SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Micro Kalium prolonged-release capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 capsule contains 600 mg of potassium chloride corresponding to 8 mmol (315 mg) of potassium ions.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Prolonged-release capsule, hard

Maroon opaque hard capsules

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment and prevention of hypokalaemia.

4.2 Posology and method of administration

Posology

Potassium deficiency prevention:
The recommended dose is 16-24 mmol (2-3 capsules) daily.

Existing potassium deficiency treatment:
The recommended dose is 16-32 mmol (2-4 capsules) 2-3 times daily.
Overall: 32-96 mmol (4-12 capsules) daily.

The dose should be adapted to serum potassium levels.

Children and adolescents
The safety and effectiveness of Micro-Kalium have not been established for children and adolescents.

Method of administration
Oral use.
The capsules should not be chewed and should be taken during or after meals with plenty of fluid. The capsules should also not be sucked.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

- Hypersensitivity to a potassium dose, e.g. for adynamia episodica hereditaria and paramyotonia congenita.
- All types of hyperkalaemia as a further potassium intake can lead to arrhythmias and even cardiac arrest.
- Hyperkalaemia can also lead to complications in the following diseases: marked renal failure, diseases with considerable cell destruction (e.g. trauma, burns, severe haemolysis, rhabdomyolysis, dissolution of tumour tissue), untreated Addison's disease, hyporeninemic hypoaldosteronism and decompensated metabolic acidosis and acute dehydration states.
- Marked renal failure even if there is no evident hyperkalaemia present.
- Concomittant use of potassium-sparing diuretics (spironolactone, triamterene, amiloride).
- As with all potassium preparations, this medicinal product is contraindicated for patients with delayed or reduced gastrointestinal transit, partial or total oesophageal occlusion, e.g. due to a carcinoma (of the oesophagus, trachea or thyroid gland), aortic aneurysm, left-ventricular dilatation, inflamed strictures due to reflux oesophagitis and oesophagus displacements following cardiac surgery (e.g. valve replacement).
- Any stenoses or atonias within the entire gastrointestinal tract (e.g. pyloric stenoses, enterosterosis).

4.4. Special warnings and precautions for use

Lesions of the gastrointestinal tract
The preparation should be stopped immediately if the following occur during treatment: marked nausea, severe vomiting, severe abdominal pains, flatulence, diarrhoea or gastrointestinal bleeding. These symptoms may be evidence of an ulceration or even a perforation of the GIT. The associated risk is increased in the presence of oesophageal stenoses, known ulcus ventriculi and duodeni, delayed intestinal transit or intestinal ischaemia due to generalised arteriosclerotic vascular changes.

Hyperkalaemia
Potassium salts may cause hyperkalaemia and cardiac arrest in patients with potassium-excretion disorders. This predominantly occurs in patients whose potassium is administered intravenously but should not be excluded for those taking it orally. Potential fatal hyperkalaemia can develop quickly and is asymptomatic. Therefore, patients with chronic renal failure or with other illnesses, which lead to potassium-excretion disorders, should be carefully monitored (Serum K^+ concentration determinations). The dosage must be adapted to the circumstances.

Metabolic acidosis
Patients with hypokalaemia and a metabolic acidosis should not receive potassium chloride, but be treated with alkalising potassium salts, like potassium bicarbonate, potassium citrate or potassium acetate.

Periodic Serum-K^+ concentration determinations are recommended throughout long-term potassium substitution therapy, particularly for the increased risk of hyperkalaemia (e.g. with renal function disorders and heart diseases). In addition, the acid-base balance, other serum electrolyte levels (e.g. Magnesium, see below), the ECG and the overall clinical status should all be monitored.

For blood samples to determine the K^+ plasma concentration it needs to be considered that artificial increases in the potassium levels may occur following an improper venous puncture or as a result of in vitro haemolysis of the blood taken.

Other pharmaceutical forms of potassium salts are favoured for patients with stomas, due to the possible change to intestinal transit.

Balancing the intracellular potassium deficiency is complicated for certain patients who have a diuretic-induced magnesium deficiency in addition to hypokalaemia. Therefore, the magnesium deficiency should be treated at the same time.

Potassium serum levels may also be influenced by reduced salt or reduced sugar diets or through regular consumption of large quantities of liquorice. Regular check-ups of serum electrolytes levels should be undertaken and an abrupt change to dietary habits should be avoided.

4.5 Interactions with other medicinal products and other forms of interaction

The concomitant use of potassium-sparing diuretics (spironolactone, triamterene, amiloride) is contraindicated (see section 4.3).

As anticholinergics inhibit gastrointestinal motility, they should only be prescribed together with fixed pharmaceutical forms of a potassium preparation if strongly indicated and with the relevant caution; this particularly applies in high doses. The medicinal product should only to be used cautiously along with other medicinal products, which are known to potentially lead to hyperkalaemia, e.g. non-steroidal antiphlogistic drugs (e.g. indomethacin), betablockers, heparin and digoxin.

ACE inhibitors can lead to potassium retention as they inhibit aldosterone production. Therefore, patients treated with ACE inhibitors should be carefully monitored if they receive a potassium preparation.

4.6 Fertility, pregnancy and lactation

Pregnancy
As intestinal motility is reduced during pregnancy, set pharmaceutical forms of potassium preparations should only be prescribed if strongly indicated.

Breast-feeding
The normal potassium content in breastmilk is approximately 13 mmol/L. As potassium intake is distributed throughout the body, the use of the medicinal product can be expected to have little or no influence on the potassium levels in breastmilk, provided that the total potassium content in the body is not excessively high.

4.7 Effects on ability to drive and use machines

Micro Kalium prolonged-release capsules has no or a negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Very common: ≥ 1/10
Common: ≥ 1/100, < 1/10
Uncommon: ≥ 1/1,000, < 1/100
Rare: ≥ 1/10,000, < 1/1,000
Very rare: < 1/10,000
Not known: Frequency cannot be estimated from the available data

System organ class	Adverse reaction	Frequency
Metabolic and nutritional disorders	Hyperkalaemia[1]	Not known
Gastrointestinal disorders	Nausea[2] Flatulence[2]	Rare

System organ class	Adverse reaction	Frequency
	Vomiting[2] Abdominal pain[2] Diarrhoea[2]	
	Occlusion[3] Bleeding[3] Ulceration[3] Perforation[3]	Very rare
Skin and subcutaneous tissue disorders	Pruritus Rash Urticaria	Rare

1 Dangerous hyperkalaemia may occur in patients whose potassium excretion or distribution in the body is disrupted (see sections 4.3 and 4.4).
2 Oral intake of potassium salts may lead to those adverse reactions. The reason for this is mucous membrane irritations of the gastrointestinal tract, which can be best reduced through increased fluid intake (as possible) and by concomitantly taking the medicinal product during or after meals or taking a reduced dosage.
3 See section 4.4. For most of these patients other simultaneous factors existed, which could be associated with such unwanted reactions (e.g. delayed intestinal passage or obstruction of the gastrointestinal tract).

Reporting 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

Clinical Symptoms
The clinical symptoms of an acute potassium overdose (poisoning) are mainly characterised by hyperkalaemia with cardiovascular and neuromuscular disorders. Renal insufficiency may already occur after relatively low doses of the medicinal product.

Cardiovascular system
Ventricular arrhythmias, bundle branch block with ventricular fibrillation accompanied by a decrease in blood pressure and states of shock ranging up to cardiac arrest may occur.
In addition to the increase of the K^+ serum concentration, the following ECG changes are typical: increased t-wave amplitude and t-wave peaking, p-wave disappearance, widening of QRS complex and ST segment reduction.

Central nervous system
Paraesthesia, seizures, loss of reflex, atonia of the striated muscle, which may range up to symptoms of respiratory paralysis.

Treatment
In acute cases of poisoning the excess potassium must be removed from the body or inactivated through:
- Induced vomiting
- Stomach flushing
- Administration of cation exchange resins, either orally or by stomach instillation, e.g. 20 g Polystyrene sodium sulfonate with 20 mL of a 70% sorbitol solution, 3-4 times a day.

For **moderate hyperkalaemia** (Plasma K^+ concentrations between 6.5 and 8 mmol/L and t-wave peaking as the only ECG change):

- Stimulation of transcellular potassium transportation through intravenous administration of 300 to 500 mL/hour of a 10% dextran solution with an insulin content of 10 to 20 units/L
- Correction of a possible acidosis through intravenous sodium bicarbonate administrations (44 to 132 mmol/L in a glucose solution)
- Correction of a possible hyponatraemia and hypovolemia.

In **severe cases of hyperkalaemia** (Plasma K^+ concentrations > 8 mmol/L or in case of considerable ECG changes including missing p-wave ,widening of the QRS complex, t-wave disappearance or the occurrence of ventricular arrhythmias):
- Glucose solution (with insulin) and/or bicarbonate infusions, as described above (leading to an extracellular to intracellular potassium displacement, onset after 30 mins)
- Correction of a possible acidosis through intravenous sodium bicarbonate administrations (44 to 132 mmol/L in a glucose solution)
- Intravenous administration of 10 to 30 mL of a 10% potassium gluconate solution for 1 to 5 minutes under ongoing ECG control (leading to a reversal of the potassium effect on the cell membranes)
- Administration of cation exchange resins through high retention enemas and namely as follows:
  30 to 50 g sodium polystyrene sulfonate in 100 mL of warm watery sorbitol solution, if possible, should be held in the sigmoid colon for a few hours. The colon will then be flushed with a sodium free solution in order to remove the resin. The enemas can be repeated, or oral ion-exchangers may be administered repeatedly so the normalised K^+ concentration is maintained.
- Haemodialysis or peritoneal dialysis may be particularly useful for patients with renal insufficiency.

When treating hyperkalaemia it should be considered that for patients under well-controlled treatment with digitalis a quick reduction of the K^+ serum levels can lead to digitalis intoxications.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Mineral supplements, potassium preparations
ATC code: A12BA01

Micro-Kalium contains potassium chloride in a micro-encapsulated form. This is a modern technology by which each KCl particle is coated with an extremely thin pharmacologically inert membrane that slowly disperses KCl in the gastrointestinal tract.
Due to these patented galenic forms highly localised KCl concentrations are avoided. The irritant effect of free potassium in the gastric mucosa and intestinal mucous membrane are limited to a minimum and thus achieve good tolerance.

Pharmacodynamic effects
K^+, the most encountered intracellular cation, plays a decisive role in different important physiological functional processes, e.g. for the transmission of nerve impulses, contraction of muscle tissues (cardiac and skeletal muscles and smooth muscle) and for maintaining normal renal function. It also contributes to the regulation of osmotic pressure and acid-base balance. K^+ concentrations vary intracellularly between 130 and 150 to 160 mmol/L and in plasma between 3.5 and 5 mmol/L. Although there is no standardised correlation between the K^+ plasma concentration and the total body content, clinical signs of a potassium deficiency usually appear if the K^+ plasma concentration falls below 3.5 mmol/L (hypokalaemia).
Signs of potassium deficiency are neuromuscular function disorders, which can range from minor muscular weakness to actual paralysis, intestinal muscle relaxation up to the paralytic ileus, and frequent disorders of the heart muscle function with ECG changes. Characteristic

are delayed PR interval, increased U waves, widened and flattened T waves and a reduction of ST-segment elevation.
Hypokalaemia can be prevented or corrected through increased potassium intake. In addition, an increased potassium intake through a potassium-rich diet, which is not always easy to do, is offered through the administration of Micro-Kalium as a suitable alternative. As there is commonly a deficiency of K^+ and Cl^- ions, potassium chloride is preferred as salt, in order to balance the majority of clinical symptoms of hypokalaemia.

5.2 Pharmacokinetic properties

Absorption
When individual doses of 5 or 6 capsules (corresponding to 40 or 48 mmoL K^+) are taken, KCl is gradually released during gastrointestinal transit over a period of approximately 4 hours. Reabsorption occurs in a way that the renal potassium-excretion is delayed around 40 to 60 minutes compared to a same dose of KCl solution.

Elimination
If potassium balance is achieved, around 90% of the potassium supplied by Micro-Kalium is excreted in urine within 8 hours and more than 98% within 24 hours.

5.3 Preclinical safety data

Potassium salts cause tissue irritation in high concentrations. Other toxic effects, including carcinogenic, mutagenic and reproductive toxicity effects, are not expected for the intended type and duration of application when considering the contraindications and other information.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule content: Ethylcellulose

Capsule shell: Gelatine
Erythrosine (E 127)
Titanium dioxide (E 171)
Ferric oxide black (E 172)

6.2 Incompatibilities
Not applicable.

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

6.4 Special precautions for storage
Do not store above 25°C.

6.5 Type and contents of container
PVC/aluminium blister packs of 50

6.6 Special precautions for disposal
No special requirements.

7. MARKETING AUTHORISATION HOLDER
A.L.MEDI-MARKET LTD, 3 Hakatif St., Emek Hefer Industrial Park, 3877701, Israel

8. **MANUFACTURER**
G.L. Pharma GmbH, Industriestrasse 1, A-8502 Lannach, Austria

9. MARKETING AUTHORISATION NUMBER
170-47-36215-00

10. DATE OF REVISION OF THE TEXT
Approved in August 2022