SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

SPASMAG INJECTABLE, solution for injection (IV) in ampoule.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Magnesium sulphate heptahydrate ..... 1.20 g
per ampoule.

Osmolarity: 550 mOsm/l.
Mg^{++}: 490 mmol/l i.e. 11800 mg/l,
4.9 mmol/ampoule i.e. 118 mg/ampoule.

3. PHARMACEUTICAL FORM:

Solution for injection

4. CLINICAL DATA

4.1. Therapeutic indications

- Curative treatment of torsades de pointes.
- Treatment of acute hypokalaemia combined with hypomagnesaemia.
- Magnesium intake in the context of correction of fluid/electrolyte disorders.
- Magnesium intake in the context of parenteral nutrition.
- Preventive and curative treatment of eclampsia.

4.2. Posology and method of administration

Posology

Curative treatment of torsades de pointes

Slow direct intravenous injection of 2 g of magnesium sulphate heptahydrate (i.e. 8 mmol of elemental magnesium) in a few minutes at the discretion of the resuscitator, followed by intravenous infusion 3 to 20 mg/minute of magnesium sulphate heptahydrate (i.e. 0.012 to 0.08 mmol of elemental magnesium per minute).

Preventive and curative treatment of eclampsia

For the prevention of eclampsia or treatment of emergent eclampsia, administer an intravenous infusion of 4 g of magnesium sulphate heptahydrate (i.e. 16 mmol of elemental magnesium) over 30 minutes.
In the event of persistence of eclampsia, administer a further intravenous infusion of 4 g without exceeding a maximum total dose of 8 g of magnesium sulphate heptahydrate (i.e. 32 mmol of elemental magnesium) during the first hour of treatment.

Thereafter, administer by intravenous infusion 2 to 3 g of magnesium sulphate heptahydrate per hour (i.e. 8 to 12 mmol of elemental magnesium) over the 24 hours following the most recent episode.

Treatment of acute hypokalaemia combined with hypomagnesaemia

Adult:

Intravenous infusion of 6 to 8 g of magnesium sulphate heptahydrate (i.e. de 24 à 32 mmol of elemental magnesium) per 24 hours.
Potassium supplementation is to be administered from a container different from that used to administer magnesium. Treatment is to be discontinued as soon as serum magnesium has normalised.

Child:

The usual dosage of the intravenous infusion is 25 to 75 mg of magnesium sulphate heptahydrate per kg of body weight and per 24 hours (i.e. 0.1 to 0.3 mmol of elemental magnesium per kg of body weight and per 24 hours).

Magnesium intake in the context of correction of fluid/electrolyte disorders and parenteral nutrition

Adult:

Intravenous infusion of 1.5 to 2 g of magnesium sulphate heptahydrate (i.e. 6 to 8 mmol of elemental magnesium) per 24 hours.

Child:
The usual dosage of the intravenous infusion is 25 to 75 mg of magnesium sulphate heptahydrate per kg of body weight and per 24 hours (i.e. 0.1 to 0.3 mmol of elemental magnesium per kg of body weight and per 24 hours).

Summary of dosages in different indications

<table>
<tr><th colspan="2">INDICATION</th><th>ROUTE</th><th>FLOW RATE
magnésium sulphate heptahydrate in mg/min
(elemental magnésium in mmol)/min</th></tr>
<tr><td rowspan="2">Curative treatment of torsades de pointes</td><td>From the outset</td><td>Slow direct IV injection</td><td>2 g (8 mmol) in a few minutes at the discretion of the resuscitator</td></tr>
<tr><td>Then</td><td>IV infusion</td><td>3 to 20 mg (0,012 à 0,08 mmol)/min</td></tr>
<tr><td rowspan="3">Preventive and curative treatment of eclampsia</td><td>For the prevention of eclampsia or treatment of emergent eclampsia</td><td rowspan="3">IV infusion</td><td>4 g (16 mmol) in 30 min

i.e. 133 mg (0,53 mmol)/min</td></tr>
<tr><td>If persistence of eclampsia</td><td>4 g (16 mmol) without exceeding a maximum total dose of 8 g (32 mmol) during the first hour of treatment

i.e. 66 to 133 mg (0,26 to 0,53 mmol)/min (first hour)</td></tr>
<tr><td>Thereafter</td><td>2 to 3 g (8 to 12 mmol)/h over the 24 hours following the most recent episode

i.e. 33 to 50 mg (0,13 to 0,2 mmol)/min (24 h)</td></tr>
<tr><td colspan="2" rowspan="2">Treatment of acute hypokalaemia combined with hypomagnesaemia</td><td rowspan="2">IV infusion</td><td><u>Adult</u> : 6 to 8 g (24 to 32 mmol)/24 h

i.e. 4 to 5 mg (0,016 to 0,022 mmol)/min (24h)</td></tr>
<tr><td><u>Child</u> : 25 to 75 mg/Kg/24h

(0,1 to 0,3 mmol/Kg/24h)</td></tr>
<tr><td colspan="2" rowspan="2">Magnesium intake in the context of correction of fluid/electrolyte disorders and parenteral nutrition</td><td rowspan="2">IV infusion</td><td><u>Adult</u> : 1,5 to 2 g (6 to 8 mmol)/24 h

i.e. 1 to 1,4 mg (0,004 to 0,005 mmol)/min (24h)</td></tr>
<tr><td><u>Child</u> : 25 to 75 mg/Kg/24h

(0,1 to 0,3 mmol/Kg/24h)</td></tr>
</table>

<u>As a general rule for IV infusion in adult:</u>

In order to prevent potentially fatal hypermagnesaemia, flow rate of the intravenous infusion is not to exceed 150 mg/minute of magnesium sulphate heptahydrate (i.e. 0.6 mmol of elemental magnesium par minute).

Method of administration
The solution of magnesium sulphate heptahydrate is to be administered:

- Either by **slow** direct intravenous injection with the patient supine and conducted in a specialised setting (intensive care unit, cardiological ICU).This method of administration is restricted to the treatment of torsades de pointes.
- Or by intravenous infusion diluted in glucose or saline solution.

4.3. Contra-indications
Severe kidney failure (creatinine clearance less than 30 mL/min/1.73 m^2).

4.4. Special warnings and precautions for use
HYPERTONIC SOLUTION FOR SLOW INJECTION.

- The first intravenous administrations are to be conducted in hospital.
- Comply with an infusion rate not exceeding 150 mg/minute of magnesium sulphate heptahydrate, i.e. 0.6 mmol/minute of elemental magnesium.
- Monitor blood pressure during intravenous injection and continuous infusion.
- Monitor serum magnesium; discontinue treatment as of serum magnesium normalisation.
- Reduce the dosage for patients with kidney failure and intensify monitoring of renal function, blood pressure and serum magnesium.

4.5. Interactions with other medicinal products and other forms of interaction
The data available to date do not suggest the existence of clinically significant interactions

4.6. Pregnancy and lactation
Pregnancy
In clinical practice, no malformation-inducing or foetotoxic effect has been observed to date.
However, the follow up of pregnancies exposed to magnesium salts administered by the IV route is not sufficient to rule out all risk.
In consequence, use of the product during pregnancy is only to be envisaged if necessary.
Lactation
In the absence of data on potential magnesium excretion in breast milk, it is preferable not to breast feed during treatment.

4.7. Effects on the ability to drive and use machines
No study of the effects on the capacity to drive vehicles and to use machines was carried out. However, no effect on this matter is expected

4.8. Adverse effects
- Pain at the injection site, vasodilatation with a feeling of heat.
- Potentially fatal hypermagnesaemia in the event of severe kidney failure or excessively fast injection.

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 Agence nationale de sécurité du medicament et des produits de santé (ANSM) in the network of the Regional Centres of Pharmacovigilance – Website: www.ansm.sante.fr

4.9. Overdose
The initial signs of hypermagnesaemia consist in inhibition of the patellar reflexes, a feeling of heat, drowsiness, spoken language disorders, muscular paralysis with difficulty breathing and even respiratory and cardiac arrest.
Treatment
- Fluids, forced diuresis,
- IV injection of 1 g of calcium gluconate,
- haemodialysis or peritoneal dialysis in the event of kidney failure.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic class: MAGNESIUM SALT SOLUTIONS.
ATC code: B05CB.
(B: Blood and Blood Forming Organs).

At physiological level

Magnesium is a mainly intracellular cation. Magnesium decreases neuronal excitability and neuromuscular transmission.
Magnesium is involved in numerous enzymatic reactions.
Magnesium is a constitutional element: 50% of the magnesium in the body is found in the bone.
At clinical level, serum magnesium:

- between 12 and 17 mg/l (1 to 1.4 mEq/l or 0.5 to 0.7 mmol/l) indicates moderate magnesium deficiency;
- less than 12 mg/l (1 mEq/l or 0.5 mmol/l) indicates severe magnesium deficiency.

Magnesium deficiency may be:

- either primary due to a congenital abnormality of metabolism (chronic congenital hypomagnesaemia),
- or secondary due to:
  - insufficient intake (severe denutrition, alcoholism, exclusive parenteral nutrition),
  - digestive malabsorption (chronic diarrhoea, digestive fistula, hypoparathyroidism),
  - excessive renal losses (tubule disease, marked polyuria, abuse of diuretics, chronic pyelonephritis, primary hyperaldosteronism, cisplatin treatment).

Non-specific clinical manifestations may occur in the context of magnesium deficiency: tremor, muscle weakness, tetany, ataxia, hyperreflexia, psychological disorders (irritability, nervousness, insomnia, etc.), cardiac rhythm disorders (extra-systoles, tachycardia), and gastrointestinal disorders (diarrhoea, etc.).

5.2. Pharmacokinetic properties:

Excretion is primarily urinary.

5.3 Preclinical safety data:

Not specified

6. PHARMACEUTICAL DATA

6.1. List of excipients:

Water for injection

6.2 Incompatibilities:

In the absence of compatibility study, this medicine must not be mixed with other medicines, the ones indicated in the section 4.2

6.3. Shelf life:

5 years.
After opening: the product should be used immediately

6.4. Special precautions for storage:

No special precautions for storage

6.5. Nature and contents of container:

10-ml ampoule (glass). Box of 5 ampoules

6.6. Method of use, instructions for handling:

No special instructions

7. PRESENTATION AND ADMINISTRATIVE IDENTIFICATION NUMBER

3400932876112 or 328 761-1: five 10-ml glass ampoules- Marketed

8. PRESCRIBING AND DISPENSING CONDITIONS: Medicinal product not subject to medical prescription

9. MARKETING AUTHORISATION HOLDER: Laboratoires GRIMBERG - 19 rue Poliveau **-** 75005 PARIS **-** France

10. DATE OF APPROVAL / REVISION: 11th April 2016