SUMMARY OF PRODUCT CHARACTERISTICS

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1 NAME OF THE MEDICINAL PRODUCT

Magnesium Sulfate 50%w/v Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Magnesium Sulfate Heptahydrate	5g/ 10ml	2.5g/ 5ml	1g/ 2ml

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Sterile Solution for Injection

A clear, colourless solution practically free from visible particles

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

- Treatment of Magnesium deficiency where the oral route of administration may be inappropriate.

- 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:
For intravenous administration, a concentration of 20% or less should be used; the rate of injection not exceeding 1.5ml/minute of a 10% solution or its equivalent.

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).

Mild magnesium deficiency
1g intramuscularly every 6 hours for 4 doses.

Severe magnesium deficiency
Up to 250mg/kg intramuscularly given within a period of 4 hours or 5g/litre of infusion solution intravenously over 3 hours

Paedriatric population
It is recommended that the solution be diluted to 20% w/v prior to intramuscular injection

Elderly
No special recommendation except in renal impairment, see below

Renal impairment:
Dosage should be reduced in renal impairment. Plasma magnesium concentrations should be monitored throughout therapy

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).

<u>Intravenous Maintenance Regimen</u>

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. 8 - 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.

**** The Eclampsia Trial Collaborative Group (Duley L et al) (1995) Which anticonvulsant for women with eclampsia? Evidence from the Collaborative Eclampsia Trial., The Lancet, Vol. 345, pp. 1455-1463.***

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.

Method of administration
Magnesium sulfate injection may be administered by intramuscular or intravenous routes.
Intramuscular therapy should be used only when peripheral venous access is impossible.

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 severely impaired renal function.

4.4 Special warnings and precautions for use

Magnesium sulfate must be used with caution in patients suspected of or known to have renal impairment.

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

Parenteral magnesium salts should be used with caution in patients with myasthenia gravis.

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

4.5 Interaction with other medicinal products and other forms of interaction

Administer with caution to patients receiving digitalis glycosides. Magnesium sulfate should not be administered concomitantly with high doses of barbiturates, opiods or hypnotics due to the risk of respiratory depression.

The action of non-depolarising muscle relaxants such as tubocurarine is potentiated and prolonged by parenteral magnesium salts.

Concomitant use of calcium channel blockers such as nifedipine or nimodipine may rarely lead to a calcium ion imbalance and could result in abnormal muscle function.
The neuromuscular blocking effects of parenteral magnesium and aminoglycoside antibacterials may be additive.

4.6 Fertility, pregnancy and lactation

Safety in human pregnancy has not been established, however, in the medical emergency of a patient having Eclampsia, Magnesium Sulfate can be administered to relieve this condition, which may be life threatening to both mother and baby.
As with all drugs it is not advisable to administer magnesium sulfate during pregnancy or breastfeeding unless considered essential, and it must be administered under medical supervision.

Magnesium crosses the placenta. When used in pregnant women, foetal heart rate should be monitored and use within 2 hours of delivery should be avoided.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects

Hypersensitivity reactions
Hypocalcaemia

Hypermagnesaemia characterised by flushing, thirst, hypotension, drowsiness, nausea, vomiting, confusion, slurred speech, double vision, loss of tendon reflexes due to neuromuscular blockade, muscle weakness, respiratory depression, electrolyte/fluid abnormalities (hypophosphataemia, hyperosmolar dehydration), ECG changes (prolonged PR, QRS and QT intervals), bradycardia, cardiac arrhythmias, coma and cardiac arrest.

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 at: www.mhra.gov.uk/yellowcard.

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.

Magnesium is the second most abundant cation in intracellular fluid and is an essential body electrolyte. Magnesium is a factor in a number of enzyme systems, and is involved in neurochemical transmission and muscular excitability.
Parenterally administered magnesium sulfate exerts a depressant effect on the central nervous system and acts peripherally to produce vasodilation.

5.2 Pharmacokinetic properties

Following intravenous administration, the onset of action is immediate and the duration approximately 30 minutes. Following intramuscular administration the onset of action occurs after approximately one hour and the duration of action is 3-4 hours.

Magnesium sulfate is excreted by the kidneys with small amounts being excreted in breast milk and saliva.

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

Streptomycin sulfate and tetramycin sulfate activity is inhibited by magnesium ions.

6.3 Shelf life

3 years

Discard any unused solution immediately after first use.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage time and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8^{o}C, unless dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Do not store above 25^{O}C.

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.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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.

Discard any unused solution at the end of the session in the appropriate manner.

7 MARKETING AUTHORISATION HOLDER

Aurum Pharmaceuticals Ltd
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8 MARKETING AUTHORISATION NUMBER(S)

PL 12064/0013

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 4th September 1996

10 DATE OF REVISION OF THE TEXT

06/06/2017