Kalcex

Package leaflet: Information for the user

Magnesium Sulfate 10% w/v Solution for Injection/Infusion

Magnesium sulfate heptahydrate

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

Magnesium Sulfate 10% w/v Solution for Injection/Infusion will be referred to as Magnesium Sulfate Injection/Infusion throughout the leaflet.

What is in this leaflet

1. What Magnesium Sulfate Injection/Infusion is and what it is used for

Magnesium Sulfate Injection/Infusion contains magnesium (as magnesium sulfate heptahydrate). Magnesium sulfate heptahydrate (hereafter referred to as magnesium sulfate) is a magnesium salt. It is used:

In adults, adolescents and children
- to treat magnesium deficiency (shortage);
- to prevent and treat low levels of magnesium in the blood in patients receiving total parenteral nutrition (nutrients that are infused into the bloodstream).

In pregnant women
- to control and prevent seizures in severe pre-eclampsia (serious complication of pregnancy characterised by high blood pressure and protein in your urine);
- to control and prevent recurrent seizures in eclampsia (convulsions as a result of pre-eclampsia).

2. What you need to know before you are given Magnesium Sulfate Injection/Infusion

You should not be given Magnesium Sulfate Injection/Infusion
- if you are allergic to magnesium sulfate, its salts or any of the other ingredients of this medicine (listed in section 6);
- you have liver failure or condition known as 'hepatic encephalopathy' (impaired brain function due to liver disease);
- you have kidney failure or severe kidney problems, or you cannot make or pass urine;
- you have heart problems or a disease causing muscle weakness and fatigue called 'myasthenia gravis' (in these cases you should not be given magnesium sulfate by injection).

If any of the above apply to you please tell your doctor or nurse before you are given Magnesium Sulfate Injection/Infusion.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before you are given Magnesium Sulfate Injection/Infusion:
- if you have kidney problems (you will need reduced dose);
- if you have liver problems.

Tell your doctor or nurse if flushing and sweating occurs.
Your magnesium and calcium blood levels will be monitored during treatment.
Your reflexes, breathing and urine output will also be checked while receiving magnesium sulfate.

Other medicines and Magnesium Sulfate Injection/Infusion
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines. Medicines which may interact with magnesium sulfate include:
- Muscle relaxants e.g. vecuronium
- Nifedipine (used to treat high blood pressure or chest pain)
- Calcium channel blockers (medicines to treat high blood pressure and chest pain)
- Diuretics (medicines that increase the passage of urine) such as thiazides and furosemide
- Calcium salts
- Digitalis glycosides e.g. digoxin (a medicine used to treat heart problems)
- Aminoglycoside antibacterial agents (medicines used to treat bacterial infections)
- Barbiturates (medicines for treating anxiety, insomnia)
- Opioids (medicines for treating chronic pain) such as morphine
- Hypnotics (medicines for sleep disorders).

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before being given this medicine.
Magnesium Sulfate Injection/Infusion may be used to treat the fits associated with pre-eclampsia and eclampsia, a serious complications of pregnancy. If you are pregnant and you are given Magnesium Sulfate Injection/Infusion, your baby's heart rate will be thoroughly monitored and use within 2 hours of delivery will be avoided. Magnesium sulfate can cause foetal skeletal adverse effects when given continuously for more than 5 to 7 days to pregnant women. In case of prolonged or repeated use of magnesium sulfate during pregnancy, your baby will be monitored for abnormal calcium or magnesium levels and skeletal adverse effects. You will not receive Magnesium Sulfate Injection/Infusion during pregnancy or breast-feeding unless considered essential by your doctor, and it will be given to you under medical supervision. Your doctor will assess that the potential benefits outweigh the risks before giving this medicine to you.
Magnesium sulfate has no effects on fertility.

Driving and using machines
Magnesium Sulfate Injection/Infusion is unlikely to affect the ability to drive and use machines. However, some people may feel dizzy or drowsy after receiving Magnesium Sulfate injection. If you experience these side effects, do not to drive or use machines.

Magnesium Sulfate Injection/Infusion contains sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per 1 ml, that is to say essentially 'sodium-free'.

3. How Magnesium Sulfate Injection/Infusion will be given

This medicine will be given to you as an injection or infusion into a vein, or as an injection or infusion into the tissue under the skin.

The following information is intended for healthcare professionals only:

Magnesium Sulfate 10% w/v Solution for Injection/Infusion
Magnesium sulfate heptahydrate

Route and method of administration
For intravenous or subcutaneous injection or infusion.

Intravenous (IV):
For intravenous injection, the 10% w/v solution does not require dilution.
For intravenous infusion, the medicinal product should be diluted.

Subcutaneous (SC):
For subcutaneous administration, the medicinal product should be diluted.

Magnesium Sulfate 10% w/v solution is not appropriate for intramuscular administration. For intramuscular injection and in case the IV loading/IM maintenance regimen below is applied, Magnesium Sulfate 50% w/v solution should be used.

For instructions on dilution before administration, see 'Instructions for use, disposal and other handling' below.

Posology
Magnesium sulfate heptahydrate 10% w/v (0.4 mmol Mg^{2+} in 1 ml).
Magnesium sulfate heptahydrate 1 g = 98.6 mg or 8.1 mEq or approximately 4 mmol magnesium (Mg^{2+}).
The concentrations of magnesium ions (Mg^{2+}) in millimoles are given as approximate values.

Therapeutic levels are reached almost immediately with appropriate intravenous doses.

Adults
Hypomagnesaemia
The dose is strictly individual. As a general guideline, 8-12 g of magnesium sulfate (32-48 mmol Mg^{2+}) can be administered in the first 24 hours followed by 4-6 g (16-24 mmol Mg^{2+}) per day for 3 or 4 days, to replete body stores. Maximum infusion rates should not exceed 2 g/hour (8 mmol Mg^{2+}/hour). The aim should be to maintain serum magnesium concentrations above 0.4 mmol/l.

Usually 10-20 ml Magnesium Sulfate 10% w/v solution (4-8 mmol Mg^{2+}) is administered slowly intravenously (at a rate of 1.5 ml/minute) or, exceptionally, subcutaneously (painful), repeatedly if necessary.

Severe pre-eclampsia or eclampsia
Intravenously an initial loading dose of 4-5 g of magnesium sulfate (16-20 mmol Mg^{2+}) diluted to an appropriate volume may be infused. This is followed by a maintenance regimen of either an intravenous (IV) infusion or regular intramuscular (IM) injections using Magnesium Sulfate 50% w/v solution as follows:

- IV maintenance regimen: the loading dose is followed by an IV infusion of 1-2 g/hour (4-8 mmol Mg^{2+}/hour);
- IM maintenance regimen: the loading dose is followed by regular IM injections of 4-5 g of magnesium sulfate (8-10 ml of undiluted Magnesium Sulfate 50% w/v solution corresponding to 16-20 mmol Mg^{2+}) into alternate buttocks every 4 hours, depending on the continuing presence of the patellar reflex and adequate respiratory function.

Therapy should continue until paroxysms cease.

Paediatric population
Hypomagnesaemia
Magnesium Sulfate 10% w/v solution may be administered intravenously to children. For the intravenous use in children the rate of administration should not exceed 0.1 ml/kg/minute (10 mg/kg/minute) Magnesium Sulfate 10% w/v solution (corresponding to 0.04 mmol/kg/minute = 0.001 g/kg/minute magnesium).

Renal insufficiency
Patients with renal insufficiency should receive 25-50% of the initial dose recommended for patients with normal kidney function. ECG monitoring is recommended with high doses and in the elderly.

Hepatic impairment
No special dosage instructions are available.

Elderly
Parenteral magnesium sulfate should be used with caution in the elderly because renal and/or hepatic disorders are more frequent in this age group and the tolerance to adverse effects may be lower.

Your doctor will decide how much magnesium sulfate should be given to you. The usual doses are given below.

Adults
For magnesium deficiency, you will be given 8-12 g of magnesium sulfate in the first 24 hours followed by 4-6 g/day for 3 or 4 days, to replete body stores.
Usually, 10-20 ml Magnesium Sulfate 10% w/v solution is given, repeatedly if needed.

For the control and prevention of seizures in severe pre-eclampsia or eclampsia, an initial loading dose of 4-5 g magnesium sulfate diluted to an appropriate volume will be given into your vein. It will be followed by either an infusion into a vein of 1-2 g/hour or regular injections into a muscle using Magnesium Sulfate 50% w/v solution, until seizures cease.

Patients with kidney problems
Patients with kidney problems will be given a reduced dose.

Patients with liver problems
There are no special dosage instructions.

Elderly
Caution should be observed as kidney and/or liver disorders and side effects are more likely in this age group.

Use in children
For magnesium deficiency, Magnesium Sulfate 10% w/v solution may be given into a vein, to replace depleted body stores in children.

If you are given too much Magnesium Sulfate Injection/Infusion
As this medicine will be given to you by a doctor or nurse, it is unlikely that you will be given too much. However, tell your doctor or nurse if you have any concerns.

If you forget to be given Magnesium sulfate Injection/Infusion
It is unlikely that you will miss a dose as your doctor or nurse will be giving it to you. You should not receive a double dose if you have missed one. Ask your doctor or nurse when you should have the next dose.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Frequency not known (cannot be estimated from the available data)
- Electrolyte/fluid abnormalities
- Breathing difficulties
- Feeling or being sick
- Drowsiness
- Confusion
- Slurred speech
- Double vision
- Loss of tendon reflexes
- Irregular heartbeat
- Cardiac arrest
- Electrocardiogram (ECG) abnormalities
- Slowed heart rate
- Flushing of the skin and low blood pressure due to dilation of blood vessels
- Muscle weakness
- Thirst
- Coma

Low blood calcium levels in pregnant women and their developing babies have been reported extremely rarely with high doses of magnesium sulfate (see 'Pregnancy, breast-feeding and fertility').

Hypersensitivity reactions cannot be ruled out.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via Yellow Card Scheme. Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Magnesium Sulfate Injection/Infusion

Keep this medicine out of the sight and reach of children.

Do not freeze.

Do not use this medicine after the expiry date which is stated on the label and carton after {EXP}. The expiry date refers to the last day of that month.

Do not use this medicine if you notice any visible signs of deterioration (e.g. particles).

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Magnesium Sulfate Injection/Infusion contains
– The active substance is magnesium sulfate heptahydrate.

Each 1 ml of solution contains 0.4 mmol Mg^{2+} (equivalent to 100 mg magnesium sulfate heptahydrate).
Each 10 ml ampoule contains 4 mmol Mg^{2+} (equivalent to 1 g magnesium sulfate heptahydrate).

– The other ingredients are sulfuric acid (for pH adjustment), sodium hydroxide (for pH adjustment), water for injections.

What Magnesium Sulfate Injection/Infusion looks like and contents of the pack
Clear colourless solution, free from visible particles.

10 ml of solution in colourless glass ampoules with red one point cut. Ampoules are packed in polyvinylchloride film liner. Liners are packed into a cardboard box.

Pack size: 5, 10 or 100 ampoules

Not all pack sizes may be marketed.

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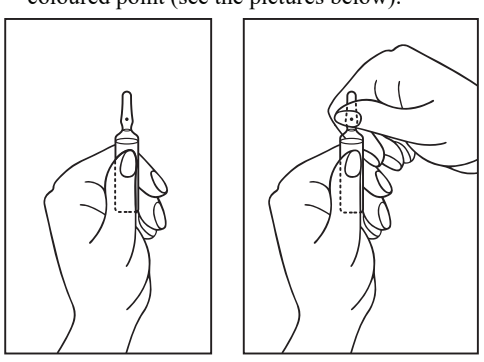
If this leaflet is difficult to see or read, please contact: Local safety officer (UK), email: kalpv.uk@biomapas.com

Place for AS Kalceks internal code
Place for manufacturer internal code

Instructions for use, disposal and other handling
For single use only. Discard any unused contents.
Can be diluted with 0.9% sodium chloride or 5% glucose solutions.
This medicinal product must not be mixed with other medicinal products except those mentioned above.
An antidote of injectable calcium gluconate solution should be immediately available.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Instruction of ampoule opening
1) Hold the ampoule upright. If there is any solution in the upper part of the ampoule, gently tap with your finger to get all the solution to the lower part of the ampoule.
2) Use both hands to open; while holding the lower part of the ampoule in one hand, use the other hand to break off the upper part of the ampoule in the direction away from the coloured point (see the pictures below).



Shelf life
Shelf life after first opening: The medicinal product should be used immediately after opening the ampoule.

Shelf life after dilution: Chemical and physical in-use stability has been demonstrated for 72 hours at 25°C and 2 to 8°C after dilution with 0.9% sodium chloride or 5% glucose solution. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibilities of the user and would normally not be longer than 24 hours at 2 to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

Overdose
Symptoms
Intravenous magnesium infusions can result in hypermagnesaemia even in the presence of normal kidney function. Clinical signs of overdose will be those of hypermagnesaemia. Patients with renal failure and metabolic derangements develop toxicity at lower doses. Disappearance of the deep tendon reflex is a useful clinical sign to detect the onset of magnesium intoxication. Magnesium intoxication is manifested by a sharp drop in blood pressure and respiratory paralysis. The potential symptoms of hypermagnesaemia are as follows:

Magnesium levels			Manifestation of overdose symptoms
mg/dl	mEq/l	mmol/l	
<1.2	<1	<0.5	Tetany Seizures Arrhythmias
1.2-1.8	1.0-1.5	0.5-0.75	Neuromuscular irritability Hypocalcaemia Hypokalaemia
1.8-2.5	1.5-2.1	0.75-1.05	Normal magnesium level
2.5-5.0	2.5-5.0	1.05-2.1	Typically asymptomatic
5.0-7.0	4.2-5.8	2.1-2.9	Lethargy Drowsiness Flushing Nausea and vomiting Diminished deep tendon reflex
7.0-12	5.8-10	2.9-5	Somnolence Loss of deep tendon reflexes Hypotension ECG changes
>12	>10	>5	Complete heart arrest Apnoea Paralysis Coma

Treatment
In symptomatic hypermagnesaemia, administration of calcium, usually at a dose of 100 to 200 mg intravenously over 5 to 10 min, antagonizes the toxic effects of magnesium.
In patients with severe renal dysfunction, peritoneal dialysis or haemodialysis will rapidly and effectively lower serum magnesium levels.