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**INDICATIONS AND USAGE**

Urocit®-K is a citrate salt of potassium indicated for the management of:

- Renal tubular acidosis with or without calcium stones (1.1)
- Hypocitraturic calcium oxalate nephrolithiasis of any etiology (1.2)
- Uric acid lithiasis with or without calcium stones (1.3)

**DOSE AND ADMINISTRATION**

Objective: 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.

- Severe hypercitraturia (urinary citrate < 150 mg/day): therapy should be initiated at 60 mEq per day; a dose of 30 mEq two times per day or 20 mEq three times per day with meals or within 30 minutes after meals or bedtime snack (2.2).
- Mild to moderate hypercitraturia (urinary citrate > 150 mg/day): therapy should be initiated at 30 mEq per day; a dose of 15 mEq two times per day or 10 mEq three times per day with meals or within 30 minutes after meals or bedtime snack (2.3).

**DOSAGE FORMS AND STRENGTHS**

- Tablets: 5 mEq, 10 mEq and 15 mEq (3)

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**CONTRAINDICATIONS**

- Hyperkalemia
- Hypochloremic alkalosis
- Severe hypocalcemia
- Severe acidosis
- Severe acidosis

**WARNINGS AND PRECAUTIONS**

- Severe acidosis
- Severe acidosis
- Severe acidosis
- Severe acidosis

**ADVERSE REACTIONS**

These may be alleviated by taking the dose with meals or snacks or by reducing the dosage (6.1).

**DRUG INTERACTIONS**

- Potassium-sparing diuretics: concurrent administration should be avoided since the simultaneous administration of these agents can produce severe hyperkalemia (7.6).
- Drugs that slow gastrointestinal transit time (7.6).

**SIDE EFFECTS**

Patients may develop mild gastrointestinal complaints such as abdominal discomfort, vomiting, diarrhea, loose bowel movements or nausea. These may be alleviated by taking the dose with meals or snacks or by reducing the dosage (6.1).
10 OVERDOSE
Treatment of Overdose: 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 Q-T interval). Late manifestations include muscle paralysis and cardiovascular collapse from cardiac arrest.

Treatment measures for hyperkalemia include the following:
1. Patients should be closely monitored for arrhythmias and electrolyte changes.
2. Elimination of medications containing potassium and of agents with potassium sparring properties such as potassium-sparing diuretics, ACE inhibitors, NSAIDs, certain nutritional supplements and many others.
3. Elimination of foods containing high levels of potassium such as almonds, apricots, bananas, beans (lima, pinto, white), cantaloupe, carrot juice (concentrate), figs, grapefruit juice, milk, oat bran, potatoes (white with skin), salmon, spinach, tuna and many others.
4. Intravenous calcium gluconate if the patient is at no risk or low risk of developing digitalis toxicity.
5. Intravenous administration of 300-500 mL of 10% dextrose solution containing 1-2 units of crystalline insulin per 1,000 mL. Correction of acidosis, if present, with intravenous sodium bicarbonate.
6. Hemodialysis or peritoneal dialysis.
7. 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 precipitate muscle paralysis and cardiovascular collapse from cardiac arrest.

11 DESCRIPTION

Urocit-K is a citrate salt of potassium. Its empirical formula is \( K_2(C_6H_5O_7) \cdot H_2O \), and it has the following chemical structure:

![Chemical Structure of Urocit-K](https://example.com/chemical_structure.png)

Urocit-K is yellowish to tan or white, wax-matrix tablets, contain 5 mEq (540 mg) potassium citrate, 10 mEq (1080 mg) potassium citrate and 15 mEq (1620 mg) potassium citrate each. Inactive ingredients include carnauba wax, magnesium stearate, and silicon dioxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

When Urocit-K is given orally, the metabolism of absorbed citrate produces an alkaline load. The increased acid load in turn increases urinary pH and raises urinary citrate by augmenting citrate clearance without measurably altering ultrafilterable 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 oxalate, 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 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. Citrate also inhibits the spontaneous nucleation of calcium oxalate and calcium phosphate stones (brushtite).

The increase in urinary pH also decreases calcium ion activity by increasing complexation to disassociated anions. The rise in urinary pH also increases the ionization 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.

In the setting of normal renal function, the rise in urinary citrate following a single dose begins the first hour and lasts for 12 hours. With multiple doses the rise in 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 mL/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 diarrheal syndrome where urinary citrate may be very low (<100 mg/day), Urocit-K may be relatively ineffective in raising urinary citrate. A higher dosage 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.

14 CLINICAL STUDIES

In the pivotal Urocit-K trials were non-randomized and non-placebo controlled where dietary management may have changed coincidentally with pharmacological treatment. Therefore, the results as presented in the following sections may overstate the effectiveness of the product.

14.1 Renal tubular acidosis (RTA) with calcium stones

The effectiveness of Urocit-K in a non-randomized, non-placebo controlled clinical study of five men and four women with calcium oxalate/calcium phosphate nephrolithiasis and documented incomplete distal renal tubular acidosis was examined. The main inclusion criterion was a history of stone passage in the 3 years prior to initiation of potassium citrate therapy. All patients began alkali treatment with 60-80 mg potassium citrate daily in 3 or 4 divided doses. Throughout treatment, patients were instructed to stay on a sodium restricted diet (100 mEq/day) and to reduce oxalate intake (limited intake of nuts, dark roughage, chocolate and tea). A moderate calcium restriction (400-900 mg/day) was imposed on patients with hypercalcemia.

K-uric acid lithiasis in 12 patients, with intravenous sodium bicarbonate. 7. Hemodialysis or peritoneal dialysis of 300-500 mL of 10% dextrose solution containing 10-20 units of crystalline insulin per 1,000 mL.

15 REFERENCES


16 HOW SUPPLIED/STORAGE AND HANDLING

Urocit-K 5 mEq tablets are uncoated, tan in yellow color, modified ball shaped, with NPC 600 debossed on one side and blank on the other, supplied in bottles as:

- Bottle of 100

Urocit-K 10 mEq tablets are uncoated, tan in yellow color, elliptical shaped, with 610 debossed on one side and MISSION on the other, supplied in bottles as:

- Bottle of 100

Urocit-K 15 mEq tablets are uncoated, tan in yellow color, modified rounded rectangle shaped, with M15 debossed on one side and blank on the other, supplied in bottles as:

- Bottle of 100

Strayer, Stone in a light container.

17 PATIENT COUNSELING INFORMATION

17.1 Administration of Drug

Tell patients to take each dose without chewing, crushing or sucking the tablet.

Tell patients to take this medicine only as directed. It is especially important if the patient is also taking both diuretics and digitalis preparations.

Tell patients to check with the doctor if there is trouble swallowing the tablet or if the tablet seems to stick in the throat.

Tell patients to check with the doctor at once if tarry stools or other evidence of gastrointestinal bleeding is noticed.

Tell patients that their doctor will perform regular blood tests and electrocardiograms to ensure safety.