SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Magnesium Sulphate Labesfal 1000 mg/10 ml solution for injection
Magnesium Sulphate Labesfal 2000 mg/10 ml solution for injection
Magnesium Sulphate Labesfal 2000 mg/20 ml solution for injection
Magnesium Sulphate Labesfal 2500 mg/10 ml solution for injection
Magnesium Sulphate Labesfal 4000 mg/20 ml solution for injection
Magnesium Sulphate Labesfal 5000 mg/20 ml solution for injection
Magnesium Sulphate Labesfal 5000 mg/10 ml solution for injection
Magnesium Sulphate Labesfal 10000 mg/20 ml solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Magnesium Sulphate Labesfal 1000 mg/10 ml solution for injection
Each ml of solution for injection contains 100 mg of magnesium sulphate heptahydrate.

Magnesium Sulphate Labesfal 2000 mg/10 ml solution for injection
Each ml of solution for injection contains 200 mg of magnesium sulphate heptahydrate.

Magnesium Sulphate Labesfal 2000 mg/20 ml solution for injection
Each ml of solution for injection contains 100 mg of magnesium sulphate heptahydrate.

Magnesium Sulphate Labesfal 2500 mg/10 ml solution for injection
Each ml of solution for injection contains 250 mg of magnesium sulphate heptahydrate.

Magnesium Sulphate Labesfal 4000 mg/20 ml solution for injection
Each ml of solution for injection contains 200 mg of magnesium sulphate heptahydrate.

Magnesium Sulphate Labesfal 5000 mg/20 ml solution for injection
Each ml of solution for injection contains 250 mg of magnesium sulphate heptahydrate.

Magnesium Sulphate Labesfal 5000 mg/10 ml solution for injection
Each ml of solution for injection contains 500 mg of magnesium sulphate heptahydrate.

Magnesium Sulphate Labesfal 10000 mg/20 ml solution for injection
Each ml of solution for injection contains 500 mg of magnesium sulphate heptahydrate.

3. PHARMACEUTICAL FORM

Solution for injection.

4. CLINICAL INFORMATION

4.1 Therapeutic information

- Treatment of hypomagnesaemia when the oral route is not appropriated due to absorption disorders. Chronic alcoholism, malnutrition, severe diarrhoea or in patients with total parenteral nutrition.

4.2 Posology and method of administration

Posology:

Adults:
6 to 8 mmol/day (1500 to 2000 mg/day), to modify according to the patient particular needs.
For intravenous use, in adults, a concentration up to 20% should be used; the administration rate should not exceed 1.5 ml/minute of a 10% solution or equivalent.

Children - 0.3 to 0.4 mmol/Kg/day.

Magnesium sulphate has anticonvulsive properties when administered parenterally and can be used in the heptahydrate form to prevent or control the effects associated with acute uremia and eclampsia. Can be given intramuscularly at doses up to 5 g; can also be used by intravenous infusion with glucose 5%. The daily dose should not exceed approximately 30 to 40 g in patients with a normal renal function. Adequate dosage reductions should be performed for patients with renal failure.

Administration method:
Solution for injection for intravenous and intramuscular administration

- Slow intravenous injection
- For venous infusion, dilute in a glucose or saline solution.

The treatment should be interrupted as soon as magnesium level is normalized.

Serum magnesium levels should be checked during the magnesium sulphate administration.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Magnesium Sulphate is not indicated in patients that suffer of cardiac arrhythmias; myocardial infarction and severe renal failure (creatinine depuration lower than 30 ml/min/1.73m^2).

4.4 Special warnings and precautions for use

Paediatric population
Intravenous use in children must be performed preferably in hospital environment.
Magnesium serum concentration must be monitored during the magnesium sulphate administration period.

In adults, in order to avoid a potentially lethal hypermagnesaemia, it is advisable to not exceed 0.6 mmol/min (about 150 mg/min). A new injection should not be performed before checking magnesium levels.
In renal failure, posology should be reduced and the renal function and magnesium levels should be checked.
Do not administer simultaneously calcium and magnesium by parenteral route.
Intravenous injection should be performed with the patient lying down with the head slightly elevated, to allow a better tolerance of the warm sensation that can occur according to the injection speed.
In severe hypomagnesaemia, magnesium sulphate should be administered through an infusion pump; blood pressure, respiratory rate, urinary output and the overdose signs (tendon reflex loss, asthenia, nausea, heat sensation, flush, vertigo and diplopia), must be monitored.

4.5 Interaction with other medicinal products and other forms of interaction

Parenteral administration of magnesium salts may potentiate neuromuscular blockers or central nervous system depressors effects.
The following incompatibilities have been described: polymyxin B sulphate, streptomycin sulphate, tobramycin sulphate, lipid emulsions, calcium gluceptate, calcium gluconate, dobutamine hydrochloride, procaine

hydrochloride, tetracyclines, soluble phosphates and alkali carbonates and bicarbonates. Incompatibility with benzylpenicillin and nafcillin has also been reported, since the effect of magnesium sulphate is pH dependent.

4.6 Fertility, pregnancy and lactation

The safety in human pregnancy and breast-feeding was not established, so, as with other medicines, it is not advisable to use magnesium sulphate during pregnancy or breast-feeding unless it is considered absolutely necessary and always performed under medical vigilance.

4.7 Effects on ability to drive and use machines

The effects of Magnesium Sulphate Labesfal on the ability to drive and use machines are negligible.

4.8 Undesirable effects

Diseases of the immune system:
- Hypersensitivity reactions

Metabolism and nutrition disorders:
- Hypocalcemia
- Hypermagnesemia potentially lethal in case of severe renal failure (see section 4.3) or very rapid injection (see section 4.4).

General disorders and administration site effects:
- Pain in the injection site, vasodilatation with a warmth sensation.

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 directly to INFARMED, I.P.:

INFARMED, I.P.
Direção de Gestão do Risco de Medicamentos
Parque da Saúde de Lisboa, Av. Brasil 53
1749-004 Lisboa
Tel: +351 21 798 73 73
Drug line: 800222444 (free call)
Fax: +351 21 798 73 97
http://www.infarmed.pt/web/infarmed/submissaoram
Email: farmacovigilancia@infarmed.pt

4.9 Overdose

By intravenous route, mainly in the renal failure with anuria: hypermagnesaemia with cardiac rhythm disorders, respiratory depression, neuromuscular transmission disorders.

Treatment: rehydration, forced diuresis; in renal failures situations, haemodialysis or peritoneal dialysis.
Neuromuscular blocking associated with hypermagnesaemia can be reverted with the administration of calcium salts as calcium gluconate which can be administered by intravenous route in a dose equivalent to 2.5 to 5 mmol of calcium.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: 12.2.3 - Electrolyte and volemic deficiency correctives. Hydroelectrolytic corrective. Magnesium, ATC code: B05XA05.

Physiologically, magnesium, mainly an intracellular cation, decreases neurons excitability and neuromuscular transmission. It intervenes in numerous enzymatic reactions; 50% of magnesium can be found in the bone.

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

This deficiency can be:
- either primary due to congenital abnormality of magnesium metabolism (congenital chronic hypomagnesaemia);
- or secondary because of inadequate supply (alcoholism, severe malnutrition, exclusive parenteral nutrition), or digestive malabsorption (chronic diarrhoea, digestive fistulae, hypoparathyroidism), or due to severe renal losses (tubulopathy, significant polyuria, chronic pyelonephritis, primary hyperaldosteronism, cisplatinum treatments).

Nonspecific clinical manifestations that can occur during hypomagnesaemia are tremors, muscular weakness, tetanus crisis, ataxia, hyper-reflexibility, psychic disorders (irritability, insomnia,…), cardiac rhythm disorders and digestive disorders.

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 sulphate easily crosses placenta and is distributed into the breast milk after parenteral administration.
Magnesium sulphate is excreted by the kidneys.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections

6.2 Incompatibilities

The following incompatibilities have been described; polymixin B sulphate, streptomycin sulphate, tobramycin sulphate, lipid emulsions, calcium gluceptate, calcium gluconate, dobutamine hydrochloride, procaine hydrochloride, tetracycline, soluble phosphates and alkaline carbonates and bicarbonates. It has also been

referred incompatibility with benzyl penicillin and nafcillin since the magnesium sulphate effect is pH dependent.

6.3 Shelf life

5 years.

6.4 Special precautions for storage

Store below 25ºC.

6.5 Nature and contents of container

Magnesium Sulphate Labesfal 1000 mg/10 ml solution for injection
Packs of 6, 12, 50 and 100 type I glass, colourless, 10 ml solution for injection ampoules.

Magnesium Sulphate Labesfal 2000 mg/10 ml solution for injection
Packs of 6, 12, 50 and 100 type I glass, colourless, 10 ml solution for injection ampoules.

Magnesium Sulphate Labesfal 2000 mg/20 ml solution for injection
Packs of 6, 12, 50 and 100 type I glass, colourless, 20 ml solution for injection ampoules.

Magnesium Sulphate Labesfal 2500 mg/10 ml solution for injection
Packs of 6, 12, 50 and 100 type I glass, colourless, 10 ml solution for injection ampoules.

Magnesium Sulphate Labesfal 4000 mg/20 ml solution for injection
Packs of 6, 12, 50 and 100 type I glass, colourless, 20 ml solution for injection ampoules.

Magnesium Sulphate Labesfal 5000 mg/20 ml solution for injection
Packs of 6, 12, 50 and 100 type I glass, colourless, 20 ml solution for injection ampoules.

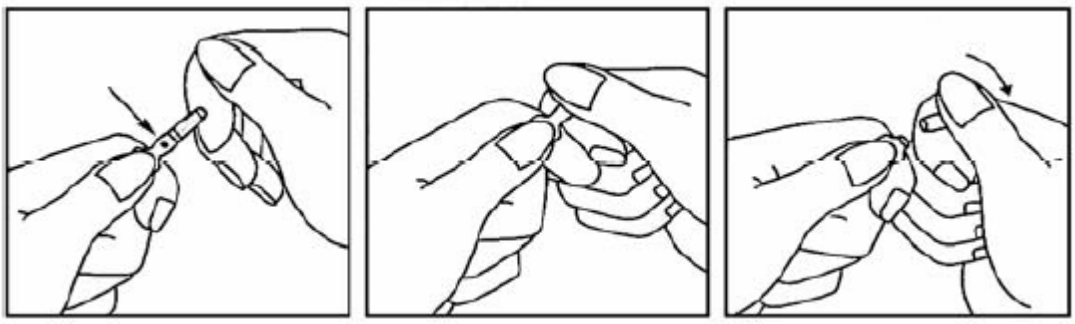
Magnesium Sulphate Labesfal 5000 mg/10 ml solution for injection
Packs of 6, 12, 50 and 100 type I glass, colourless, 10 ml solution for injection ampoules.

Magnesium Sulphate Labesfal 10000 mg/20 ml solution for injection
Packs of 6, 12, 50 and 100 type I glass, colourless, 20 ml solution for injection ampoules.

6.6 Special precautions for disposal

Instructions to open the OPC ampoules (One-Point-Cut)
- Hold the ampoule body between your thumb and index finger, with the point facing upwards;
- Put your other hand index finger supporting the upper part of the ampoule.

Put your thumb over the point, as shown in the figure below.
- With your index fingers close to each other, press the point area to open the ampoule.



Medicinal products intended for parenteral administration should be visually inspected prior to use. It should only be administered if the solution is clear and without particles in suspension, and the container is intact.
This medicinal product is for single use only. Unused content should be disposed of immediately.
After opening the ampoule, the solution for injection should be used immediately.

7. MARKETING AUTHORISATION HOLDER

Labesfal - Laboratórios Almiro, S.A.
Zona Industrial do Lagedo
3465-157 Santiago de Besteiros
Portugal

8. MARKETING AUTHORISATION NUMBER(S)

Magnesium Sulphate Labesfal 1000 mg/10 ml solution for injection
N.º of register: 3256997 – 6 ampoules of 10 ml solution for injection, 1000 mg/10 ml, type I glass ampoules.
N.º of register: 3257094 - 12 ampoules of 10 ml solution for injection, 1000 mg/10 ml, type I glass ampoules.
N.º of register: 3257193 - 50 ampoules of 10 ml solution for injection, 1000 mg/10 ml, type I glass ampoules.
N.º of register: 3257292 - 50 ampoules of 10 ml solution for injection, 1000 mg/10 ml, type I glass ampoules.

Magnesium Sulphate Labesfal 2000 mg/10 ml solution for injection
N.º of register: 3257797 – 6 ampoules of 10 ml solution for injection, 2000 mg/10 ml, type I glass ampoules.
N.º of register: 3257896 – 12 ampoules of 10 ml solution for injection, 2000 mg/10 ml, type I glass ampoules.
N.º of register: 3257995 – 50 ampoules of 10 ml solution for injection, 2000 mg/10 ml, type I glass ampoules.
N.º of register: 3258092 – 100 ampoules of 10 ml solution for injection, 2000 mg/10 ml, type I glass ampoules.

Magnesium Sulphate Labesfal 2000 mg/20 ml solution for injection
N.º of register: 3257391 – 6 ampoules of 20 ml solution for injection, 2000 mg/20 ml, type I glass ampoules.
N.º of register: 3257490 – 12 ampoules of 10 ml solution for injection, 2000 mg/20 ml, type I glass ampoules.
N.º of register: 3257599 – 50 ampoules of 10 ml solution for injection, 2000 mg/20 ml, type I glass ampoules.
N.º of register: 3257698 – 100 ampoules of 20 ml solution for injection, 2000 mg/20 ml, type I glass ampoules.

Magnesium Sulphate Labesfal 2500 mg/10 ml solution for injection
N.º of register: 3258993 – 6 ampoules of 10 ml solution for injection, 2500 mg/10 ml, type I glass ampoules.
N.º of register: 3259090 – 12 ampoules of 10 ml solution for injection, 2500 mg/10 ml, type I glass ampoules.
N.º of register: 3259199 – 50 ampoules of 10 ml solution for injection, 2500 mg/10 ml, type I glass ampoules.
N.º of register: 3259298 – 100 ampoules of 10 ml solution for injection, 2500 mg/10 ml, type I glass ampoules.

Magnesium Sulphate Labesfal 4000 mg/20 ml solution for injection
N.º of register: 3258191 – 6 ampoules of 10 ml solution for injection, 4000 mg/20 ml, type I glass ampoules.
N.º of register: 3258290 – 12 ampoules of 10 ml solution for injection, 4000 mg/20 ml, type I glass ampoules.
N.º of register: 3258399 – 50 ampoules of 10 ml solution for injection, 4000 mg/20 ml, type I glass ampoules.
N.º of register: 3258498 – 6 ampoules of 10 ml solution for injection, 4000 mg/20 ml, type I glass ampoules.

Magnesium Sulphate Labesfal 5000 mg/20 ml solution for injection
N.º of register: 3258597 – 6 ampoules of 20 ml solution for injection, 5000 mg/20 ml, type I glass ampoules.
N.º of register: 3258696 – 12 ampoules of 20 ml solution for injection, 5000 mg/20 ml, type I glass ampoules.
N.º of register: 3258795 – 50 ampoules of 20 ml solution for injection, 5000 mg/20 ml, type I glass ampoules.
N.º of register: 3258894 – 100 ampoules of 20 ml solution for injection, 5000 mg/20 ml, type I glass ampoules.

Magnesium Sulphate Labesfal 5000 mg/10 ml solution for injection
N.º of register: 3259397 – 6 ampoules of 10 ml solution for injection, 5000 mg/10 ml, type I glass ampoules.
N.º of register: 3259496 – 12 ampoules of 10 ml solution for injection, 5000 mg/10 ml, type I glass ampoules.

N.º of register: 3259595 – 50 ampoules of 10 ml solution for injection, 5000 mg/10 ml, type I glass ampoules.
N.º of register: 3259694 – 100 ampoules of 10 ml solution for injection, 5000 mg/10 ml, type I glass ampoules.

Magnesium Sulphate Labesfal 10000 mg/20 ml solution for injection
N.º of register: 3259793 – 6 ampoules of 20 ml solution for injection, 10000 mg/20 ml, type I glass ampoules.
N.º of register: 3259892 – 12 ampoules of 20 ml solution for injection, 10000 mg/20 ml, type I glass ampoules.
N.º of register: 3259991 – 50 ampoules of 20 ml solution for injection, 10000 mg/20 ml, type I glass ampoules.
N.º of register: 3260098 – 100 ampoules of 20 ml solution for injection, 10000 mg/20 ml, type I glass ampoules.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of firs authorisation: 17 August, 2000
Date of last renovation: 17 August, 2005

10. DATE OF REVISION OF THE TEXT

March 2018