

FORCULI Solution (Potassium citrate + Magnesium citrate + Pyridoxine hydrochloride)

Prescribing Information

Composition

Each 5ml contains

Pyridoxine hydrochloride.....20 mg

Potassium citrate.....1100 mg

Magnesium citrate375 mg

(Each ml contains approx. 1 mEq. magnesium ion, 2 mEq. potassium ion, 3 mEq. citrate ion and 4 mg of pyridoxine hydrochloride)

Dosage Form

Oral solution

Pharmacology

Mechanism of Action

Potassium citrate and magnesium citrate solution when given orally, the metabolism of absorbed citrate produces an alkaline load.

In addition to raising urinary pH and citrate, this also increases urinary potassium and magnesium. In some patients, potassium citrate causes a transient reduction in urinary calcium.

These changes produce urine that is less conducive to the crystallization 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. Increased magnesium in the urine, by complexing with oxalate decreases the oxalate ion activity and thus the saturation of calcium oxalate. Citrate and magnesium also inhibits the spontaneous nucleation of calcium oxalate and 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 ionization of uric acid to more soluble urate ion.

Potassium citrate 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.

Pyridoxine is a co-factor of the Alanine-Glyoxylate-Transaminase (AGT) enzyme. Pyridoxine increases the activity of the enzyme AGT, thus glyoxylate is converted to glycine rather than oxalate, which decreases the urinary oxalate level.

Indications

FORCULI is indicated for the management of

- Calcium oxalate nephrolithiasis and uric acid lithiasis with or without calcium stones.
- Renal tubular acidosis with calcium stones.

Dosage and Administration

Three teaspoons (15ml) of FORCULI oral solution diluted with one glass of water, after meals/at bedtime twice daily or as directed by the physician.

Contraindications

FORCULI is contraindicated

- In patients with hyperkalemia (or who have conditions pre-disposing them to hyperkalemia), 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, extensive tissue breakdown, or the administration of a potassium-sparing agent (such as triamterene, spironolactone or amiloride).

- In patients in whom there is cause for arrest or delay in passage through the gastrointestinal tract, such as those suffering from delayed gastric emptying, esophageal compression, intestinal obstruction or stricture, or those taking anticholinergic medication.
- In patients with peptic ulcer disease because of its ulcerogenic potential.
- 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 FORCULI to increase urinary citrate may be attenuated by bacterial enzymatic degradation of citrate. Moreover, the rise in urinary pH resulting from FORCULI therapy might promote further bacterial growth.
- In patients with renal insufficiency (glomerular filtration rate of less than 0.7 ml/kg/min), because of the danger of soft tissue calcification and increased risk for the development of hyperkalemia.

Warnings and Precautions

General

Hyperkalemia

In patients with impaired mechanisms for excreting potassium, potassium citrate administration can produce hyperkalemia and cardiac arrest. Potentially fatal hyperkalemia can develop rapidly and be asymptomatic. The use of potassium citrate 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. Closely monitor for signs of hyperkalemia with periodic blood tests and ECGs.

Gastrointestinal Lesions

Because of reports of upper gastrointestinal mucosal lesions following administration of potassium chloride (wax-matrix), and endoscopic examination of the upper gastrointestinal mucosa was performed in 30 normal volunteers after they had taken glycopyrrolate 2 mg. p.o. t.i.d., potassium citrate 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. Potassium citrate 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 tablets, which injured the bowel. In addition, perhaps because 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 potassium citrate is limited, but a similar frequency of gastrointestinal lesions should be anticipated.

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

Drug Interactions

Potential Effects of Potassium Citrate on Other Drugs

Potassium-sparing Diuretics

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

Potential Effects of Other Drugs on Potassium Citrate

Drugs that slow gastrointestinal transit time:

These agents (such as anticholinergics) can be expected to increase the gastrointestinal irritation produced by potassium salts.

Renal Impairment

Potassium citrate is contraindicated in patients with renal insufficiency (glomerular filtration rate of less than 0.7 ml/kg/min), because of the danger of soft tissue calcification and increased risk for the development of hyperkalemia.

Pregnancy

Pregnancy Category C

Animal reproduction studies have not been conducted. It is also not known whether potassium citrate can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Potassium citrate should be given to a pregnant woman only if clearly needed.

Lactation

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

Paediatric Use

Safety and effectiveness in children have not been established.

Information for Patients

Physician should advise their patients to take this medicine only as directed. This is especially important if the patient is also taking both diuretics and digitalis preparations.

Patients should be advised to check with the doctor at once if tarry stools or other evidence of gastrointestinal bleeding is noticed.

Patients should be advised to perform regular blood tests and electrocardiograms to ensure safety.

Undesirable Effects

Post marketing Experience

Some patients may develop minor gastrointestinal complaints during potassium citrate therapy, such as abdominal discomfort, vomiting, diarrhea, 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 snack, or by reducing the dosage. Patients may find intact matrices in feces.

Long-term use of large doses of pyridoxine is associated with the development of severe peripheral neuropathies; the dose at which these occur is controversial.

Overdose

Treatment of over dosage

The administration of potassium salts to persons without predisposing conditions for hyperkalemia rarely causes serious hyperkalemia at recommended dosages. It is important to recognize that hyperkalemia 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 hyperkalemia include the following:

- Patients should be closely monitored for arrhythmias and electrolyte changes.
- Elimination of medications containing potassium and of agents with potassium-sparing properties such as potassium-sparing diuretics, ARBs, ACE inhibitors, NSAIDs, certain nutritional supplements and many others.
- Elimination of foods containing high levels of potassium such as almonds, apricots, bananas, beans (lima, pinto, white), cantaloupe, carrot juice (canned), figs, grapefruit juice, halibut, milk, oat bran, potato (with skin), salmon, spinach, tuna and many others.
- Intravenous calcium gluconate if the patient is at no risk or low risk of developing digitalis toxicity.
- Intravenous administration of 300-500 mL/hr of 10% dextrose solution containing 10-20 units of crystalline insulin per 1,000 mL.
- Correction of acidosis, if present, with intravenous sodium bicarbonate.
- Hemodialysis or peritoneal dialysis.
- Exchange resins may be used. However, this measure alone is not sufficient for the acute treatment of hyperkalemia.

Lowering potassium levels too rapidly in patients taking digitalis can produce digitalis toxicity.

Packaging Information: FORCULI 200 ml & 450 ml *Last Updated: Mar20 & Reviewed April 20*