

SLOW-K®

potassium chloride

DESCRIPTION

Active substance:

Potassium Chloride B.P. 600 mg (approximately 8 mEq) in a slow-release wax core.

Active moiety:

Potassium

Excipients:

Cetostearyl alcohol, gelatin, magnesium stearate, acacia, titanium dioxide, purified talc, sucrose, red iron oxide, yellow iron oxide and Carnauba Wax.

PHARMACOLOGY

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-base 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 may be observed whenever the plasma potassium concentration falls below 3.5 mmol/L (hypokalaemia). These signs include: impaired neuromuscular function, which may vary from minimal weakness to frank paralysis; intestinal dilatation and ileus; and, more frequently, abnormalities of myocardial function, with disturbed ECG patterns including an exaggerated U wave, a broad and flat T wave, and a depressed ST segment.

Hypokalaemia 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 hypokalaemia.

Pharmacokinetics

Absorption

The potassium chloride in SLOW-K is gradually released from the insoluble neutral wax core during transit through the alimentary tract, and is completely absorbed. The wax core is excreted in a softened form in the faeces, but its presence there is not indicative of incomplete absorption of the active ingredient.

The characteristic slow release, sustained over a period of 3 to 4 hours, virtually precludes high concentrations of potassium chloride accumulating in localised areas of the gut, which otherwise might irritate, or damage, the mucosa. The release of potassium is largely independent of pH.

Hyperkalaemia is rarely encountered because any excess of potassium is normally rapidly excreted via the kidneys. The pattern of absorption of potassium from SLOW-K is such that renal excretion occurs 30 to 60 minutes later than when a dose of the same size is given in solution.

Elimination

In the presence of a normal potassium balance, approximately 90% of the potassium supplied by SLOW-K is excreted via the kidneys within 7 hours, and more than 98% within 24 hours.

The chloride salt is usually preferable to the bicarbonate, citrate or tartrate as potassium and chloride loss are often associated. A potassium supplement which does not contain the chloride ion may be largely excreted in the urine.

SLOW-K does not taste unpleasant and is readily acceptable to patients.

Special population

Elderly Patients

No pharmacokinetics studies of potassium chloride are reported in elderly population. However, these patients are more likely to develop hyperkalaemia 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 hyperkalaemia 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.

CLINICAL TRIALS

No clinical trials have been conducted with SLOW-K.

INDICATIONS

For the treatment and specific prevention of hypokalaemia in patients who cannot tolerate oral potassium drinks or who find their taste unacceptable:

- during protracted or intensive diuretic medication for hypertension, massive oedema, or congestive heart failure (potassium supplementation is of particular importance in patients under concomitant digitalisation, because hypokalaemia increases the toxicity of digitalis)
- in liver cirrhosis, especially during diuretic therapy
- in renal diseases associated with increased potassium excretion (e.g. salt wasting nephropathies, hereditary tubular disorders)
- in gastro-intestinal disorders which induce potassium loss (e.g. severe or chronic diarrhoea, vomiting, fistula drainage, enterostomy or abuse of laxatives)
- in hypochloraemic alkalosis or in patients receiving a low salt diet or a diet deficient in potassium
- during prolonged or intensive treatment with corticosteroids, ACTH, carbenoxolone or high doses of carbenicillin or benzylpenicillin
- in Cushing's syndrome or hyperaldosteronism
- in megaloblastic anaemia during the early stages of treatment

In these conditions, SLOW-K is particularly indicated if a diet rich in potassium cannot be guaranteed.

CONTRAINDICATIONS

- Hypersensitivity to potassium administration (e.g. adynamia episodica hereditaria, congenital paramyotonia) or hypersensitivity to any of the excipients (see Description).
- All forms of hyperkalaemia, as encountered in marked renal failure, in conditions involving extensive cell destruction (e.g. trauma, severe burns, crush syndrome, massive haemolysis, rhabdomyolysis, tumour lysis), in untreated Addison's disease, in hyporeninemic hypoaldosteronism, or in decompensated cases of metabolic acidosis and acute dehydration.
- Hyperkalaemic periodic paralysis (an inherited autosomal dominant disorder affecting sodium channels in muscle cells and the ability to regulate potassium levels in the blood). Potassium administration precipitates attacks. Serum potassium might be slightly elevated but may also be normal during an attack
- Marked renal failure, even where hyperkalaemia is not yet manifest.
- All conditions in which passage through the digestive tract is retarded or obstructed (e.g. diverticula, compression of the oesophagus, gastro-intestinal stenosis or atony).
- Gastric and/or intestinal ulcers
- Concomitant treatment with potassium-sparing diuretics (aldosterone antagonists, triamterene, amiloride) (see Precautions and Interactions with Other Medicines).
- Patients in whom there is cause for arrest or delay in tablet passage through the gastrointestinal tract, such as partial or complete oesophageal obstruction (e.g. by oesophageal, postcricoidal or thyroidal carcinomas, aortic aneurysm, left-atrial enlargement,

inflammatory stricture due to reflux oesophagitis, oesophageal displacement due to cardiac surgery), stenosis or atony in any part of the gastrointestinal tract.

PRECAUTIONS

Gastrointestinal Disorders

If a patient receiving SLOW-K develops pronounced nausea, severe vomiting, severe abdominal pains or flatulence, diarrhoea or gastrointestinal haemorrhage, the preparation should be withdrawn at once, because these signs and symptoms may indicate ulceration or perforation in the gastro-intestinal tract (see Adverse Effects).

Such risks may be increased in patients with oesophageal stasis, known peptic and/or gastric ulcers, delayed intestinal transit, or intestinal ischemia due to generalised atherosclerotic vascular disease.

Caution should be exercised when prescribing solid oral potassium preparations, particularly in high dosage, patients concurrently receiving anticholinergic agents because of their potential to reduce gastrointestinal motility (see Interactions with other medicines).

Because of the possibility of their causing gastrointestinal irritation, oral potassium preparations should be prescribed with particular caution in patients with a history of peptic ulcer.

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

SLOW-K is advised to be given with or after food to minimise gastric irritation. The sugar-coated tablets should be swallowed whole as described in section "Dosage and Administration".

Hyperkalaemia

Owing to the risk of producing hyperkalaemia, potassium salts should not be given concomitantly with potassium-sparing diuretics (aldosterone antagonists, triamterene or amiloride).

SLOW-K is contraindicated in patients with marked renal failure (see Contraindications). In patients with mild to moderately impaired renal function, special care should be exercised when prescribing potassium salts in view of the risk of their producing hyperkalaemia and cardiac arrest. This arises most commonly in patients given potassium by the intravenous route, but it may also occur in patients receiving potassium orally. Potentially fatal hyperkalaemia can develop rapidly and may be asymptomatic.

SLOW-K should be used with caution in patients receiving any drug known to have a potential for hyperkalaemia (see Interactions with other Medicines). Particularly careful monitoring of

serum electrolytes and appropriate dosage adjustments is indicated in cases of protracted therapy with large doses of potassium, and must invariably be carried out in patients with impaired renal function or heart disease.

Metabolic Acidosis

Hypokalaemia occurring in cases of metabolic acidosis should be treated, not with potassium chloride, but with the potassium salt of a weak acid (e.g. potassium bicarbonate).

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 hyperkalaemia, SLOW-K is contraindicated in patients with severe renal impairment.

Patients with 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.

Treatment Monitoring

Periodic serum potassium determinations are recommended during long-term potassium supplementation, especially in clinical conditions which carry a risk of hyperkalaemia (e.g. impairment of renal function, heart disease).

In addition, careful attention should be paid to the acid-base balance, to other serum electrolyte levels (e.g. magnesium), to the ECG, and to the clinical status of the patient.

When blood samples are taken for analysis of plasma potassium, it is important to bear in mind that artifactual elevations can occur after an improper vein puncture technique or as a result of *in vitro* haemolysis of the sample.

Other

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

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

Effects on fertility

No specific fertility studies with potassium chloride have been conducted. There are no special recommendations.

Use in Pregnancy

No adverse effects on embryonal development were observed in mice and rats administered potassium chloride during gestation at oral doses up to 235 and 310 mg / kg / day. Oral potassium preparations in solid dosage forms should be given to pregnant women only if clearly needed, because the gastro-intestinal hypomotility associated with pregnancy increases the possibility of adverse reactions.

Use in Lactation

Potassium is distributed into breast milk. The excretion of potassium in milk after administration of potassium chloride has not been studied in animals or human.

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

Paediatric Use

Keep out of reach of children. Safety and effectiveness of SLOW-K for use in children have not been established. SLOW-K is only suitable for use in adults and should not be used in children.

Use in the Elderly

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

Genotoxicity

Potassium chloride was negative in the Ames test, with and without metabolic activation. The compound was weakly mutagenic in *L5178Y* mouse lymphoma cells at high concentrations. In chromosome aberration tests with Chinese hamster ovary cells, positive results were obtained without metabolic activation. Increases in mutagenicity and chromosome aberrations observed with potassium chloride *in vitro* occurred in association with cytotoxicity and / or at high concentrations and are considered most likely to not reflect a direct genotoxic effect.

No *in vivo* genotoxicity study has been conducted.

Carcinogenicity

No carcinogenic effects were observed for potassium chloride in studies in rats involving dietary administration at doses up to 1820 mg/kg/day in males for 2 years, and up to 1454 mg/kg/day in males and up to 1685 mg/kg/day in females for 30 months.

INTERACTIONS WITH OTHER MEDICINES

Observed interactions resulting in a contraindication

Potassium-sparing Diuretics

Drugs which interfere with potassium excretion may promote hyperkalaemia when given together with SLOW-K.

Concomitant treatment with potassium-sparing diuretics (aldosterone antagonists such as spironolactone, triamterene, amiloride) is contraindicated (see Contraindications).

Anticipated interactions resulting in concomitant use not being recommended

Drugs Causing Hyperkalaemia

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 Precautions).

Interactions to be considered

Drugs causing hyperkalaemia

Other drugs such as direct renin inhibitors (e.g. aliskiren) and proton pump inhibitors can cause hyperkalaemia when used concomitantly with SLOW-K. Thus, concomitant use should be exercised with caution.

Serum potassium monitoring is recommended.

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 Precautions).

ADVERSE EFFECTS

Oral potassium preparations, particularly if their passage through the gastrointestinal tract is retarded or obstructed, may cause local irritation of the mucosa and thus provoke gastrointestinal disturbances (nausea, flatulence, vomiting, abdominal pains, diarrhoea or gastrointestinal bleeding).

Such unwanted effects, however, are encountered only occasionally if SLOW-K is employed in its proper indications. Though very rare, the possibility of ulceration with serious consequences cannot be completely excluded (see Precautions).

Post-marketing Experience

The following adverse reactions have been reported during post-marketing of 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 categorised as not known.

Adverse reactions are listed according to system organ classes in MedDRA. Within each system organ class, adverse reactions are presented in order of decreasing seriousness.

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

<p>Gastrointestinal disorders Gastrointestinal obstruction, gastrointestinal hemorrhage, gastrointestinal ulcer, with or without perforation of the upper or lower GIT, delayed intestinal transit or obstruction in the GIT. Nausea, flatulence, vomiting, abdominal pain, diarrhea</p> <p>Skin and subcutaneous tissue disorders Urticarial, rash, pruritus</p> <p>Metabolism and nutrition disorders Hyperkalaemia: either with renal potassium excretion or with internal disposal</p>

DOSAGE AND ADMINISTRATION

General populations

The dosage of SLOW-K should be adjusted to suit the cause and extent of the potassium deficiency in each case. Depending on the patient's individual requirements, 2 to 6 tablets daily, given in several fractional doses, will generally suffice. In severe potassium deficiency, however, it may be necessary for a patient to take 9 to 12 tablets daily. When SLOW-K is administered in conjunction with an oral diuretic agent, 1 or 2 tablets daily may be sufficient.

Renal impairment

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

Method of administration

SLOW-K should be given with or after food to minimise 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. Medication with SLOW-K should be continued until the potassium deficiency has been corrected.

OVERDOSAGE

Signs and Symptoms

Cardiovascular:

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

Neuromuscular:

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

Elevation of the serum potassium concentration.

ECG changes:

Increased amplitude and peaking of T waves, disappearance of P wave, widening of QRS complex, and S-T depression.

Pharmacobezoar:

Rare cases of pharmacobezoar have been reported in association with large overdose of Slow-K tablets. Presence of radiopaque tablets on abdominal X-ray, will confirm the ingestion. Formation of pharmacobezoar may cause continual release of potassium chloride, hours after drug ingestion.

Treatment

Gastric lavage, administration of cation-exchange agents, infusion of glucose + insulin, forced diuresis and possibly peritoneal dialysis or haemodialysis.

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.

Contact the Poison Information Centre on 131 126 for advice on management.

PRESENTATION AND STORAGE CONDITIONS

Tablet 600 mg; containers of 100 tablets.

Information to be Given to the Patient

Please note that the tablets should be swallowed whole with fluid at mealtimes. If you notice any of the following signs while under treatment with SLOW-K, i.e. marked nausea or vomiting, pronounced flatulence, pain in the abdomen, diarrhoea with black or blood-stained stools, you should stop taking the medicine at once and notify your doctor without delay.

Storage

Store below 30°C.

NAME AND ADDRESS OF THE SPONSOR

NOVARTIS Pharmaceuticals Australia Pty. Limited
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54 Waterloo Road
MACQUARIE PARK NSW 2113

POISON SCHEDULE OF THE MEDICINE

Schedule 4 – Prescription Only Medicine

DATE OF FIRST INCLUSION IN THE ARTG

13 November 2000

DATE OF MOST RECENT AMENDMENT

12 November 2015

(slk121115i.doc) based on CDS 18.08.2015