1. NAME OF THE DRUG

Magnesium sulfate S.A.L.F. 1 g/10 ml concentrate for solution for infusion
Magnesium sulfate S.A.L.F. 2 g/10 ml concentrate for solution for infusion
Magnesium sulfate S.A.L.F. 2.5 g/10 ml concentrate for solution for infusion
Magnesium sulfate S.A.L.F. 2 mEq / ml concentrate for solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Magnesium sulfate S.A.L.F. 1 g/10 ml concentrate for solution for infusion
Magnesium sulfate S.A.L.F. 2 g/10 ml concentrate for solution for infusion
Magnesium sulfate S.A.L.F. 2.5 g/10 ml concentrate for solution for infusion

Each ampoule contains:

	1 g/10 ml	***2 g/10 ml***	***2,5 g/10 ml***
Magnesium sulfate heptahydrate	1000 mg	2000 mg	2500 mg
Water for injections q.s to	10 ml	10 ml	10 ml
mEq/liter (Mg^{++})	811	1623	2028
(SO_4^{--})	811	1623	2028
pH: between 5,5 and 7,0			

Magnesium sulfate S.A.L.F. 2 mEq / ml concentrate for solution for infusion

Each ml of solution contains:

Magnesium sulfate heptahydrate, 0.246 g (equivalent to 2 mEq of Mg + +)
pH: between 5.5 and 7.0

For a full list of the excipients, see section 6.1

3. PHARMACEUTICAL FORM

Concentrate for solution for infusion.

4. CLINICAL INFORMATION

4.1. Therapeutic indications

- Prevention and control of seizures in case of a severe pregnancy toxemia in women during pregnancy (preeclampsia and eclampsia).
- Replacement therapy in case of magnesium deficiency, especially in case of acute hypomagnesemia accompanied by signs of tetany.
- Prevention and treatment of hypomagnesemia in patients receiving a total parenteral nutrition.

4.2. Posology and method of administration

Magnesium sulfate S.A.L.F. must be diluted in glucose 5% or sodium chloride 0.9%.

- Prevention and control of seizures in case of a severe pregnancy toxemia in women during pregnancy (preeclampsia and eclampsia).
- Replacement therapy in magnesium deficiency, especially in case of acute hypomagnesemia accompanied by signs of tetany.
  The total initial dose is 10-14 g of magnesium sulfate. Do not exceed the dose of 30-40 g in 24 hours.
- Prevention and treatment of hypomagnesemia in patients receiving a total parenteral nutrition.
  From 1 g to 3 g (8-24 mEq) per day.

In the presence of a severe renal impairment, the maximum dose of magnesium sulfate is 20 g/48 hours.
The serum magnesium concentration of 6 mg/100 ml is considered optimal for the control of seizures.

4.3. Contraindications
Hypersensitivity to the active ingredient or to any of the excipients;
patients with cardiac arrhythmias or myocardial damage;
patients with a severe renal impairment.

4.4. Special warnings and precautions for use
Use at a controlled rate after an appropriate dilution. Use the solution only if clear.
Use with caution in cases of less severe renal impairment and in patients with myasthenia gravis.
Intravenous use in the presence of a renal insufficiency may lead to a magnesium intoxication.
To promptly detect clinical signs of magnesium overdose, it is necessary to closely monitor patients receiving magnesium sulfate for eclampsia.
The intravenous use in eclampsia should be reserved for an immediate check of life-threatening seizures.

Magnesium sulfate S.A.L.F. 1 g/10 ml concentrate for solution for infusion
Magnesium sulfate S.A.L.F. 2 g/10 ml concentrate for solution for infusion
Magnesium sulfate S.A.L.F. 2.5 g/10 ml concentrate for solution for infusion
The product should be used immediately after opening the ampoule: any unused residue should be discarded.

Check the integrity of the ampoule / vial: it must not have any cracks or other damage that could impair the seal.

Important information about some of the ingredients:

Magnesium sulfate S.A.L.F. 2 mEq / ml concentrate for solution for infusion contains benzyl alcohol:
This medicine should not be given to premature babies or newborns.
Because of the risk of fatal toxic reactions related to the exposure to benzyl alcohol in quantities exceeding 90 mg / kg / day, this product must not be given to children under 3 years of age.
For exposures up to 90 mg / kg / day it can cause toxic and allergic reactions in children up to 3 years of age.

4.5. Interaction with other medicinal products and other forms of interaction
Magnesium sulfate may interact with the following medicines:

Drugs that depress the central nervous system
When barbiturates, narcotics or other hypnotics (or systemic anesthetics) or other drugs that depress the central nervous system are co-administered with magnesium, their dosage should be carefully modified due to the additional depressing effect of magnesium on the central nervous system.
The depression of the central nervous system and of the peripheral transmission caused by magnesium can be antagonized by calcium.

Cardiac glycosides
Magnesium sulfate should be administered with extreme caution in patients taking digitalis drugs, because of changes in the cardiac conduction that may develop into cardiac arrhythmia in case it should be necessary to administer calcium to treat poisoning by magnesium.

Competitive and depolarizing neuromuscular junction blockers
The parenteral administration of magnesium sulfate potentiates the effect of competitive and depolarizing neuromuscular junction blockers.

Aminoglycoside antibiotics
The effect of magnesium via parenteral administration and of aminoglycoside antibiotics on the neuromuscular blockade can be additive.

Eltrombopag
The administration of products containing aluminum, calcium or magnesium may decrease the plasmatic concentrations of eltrombopag.

Rocuronium
A co-administration of rocuronium and magnesium may increase the risk of toxicity by rocuronium (prolongation of neuromuscular blockade, respiratory depression and apnea).

Labetalol
A co-administration of labetalol and magnesium can cause bradycardia and decreased cardiac output (shortness of breath, dizziness, or fainting).

Calcium channel blockers (isradipine, felodipine, nicardipine and nifedipine)
A concomitant administration of magnesium with a calcium antagonist may cause hypotension.

4.6. Pregnancy and lactation

Pregnancy
Studies in pregnant women have not shown an increased risk of fetal abnormalities during all the trimesters of pregnancy. The possibility of a fetal damage following an administration of magnesium sulphate during pregnancy seems to be remote. However, since studies can not rule out the possibility that there may be a damage and magnesium sulfate crosses the placenta, this drug must not be used during pregnancy, unless clearly necessary.
In addition, you should monitor the fetal heart rate, when it is administered to pregnant women.
Avoid the use of magnesium sulfate 2 hours before giving birth.
If magnesium sulfate is administered (especially for more than 24 hours before parturition) to control seizures in mothers with pregnancy toxemia, babies may show signs of magnesium toxicity, including neuromuscular and respiratory depression.

Lactation
The use of magnesium sulfate is considered compatible with lactation, although its presence has been detected in breast milk.

4.7. Effects on ability to drive and use machines
Not applicable.

4.8. Side effects
Here below are the possible side effects of magnesium sulfate organized according to MedDRA system organ classification. There are insufficient data to determine the frequency of the each effect listed.

Gastrointestinal disorders
Paralytic ileus
Delayed intestinal transit

General disorders and administration site conditions
Hypersensitivity reactions
Hives

Metabolism and nutrition disorders
Metabolic acidosis

Hypocalcemia

Injury, poisoning and procedural complications
You may experience the following symptoms of magnesium toxicity: flushing, sweating, hypotension, flaccid paralysis, hypothermia, circulatory collapse, cardiac depression and central nervous system that can evolve into respiratory paralysis.

4.9. Overdose

Symptoms
Magnesium intoxication is manifested by a spike in blood pressure and respiratory paralysis.
The disappearance of the patellar reflex is a useful clinical sign to identify the beginning of intoxication.

Treatment
It is necessary to resort to artificial respiration. To counteract the effects of hypermagnesemia it is necessary to administer calcium gluconate intravenously (10-20 ml of 5% solution).
The sub-cutaneus administration of 0.5-1 mg of physostigmine can be helpful.
The hypermagnesaemia in newborns may require resuscitation and an assisted ventilation for endotracheal intubation or an intermittent ventilation at a positive pressure, as well as the intravenous administration of calcium gluconate.

5. PHARMACOLOGICAL PROPERTIES
5.1. Pharmacodynamic properties
Pharmacotherapeutic group: Electrolyte solutions.
ATC code: B05XA05
Magnesium is an important co-factor for the enzyme reactions and plays an important role in neurochemical transmission and muscular excitability.
Magnesium prevents or controls convulsions by blocking the neuromuscular transmission and decreasing the amount of acetylcholine released in the neuromuscular junction by the impulse of the motor neuron.

5.2. Pharmacokinetic properties
After an intravenous administration of magnesium, the anticonvulsant effect is immediate and lasts about 30 minutes.
Ater an intramuscular administration, the onset of the effect is observed in about 1 hour and lasts for 3-4 hours.
The anticonvulsant efficacy is observed in serum concentrations between 2.5 and 7.5 mEq / l.
Magnesium is excreted solely by the kidneys with a speed proportional to the plasmatic concentration and glomerular filtration.

5.3. Preclinical safety data
Preclinical data have little clinical relevance in light of the extensive experience gained with the use of this drug in humans.

6. PHARMACEUTICAL INFORMATION
6.1. List of the excipients.

6.2. Incompatibility.
The magnesium sulfate in solution can lead to the formation of a precipitate, when mixed with solutions containing: alcohol (at high concentrations), heavy metals, carbonates and bicarbonates, sodium hydrocortisone, succinates, phosphates, polymyxin B sulfate, procaine hydrochloride, calcium salicylate, clindamycin phosphate, tartrates.
The potential incompatibility is often influenced by the change in the concentration of the reactants and the pH of the solutions.

6.3. Shelf life
3 years in its unopened original package.

6.4. Special precautions for storage
Store in the original package.
No special storage conditions in relation to temperature. Do not freeze.

6.5. Nature and capacity of the container
Magnesium sulfate S.A.L.F. 1 g/10 ml concentrate for solution for infusion
Magnesium sulfate S.A.L.F. 2 g/10 ml concentrate for solution for infusion
Magnesium sulfate S.A.L.F. 2.5 g/10 ml concentrate for solution for infusion
Glass ampoule of 10 ml.

Magnesium sulfate S.A.L.F. 2.5 g/10 ml concentrate for solution for infusion
Glass vial of 30 ml.

6.6. Special precautions for disposal and other handling
Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER
S.A.L.F. S.p.A. Laboratorio Farmacologico - Via Marconi, 2 - Dine Sotto (BG) – Tel. 035-940097

8. MARKETING AUTHORISATION NUMBER
Magnesium sulfate S.A.L.F. 1 g/10 ml concentrate for solution for infusion
5 ampoules of 10 ml A.I.C. 030676011

Magnesium sulfate S.A.L.F. 2 g/10 ml concentrate for solution for infusion
5 ampoules of 10 ml A.I.C. 030676035

Magnesium sulfate S.A.L.F. 2.5 g/10 ml concentrate for solution for infusion
5 ampoules of 10 ml A.I.C. 030676050

Magnesium sulfate S.A.L.F. 2 mEq / ml concentrate for solution for infusion
1 vial of 30 ml A.I.C. 030676098

9. DATE OF RENEWAL OF THE AUTHORISATION
May 5th, 2008

10. DATE OF REVISION OF THE TEXT
July 2012