SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Magnesium Sulfate 20% w/v solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Magnesium sulfate heptahydrate 200 mg/ml (approximately 0.8 mmol Mg^{2+}/ml)

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion.

Clear and colourless solution, pH 5.5 - 7.0.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of magnesium deficiency in hypomagnesaemia.

Prevention of recurrent seizures in eclampsia.

4.2 Posology and method of administration

Posology

Dosage should be tailored according to the individual patient's needs and responses. Plasma magnesium concentrations should be measured to determine the rate and duration of infusion and should be monitored throughout therapy.

Treatment of magnesium deficiency in hypomagnesaemia

Up to 40 g or 160 mmols of magnesium ions (200ml of a 20% solution) by slow intravenous infusion (in glucose 5%) over up to 5 days, may be required to replace the deficit (allowing for urinary losses).

Elderly

No special recommendation. Use with caution due to risk of renal impairment in this age group, see below.

Renal impairment

Doses must be reduced in renal impairment. Caution must be observed to prevent exceeding the renal excretory capacity. The dosage should not exceed 20g in 48 hours (100ml of a 20% solution or 80mmols of magnesium ions).

Prevention of recurrent seizures in eclampsia

A loading dose of 4g (16 mmols) of magnesium ions IV (20ml of a 20% solution) or in some cases 5g (20 mmols) og magnesium ions IV (25 ml of a 20% solution), given over 5-15 minutes, is followed by an infusion of 1g (4mmols)/h (5ml of a 20% solution) continued for 24h after the last fit.

Recurrent Convulsions: If convulsions recur, a further 2-4g (8-16 mmols) of magnesium ions (10-20 ml of a 20% solution,depending on the woman's weight, 2g (8 mmols) 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 (80 mmols of magnesium ions) over 48 hours.

For instructions on dilution of the product before administration, see section 6.6.

Paediatric population

No special recommendation.

Method of administration

Intravenous infusion.

4.3 Contraindications

Hypersensitivity to magnesium and its salts.

Renal failure.

Hepatic encephalopathy, hepatic failure.

Parenteral magnesium salts should generally be avoided in patients with heart block.

4.4 Special warnings and precautions for use

Magnesium salts should be administered with caution to patients with impaired renal function and appropriate dosage reduction should be made. See section 4.2.

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

Respiratory depression may occur and caution is required in patients with respiratory disease.

Parenteral magnesium should be used with caution in individuals with myasthenia gravis, to prevent an exacerbation of the condition or the precipitation of a myasthenic crisis. A risk-benefit assessment should be performed in individual cases prior to initiation of treatment.

Serum calcium levels should be routinely monitored in patients receiving magnesium sulfate.

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.

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. The neuromuscular blocking effects of parenteral magnesium and aminoglycoside antibacterials may be additive.

CNS Depressants: When barbiturates, opiates, general anaesthetics, or other CNS depressants are administered concomitantly with magnesium sulfate, dosage of these agents must be carefully adjusted because of the additive central depressant effects.

Intravenous calcium will antagonise the effects of magnesium.

The muscle stimulating effects of barium toxicity are reduced by magnesium.

4.6 Fertility, pregnancy and lactation

Pregnancy

As eclampsia may be life-threatening to mother and baby, magnesium sulfate may be administered in this condition.

Magnesium crosses the placenta and may produce hypotonia, hypoflexia, hypotension. If administered during labour it may cause respiratory depression of the newborn infant. When used in pregnant women, fetal heart rate should be monitored and use within 2 hours of delivery should be avoided.

Magnesium sulfate can cause skeletal adverse effects when administered continuously for more than 5 to 7 days to pregnant women. There are retrospective epidemiological studies and case reports documenting fetal adverse effects including hypocalcaemia, skeletal demineralization, osteopenia and other skeletal adverse effects with maternal administration of magnesium sulfate for more than 5 to 7 days. The clinical significance of the observed effects is unknown.

If prolonged or repeated exposure to magnesium sulfate occurs during pregnancy monitoring of neonates for abnormal calcium or magnesium levels and skeletal adverse effects should be considered.

Breastfeeding

Safety during breast feeding has not been established. Therefore, as with all drugs, it is not advisable to administer magnesium sulfate during breastfeeding unless considered essential.

Fertility

There is no information on the effects of magnesium sulfate on fertility.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Immune system disorders

Hypersensitivity reactions.

Excessive administration of magnesium leads to the development of symptoms of hypermagnesaemia which may include:

Metabolism and Nutritional disorders

Electrolyte/fluid abnormalities (hypophosphataemia, hyperosmolar dehydration)

There have been isolated reports of maternal and fetal hypocalcaemia with high doses of magnesium sulfate (see section 4.6).

Nervous system disorders

Respiratory depression

Nausea, vomiting, drowsiness and confusion

Coma

Slurred speech, double vision

Cardiac disorders

Cardiac arrhythmias, cardiac arrest

ECG changes (prolonged PR, QRS and QT intervals), bradycardia

Vascular disorders

Flushing of the skin and hypotension due to peripheral vasodilatation

Musculoskeletal and connective tissue disorders

Loss of tendon reflexes due to neuromuscular blockade, muscle weakness

Other undesirable effects

Thirst

There have been isolated reports of maternal and foetal hypocalcaemia with high doses of magnesium sulfate.

Especially in patients with impaired renal function, there may be sufficient accumulation of magnesium sulfate to produce toxic effects.

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 Yellow Card Scheme.

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Signs

Clinical signs of overdosage will be those of hypermagnesaemia, see section 4.8.

Treatment

Appropriate action should be taken to reduce the blood level of magnesium. 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: electrolyte solutions, ATC code: B05XA05.

Mechanism of action

Magnesium is the second most abundant cation in intracellular fluid and is an essential body electrolyte. It is a cofactor in numerous enzyme systems and is involved in phosphate transfer, muscle contractility and neuronal transmission.

The precise site of action of magnesium sulfate in eclampsia is not known. Experimentally, magnesium has been shown to block the NMDA subtype of glutamate channel through which calcium enters the cell and causes neuronal damage during cerebral ischaemia. Ischaemia leads to lowering of the transmembrane potential allowing calcium ion influx across the membrane and from the endoplasmic reticulum and mitochondria. This leads to further calcium influx as membrane phospholipids are hydrolysed by activated enzymes. Magnesium blocks calcium at intracellular sites in addition to the outer lipid membrane.

Pharmacodynamic effects

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.

Clinical efficacy and safety

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

Distribution

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

When given intravenously, Magnesium Sulfate has an immediate onset of action, and its duration of activity is about 30mins.

Elimination

Small and clinically irrelevant amounts of magnesium are excreted in milk. The major excretory pathway is renal and parenteral loads are rapidly eliminated in this way. In renal impairment, there may be accumulation of magnesium. Faecal loss is very limited; small amounts are excreted in saliva and magnesium crosses the placenta.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber additional to those already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections.

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

The product must be used immediately after the opening of the container and the storage of opened ampoules should be avoided.

6.5 Nature and contents of container

Transparent and colourless 10 ml or 20 ml glass ampoule type I. The ampoules are inserted into polypropylene blisters and packed in carton boxes. Each carton box contains 10 ampoules of 10 ml or 5 ampoules of 20 ml.

6.6 Special precautions for disposal

Magnesium sulfate can be diluted with Glucose 5% and Sodium chloride 0.9% solutions.

Disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Synchrony Pharma Limited
3 Bunhill Row
London
EC1Y 8YZ
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 39280/0007

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

21/03/2018

10 DATE OF REVISION OF THE TEXT

31/05/2023