

1. NAME OF THE MEDICINAL PRODUCT

Slow-K

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One sugar-coated prolonged release tablet contains 600mg potassium chloride as active substance equivalent to 8mmol potassium ion (K⁺)

Excipients: Each tablet contains 96.4mg sucrose

For a full list of excipients, see section 6.1 List of Excipients.

3. PHARMACEUTICAL FORM

Sugar coated prolonged release tablet

Pale orange, round, biconvex, sugar-coated tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment and prevention of hypokalaemia.

4.2 Posology and method of administration

It is important that the tablets should be swallowed whole, with fluid during meals, whilst the patient is sitting upright.

General Populations:

The dosage of Slow-K should be adjusted to the individual needs of each patient. 2-3 tablets daily are usually an adequate supplement to prevent hypokalaemia. In states of potassium deficiency doses of 5 to 6 tablets daily may be needed increasing up to 12 tablets daily in severe deficiency. If the dosage exceeds 16mmol K⁺ (2 tablets) it should be taken in divided doses. Where intermittent diuretic therapy is being used, it is advisable to give Slow K on intervening days between administration of the diuretic. The response to treatment should preferably be monitored by repeat determination of plasma potassium and Slow K continued until the hypokalaemia has been corrected.

Special populations

Renal impairment

In patients with mild to moderate renal impairment, Slow K should be given with extreme caution with frequent serum potassium monitoring due to increased risk of hyperkalemia. Slow-K is contraindicated in patients with severe renal impairment (see also section 4.3 Contraindications).

Hepatic impairment

No studies have been performed in hepatically impaired patients. However, Slow-K should be given with caution due to increased likelihood of electrolyte disturbances in patients with hepatic impairment (see also section 4.3 Contraindications).

Paediatrics

Safety and effectiveness in children have not been established, Slow-K is therefore not recommended for paediatric use.

Geriatrics (older than 65 years)

Slow-K should be given with caution and with frequent serum potassium monitoring due to increased risk of hyperkalemia.

Method of administration

Slow-K is advised to be given with or after food to minimize gastric irritation. The sugar-coated tablets must not be crushed, chewed, or sucked, but should be swallowed whole with an adequate amount of fluid while the patient is sitting upright.

4.3 Contraindications

All forms of hyperkalaemia as may occur in marked renal failure (even when not yet associated with manifest hyperkalaemia), untreated Addison's disease, hyporeninaemic hypoaldosteronism, acute dehydration and conditions involving extensive cell destruction (e.g. severe burns).

Hypersensitivity to potassium administration e.g. hyperkalaemic periodic paralysis and congenital paramyotonia, or hypersensitivity to any of the excipients.

Hyperkalemic periodic paralysis: It is an inherited autosomal dominant disorder which affects sodium channels in muscle cells and the ability to regulate potassium levels in the blood. The term hyperkalemic is misleading since patients are often normokalemic during attacks. The fact that attacks are precipitated by potassium administration best defines the disease.

All solid forms of potassium medication are contraindicated in the presence of obstructions in the digestive tract (e.g. resulting from compression of the oesophagus due to dilation of the left atrium or from stenosis of the gut).

In cases of metabolic acidosis, the hypokalaemia should be treated not with potassium chloride but with an alkaline potassium salt (e.g. potassium bicarbonate).

Concomitant treatment with potassium sparing diuretics (e.g. spironolactone, triamterene, amiloride) (See also section 4.5 Interaction with other medicinal products and other forms of interaction).

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

4.4 Special warnings and precautions for use

Gastrointestinal disorders

Potassium chloride, alone or in combination with other medications may induce ulceration in the gastrointestinal tract, in particular the lower oesophagus and small bowel. This possibility is increased in patients with local, functional or mechanical disorders of the gastrointestinal tract, with cardiovascular disease, or in those on prolonged therapy or receiving anticholinergics. Symptoms or signs suggesting ulceration or obstruction of the tract should be regarded as reasons to discontinue medication immediately (See also section 4.8 Undesirable effects).

Patients with ostomies may have altered intestinal transit times and are better treated with other forms of potassium salts.

Hyperkalaemia

Potassium salts should only be administered with extreme caution to patients with renal dysfunction, hepatic disease (because of the risk of hyperkalaemia), history of or existent peptic ulceration. Monitoring of serum potassium and other electrolytes is particularly necessary in patients with diseases of the heart and kidneys.

Slow K should be used with caution in patients receiving any drug known to have a potential for hyperkalaemia, such as ACE inhibitors, angiotensin –II-receptor antagonists, NSAIDs (e.g. indomethacin), beta-blockers, heparin, digoxin and ciclosporin (see also section 4.5 Interaction with other medicinal products and other forms of interaction).

Treatment Monitoring

Periodic serum potassium determinations are recommended during long term supplementation, especially in clinical conditions which carry a risk of hyperkalaemia (e.g. impaired renal function or heart disease) (see also section 4.5 Interaction with other medicinal products and other forms of interaction).

Other

In some patients, diuretic induced magnesium deficiency will prevent restoration of intracellular deficits of potassium so that hypomagnesaemia should be corrected at the same time as hypokalaemia.

Slow-K contains sucrose (=saccharose). Patients with rare hereditary disorders like fructose-intolerance, glucose-galactose malabsorption, or sucrase-isomaltase insufficiency should not use this medicine

4.5 Interaction with other medicinal products and other forms of interaction

Observed Interactions resulting in a contraindication

Potassium-sparing diuretics:

Concomitant treatment with potassium-sparing diuretics (spironolactone, triamterene, amiloride) is contraindicated (see also section 4.3 Contraindications). Drugs which interfere with potassium excretion may promote hyperkalemia when given together with Slow-K.

Anticipated interactions resulting in concomitant use not being recommended

Drugs causing hyperkalemia:

Slow-K should be used with caution in patients receiving any drug known to have a potential for hyperkalemia, such as ACE inhibitors, angiotensin-II-receptor-antagonists, NSAIDs (e.g. indomethacin), beta-blockers, heparin, digoxin ciclosporin (see also section 4.4 Special warnings and precautions for use).

Interactions to be considered

Drugs causing hyperkalemia:

Other drugs such as direct renin inhibitors (e.g. aliskerin) and proton pump inhibitors can cause hyperkalemia when used concomitantly with Slow-K. Thus, caution should be exercised in their concomitant use.

Anticholinergics:

Since anticholinergic drugs may reduce gastrointestinal motility, they should be prescribed with great care when given concomitantly with solid oral potassium preparations, particularly in high dosage (see also section 4.4 Special warnings and precautions for use).

4.6 Fertility, pregnancy and lactation

Pregnancy

For Slow-K no clinical data on exposed pregnancies are available.

There is no indication in animal studies of direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development (see also section 5.3 Preclinical safety data).

Because of gastrointestinal hypomotility associated with pregnancy, solid forms of oral potassium preparations should be given to pregnant women only if considered essential.

Lactation

The excretion of potassium in milk has not been studied in animals or human.

The normal K⁺ content of human milk is about 13mmol/litre. Since oral potassium becomes part of the body's potassium pool, provided this is not excessive, Slow K can be expected to have little or no effect on the potassium level in human milk.

Slow-K should only be given during breast-feeding when the expected benefit to the mother outweighs the potential risk to the baby.

Fertility

There are no special recommendations.

4.7 Effects on ability to drive and use machines

None known to date.

4.8 Undesirable Effects

Side-effects are rare with Slow-K, as any excess potassium is rapidly excreted in the urine.

Adverse drug reactions from post-marketing experience (frequency not known)

The following adverse drug reactions have been derived from post-marketing experience with Slow-K. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency which is therefore categorized as not known. Adverse drug reactions are listed according to system organ classes in MedDRA. Within each system organ class, ADRs are presented in order of decreasing seriousness.

Table 4-1 Adverse drug reactions from post-marketing experience (frequency not known)

Gastrointestinal disorders Gastrointestinal obstruction, gastrointestinal hemorrhage, gastrointestinal ulcer, with or without perforation of the upper or lower GIT. Nausea, flatulence, vomiting, abdominal pain, diarrhea
Skin and subcutaneous tissue disorders Urticarial, rash, pruritus
Metabolism and nutrition disorders Hyperkalemia can develop in patients having difficulties, either with renal potassium excretion or with internal disposal (metabolism).

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

<http://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il>

4.9 Overdose

The clinical picture of acute overdosage (intoxication) with potassium is characterized chiefly by hyperkalemia together with cardiovascular and neuromuscular disturbances, which, in the presence of renal impairment, may already develop after relatively low doses of Slow-K. Presence of radiopaque tablets on abdominal X-ray, will confirm the ingestion.

Cardiovascular system

Hypotension, shock, ventricular arrhythmias, bundle-branch block, ventricular fibrillation leading possibly to cardiac arrest.

Besides elevation of serum potassium concentration, typical ECG changes are also encountered (increasing amplitude and peaking of T waves, disappearance of P wave, widening of QRS complex and S-T segment depression).

Central nervous system and muscles

Paraesthesiae, convulsions, areflexia, flaccid paralysis of striated muscle leading possibly to respiratory paralysis.

Pharmacobezoar

Rare cases of pharmacobezoar have been reported in association with large overdose of Slow-K tablets. Formation of pharmacobezoar may cause continual release of potassium chloride, hours after drug ingestion.

Treatment

In cases of acute poisoning, remove and/or inactivate excess potassium by:

- Induction of vomiting
- Gastric lavage
- Administration of cation exchange resin by mouth or gastric instillation (e.g. 20 g sodium polystyrene sulfonate with 20 mL 70% sorbitol solution).
- In case of moderate/severe hyperkalemia, standard treatment should be initiated after monitoring the serum potassium levels and should be managed accordingly.
- In case of pharmacobezoar consideration should be given to vigorous gastrointestinal decontamination procedures for effective removal of the pharmacobezoar which may include, but are not limited to, endoscopy or surgery in selected patients, depending on the size of bezoar and the number of tablets ingested.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Potassium supplement, ATC code: A12BA01

Potassium, as the most abundant intracellular cation, plays an essential role in several important physiological functions, including transmission of nerve impulses, contraction of cardiac, skeletal, and smooth-muscle tissues, and maintenance of normal renal function. It also aids in the regulation of osmotic pressure and the acid-based balance. Concentrations of K⁺ range in intracellular fluid from 130 to 150 up to 160 mmol/L and in plasma from 3.5 to 5 mmol/L. Although there is no uniform correlation between plasma concentrations of potassium and total body stores, clinical signs of K⁺ deficiency are usually observed whenever the plasma potassium concentration falls below 3.5 mmol/L (hypokalemia). These signs include: impaired neuromuscular function, which may vary from minimal weakness to frank paralysis; intestinal dilatation and ileus; and, more frequently, abnormalities myocardial function with disturbed ECG patterns characterized by a prolonged PR interval, an exaggerated U wave, a broad and flat T wave, and a depressed ST segment.

Hypokalemia can be prevented and/or corrected by giving supplementary potassium. Apart from increasing dietary intake of potassium-rich foods, which may not always be practicable, a suitable alternative is to administer Slow-K. In view of the frequency with which deficits of K⁺ and CL⁻ coexist, potassium chloride is the preferred salt for most of the clinical conditions associated with hypokalemia.

5.2 Pharmacokinetic properties

Absorption

Following a single dose of Slow K, potassium chloride is released over a period of approximately 4 hours. Renal excretion of potassium chloride following ingestion of Slow K occurs 30-60 minutes later than when the same dose is given in the form of a solution.

Elimination

In the presence of a normal potassium balance 90% of the potassium supplied by Slow K is excreted renally within 8 hours and more than 98% by 24 hours.

Special population

Elderly Patients

No pharmacokinetics studies of potassium chloride are reported in elderly population. However, these patients are more likely to develop hyperkalemia due to physiological changes, and reduced renal function.

Pediatrics

No pharmacokinetics studies of potassium chloride are reported in the pediatric population.

Hepatic impairment

No pharmacokinetics studies of potassium chloride are reported in patients with hepatic impairment.

Renal impairment

Potassium is almost completely excreted via urine and its excretion rate highly correlates with the glomerular filtration rate. Considering the possibility of hyperkalemia in these patients and severity of outcome, Slow-K is contraindicated in patients with severe renal impairment. If used in patients with mild to moderate renal impairment, extreme caution along with frequent serum potassium monitoring is recommended.

5.3 Preclinical safety data

Preclinical data do not support a special hazard for humans based on conventional studies of acute toxicity, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction.

The acute and repeated-dose oral toxicity of potassium chloride (KCl) in animals is low. Gastrointestinal irritant effects have been observed in rhesus monkeys at high oral dosages of Slow-K. Some positive results in *in vitro* genotoxicity assays were attributed to very high concentrations of KCl. Carcinogenicity studies in rats administered KCl in-feed were negative. Limited information from oral developmental studies in rodents indicates there is no ill effect on offspring. There is no evidence from animal experiments that oral KCl exerts any teratogenic effects or reproductive toxicity which would be relevant to man.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet Core:

Cetostearyl alcohol

Gelatin

Magnesium stearate

Tablet Coating:

Acacia

Gelatin

Titanium dioxide

Talc

Sucrose

Dispersed buff 70753 containing red iron oxide (E172), yellow iron oxide (E172) and Titanium dioxide (E171)

Carnauba Wax

6.2 Incompatibilities

Not applicable

6.3 Special Precautions for Storage

Store below 30°C.

Protect from moisture.

Store in the original package.

Keep the container tightly closed.

Shelf life after first opening: 60 days.

Slow-K must be kept out of the reach and sight of children.

6.4 Nature and Contents of Container

Plastic container containing 100 sugar coated prolonged release tablets.

6.5 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements

7. REGISTRATION HOLDER

Novartis Israel Ltd., 36 Shacham St., Petach-Tikva

8. Manufacturer:

Sandoz Grup, Gebze, Turkey

For Novartis Pharma AG., Basel, Switzerland

REGISTRATION NUMBER

115-88-22133