Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Magnesium Sulfate 50 % w/v Solution for Injection/Concentrate for solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1ml contains Magnesium Sulfate Heptahydrate 0.5g (2mmol Mg 2+)
2ml contains Magnesium Sulfate Heptahydrate 1g (4mmol Mg 2+)
5ml contains Magnesium Sulfate Heptahydrate 2.5g (10mmol Mg 2+)
10ml contains Magnesium Sulfate Heptahydrate 5g (20mmol Mg 2+)

Excipients with known effect

Each ml solution for injection/Concentrate for solution for infusion contains 3.54mg of sodium

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for Injection
Concentrate for solution for infusion
Clear, colourless sterile solution

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of Magnesium deficiency in hypomagnesaemia.
To prevent further seizures associated with eclampsia.

4.2 Posology and method of administration

Dosage should be individualised according to patient's needs and responses.
Plasma levels should also be monitored throughout therapy.

a) Treatment of magnesium deficiency in hypomagnesaemia:

Up to 40g $MgSO_4$ (equivalent to 160mmol Mg^{2+}) by slow intravenous infusion (in glucose 5%) over up to 5 days, may be required to replace the deficit (allowing for urinary losses).

b) To prevent further seizures associated with eclampsia:
An initial intravenous (IV) loading dose is followed for 24h by either an IV infusion, or regular intramuscular (IM) injections.

Intramuscular Maintenance Regimen

A loading dose of 4g $MgSO_4$ (approx. 16mmol Mg^{2+}) IV (usually in 20% solution) over 5min (minimum, preferably 10-15 min) is followed immediately by 5g $MgSO_4$ (approx. 20mmol Mg^{2+}) (usually in 50% solution) as a deep IM injection into the upper outer quadrant of each buttock.

Maintenance therapy is a further 5g $MgSO_4$ (approx. 20mmol Mg^{2+}) IM every 4h, continued for 24h after the last fit (provided the respiratory rate is >16/min, urine output >25ml/h, and knee jerks are present).
Intravenous Maintenance Regimen

A loading dose of 4g $MgSO_4$ (approx. 16mmol Mg^{2+}) IV (or in some cases 5g $MgSO_4$ (approx. 20mmol Mg^{2+}) IV), as described above, is followed by an infusion of 1g/h continued for 24h after the last fit.

Recurrent Convulsions: In both the IM and IV regimens, if convulsions recur, a further 2-4g $MgSO_4$ (approx. 16mmol Mg^{2+}) (depending on the woman's weight, 2g $MgSO_4$ (approx. 8mmol Mg^{2+}) if less than 70Kg) is given IV over 5 min.

Appropriate reductions in dosage should be made for patients with renal impairment; a suggested dose reduction in severe renal impairment is a maximum of 20g $MgSO_4$ (approx. 80mmol Mg^{2+}) over 48 hours

4.3 Contraindications

Hypersensitivity to magnesium and its salts or to any of the excipients listed in section 6.1.
Magnesium sulfate is contraindicated in patients with hepatic encephalopathy, hepatic failure or renal failure, myasthenia gravis or cardiac disease.

4.4 Special warnings and precautions for use

Magnesium salts should be administered with caution to patients with impaired renal function; appropriate reductions in dosage should be made (Refer to 'section 4.2' above). Magnesium salts should also be administered with caution to those receiving digitalis glycosides. Parenteral administration of magnesium salts may enhance the effects of neuromuscular blocking agents or of central nervous system depressants.

For intramuscular use a 25% or 50% solution is used. For intravenous use this solution must be diluted before use. Concentrations of up to 20% are usually employed.

Magnesium sulfate should not be used in hepatic coma if there is risk of renal failure.

Magnesium sulfate 50% w/v Solution for Injection/Concentrate for solution for infusion contains Sodium
This medicine contains less than 1 mmol sodium (23mg) per ml, that is to say essentially sodium free

4.5 Interaction with other medicinal products and other forms of interaction

Muscle Relaxants: non-depolarising muscle relaxants such as tubocurarine are enhanced by parenteral magnesium salts.
Nifedipine: profound hypotension was produced in two women who were given oral Nifedipine.

4.6 Fertility, pregnancy and lactation

In the medical situation of a patient having Eclampsia, Magnesium Sulfate can be administered to relieve this condition, which may be life threatening to mother and baby.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Excessive administration of magnesium leads to the development of hypermagnesaemia. Symptoms of hypermagnesaemia may include nausea, vomiting, flushing of the skin, thirst, hypotension due to peripheral vasodilatation, drowsiness, confusion, loss of tendon reflexes due to neuromuscular blockade, muscle weakness, respiratory depression, cardiac arrhythmias, coma, and cardiac arrest.

Acute ingestion of Magnesium Sulfate and similar magnesium-containing compounds may also cause gastrointestinal irritation and watery diarrhoea.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Appropriate action should be taken to reduce the blood level of magnesium to avoid hypermagnesaemia. Neuromuscular blockade associated with hypermagnesaemia may be reversed with calcium salts, such as Calcium Gluconate, which should be administered intravenously in a dose equivalent to 2.5 to 5mmol of calcium.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Mineral Supplements,
ATC code: A12CC 02.

Serum magnesium levels in the range of 1.5 - 2.5mmol/l cause vasodilatation in the peripheral and coronary circulation, and corresponding increases of 20-25% in cardiac output and coronary blood flow. There is little change in heart rate or blood pressure. The Atrium-His interval is slightly prolonged as a result of the electrophysiological actions of magnesium. Any direct inhibition is offset by the reflex response to a drop in peripheral vascular resistance, and the Q- T interval is unchanged, thus the function of the SAN is little altered. Within this concentration range there are no detectable effects on CNS function or neuromuscular transmission.

At a serum magnesium level of 1-3mmol/l platelet disaggregation has been reported; possibly mediated by stimulation of prostacyclin release from vascular endothelium.

5.2 Pharmacokinetic properties

The concentration of magnesium in plasma is normally tightly regulated in the range of 0.75-0.95mmol/l.

Small and clinically irrelevant amounts are excreted in breast milk. The major excretory pathway of magnesium is renal, and both oral and intravenous loads are rapidly eliminated in this way. In renal impairment there may be accumulation of magnesium.

The potential for magnesium toxicity is greater in parenteral administration than with oral dosing.

At plasma concentrations of up to 4mmol/l, the only adverse effect likely to be seen is flushing due to peripheral vasodilatation. At about 4-5mmol/l, concentration-dependant toxicity is heralded by loss of deep-tendon reflexes, then successively by hypotension, bradycardia and ultimately neuromuscular blockade leading to respiratory arrest.

When given intravenously, Magnesium Sulphate has an immediate onset of action, and its duration of activity is about 30 mins. The onset of action of intramuscular magnesium sulphate is about one hour, and its duration of action is three to four hours.

5.3 Preclinical safety data

This product has been available for many years and its side effects and clinical profile are well-understood, therefore no further data is provided.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for Injections

Hydrochloric Acid
Sodium Hydroxide

6.2 Incompatibilities

Magnesium sulfate is incompatible with alkali hydroxides (forming insoluble magnesium hydroxide), alkali carbonates (forming insoluble magnesium carbonate) and salicylates. Streptomycin sulfate and Tetramycin sulfate activity is inhibited by magnesium ions.

6.3 Shelf life

Unopened: 3 years
The product should be used immediately after opening

6.4 Special precautions for storage

Do not store above 25ºC.

6.5 Nature and contents of container

Neutral Type 1 glass ampoules 2, 5 and 10ml, containing a 50% w/v sterile solution for injection of Magnesium Sulfate. 10 ampoules are packed in a carton.

6.6 Special precautions for disposal and other handling

For intramuscular use a 25% or 50% solution is used. For intravenous use, this solution must be diluted before use. Concentrations of up to 20% are usually employed.

Magnesium Sulfate Injection must be diluted prior to administration by intravenous infusion. The following infusion fluids may be used: - 5% dextrose in water. 0.9% Sodium Chloride and Water for Injections.

For single use only
Discard any unused contents

7 MARKETING AUTHORISATION HOLDER

Ethypharm
194 Bureaux de la Colline - Bâtiment D
92213 Saint-Cloud Cedex
France

8 MARKETING AUTHORISATION NUMBER

PA0549/020/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26th May 2006
Date of last renewal: 25th May 2011

10 DATE OF REVISION OF THE TEXT

February 2023