Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

Magnesium sulfate 50% Inresa

Concentrate for solution for injection or infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One 10 ml ampoule contains:

5.0 g magnesium sulfate heptahydrate, equivalent to 493 mg magnesium ions (equivalent to 20.25 mmol Mg).

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Concentrate for solution for injection or infusion

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Pre-eclampsia, eclampsia

4.2 Posology, method and duration of administration

Posology

Pre-eclampsia and eclampsia: initial dose:
4 g magnesium sulfate heptahydrate IV for 5 – 15 min.; maintenance dose: 1 g/hour for 24 hours (infusion)

Method and duration of administration:

Concentrate for solution for infusion for IV use

Do not administer Magnesium sulfate 50% Inresa concentrate for solution for infusion undiluted into peripheral veins. For slow intravenous injection, a 20% solution (e.g. 1 ampoule + 15 ml solution for dilution) should be made, whilst a 2% solution (2 ampoules + 480 ml solution for dilution) should be made for continuous intravenous infusions.
As a solution for dilution, 5% glucose, 5% xylitol or 0.9% sodium chloride solutions are suitable. It is recommended that patients be allowed to rest for a further 10 - 20 minutes after the injection.

4.3 Contraindications

Marked bradycardia (slow heart beat), myasthenia gravis (muscle weakness) and AV block (disruption of the heart's impulse conduction system) or other cardiac conduction disturbances and diathesis for infection stones (calcium, magnesium ammonium phosphate stones), severe renal dysfunction, anuria, dehydration.

Magnesium sulfate 50% Inresa should not be co-administered with barbiturates, narcotics or hypnotics, due to the risk of respiratory depression.

4.4 Special warnings and precautions for use

To be used only with special caution in patients with mild to moderately pronounced renal insufficiency.

See also 4.9 Overdose.

4.5 Interaction with other medicinal products and other forms of interaction

The effect of magnesium is reduced (antagonism) upon concomitant IV administration of calcium salts. Muscle relaxants of the curare type potentiate the effect of magnesium on the motor end plate. Diuretics, aminoglycoside antibiotics (such as gentamycin, tobramycin, amphotericin B), immunosuppressants (such as ciclosporin A) and cytostatics (such as cisplatin) and digitalis glycosides cause increased excretion of magnesium via the kidneys. Interaction with nifedipine should furthermore be taken into consideration, which can lead to severe hypotension and neuromuscular blockade.

For more details, see also under 4.3 Contraindications.

4.6 Pregnancy and lactation

There is no evidence of a risk of malformation. However, documented experience in humans is limited with regard to use during early pregnancy. Therefore, Magnesium sulfate 50% Inresa should only be used during pregnancy after a careful benefit/risk assessment.

If magnesium is administered shortly before childbirth, the newborn infant should be monitored during the first 24 – 48 hours of life for signs of toxicity (neurological depression with respiratory depression, muscle weakness, loss of reflexes).

4.7 Effects on ability to drive and use machines

Magnesium sulfate 50% Inresa has no influence on the ability to drive and use machines.

4.8 Undesirable effects

The following categories are used for stating the frequency of undesirable effects:

Very common (≥ 1/10)

Common (≥ 1/100 to < 1/10)

Uncommon (≥ 1/1,000 to < 1/100)

Rare (≥ 1/10,000 to < 1/1,000)

Very rare (< 1/10,000)

Not known (cannot be estimated from the available data)

Very common: flushing

Common: nausea or vomiting, muscle weakness, absent or reduced tendon reflexes, respiratory depression, reactions at the injection site (pain, burning, swelling, inflammation)

Uncommon: thirst, headache; hypotension, heart palpitations, tachycardia; dizziness, drowsiness or confusion, itching or tingling

In addition, the following may occur: skin rash, hyperkalaemia, prolonged bleeding time as well as visual disturbances.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the *Bundesinstitut für Arzneimittel und Medizinprodukte (*Federal Institute for Drugs and Medical Devices)*, Abt. Pharmakovigilanz (*Department of Pharmacovigilance), Kurt-Georg-Kiesinger-Allee 3, D-53175 Bonn, website: www.bfarm.de.

4.9 Overdose

a) Symptoms of intoxication

Magnesium intoxication is unlikely when renal function is intact and at the dosage stated. If magnesium intoxication should nevertheless occur, the following symptoms can be observed (see Table):

Mg plasma concentration in mmol/l	Possible symptoms, possible undesirable effects
> 1.5	Decrease in blood pressure, retching, vomiting
> 2.5	CNS depression
> 3.5	Hyporeflexia, ECG changes
> 5.0	Incipient respiratory depression
> 5.5	Coma
> 7.0	Cardiac arrest, Respiratory paralysis

b) Treatment of intoxication

Reduction of the dose or discontinuation of the medication leads to rapid regression of the undesirable effects.

As an immediate measure (antidote), a slow intravenous calcium injection (10 – 20 ml of a 10% calcium gluconate solution) can be used.

See also 4.6 Pregnancy and lactation

With high-dose magnesium sulfate therapy, the following must be checked:

1. Monitoring of cardiovascular function

2. Patellar tendon reflexes (knee tendon reflexes); these must be maintained. Dose reduction if they are no longer responsive.

3. The respiratory rate should be no less than 16 breaths/min.

4. Urine output should be 25 ml per hour or 100 ml per 4 hours. If it is any lower, there is a risk of hypermagnesaemia (excessive high magnesium concentrations in the blood).

5. As an antidote, 10% calcium gluconate ampoules must be readily available.

6. If the antidote is not sufficient in life-threatening conditions, intensive care measures must be taken.

To be used only with special caution in patients with mild to moderately pronounced renal insufficiency.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: magnesium preparation

ATC code: A12CC02

A decrease in the plasma magnesium concentration is followed by increased excitability of the central nervous system and even seizures and disorientation or psychotic syndromes. Magnesium deficiency promotes a tendency for preterm labour and gestosis. High magnesium concentrations cause flaccid paralysis of the musculoskeletal system. This is due to a reduction in acetylcholine release at the neuromuscular end plates. A relaxant effect is also achieved by magnesium ions on the smooth muscles. On the heart, the effect of magnesium ions is equivalent to that of potassium ions. High concentrations (20 – 30 mmol/l plasma) prolong the conduction time; higher concentrations lead to diastolic cardiac arrest. Hypomagnesaemic tetany can be abolished by magnesium ions, but not by calcium ions. Magnesium plays a role in a large number of biochemical reactions, the most important being its involvement as a co-factor in all enzymes that may be associated with nucleotide-dependent transphosphorylation reactions.

5.2 Pharmacokinetic properties

Normal values for magnesium serum concentrations are within the range of 0.75 - 1.1 mmol/1.

Distribution in organs and tissues

In the adult human body, reserves of magnesium are approximately 100 mg, half of which is found in bone. Approximately 45% is found inside cells and 5% in the extracellular fluid. The intracellular concentration varies between 10 and 60 mmol/l, whilst that in plasma is between 3 and 4.4 mmol/l. Of this, ⅔ are present as free Mg^{2+} ions and ⅓ is bound to proteins.

Elimination

Renal magnesium excretion is rapidly adjusted to the supply of magnesium. Normally, about 1.5 mg/kg/day is excreted with the urine. Following parenteral administration, a half-life of almost 4 hours can be assumed.

5.3 Preclinical safety data

There is no available information of relevance to safety other than the statements made in other sections of this prescribing information.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections, 95 – 98% sulphuric acid for pH adjustment

6.2 Incompatibilities

The solution for injection should not be mixed with solutions containing calcium or phosphate, or with alkaline solutions (risk of precipitation).

6.3 Shelf life

The shelf life is 5 years.
After opening the ampoule, the concentrate for solution for injection or infusion must be used immediately.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Original packs with 5 ampoules and 50 ampoules (hospital pack), each with 10 ml concentrate for solution for injection or infusion

Original packs with 10 ampoules and 100 ampoules (hospital pack), each with 10 ml concentrate for solution for injection or infusion

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Inresa Arzneimittel GmbH
Obere Hardtstrasse 18
D-79114 Freiburg

8. MARKETING AUTHORISATION NUMBER

6914444.00.00

9. DATE OF AUTHORISATION

07/01/2008

10. DATE OF REVISION OF THE TEXT

July 2024

11. GENERAL CLASSIFICATION FOR SUPPLY

Only available from pharmacies