MAGNESIUM SULFATE - magnesium sulfate heptahydrate injection, solution
Gland Pharma Limited

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MAGNESIUM SULFATE IN WATER FOR INJECTION
For Intravenous Use Only
Rx Only

DESCRIPTION
Magnesium Sulfate in Water for Injection is a sterile, nonpyrogenic solution of magnesium sulfate heptahydrate in water for injection. May contain sulfuric acid and/or sodium hydroxide for pH adjustment. The pH is 4.5 (3.5 to 6.5). It is available in 4% concentration. See HOW SUPPLIED section for the content and characteristics of available dosage forms and sizes.

Magnesium Sulfate heptahydrate, USP is chemically designated MgSO₄ • 7H₂O, colorless crystals or white powder freely soluble in water.

Water for Injection, USP is chemically designated H₂O.

The flexible plastic container is fabricated from a specially formulated polypropylene. Water can permeate from inside the container into the overwrap 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.

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

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 serum magnesium levels range from 1.3 to 2.1 mEq/liter.

As serum magnesium rises above 4 mEq/liter, the deep tendon reflexes are first decreased and then disappear as the serum level approaches 10 mEq/liter. At this level respiratory paralysis may occur. Heart block also may occur at this or lower serum 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 to 7.5 mEq/liter.

Pharmacokinetics:
Absorption: Intravenously administered magnesium is immediately absorbed.
Distribution: Approximately 1 to 2% of total body magnesium is located in the extracellular fluid
space. Magnesium is 30% bound to albumin.

**Metabolism:** Magnesium is not metabolized.

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

**Special Populations:**

**Renal Insufficiency:** Magnesium is excreted solely by the kidney. In patients with severe renal insufficiency, the dose should be lower and frequent serum magnesium levels must be obtained (see **DOSAGE AND ADMINISTRATION**).

**Hepatic Insufficiency:** Magnesium is excreted solely by the kidney. No dosing adjustments are necessary in hepatic insufficiency.

**Drug-Drug Interactions:** Drug induced renal losses of magnesium occur with the following drugs or drug classes:

- Aminoglycosides
- Amphotericin B
- Cyclosporine
- Diuretics
- Digitalis
- Cisplatin
- Alcohol

**INDICATIONS AND USAGE**

Magnesium Sulfate in Water for Injection is indicated for the prevention and control of seizures in preeclampsia and eclampsia, respectively. 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.

**CONTRAINDICATIONS**

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

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

**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 mEq/liter). The strength of the deep tendon reflexes begins to diminish when serum 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.

Magnesium Sulfate in Water for Injection should be administered slowly to avoid producing hypermagnesemia.

**Carcinogenesis, Mutagenesis, Impairment of Fertility**

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

**Pregnancy (See WARNINGS and PRECAUTIONS)**

**Teratogenic Effects:**

Magnesium Sulfate in Water for Injection 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’s, osteopenia and other skeletal abnormalities with continuous maternal administration of magnesium sulfate for more than 5-7 days.¹-¹² Magnesium Sulfate in Water for 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 IV 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 in Water for Injection 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**

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Magnesium Sulfate in Water for Injection is administered to a nursing mother.

**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 IV 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 IV calcium.

**DOSAGE AND ADMINISTRATION**

Magnesium Sulfate in Water for Injection is intended for intravenous use only. For the management of pre-eclampsia or eclampsia, intravenous infusions of dilute solutions of magnesium (1% to 8%) are often given in combination with intramuscular injections of 50% Magnesium Sulfate Injection, USP. Therefore, in the clinical conditions cited below, both forms of therapy are noted, as appropriate.

Continuous maternal administration of magnesium sulfate in pregnancy beyond 5 to 7 days can cause fetal abnormalities.

**In Eclampsia**

In severe pre-eclampsia or eclampsia, the total initial dose is 10 to 14 g of magnesium sulfate. To initiate therapy, 4 g of Magnesium Sulfate in Water for Injection may be administered intravenously. The rate of I.V. infusion should generally not exceed 150 mg/minute, or 3.75 mL of a 4% concentration (or its equivalent) per minute, except in severe eclampsia with seizures. Simultaneously, 4 to 5 g (32.5 to 40.6 mEq) of magnesium sulfate may be administered intramuscularly into each buttock using undiluted 50% Magnesium Sulfate Injection, USP. After the initial I.V. dose, some clinicians administer 1 to 2 g/hour by constant I.V. infusion.

Subsequent intramuscular doses of 4 to 5 g of magnesium sulfate may be injected into alternate buttocks every four hours, depending on the continuing presence of the patellar reflex, adequate respiratory function, and absence of signs of magnesium toxicity. 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 magnesium sulfate should not be exceeded. In the presence of severe renal insufficiency, frequent serum magnesium concentrations must be obtained and the maximum dosage of magnesium sulfate is 20 g per 48 hours.

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. Discard unused portion.

**HOW SUPPLIED**

Magnesium Sulfate in Water for Injection is supplied as clear colorless solution in single-dose flexible plastic containers as follows:
<table>
<thead>
<tr>
<th>NDC No.</th>
<th>Size Container</th>
<th>Total Magnesium Sulfate**</th>
<th>Total Magnesium Ion</th>
<th>Magnesium Sulfate** Concentration</th>
<th>Magnesium Ion Concentration</th>
<th>Osmolarity (Calc.)</th>
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<tbody>
<tr>
<td>68083-396-01</td>
<td>50 mL*</td>
<td>2 g</td>
<td>16.25 mEq</td>
<td>4% (40 mg/mL)</td>
<td>16.25 mEq/50 mL</td>
<td>325 mOsmol/Liter</td>
</tr>
<tr>
<td>68083-397-01</td>
<td>100 mL</td>
<td>4 g</td>
<td>32.5 mEq</td>
<td>4% (40 mg/mL)</td>
<td>32.5 mEq/100 mL</td>
<td>325 mOsmol/Liter</td>
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</tbody>
</table>

* Partial fill container 50 mL volume in 100 mL container.
** As the heptahydrate.

**WARNING: DO NOT USE FLEXIBLE CONTAINER IN SERIES CONNECTIONS.**

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

**REFERENCES**


Manufactured by:
Gland Pharma Limited
D.P.Pally,
Hyderabad -500043, INDIA
Revised date: December 2019

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL
NDC 68083-396-01
Magnesium Sulfate in Water for Injection
2 g/50 mL
50 mL Bag Label
Magnesium Sulfate in Water for Injection 2 g/50 mL

(0.325 mEq Mg²⁺/mL) 40 mg/mL

FOR INTRAVENOUS INFUSION

EACH 50 mL CONTAINS: MAGNESIUM SULFATE HEPTAHYDRATE 2 g (EQUIVALENT TO 16.25 mEq MAGNESIUM) IN WATER FOR INJECTION. MAY CONTAIN SULFURIC ACID AND/OR SODIUM HYDROXIDE FOR pH ADJUSTMENT.

325 mOsmol/LITER (CALC.)  pH 4.5 (3.5 TO 6.5)

DISCARD UNUSED PORTION. FOR I.V. USE. STERILE, NONPYROGENIC. USE ONLY IF SOLUTION IS CLEAR AND CONTAINER IS UNDAMAGED. MUST NOT BE USED IN SERIES CONNECTIONS.

THE BAG IS NOT MADE WITH LATEX, PVC OR DEHP.

STORE AT 20 TO 25°C (68 TO 77°F). [SEE USP CONTROLLED ROOM TEMPERATURE.] PROTECT FROM FREEZING. USUAL DOSAGE: SEE INSERT.

MANUFACTURED BY:
GLAND PHARMA LIMITED
D.P.PALLY, HYDERABAD - 500043, INDIA.
ML NO: 103/AP/RR/97/F/R

LOT:
EXP:

The prefix and variable Batch details to be printed during text matter printing
NDC 68083-396-01
Magnesium Sulfate in Water for Injection
2 g/50 mL
50 mL Pouch Label
Magnesium Sulfate in Water for Injection 2 g/50 mL

(0.325 mEq Mg++/mL) 40 mg/mL

For Intravenous Infusion

Each 50 mL contains: magnesium sulfate heptahydrate 2 g (equivalent to 16.25 mEq magnesium) in water for injection. May contain sulfuric acid and/or sodium hydroxide for pH adjustment.

325 mOsmol/Liter (CALC.)

pH 4.5 (3.5 to 6.5)

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

For I.V. Use. 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.] Avoid excessive heat. Protect from freezing. Usual Dosage: See insert.

The Bag is not made with natural rubber latex, PVC or DEHP.

Manufactured by:
Gland Pharma Limited
D.P.Pally, Hyderabad - 500043, INDIA.
ML No: 103/AP/RR/97/F/R
NDC 68083-397-01
Magnesium Sulfate in Water for Injection
4 g/100 mL
100 mL Bag Label
Magnesium Sulfate in Water for Injection 4 g/100 mL

(0.325 mEq Mg²⁺/mL) 40 mg/mL

FOR INTRAVENOUS INFUSION

EACH 100 mL CONTAINS: MAGNESIUM SULFATE HEPTAhydrate 4 g (EQUIVALENT TO 32.5 mEq MAGNESIUM) IN WATER FOR INJECTION. MAY CONTAIN SULFURIC ACID AND/OR SODIUM HYDROXIDE FOR pH ADJUSTMENT.

325 mOsmol/LITER (CALC.) pH 4.5 (3.5 TO 6.5)

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THE BAG IS NOT MADE WITH LATEX, PVC OR DEHP.

STORE AT 20 TO 25°C (68 TO 77°F). [SEE USP CONTROLLED ROOM TEMPERATURE.] PROTECT FROM FREEZING. USUAL DOSAGE: SEE INSERT.

MANUFACTURED BY:
GLAND PHARMA LIMITED
D.P.PALLY, HYDERABAD - 500043, INDIA.
ML No: 01/RR/AP/2008/LVP/R

LOT:
EXP:

The prefix and variable Batch details to be printed during text matter printing.
NDC 68083-397-01
Magnesium Sulfate in Water for Injection
4 g/100 mL
100 mL Pouch Label
Magnesium Sulfate in Water for Injection 4 g/100 mL

(0.325 mEq Mg^{++}/mL) 40 mg/mL

For Intravenous Infusion

Each 100 mL contains: magnesium sulfate heptahydrate 4 g (equivalent to 32.5 mEq magnesium) in water for injection. May contain sulfuric acid and/or sodium hydroxide for pH adjustment.

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

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D.P.Pally, Hyderabad - 500043, INDIA.
ML No: 01/RR/AP/2008/LVP/R
MAGNESIUM SULFATE
magnesium sulfate heptahydrate injection, solution

Product Information
Product Type: HUMAN PRESCRIPTION DRUG
Item Code (Source): NDC:68083-396
Route of Administration: INTRAVENOUS

Active Ingredient/Active Moiety

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<th>Ingredient Name</th>
<th>Basis of Strength</th>
<th>Strength</th>
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<tr>
<td>MAGNESIUM SULFATE HEPTAHYDRATE (UNII: SK47B8698T) (MAGNESIUM CATION - UNII:T6V3LHY838)</td>
<td>MAGNESIUM SULFATE HEPTAHYDRATE</td>
<td>2 g in 50 mL</td>
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Inactive Ingredients

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<tr>
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<td>SULFURIC ACID (UNII: 040UQP6WCF)</td>
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<td>WATER (UNII: 059QF0KO0R)</td>
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Packaging

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<td>NDC:68083-396-01</td>
<td>24 in 1 CASE</td>
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<td>07/10/2020</td>
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<tr>
<td>1</td>
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<td>1 in 1 POUCH</td>
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<td>50 mL in 1 BAG; Type 9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)</td>
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<td>ANDA213917</td>
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**MAGNESIUM SULFATE**
magnesium sulfate heptahydrate injection, solution

### Product Information

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**Labeler** - Gland Pharma Limited (918601238)

### Establishment

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<th>Name</th>
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Revised: 7/2020