For the use only of registered medical practitioners or a hospital or a laboratory

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Magnesium Sulphate Intravenous Infusion 4% w/v

iv-Mag™

1. Generic Name: Magnesium Sulphate Intravenous Infusion 4% w/v

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:
Each 100 ml contains:
Magnesium Sulphate Heptahydrate..... 4g
(equivalent to 32.5 mEq of Magnesium)
Excipients..... qs
Water for injection..... qs to 100ml

3. DOSAGE FORM AND STRENGTH
Solution for Intravenous Infusion 4% w/v

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
Magnesium sulphate intravenous infusion is indicated for the prevention and control of seizures in pre-eclampsia and eclampsia, respectively. When used judiciously it effectively prevents and controls convulsions of eclampsia without producing deleterious depression of the central nervous system of the mother or infant.

4.2 Posology and method of administration
This formulation 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 sulphate injection. Therefore, in the clinical conditions cited below, both forms of therapy are noted, as appropriate. Continuous maternal administration of magnesium sulphate 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 sulphate. To initiate therapy, 4 g of magnesium sulphate intravenous infusion may be administered intravenously. The rate of IV 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 sulphate may be administered intramuscularly into each buttock using an undiluted 50% magnesium sulphate injection. 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 sulphate 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 the control of seizures. A total daily (24 hr) dose of 30 to 40 g magnesium sulphate should not be exceeded. In the presence of severe renal insufficiency, frequent serum magnesium concentrations must be obtained and the maximum dosage of magnesium sulphate 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 a solution is clear. Discard unused portions.

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

4.4 Special warnings and precautions for use
WARNINGS:
FETAL HARM: Continuous administration of magnesium sulphate 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 sulphate should be used during pregnancy only if clearly needed. If magnesium sulphate is given for the 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 sulphate 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 over dosage in toxemia. Clinical indications of a safe dosage regimen include the presence of the patellar reflex (knee jerk) and the absence of a respiratory depression (approximately 16 breaths or more/minute). Serum magnesium levels are 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 sulphate intravenous infusion should be administered slowly to avoid producing hypermagnesemia.

4.5 Drug Interactions
Drug induced renal losses of magnesium occur with the following drugs or drug classes:
Aminoglycosides
Cyclosporine
Digitalis
Alcohol
Amphotencin B
Diuretics
Cisplatin

4.6 Use in special population (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)
Teratogenic Effects:
Magnesium sulphate intravenous infusion, 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 sulphate for more than 5 to 7 days. Magnesium sulphate intravenous infusion 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 sulphate is an unapproved treatment for preterm labor. The safety and efficacy of such use have not been established. The administration of magnesium sulphate intravenous infusion 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 sulphate intravenous infusion is administered to a nursing mother.

Paediatric & Geriatric population:
There is no relevant use.

4.7 Effects on ability to drive and use machines
Not relevant.

4.8 Undesirable effects:
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 sulphate therapy for eclampsia has been reported.

4.9 Overdose
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.

5. PHARMACOLOGICAL PROPERTIES
5.1 Mechanism of Action
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.

5.2 Pharmcodynamics
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 a 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.

5.3 Pharmakokinetics
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.

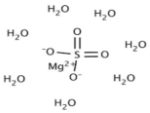
Excretion
Magnesium is excreted solely by the kidney at a rate proportional to the serum concentration and glomerular filtration.

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.

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

6. NON CLINICAL PROPERTIES
6.1 Animal Toxicology or Pharmacology
Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.

7. DESCRIPTION
Drug Substance: Magnesium Sulphate Heptahydrate
Chemical Name: Magnesium Sulphate Heptahydrate
Chemical Structure:



Chemical Formula: $MgSO_4, 7H_2O$
Molecular Weight: 246.47
Drug Product: Magnesium Sulphate Intravenous Infusion (4% w/v)
A clear colourless liquid free from visible particles.

8. PHARMACEUTICAL PARTICULARS.
8.1 Incompatibilities
In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

8.2 Shelf life
24 Months

8.3 Packaging information
100 ml LDPE bottle.

8.4 Storage and handling instructions.
Store at a temperature not exceeding 30°C. Do not Freeze.

9. PATIENT COUNSELING INFORMATION
The active substance in this product is magnesium sulphate heptahydrate.
This medicine will be given to the patient as an infusion into a vein.
Magnesium sulphate intravenous infusion is indicated

- to control and prevent seizures in severe pre-eclampsia (a serious complication of pregnancy characterized by high blood pressure and protein in your urine);
- to control and prevent recurrent seizures in eclampsia (convulsions as a result of pre-eclampsia).

Do not use this medicine if the patient is allergic to magnesium sulphate.
Please inform the doctor if the patient has any liver, kidney or heart problems.
In general, healthcare professionals may counsel their patients and/or their relatives about the special warnings and precautions for use, drug interactions, undesirable effects, and any relevant contra-indications of the medicine. Patients may also be informed about posology, method of administration and storage/handling Information as applicable.

10. DETAILS OF MANUFACTURER
M/s Precise Biopharma Pvt. Ltd.
At. Plot No.876, N.H. No.8, Village Hariyala, Tal.Matar, Dist. Kheda-387411, Gujarat.

11. DETAILS OF PERMISSION NUMBER WITH DATE
Permission No.: MF/SND/22/000130 Date: 11.05.2022

12. DATE OF REVISION: NA

13. MARKETED BY:
Blisson Medica Pvt. Ltd.
Gala No.: 9, Building I-3, Shree Arihant Compound, Kopar, Bhiwandi, Thane - 421302.
Corporate Office:
E-311, EBD, Neptune Mall, LBS Road, Bhandup (W), Mumbai - 400 078, India.

For reporting suspected adverse drug reactions, email pvglobal@precisegroup.co.in