SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Magnesium sulfate Kalceks 50%

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains 500 mg magnesium sulfate heptahydrate (2 mmol = 49 mg or 4 mEq) magnesium (Mg^{2+}).
Each 2 ml ampoule contains 1 g magnesium sulfate heptahydrate.
Each 10 ml ampoule contains 5 g magnesium sulfate heptahydrate.
1 g of magnesium sulfate heptahydrate provides 4 mmol (8.1 mEq) of elemental magnesium (Mg^{2+}).

The concentrations of magnesium ions (Mg^{2+}) in millimoles are given as approximate values.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection or infusion, with a pH of between 5.5 and 7.
Clear colourless solution, free from visible particles.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Magnesium sulfate Kalceks 50% is indicated for:
1) the treatment of magnesium deficiency in hypomagnesaemia.
2) the prevention and treatment of hypomagnesaemia in patients receiving total parenteral nutrition.
3) the control and prevention of seizures in severe pre-eclampsia.
4) the control and prevention of recurrent seizures in eclampsia.

4.2 Posology and method of administration

Magnesium sulfate Kalceks 50% may be administered by the intravenous (preferred method) or intramuscular (painful, avoid if possible) routes (see below for method of administration and section 4.4).

Posology
Dosage should be tailored according to the individual's needs and responses and should be reduced in renal impairment. Plasma magnesium concentrations should be measured to determine the rate and duration of infusion and should be monitored throughout therapy.

1 g magnesium sulfate heptahydrate = 98.6 mg or 8.1 mEq or 4 mmol Mg^{2+}.

Treatment of magnesium deficiency in hypomagnesaemia
Adults:
Intravenous Route: Up to 80 ml Magnesium sulfate Kalceks 50% (corresponding to 160 mmol ≈ 4 g Mg^{2+}) diluted should be administered by slow intravenous infusion over a period of up to five days and titrated to clinical need. The usual regimen is 16 – 24 ml Magnesium sulfate Kalceks 50% (corresponding to 32 – 48 mmol ≈ 0.8 – 1.2 g Mg^{2+}) diluted in the first 24 hours followed by 8 – 12 ml Magnesium sulfate Kalceks 50% (corresponding to 16 – 24 mmol ≈ 0.4 – 0.6 g Mg^{2+}) diluted per day for 3 or 4 days.

Intramuscular Route:
2 – 4 ml Magnesium sulfate Kalceks 50% (corresponding to 4 – 8 mmol ≈ 0.1 – 0.2 g Mg^{2+}) undiluted or 4 – 8 ml of Magnesium sulfate Kalceks 50% diluted to 25% solution can be given intramuscularly every 6 hours for 24 hours (a total of 4 doses).

Children and adolescents:
Neonate
0.2 ml/kg Magnesium sulfate Kalceks 50% (corresponding to 0.4 mmol/kg ≈ 0.01 g/kg Mg^{2+}) diluted to 20% solution (i.e. 0.5 ml/kg of a 20% solution) every 6 – 12 hours as required, to be given by intravenous injection over at least

10 minutes.
Child 1 month – 11 years
0.1 ml/kg Magnesium sulfate Kalceks 50% (corresponding to 0.2 mmol/kg ≈ 0.005 g/kg Mg^{2+}) diluted to 20% solution (i.e. 0.25 ml/kg of a 20% solution) every 12 hours as required, to be given by intravenous injection over at least 10 minutes.
Adolescent 12 – 17 years
2 ml Magnesium sulfate Kalceks 50% (corresponding to 4 mmol ≈ 0.1 g Mg^{2+}) diluted to 20% solution (i.e. 5 ml of a 20% solution) every 12 hours as required, to be given by intravenous injection over at least 10 minutes.

Elderly:
There are no specific recommendations for dosage in elderly adults. Magnesium sulfate Kalceks 50% should be used with caution in elderly because of often renal impairment in this age group.

Prevention of hypomagnesaemia in patients receiving total parenteral nutrition
Adults:
5 – 10 ml Magnesium sulfate Kalceks 50% (corresponding to 10 – 20 mmol ≈ 0.25 – 0.5 g Mg^{2+}) diluted daily, usual dose 6 ml Magnesium sulfate Kalceks 50% (corresponding to 12 mmol ≈ 0.3 g Mg^{2+}) diluted daily, by intravenous infusion or intramuscular injection.

Neonates and infants (up to 12 months):
0.1 ml/kg Magnesium sulfate Kalceks 50% (corresponding to 0.2 mmol/kg ≈ 0.005 g/kg Mg^{2+}) diluted daily by intravenous infusion.

Children (1 – 13 years) and adolescents (14 – 18 years):
0.05 ml/kg Magnesium sulfate Kalceks 50% (corresponding to 0.1 mmol/kg ≈ 0.0025 g/kg Mg^{2+}) diluted daily by intravenous infusion.

Control and prevention of recurrent seizures in severe pre-eclampsia and eclampsia
Adult women:
Loading dose: An initial IV loading dose of approximately 8 – 10 ml Magnesium sulfate Kalceks 50% (corresponding to 16 – 20 mmol ≈ 0.4 – 0.5 g Mg^{2+}) diluted to an appropriate volume is administered over 5 – 15 minutes, followed either by maintenance intravenous infusion or regular IM injections for 24 hours, as follows:
IV Maintenance Regimen
The IV loading dose (above) is followed by an infusion of approximately 2 ml Magnesium sulfate Kalceks 50% (corresponding to 4 mmol ≈ 0.1 g Mg^{2+}) diluted per hour for at least 24 hours after the last fit.
IM Maintenance Regimen
The IV loading dose (above) is immediately followed by deep IM injection of 10 ml Magnesium sulfate Kalceks 50% (corresponding to 20 mmol ≈ 0.5 g Mg^{2+}) undiluted.

Maintenance therapy is a further 10 ml Magnesium sulfate Kalceks 50% (corresponding to 20 mmol ≈ 0.5 g Mg^{2+}) undiluted IM every four hours, continued for 24 hours after the last fit (provided respiratory rate is > 16/min, urine output > 25ml/min and knee jerks are present).

Recurrent convulsions: In both IV and IM regimens, a further 4 – 8 ml Magnesium sulfate Kalceks 50% (corresponding to 8 – 16 mmol ≈ 0.2 – 0.4 g Mg^{2+}) diluted depending on body weight [if less than 70 kg 4 ml Magnesium sulfate Kalceks 50% (corresponding to 8 mmol ≈ 0.2 g Mg^{2+}) diluted] are given IV over a period of 5 minutes.

Renal impairment
Magnesium sulfate Kalceks 50% is contraindicated in patients with severe renal impairment (see section 4.3). Magnesium sulfate Kalceks 50% should be used with caution in mild to moderate renal impairment. A reduction in dosage to 40 ml Magnesium sulfate Kalceks 50% (corresponding to 80 mmol ≈ 2 g Mg^{2+}) diluted over 48 hours may be given.

Patients with impaired liver function
There are no recommended special dosage instructions for patients with impaired liver function because of insufficient data.

Method of administration
Intravenous use in adults and adolescents

Intravenous infusion: For the intravenous route, the 50% solution requires dilution to a concentration of not more than 20% (≤ 200 mg/ml magnesium sulfate heptahydrate) – with a suitable diluent, such as 5% glucose or 0.9% sodium chloride solution. Infuse *via* a volumetric infusion device at a rate appropriate to the indication (see posology above).

Intravenous injection: Give by slow IV injection at a rate appropriate to the indication (see posology above).

Intravenous use in children:
Rate of administration should not exceed 0.02 ml/kg/min of appropriately diluted Magnesium sulfate Kalceks 50% (corresponding to 0.04 mmol/kg/min ≈ 0.001 g/kg/min Mg^{2+}).

Deep Intramuscular injection (adults only)
For the intramuscular route, the 50% solution should be used undiluted or diluted to 25%. If the total dose to be administered exceeds 5 ml, the injection volume should be divided between more than one deep muscular injection site.

4.3 Contraindications

- Hypersensitivity to magnesium and its salts or to any of the excipients listed in section 6.1.
- Hepatic encephalopathy, hepatic failure.
- Severe renal impairment (glomerular filtration rate under 25 ml/h), renal failure, anuria.
- Parenteral administration of the medicinal product is contraindicated in patients with heart block (class I-III) or myocardial damage and myasthenia gravis.

4.4 Special warnings and precautions for use

Magnesium salts should be administered with caution to patients with impaired renal function and appropriate dosage reduction should be made (see section 4.2).

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

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

The serum magnesium level should be monitored during the treatment.

Monitoring of the absence of respiratory depression: the breath rate should not be under 16 breaths/min.

The excretion of urine should not be under 25 ml/h, as it could lead to hypermagnesaemia.

The presence of the patellar reflex should be checked.

The medicine should be administered with caution if flushing and sweating occurs.

An antidote of injectable calcium gluconate solution should be immediately available.

For the intravenous use in children the rate of administration should not exceed 0.02 ml/kg/min of appropriately diluted Magnesium sulfate Kalceks 50% (corresponding to 0.04 mmol/kg/min = 0.001 g/kg/min Mg^{2+}) (see section 4.2).

The 50% w/v solution MUST be diluted before use for IV administration; concentrations up to 20% are usually employed.

For the intramuscular route, use good clinical practice for intramuscular injections. The 50% solution should be used undiluted or diluted to 25%. The medicine should not be administered into muscles which are emaciated or atrophied.
For intramuscular administration, dorsogluteal muscle and sciatic nerve should be avoided.

If the total dose to be administered exceeds 5 ml, the injection volume should be divided between more than one deep muscular injection site.

Use caution in older or thin patients who may only tolerate up to 2 ml in a single injection. Do not use an injection

site that has evidence of infection or injury. If repeating an intramuscular dose, rotate injection sites to avoid injury or discomfort to the muscles.

4.5 Interaction with other medicinal products and other forms of interaction

Muscle relaxants
The action of non-depolarizing muscle relaxants is potentiated and prolonged by parenteral magnesium salts and magnesium sulfate enhances non-depolarizing muscle relaxant vecuronium action at adult muscle type nicotinic acetylcholine receptor *in vitro*.

Nifedipine
Profound hypotension has been reported.

Calcium channel blockers or diuretics
There is a risk of cardiopulmonary events when intravenous magnesium sulfate is used concomitantly with calcium channel blockers or diuretics (such as thiazides and furosemide).

Calcium salts
Calcium salts may reduce the efficacy of magnesium. Several magnesium activated enzymes are inhibited by calcium.

Digitalis glycosides
Magnesium salts should also be administered with caution to those patients receiving digitalis glycosides. Magnesium has been shown to block the transient inward current carried by calcium, which digitalis glucosides generate.

Neuromuscular blocking agents
Parenteral administration of magnesium salts may enhance the effects of neuromuscular blocking agents. The neuromuscular blocking effects of parenteral magnesium and aminoglycoside antibacterial agents may be additive.

CNS depressants
When barbiturates, narcotics or other hypnotics (or systemic anesthetics) are to be given in conjunction with magnesium, their dosage should be adjusted with caution because of additive depressant effects of magnesium and the risk of respiratory depression.

Drug transporters
Pretreatment with magnesium has been reported in the rat to attenuate cisplatin (CDDP)-induced nephrotoxicity (CIN). Magnesium co-administration reduced platina accumulation by regulating the expression of the renal transporters, rOct2 and rMate1 and, thereby, attenuated CIN.

4.6 Fertility, pregnancy and lactation

Pregnancy
Magnesium sulfate easily crosses the placenta, and fetal serum levels will closely mirror maternal estimations.

As eclampsia may be life-threatening to mother and baby, magnesium sulfate may be administered in this condition. Sufficient amount of magnesium may cross the placenta in mothers treated with high doses e.g. in pre-eclampsia, causing hypotonia and respiratory depression in newborns. When used in pregnant women, fetal heart rate should be monitored and use within 2 hours of delivery should be avoided.
Magnesium sulfate can cause skeletal adverse effects when administered continuously for more than 5 to 7 days to pregnant women. There are retrospective epidemiological studies and case reports documenting fetal adverse effects including hypocalcemia, skeletal demineralization, osteopenia and other skeletal adverse effects with maternal administration of magnesium sulfate for more than 5 to 7 days. The clinical significance of the observed effects is unknown.
If prolonged or repeated exposure to magnesium sulfate occurs during pregnancy monitoring of neonates for abnormal calcium or magnesium levels and skeletal adverse effects should be considered. Serum magnesium levels in preterm infants are higher than adult levels.

Breast-feeding
Magnesium concentration of mature human milk is 31 mg/l. Based on a mean milk transfer of 0.8 l/day and a concentration of magnesium in mature breast milk of 31 mg/l, a secretion of 25 mg/day of magnesium in breast milk

is estimated during the first six months of lactation.
Safety during breast-feeding has not been established. Therefore, it is not advisable to administer magnesium sulfate during breast-feeding unless considered essential.

Fertility
Based on long-term experience, no effects of magnesium on male and female fertility are anticipated.

4.7 Effects on ability to drive and use machines

Parenteral magnesium sulfate is unlikely to affect the ability to drive or to operate machinery.
However, on the basis of the potential adverse effects, some people may feel dizzy or drowsy after receiving parenteral magnesium sulfate. Patients should be advised not to drive or operate machinery.

4.8 Undesirable effects

The frequency of undesirable effects is not known (cannot be estimated from the available data).

Immune system disorders
As with all medicines, hypersensitivity reactions cannot be ruled out.

Excessive administration of magnesium leads to the development of symptoms of hypermagnesaemia which may include:

Metabolism and nutrition disorders
Electrolyte/fluid abnormalities (hypophosphataemia, hypertonic dehydration).
There have been isolated reports of maternal and fetal hypocalcaemia with high doses of magnesium sulfate (see section 4.6).

Nervous system disorders
Respiratory depression.
Nausea, vomiting, drowsiness and confusion.
Coma.
Slurred speech, double vision.
Loss of tendon reflexes due to neuromuscular blockade.

Cardiac disorders
Cardiac arrhythmias, cardiac arrest.
ECG abnormal (prolonged PR, QRS and QT intervals), bradycardia.

Vascular disorders
Flushing of the skin and hypotension due to peripheral vasodilatation.

Musculoskeletal and connective tissue disorders
Muscle weakness.

General disorders and administration site conditions
Thirst.

Especially in patients with impaired renal function, there may be sufficient accumulation of magnesium sulfate to produce toxic effects.

Injection/infusion-related effects
Too rapid administration: quickly developing vasodilatation, reduced blood pressure.

Local: as all parenteral medicines, magnesium sulfate injections may be irritant to veins; extravasation may cause tissue damage.
Intramuscular: pain, redness, swelling or warmth at the injection site, drainage at the injection site, prolonged bleeding, cellulitis, sterile abscess, signs of an allergic reaction, such as difficulty breathing or facial swelling, injury to nearby structures (blood vessels, bones, or nerves), inadvertent intravascular or intra-ostial injection, tissue necrosis, poor absorption due to high injection volume have been described for other magnesium sulfate solutions for 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.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form: https://sideeffects.health.gov.il

4.9 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 listed in the table below:

Magnesium levels			**Manifestation of hypomagnesaemia/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	2.1-4.2	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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other mineral supplements, magnesium sulfate ATC code: A12CC02

Magnesium is a cofactor of more than 300 enzymatic reactions, acting either on the substrate (especially for reactions involving ATP, where its binding to the nucleotide induces an adequate conformation and helps to weaken the terminal O–P bond of ATP, thereby facilitating the transfer of phosphate) or on the enzyme itself as a structural or catalytic component. As ATP utilisation is involved in many metabolic pathways, magnesium is essential in the intermediary metabolism for the synthesis of carbohydrates, lipids, nucleic acids and proteins, as well as for specific

actions in various organs such as the neuromuscular or cardiovascular system. Magnesium can interfere with calcium at the membrane level or bind to membrane phospholipids, thus modulating membrane permeability and electrical characteristics. Magnesium has an impact on bone health through its role in the structure of hydroxyapatite crystals in bone.

5.2 Pharmacokinetic properties

The approximate amount of magnesium: each 1 g of magnesium sulfate heptahydrate will provide 4.1 mmol magnesium.

Absorption and distribution
Magnesium is approximately equally distributed in bone and soft tissues, less than 1% being present in blood compartments. Cellular magnesium concentrations are constantly in the range of 17-20 mmol/l, despite rapid movements across cell membranes through multiple carriers and channels. Intracellular concentrations have been observed to decrease linearly with increasing age, without parallel changes in plasma magnesium concentration.

Total body magnesium content in a healthy adult is around 20-28 g. Approximately 99% of total body magnesium is intracellular. Of this, about 60% is in bone, either strongly bound to apatite, where it is difficult to mobilise, or loosely adsorbed at the surface of mineral crystals, where it can be easily mobilised in response to variation in dietary supply. About 25% of body magnesium is in muscle, where mitochondria are considered to be the intracellular storage site.

About 20-33% is bound to proteins, the remaining about 80% is unbound.
Only the ionized magnesium is physiologically active.

In the whole body, compartmental analysis using stable isotopes showed the existence of at least two major extraplasma compartments: the first compartment represents 80% of the rapidly exchangeable pool with an exchange rate of 48 mg/h; the second pool has a faster exchange rate of 179 mg/h. The sum of these rapidly exchangeable compartments amounts to around 25% of the magnesium body pool.

The most important transport system to tissues appears to be the transient receptor potential melastatin 7 (TRPM7).

Biotransformation
Magnesium sulfate is not metabolized.

Elimination
The kidney plays a major role in magnesium homeostasis and maintenance of serum concentrations. Around 80% of serum magnesium is ultrafiltrable through the glomerulus, but only around 3% of the filtered fraction appears in the urine, owing to an efficient reabsorption taking place mainly (60-70%) in the thick ascending loop of Henle.

The main stimuli that increase urinary magnesium excretion are high natriuresis, osmotic load and metabolic acidosis; those that reduce it are metabolic alkalosis, parathyroid hormone and, possibly, calcitonin. The remaining part of the reabsorption takes place in the distal convoluted tubule via an active transcellular mechanism that finally controls the amount excreted in the urine.

Faecal loss is very limited. The endogenous routes of elimination of absorbed magnesium through the digestive tract are bile, pancreatic and intestinal juices, and intestinal cells; part of these endogenous losses can be reabsorbed. Using stable isotopes, endogenous faecal excretion has been determined to be 49 ± 11 mg/day in six healthy men aged 26-41 years, around 15 mg/day (0.1-0.9 mg/kg body weight/day) in 9- to 14-year-old boys and girls and from 4.7 to 21.7 mg/day in five girls aged 12-14 years, without influence of calcium intake.

Magnesium losses through sweat are likely to be modest, in the range of 1-5 mg/day, on the basis of a daily sweat volume of around 0.5 l/day.

Magnesium losses through menstruation in women are negligible.

Special populations

Paediatric population
The pharmacokinetics of intravenous magnesium sulfate have been studied in 2-14 years old children. The covariate analysis found that **only weight** was a significant predictor of magnesium concentrations in children. Estimated

model parameters suggested that magnesium exhibits a short serum half-life (2.7 h) in children.

No intramuscular or subcutaneous pharmacokinetic data are available in children.

Elderly
No specific pharmacokinetic studies have been performed with parenteral (i.v., i.m. or s.c.) magnesium sulfate in the elderly.

Hepatic impairment
Liver diseases are often accompanied by hypoalbuminemia, which per se may have an effect on the level of total serum magnesium. The serum ionized/total magnesium ratio is inversely related to serum albumin. According to a study patients with the lowest levels of serum albumin have a greater part of their serum magnesium in free biologically active form, as ionized magnesium. In patients with alcoholic hepatopathy the mean concentrations of both serum total and ionized magnesium were lower than normal.

Renal impairment
In renal impairment, there may be accumulation of magnesium.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sulfuric acid (for pH adjustment)
Sodium hydroxide (for pH adjustment)
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6. Magnesium sulfate is incompatible with alkali hydroxides (forming insoluble magnesium hydroxide), alkali carbonates (forming insoluble magnesium carbonate) and salicylates. The activities of streptomycin sulfate and tetramycin sulfate are inhibited by magnesium ions.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

Shelf life after first opening:
The medicinal product should be used immediately after opening the ampoule (see section 6.6).

Shelf life after dilution:
Chemical and physical in-use stability has been demonstrated for 72 hours at 30°C and 2 – 8°C when diluted to a concentration of not more than 200 mg/ml magnesium sulfate heptahydrate in 0.9% sodium chloride or 5% glucose solution.
Solutions diluted to 25% should be used immediately.
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 – 8°C unless dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Store below 30ºC, do not freeze.
For storage conditions after dilution or first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

2 ml or 10 ml of solution in type I hydrolytic class colourless borosilicate glass ampoules with one point cut. Ampoules are packed in liner. Liners are packed into outer carton.
Pack size:
10 ampoules

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

For intramuscular use, a 50% solution is used undiluted or diluted to 25%. For intravenous use, the 50% solution must be diluted before use, with a suitable diluent, such as 5% glucose or 0.9% sodium chloride solution.

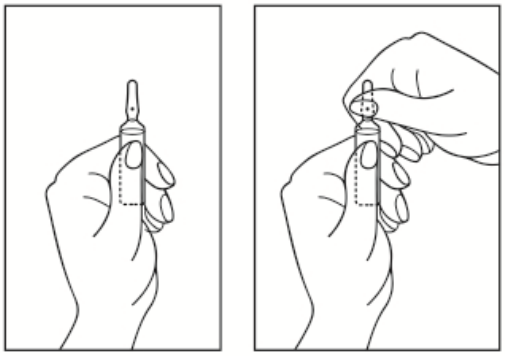
For single use only. Discard any unused contents.

This medicinal product should be used immediately after opening the ampoule (section 6.3).

This medicine should not be used if there are any visible signs of deterioration (e.g. particles).

Instruction of ampoule opening:

1) Turn the ampoule with coloured point up. 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).



Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

A.L.Medi-Market Ltd., 3 Hakatif street, Emek Hefer Industrial Park, 3877701, Israel

8. MANUFACTURER

AS Kalceks, Krustpils iela 71E, Rīga, LV-1057, Latvia

9. MARKETING AUTHORISATION NUMBER(S)

165-51-35894-00

10. DATE OF REVISION OF THE TEXT

Revised in October 2025