MAGNESIUM SULFATE IN 5% DEXTROSE- magnesium sulfate heptahydrate injection, solution
Fresenius Kabi USA, LLC

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Magnesium Sulfate in 5% Dextrose Injection, USP

For Intravenous Use Only
Rx only

DESCRIPTION
Magnesium Sulfate in 5% Dextrose Injection, USP is a sterile, nonpyrogenic solution of magnesium sulfate heptahydrate and dextrose in water for injection. Each 100 mL contains 1 g magnesium sulfate heptahydrate and dextrose, hydrous 5 g 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 a 1% concentration. See HOW SUPPLIED section for the content and characteristics of available dosage form and size.

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

Dextrose, USP is chemically designated D-glucose, monohydrate, a hexose sugar freely soluble in water. It has the following structural formula:

![Dextrose Structural Formula](image)

C₆H₁₂O₆ • H₂O M.W. 198.17

Water for injection, USP is chemically designated H₂O.

The flexible container is fabricated from a specially formulated non-plasticized, film containing polypropylene and thermoplastic elastomers (freeflex® bag). The amount of water that can permeate from the container into the overwrap is insufficient to affect the solution significantly. Solutions in contact with the flexible container can leach out certain of the container’s chemical components in very small amounts within the expiration period. The suitability of the container material has been confirmed by tests in animals according to USP biological tests for plastic containers. 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 5% dextrose injection, USP is indicated for the prevention and control of seizures in pre-eclampsia and eclampsia, respectively. When used judiciously it effectively prevents and controls the convulsions of eclampsia without producing deleterious depression of the central nervous system.
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 5% dextrose injection, USP should be administered slowly to avoid producing hypermagnesemia.

Carcinogenesis, Mutagenesis, Impairment of Fertility
Studies with magnesium sulfate in 5% dextrose injection, USP have not been performed to evaluate carcinogenic potential, mutagenic potential or effects on fertility.

Pregnancy
Teratogenic Effects
Pregnancy Category D (see WARNINGS and PRECAUTIONS)
See WARNINGS and PRECAUTIONS.

Magnesium sulfate in 5% dextrose injection, USP 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 demineralizations, osteopenia and other skeletal abnormalities with continuous maternal administration of magnesium sulfate for more than 5 to 7 days. Magnesium sulfate in 5% dextrose injection, USP 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 5% dextrose injection, USP 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 5% dextrose injection, USP is administered to a nursing woman.

**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 5% dextrose injection, USP 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 Pre-eclampsia or 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 5% dextrose injection, USP may be administered intravenously. The rate of IV infusion should generally not exceed 150 mg/minute, or 7.5 mL of a 2% 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 IV dose, some clinicians administer 1 to 2 g/hour by constant IV 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 recommended 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 5% Dextrose Injection, USP is supplied in a single-dose flexible plastic container as follows:

<table>
<thead>
<tr>
<th>Product Code</th>
<th>Unit of Sale</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>
<th>Unit of Use</th>
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<tbody>
<tr>
<td>610801</td>
<td>NDC 63323-108-01 Packages of 24</td>
<td>1 g</td>
<td>8.1 mEq</td>
<td>1% (10 mg/mL)</td>
<td>8.1 mEq/100 mL</td>
<td>333 m0smol/Liter</td>
<td>NDC 63323-108-00 100 mL fill in a 100 mL freeflex Bag</td>
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*As the heptahydrate.

WARNING: DO NOT USE FLEXIBLE CONTAINER IN SERIES CONNECTIONS.

The container closure is not made with natural rubber latex. Non-PVC, Non-DEHP, Sterile.

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

REFERENCES

4. Malaeb SN, Rassi A, Haddad MC. Bone mineralization in newborns whose mothers received

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Manufactured for:

www.fresenius-kabi.com/us

Made in Norway

451340B

Revised: November 2018

**PACKAGE LABEL - PRINCIPAL DISPLAY PANEL - Magnesium Sulfate 100 mL Foil Overwrap**
Magnesium Sulfate
in 5% Dextrose Injection, USP

1g total in 100 mL
(0.081 mEq Mg²⁺/mL)
10 mg per mL

For Intravenous Infusion
Rx Only

USE IMMEDIATELY ONCE REMOVED FROM OVERWRAP.

Each 100 mL of sterile solution contains: Magnesium Sulfate
Heptahydrate 1 g (equivalent to 8.1 mEq magnesium) and dextrose,
hydrous 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 Use Only — Discard Unused Portion.

Usual dosage: see insert. Use only if solution is clear and container
is undamaged.

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

After removing the overwrap, check for leaks by squeezing container.
If leaks are found, discard, as sterility may be impaired.

Overwrap is a moisture barrier and is heat-sterilized.

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

The container closure is not made with natural rubber latex.
Non-PVC, Non-DEHP, Sterile.

Manufactured for:

Fresenius Kabi USA, LLC
Lake Zurich, IL 60047
Made in Norway

To Open Overwrap — Tear at Notch
Magnesium Sulfate in 5% Dextrose Injection, USP

1 g total in 100 mL (0.081 mEq Mg^{++}/mL) 10 mg per mL

For Intravenous Infusion

Rx only
Magnesium Sulfate
in 5% Dextrose Injection, USP

1 g total in 100 mL

(0.081 mEq Mg²⁺/mL) 10 mg per mL

For Intravenous Infusion  Rx Only

Each 100 mL of sterile solution contains:
Magnesium Sulfate Heptahydrate 1 g
(equivalent to 8.1 mEq magnesium) and
dextrose, hydrous 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 Use Only — Discard Unused Portion.

Usual dosage: see insert. Use only if solution
is clear and container is undamaged.
The container closure is not
made with natural rubber latex. Non-PVC, Non-
DEHP, Sterile.

Manufactured for:
Fresenius Kabi USA, LLC
Lake Zurich, IL 60047  402855C
Made in Norway  01-69-13-001  1234567890

PACKAGE LABEL - PRINCIPAL DISPLAY Magnesium Sulfate 100 mL Bag Case Label

Product No. 610801

Magnesium Sulfate in 5% Dextrose Injection, USP

1 g total in 100 mL (10 mg per mL)

NDC 63323-108-01 Rx only
# Product Information

**Product Type**
- HUMAN PRESCRIPTION DRUG

**Route of Administration**
- INTRAVENOUS

## Active Ingredient/Active Moiety

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<td>MAGNESIUM SULFATE HEPTAhydrate</td>
<td>1 g in 100 mL</td>
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## Inactive Ingredients

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### Packaging

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### Marketing Information
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**Labeler** - Fresenius Kabi USA, LLC (608775388)

**Establishment**

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<td>731170932</td>
<td>manufacture(63323-108), analysis(63323-108)</td>
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Revised: 12/2019