% Dextrose Injection. Artificial respiration may be required. Administer an injectable calcium salt to counteract the potential hazards of magnesium toxicity [see *Warnings and Precautions (5.2)*].

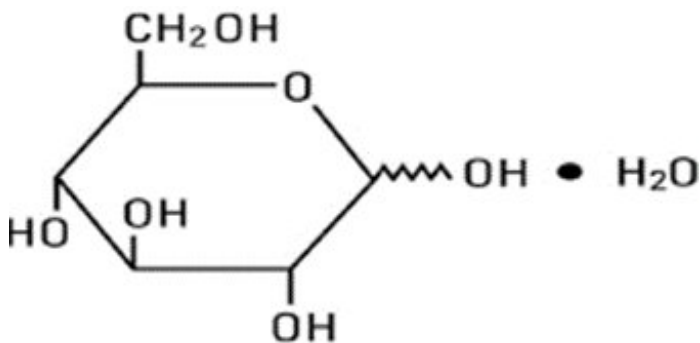
Hypermagnesemia in the newborn (after administration of Magnesium Sulfate in 5% Dextrose Injection to the mother) may require resuscitation and assisted ventilation via endotracheal intubation or intermittent positive pressure ventilation as well as intravenous calcium.

11 DESCRIPTION

Magnesium Sulfate in 5% Dextrose Injection, USP is a sterile, nonpyrogenic, clear, colorless solution of magnesium sulfate heptahydrate and dextrose in water for injection for intravenous use. Each 100 mL contains 1 gram of magnesium sulfate heptahydrate and dextrose monohydrate 5 grams in water for injection [see *How Supplied/Storage and Handling (16)*]. Magnesium Sulfate in 5% Dextrose Injection, USP may contain sulfuric acid and/or sodium hydroxide for pH adjustment. The pH is 4.5 (3.5 to 6.5).

Magnesium Sulfate, USP heptahydrate is chemically known as sulfuric acid magnesium salt (1:1), heptahydrate and chemically designated $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$, with a molecular weight of 246.47. It occurs as small colorless crystals freely soluble in water.

Dextrose, USP is chemically designated D-glucose, monohydrate, a hexose sugar freely soluble in water. The molecular formula is $\text{C}_6\text{H}_{12}\text{O}_6 \cdot \text{H}_2\text{O}$ and the molecular weight is 198.17. It has the following structural formula:



Water for Injection, USP is chemically designated H_2O .

Water can permeate from inside the flexible plastic container (polyvinylchloride) into the overwrap [see *Dosage and Administration (2.1)*] but not in amounts sufficient to affect the solution significantly. 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 plastic container materials. Exposure to temperatures above 25°C (77°F) during transport and storage will lead to minor losses in moisture content. Higher temperatures lead to greater losses. It is unlikely that these minor losses will lead to clinically significant changes within the expiration period.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Magnesium prevents seizures in patients with preeclampsia and controls seizures in patients with eclampsia by blocking neuromuscular transmission and decreasing the amount of acetylcholine liberated at the end plate by the motor nerve impulse. Magnesium has a depressant effect on the central nervous system [see *Drug Interactions (7)*]. Magnesium acts peripherally to produce vasodilation.

12.2 Pharmacodynamics

With intravenous administration of magnesium sulfate the onset of anticonvulsant action is immediate and lasts about 30 minutes. The estimated magnesium concentration (above baseline) required to elicit half-maximum effect (EC₅₀) on systolic and diastolic blood pressure in pregnant women with preeclampsia that received intravenous magnesium sulfate therapy was reported to be 1.5 and 1.8 mEq per liter (1.9 and 2.2 mg per dL), respectively, in a published study. Effective anticonvulsant serum concentrations range from 2.5 to 7.5 mEq per liter.

Drug Interaction Studies

The following information is based upon published case reports and clinical studies that could not be confirmed by an adequately controlled study, but still warrant consideration given the potential risks involved [*see Drug Interactions (7)*].

Neuromuscular Blocking Agents:

Potential and prolongation of neuromuscular blockade requiring modification of the neuromuscular blocking agent dosage and/or increased reversal agent requirements were reported in preeclamptic women who received magnesium sulfate treatment who underwent subsequent surgery (for example, caesarian section) with anesthesia that included either a depolarizing (d-tubocurarine, succinylcholine) or nondepolarizing neuromuscular blocking agent (vecuronium, rocuronium).

Narcotics and/or Propofol:

Potential and prolongation of analgesic and/or sedative effects as well as a reduced requirement for an intravenous narcotic (fentanyl, sufentanil, tramadol), intrathecal narcotic (fentanyl), and/or intravenous propofol was reported in magnesium sulfate treated patients who required surgery or intensive care that also included narcotic and/or propofol therapy.

Dihydropyridine Calcium Channel Blockers:

An exaggerated hypotensive response (blood pressure 80 to 93/49 to 60 mm Hg) was reported in preeclamptic women who received oral nifedipine in addition to magnesium sulfate treatment. Blood pressure returned to previous levels within approximately 30 minutes with supportive care.

12.3 Pharmacokinetics

Distribution

Approximately 1 to 2% of total body magnesium is located in the extracellular fluid space. Magnesium is 30% bound to albumin.

Elimination

The average half-life and systemic clearance of magnesium sulfate in preeclamptic women is approximately 4 to 5 hours and 4 to 5 liters per hour, respectively.

Excretion:

Magnesium is excreted solely by the kidney at a rate proportional to the serum concentration and glomerular filtration.

Specific Populations

Patients with Renal Impairment:

Plasma magnesium concentrations of 7 to 12.3 mEq per liter (8.6 to 15.1 mg per dL) were reported in preeclamptic women with a urine output less than 100 mL per 4 hours that received 20 grams of magnesium sulfate intravenously over 2 to 8 hours in a published study [*see Dosage and Administration (2.3)* and *Use in Specific Populations (8.6)*].

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies with Magnesium Sulfate in 5% Dextrose Injection have not been performed to evaluate carcinogenic potential, mutagenic potential or effects on fertility.

16 HOW SUPPLIED/STORAGE AND HANDLING

Magnesium Sulfate in 5% Dextrose Injection, USP is a clear, colorless solution supplied in single-dose flexible plastic containers (see Table 2).

Table 2: How Supplied Information

Magnesium Sulfate* Concentration	NDC Number	Container Size	Total Magnesium Sulfate*	Total Magnesium Ion	Magnesium Ion Concentration	Osmolarity**
0.01 grams/mL (1%)	67457-567-00	100 mL	1 gram	8.1 mEq	8.1 mEq/100 mL	333 mOsmol/liter

*As the heptahydrate; **Osmolarity was calculated

Storage

Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.] Protect from freezing.

17 PATIENT COUNSELING INFORMATION

Magnesium Sulfate in 5% Dextrose Injection is typically administered to pregnancy women in emergent situations. When feasible, advise the patient and family of the following:

Fetal-Neonatal Toxicity Reported With Prolonged Use

Continuous administration of Magnesium Sulfate in 5% Dextrose Injection in pregnant women beyond 5 to 7 days can lead to hypocalcemia and bone abnormalities in the developing fetus, including skeletal demineralization and osteopenia. In addition, cases of neonatal fracture have been reported [see *Warnings and Precautions (5.1)*].

Risk of Magnesium Toxicity

Pregnant women receiving Magnesium Sulfate in 5% Dextrose Injection are at risk for magnesium toxicity, including facial edema, diminished strength of deep tendon reflexes, and respiratory depression [see *Warnings and Precautions (5.2)*].

Manufactured for:

Mylan Institutional LLC

Rockford, IL 61103 U.S.A.

Manufactured by:

Terumo BCT Ltd

Larne, United Kingdom

JUNE 2019

PACKAGE/LABEL PRINCIPAL DISPLAY PANEL

NDC 67457-567-00

100 mL

Magnesium Sulfate in 5% Dextrose Injection, USP

(0.081 mEq Mg⁺⁺/mL)

1 g/100 mL

10 mg/mL

1 g TOTAL

For Intravenous Use

Rx only

Mylan

Each 100 mL contains: Magnesium sulfate heptahydrate 1 g (equivalent to 8.1 mEq magnesium) and dextrose monohydrate 5 g in Water for Injection. May contain sulfuric acid and/or sodium hydroxide for pH adjustment.

pH 4.5 (3.5 to 6.5) 333 mOsmol/Liter (CALC.)

DO NOT ADD SUPPLEMENTARY MEDICATION. WHENEVER POSSIBLE USE CENTRAL ROUTE.

Single-Dose Container. **Usual dosage:** See insert. Sterile, Nonpyrogenic. Use only if solution is clear. After removing the overwrap, check for minute leaks by squeezing container firmly. If leaks are found, discard unit as sterility may be impaired. Must not be used in series connections.

The overwrap is a moisture barrier. Do not remove unit from overwrap until ready for use. Use unit promptly when pouch is opened. Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.] Protect from freezing. See insert.

THE INFUSION BAG AND PORTS ARE NOT MADE WITH NATURAL RUBBER LATEX.

Manufactured in UK for:

Mylan Institutional LLC

Rockford, IL 61103 U.S.A.

NDC 67457-567-00

100 mL

Magnesium Sulfate in 5% Dextrose

Injection, USP

(0.081 mEq Mg⁺⁺/mL)
1 g/100 mL

10 mg/mL

For Intravenous Use

Rx only



 Mylan®

Each 100 mL contains: Magnesium sulfate heptahydrate 1 g (equivalent to 8.1 mEq magnesium) and dextrose monohydrate 5 g in Water for Injection. May contain sulfuric acid and/or sodium hydroxide for pH adjustment.

pH 4.5 (3.5 to 6.5) 333 mOsmol/Liter (CALC.)

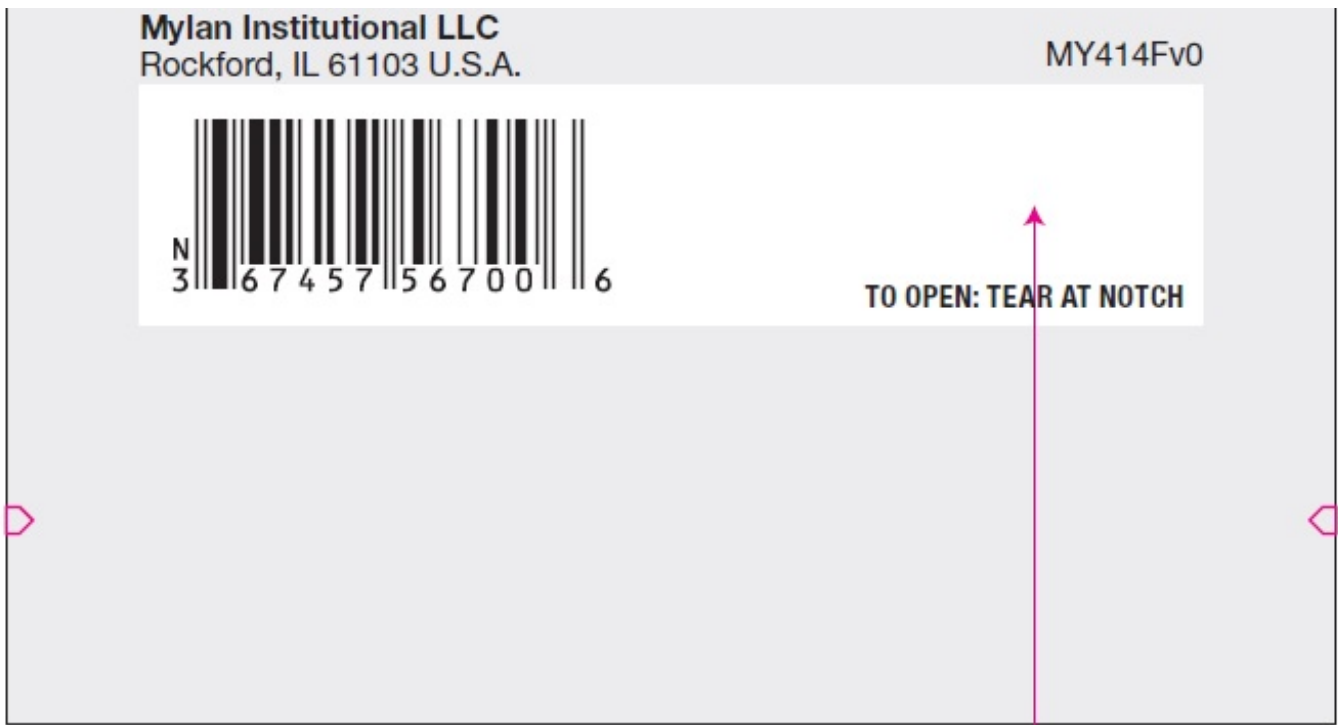
DO NOT ADD SUPPLEMENTARY MEDICATION. WHENEVER POSSIBLE USE CENTRAL ROUTE.

Single-Dose Container. **Usual dosage:** See insert. Sterile, Nonpyrogenic. Use only if solution is clear. After removing the overwrap, check for minute leaks by squeezing container firmly. If leaks are found, discard unit as sterility may be impaired. Must not be used in series connections.

The overwrap is a moisture barrier. Do not remove unit from overwrap until ready for use. Use unit promptly when pouch is opened. Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.] Protect from freezing. See insert.

THE INFUSION BAG AND PORTS ARE NOT MADE WITH NATURAL RUBBER LATEX.

Manufactured in U.K. for:



▷ Notch to tear

Overcoding Area with White Background

LOT:XXXXXXXX
EXP:mm/yyyy

PACKAGE/LABEL PRINCIPAL DISPLAY PANEL

NDC 67457-567-00

100 mL

Magnesium Sulfate in 5% Dextrose Injection, USP

(0.081 mEq Mg⁺⁺/mL)

1 g/100 mL

10 mg/mL

1 g TOTAL

For Intravenous Use

Each 100 mL contains: Magnesium sulfate heptahydrate 1 g (equivalent to 8.1 mEq magnesium) and dextrose monohydrate 5 g in Water for Injection. May contain sulfuric acid and/or sodium hydroxide for pH adjustment.

pH 4.5 (3.5 to 6.5) 333 mOsmol/Liter (CALC.)

Single-Dose Container. DISCARD UNUSED PORTION.

USUAL DOSAGE: SEE INSERT. STERILE, NONPYROGENIC. USE ONLY IF SOLUTION IS CLEAR AND CONTAINER IS UNDAMAGED. MUST NOT BE USED IN SERIES CONNECTIONS.

THE INFUSION BAG AND PORTS ARE NOT MADE WITH NATURAL RUBBER LATEX.

Manufactured in UK for:

Mylan Institutional LLC

Rockford, IL 61103 U.S.A.

Rx only

Mylan

NDC 67457-567-00

100 mL

Magnesium Sulfate in 5% Dextrose

Injection, USP

(0.081 mEq Mg⁺⁺/mL)
1 g/100 mL



10 mg/mL

For Intravenous Use

Each 100 mL contains: Magnesium sulfate heptahydrate 1 g (equivalent to 8.1 mEq magnesium) and dextrose monohydrate 5 g in Water for Injection. May contain sulfuric acid and/or sodium hydroxide for pH adjustment. pH 4.5 (3.5 to 6.5) 333 mOsmol/Liter (CALC.)

Single-Dose Container. DISCARD UNUSED PORTION.

USUAL DOSAGE: SEE INSERT. STERILE, NONPYROGENIC. USE ONLY IF SOLUTION IS CLEAR AND CONTAINER IS UNDAMAGED. MUST NOT BE USED IN SERIES CONNECTIONS.

THE INFUSION BAG AND PORTS ARE NOT MADE WITH NATURAL RUBBER LATEX.

Manufactured in U.K. for: **Mylan Institutional LLC**
Rockford, IL 61103 U.S.A.

Rx only



MY414Bv0



(01)00367457567006

Batch details to be
overcoded on suitable area

LOT:XXXXXXXX
EXP:mm/yyyy

MAGNESIUM SULFATE IN DEXTROSE

magnesium sulfate heptahydrate injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:67457-567
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
MAGNESIUM SULFATE HEPTAHYDRATE (UNII: SK47B8698T) (MAGNESIUM CATION - UNII:T6V3LHY838)	MAGNESIUM SULFATE HEPTAHYDRATE	1 g in 100 mL

Inactive Ingredients

Ingredient Name	Strength
SULFURIC ACID (UNII: O40UQP6WCF)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
DEXTROSE MONOHYDRATE (UNII: LX22YL083G)	
WATER (UNII: 059QF0K00R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:67457-567-00	1 in 1 POUCH	10/13/2020	
1		100 mL in 1 BAG; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA209932	10/13/2020	

Labeler - Mylan Institutional LLC (790384502)

Revised: 6/2019

Mylan Institutional LLC