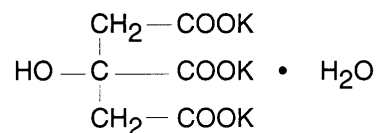


PRODUCT INFORMATION**UROCIT[®]-K****Wax matrix tablets****NAME OF DRUG**

Potassium Citrate

CAS number- 6100-05-6

The empirical formula of potassium citrate is $K_3C_6H_5O_7 \cdot H_2O$, and its structural formula is:

**DESCRIPTION**

Potassium citrate is a white granular powder that is soluble in water at 154 g/100mL, almost insoluble in alcohol, and insoluble in organic solvents.

UROCIT-K is supplied as wax matrix tablets for oral administration. Each tablet contains 1.08 g of potassium citrate, which is equivalent to 10 mEq potassium citrate, or 10 mmols of potassium and 3.3 mmols of citrate.

UROCIT-K tablets also contain the inactive ingredients: magnesium stearate and carnauba wax.

PHARMACOLOGY**Pharmacodynamic Properties**

When UROCIT-K is given orally, the metabolism of absorbed citrate produces an alkaline load. The induced alkaline load in turn increases urinary pH and raises urinary citrate by augmenting citrate clearance without measurably altering ultra-filterable serum citrate. Thus, UROCIT-K therapy appears to increase urinary citrate principally by modifying the renal handling of citrate, rather than by increasing the filtered load of citrate. The increased filtered load of citrate may play some role, however, as in small comparisons of oral citrate and oral bicarbonate, citrate had a greater effect on urinary citrate.

In addition to raising urinary pH and citrate, UROCIT-K increases urinary potassium by approximately the amount contained in the medication. In some patients, UROCIT-K causes a transient reduction in urinary calcium.

The changes induced by UROCIT-K produce a urine that is less conducive to the crystallisation of stone-forming salts (calcium oxalate, calcium phosphate and uric acid). Increased citrate in the urine, by complexing with calcium, decreases calcium ion activity and thus the saturation of calcium oxalate. Citrate also inhibits the spontaneous nucleation of calcium oxalate and crystal growth of calcium phosphate (brushite).

The increase in urinary pH also decreases calcium ion activity by increasing calcium complexation to dissociated anions. The rise in urinary pH also increases the ionisation of uric acid to the more soluble urate ion.

UROCIT-K therapy does not alter the urinary saturation of calcium phosphate, since the effect of increased citrate complexation of calcium is opposed by the rise in pH-dependent dissociation of phosphate. Calcium phosphate stones are more stable in alkaline urine.

Pharmacokinetic Properties

In the setting of normal renal function, the rise in urinary citrate following a single dose begins by the first hour and lasts for 12 hours. With multiple doses the rise in the citrate excretion reaches its peak by the third day and averts the normally wide circadian fluctuation in urinary citrate, thus maintaining urinary citrate at a higher, more constant level throughout the day. When the treatment is withdrawn, urinary citrate begins to decline toward the pre-treatment level on the first day.

The rise in citrate excretion is directly dependent on the UROCIT-K dosage. Following long-term treatment, UROCIT-K at a dosage of 60 mEq/day raises urinary citrate by approximately 400 mg/day and increases urinary pH by approximately 0.7 units.

In patients with severe renal tubular acidosis or chronic diarrhoeal syndrome where urinary citrate may be very low (<100 mg/day), UROCIT-K may be relatively ineffective in raising urinary citrate. A higher dose of UROCIT-K may therefore be required to produce a satisfactory citraturic response. In patients with renal tubular acidosis in whom urinary pH may be high, UROCIT-K produces a relatively small rise in urinary pH.

INDICATIONS

UROCIT-K wax matrix tablets aid in the management of, and reduces the risk of formation of, kidney stones.

CONTRAINDICATIONS

UROCIT-K is contraindicated in patients with hyperkalaemia and in those who have conditions predisposing them to untoward hyperkalaemia, as a further rise in serum potassium concentration may produce cardiac arrest. Such conditions include: chronic renal failure, uncontrolled diabetes mellitus, acute dehydration, strenuous physical exercise in unconditioned individuals, adrenal insufficiency, or extensive tissue breakdown. Concomitant administration of UROCIT-K and a potassium-sparing diuretic should best be avoided (see **PRECAUTIONS- Interactions with other drugs**).

UROCIT-K is contraindicated in patients in whom there is cause for arrest or delay in tablet passage through the gastrointestinal tract, such as those suffering from delayed gastric emptying, oesophageal compression, intestinal obstruction or stricture or those taking anticholinergic medication. Because of its ulcerogenic potential, UROCIT-K should not be given to patients with peptic ulcer disease.

UROCIT-K is contraindicated in patients with active urinary tract infection (with either urea-splitting or other organisms, in association with either calcium or struvite stones). The ability of UROCIT-K to increase urinary citrate may be attenuated by bacterial enzymatic degradation of citrate. Moreover, the rise in urinary pH resulting from UROCIT-K therapy might promote further bacterial growth.

UROCIT-K is contraindicated in patients with renal insufficiency (glomerular filtration rate of less than 0.7 mL/kg/min), because of increased risk for the development of hyperkalaemia and severe alkalosis.

PRECAUTIONS

Hyperkalaemia: In patients with impaired mechanisms for excreting potassium, UROCIT-K administration can produce hyperkalaemia and cardiac arrest. Potential fatal hyperkalaemia can develop rapidly and be asymptomatic. The use of UROCIT-K in patients with chronic renal failure, or any other condition which impairs potassium excretion such as severe myocardial damage or heart failure, should be avoided.

Gastrointestinal lesions: Owing to the reports of upper gastrointestinal mucosal lesions following administration of potassium chloride (wax-matrix), an endoscopic examination of the upper gastrointestinal mucosa was performed in 30 normal volunteers after they had taken glycopyrrolate 2 mg per p.o. t.i.d., UROCIT-K 95 mEq/day, wax-matrix potassium chloride 96 mEq/day or wax matrix placebo, in thrice daily schedule in the fasting state for one week. UROCIT-K and the wax-matrix formulation of potassium chloride were indistinguishable but both were significantly more irritating than the wax-matrix placebo. In a subsequent similar study, lesions were less severe when glycopyrrolate was omitted.

Solid dosage forms of potassium chloride have produced stenotic and/or ulcerative lesions of the small bowel and deaths. These lesions are caused by a high local concentration of potassium ions in the region of the dissolving tablet, which injured the bowel. In addition, perhaps because the wax-matrix preparations are not enteric-coated and release some of their potassium content in the stomach, there have been reports of upper gastrointestinal bleeding associated with these products. The frequency of gastrointestinal lesions with wax-matrix potassium chloride products is estimated at one per 100,000 patient-years. Experience with UROCIT-K is limited, but a similar frequency of gastrointestinal lesions should be anticipated.

If there is severe vomiting, abdominal pain or gastrointestinal bleeding, UROCIT-K should be discontinued immediately and the possibility of bowel perforation or obstruction investigated.

Carcinogenicity/mutagenicity/fertility

Long-term carcinogenicity studies in animals have not been performed.

Use in pregnancy

Animal reproduction studies have not been conducted with UROCIT-K. It is also not known whether UROCIT-K can cause foetal harm when administered to a pregnant woman or can affect reproduction capacity. UROCIT-K should be given to a pregnant woman only if clearly needed.

Use in lactation

The normal potassium ion content of human milk is about 13 mEq/L. It is not known if UROCIT-K has an effect on this content. Caution should be exercised when UROCIT-K is administered to a nursing woman.

Use in children

Safety and effectiveness in children have not been established.

Interactions with other drugs

Concomitant administration of UROCIT-K and a potassium-sparing diuretic (such as triamterene, spironolactone or amiloride) should be best avoided, since the simultaneous administration of these agents can produce severe hyperkalaemia.

Drugs that slow gastrointestinal transit time (such as anticholinergics) can be expected to increase the gastrointestinal irritation produced by potassium salts (see **CONTRAINDICATIONS**).

Effects on laboratory tests

Regular serum potassium determinations are recommended. Careful attention should be paid to acid-base balance, other serum electrolyte levels, the electrocardiogram, and the clinical status of the patient, particularly in the presence of cardiac disease, renal disease or alkalosis.

ADVERSE REACTIONS

Some patients may develop minor gastrointestinal complaints during UROCIT-K therapy, such as abdominal discomfort, vomiting, diarrhoea, loose bowel movements or nausea. These symptoms are due to the irritation of the gastrointestinal tract, and may be alleviated by taking the dose with meals or a snack, or by reducing the dosage. Patients may find intact wax matrices in their faeces.

DOSAGE AND ADMINISTRATION

Treatment with UROCIT-K should be added to a regimen that limits salt intake (avoidance of foods with high salt content and of added salt at the table) and encourages high fluid intake (urine volume should be at least two litres per day). The objective of treatment with UROCIT-K is to provide UROCIT-K in sufficient dosage to restore normal urinary citrate (greater than 320 mg/day and as close to the normal mean of 640 mg/day as possible), and to increase urinary pH to a level of 6.0 to 7.0.

In patients with severe hypocitraturia (urinary citrate of less than 150 mg/day), therapy should be initiated at a dosage of 60 mEq/day in two or three divided doses (with meals or within 30 minutes after meals or bedtime snack). In patients with mild-moderate hypocitraturia (150 to 320 mg/day), UROCIT-K should be initiated at a dosage of 30-40 mEq/day in three or two divided doses respectively. Twenty-four hour urinary citrate and/or urinary pH measurements should be used to determine the adequacy of the initial dosage and to evaluate the effectiveness of any dosage change. In addition, urinary citrate and/or pH should be measured every four months.

Doses of UROCIT-K greater than 100 mEq/day have not been studied and should be avoided.

Serum electrolytes (sodium, potassium, chloride and carbon dioxide), serum creatinine, and complete blood count should be monitored every four months. The treatment should be discontinued if there is hyperkalaemia, a significant rise in serum creatinine or a significant fall in blood haematocrit or haemoglobin.

OVERDOSAGE

The administration of potassium salts to persons without predisposing conditions for hyperkalaemia (see **CONTRAINDICATIONS**) rarely causes serious hyperkalaemia at recommended dosages. It is important to recognise that hyperkalaemia is usually asymptomatic and may be manifested only by an increased serum potassium concentration and characteristic electrocardiographic changes (peaking of T-wave, loss of P-wave, depression of S-T segment and prolongation of the QT interval). Late manifestations include muscle paralysis and cardiovascular collapse from cardiac arrest.

Treatment measures for hyperkalaemia include the following:

- (1) elimination of potassium-rich foods, medications containing potassium, and of potassium-sparing diuretics;
- (2) intravenous administration of 300 – 500 mL/h of 10% glucose solution containing 10 – 20 units of insulin/1000 mL
- (3) correction of acidosis, if present, with intravenous sodium bicarbonate; and
- (4) use of exchange resins, haemodialysis or peritoneal dialysis.

In treating hyperkalaemia, one should be mindful that in patients who have been stabilised on digitalis, too rapid a lowering of the serum potassium concentration can produce digitalis toxicity.

PRESENTATION

UROCIT-K 10 mEq is available for oral administration in a tablet form in bottles of 100 each.

STORAGE CONDITION

Store below 25°C.

NAME AND ADDRESS OF THE SPONSOR

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