1. **INDICATIONS AND USAGE**

Potassium citrate is indicated for the management of renal tubular acidosis (see Clinical Studies (14.2)).

2. **DOSE AND ADMINISTRATION**

   - **Dosing Instructions**
     - Treatment with extended release potassium citrate 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 liters per day). The objective of treatment with Potassium Citrate Extended-release Tablets is to provide Potassium Citrate Extended-release Tablets in sufficient dosage to restore normal urinary citrate (greater than 320 mg/dl) and as close to the normal mean of 640 mg/dl as possible, and to increase urinary pH to a level of 6.0 to 7.0.

3. **ADVERSE REACTIONS**

   - **Gastrointestinal Lesions**
     - Some patients may develop minor gastrointestinal complaints such as abdominal discomfort, vomiting, diarrhea, loose bowel movements, or eructations. These may be alleviated by taking the dose with meals or snacks or by reducing the dosage (6.1). To prevent these effects, some gastrointestinal irritation produced by potassium salts (7.2) should be anticipated.

4. **CONTRAINDICATIONS**

   - **Patients with hyperkalemia** (or who have conditions predisposing them to hyperkalemia). Such conditions include chronic renal failure, untreated diabetes mellitus, acute dehydration, strenuous physical exercise in unconditioned individuals, adrenal insufficiency, extensive tissue breakdown (4)

5. **WARNINGS AND PRECAUTIONS**

   - **Hyperkalemia**
     - In patients with impaired mechanisms for excreting potassium, Potassium Citrate Extended-release Tablets administration can produce hyperkalemia and cardiac arrest. Potentially fatal hyperkalemia can develop rapidly and be asymptomatic.
     - The use of Potassium Citrate Extended-release Tablets 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 (5.1).
     - **Gastrointestinal lesions**: if there is severe vomiting, abdominal pain or gastrointestinal bleeding, Potassium Citrate Extended-release Tablets should be discontinued immediately and the possibility of bowel perforation or obstruction investigated (5.2).

6. **DOSE FORMS AND STRENGTHS**

   - Tablets: 5 mEq, 10 mEq (3)

7. **DRUG INTERACTIONS**

   - **Gastrointestinal Lesions**
     - With prolonged use, gastrointestinal irritation produced by potassium salts (7.2) and increased fluid intake, the frequency of gastrointestinal lesions with wax-matrix potassium chloride products is estimated at one per 100,000 patient-years. Lesions should be anticipated.

8. **USE IN SPECIFIC POPULATIONS**

   - **Pregnancy**
     - Pregnancy Category C: animal reproduction studies have not been conducted. It is not known whether Potassium Citrate Extended-release Tablets can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Potassium Citrate Extended-release Tablets should be given to a pregnant woman only if clearly needed (8.1).

   - **Nursing Mothers**
     - It is not known if Potassium Citrate Extended-release Tablets have an effect on this content. Potassium Citrate Extended-release Tablets should be given to a woman who is breast feeding only if clearly needed (8.3).

   - **Pediatric Use**
     - Safety and effectiveness in children have not been established (8.4).

9. **REFERENCES**

   - See 17 for PATIENT COUNSELING INFORMATION

10. **FULL PRESCRIBING INFORMATION CONTENTS**

   - Revised: 09/2012

11. **HIGHLIGHTS OF PRESCRIBING INFORMATION**

   - These highlights do not include all the information needed to use Potassium Citrate Extended-release Tablets safely and effectively. See full prescribing information for Potassium Citrate Extended-release Tablets.

12. **CLINICAL PHARMACOLOGY**

   - 12.1 Mechanism of Action

13. **CLINICAL STUDIES**

   - 13.1 Renal tubular acidosis (RTA) with calcium stones
   - 13.2 Hypertrophic calcium oxalate nephropathy of any etiology

14. **REFERENCES**

   - 14. REFERENCES

15. **HOW SUPPLIED/STORAGE AND HANDLING**

   - 15.1 Potassium carbonate tablets (7.3) or with without calcium stones (7.3)
Citrate Extended-release Tablets produce a relatively small rise in urinary pH. To produce a satisfactory citraturic response. In patients with renal tubular acidosis in whom urinary pH may be high, Potassium Citrate Extended-release Tablets may be relatively ineffective in raising urinary citrate in whom urinary pH may be high. Potassium Citrate Extended-release Tablets produce a relatively small rise in urinary pH.

14 CLINICAL STUDIES

The pivotal Potassium Citrate Extended-release Tablets trials were non-randomized and non-placebo controlled where dietary management may have changed concurrently with pharmacological treatment. Therefore, the results as presented in the following sections may overestimate the efficacy of the test.

14.1 Renal tubular acidosis (FTA) with calcium stones

The effect of oral potassium citrate therapy 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 one inclusion criterion was a history of spontaneous passage or surgical removal of stones during 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/d) and to reduce oxalate intake by limiting intake of dark roughage, dark leafy greens, chocolate and tea. A moderate calcium restriction (400-800 mg/d) was imposed on patients with hypercalcemia.

X-rays of the urinary tract, available in all patients, were reviewed to determine presence of pre-existing stones, appearance of new stones, or change in the number of stones.

Potassium citrate therapy was associated with inhibition of new stone formation in patients with distal tubular acidosis. Three of the new patients continued to pass stones during the on-treatment phase. While it is likely that these patients passed pre-existing stones during therapy, the most conservative assumption is that the passed stones were newly formed. Using this assumption, the stone-passage remission rate was 67%. All patients had a reduced stone formation rate. Over the first 2 years of the on-treatment phase, the stone formation rate reduction was from 1.62 to 1.0 per year.

14.2 Hypocitraturic calcium oxalate nephrolithiasis of any etiology

Eighty-nine patients with hypocitraturic calcium nephrolithiasis or uric acid lithiasis with or without calcium nephrolithiasis participated in a parallel non-randomized, non-placebo controlled clinical study. Four groups of patients were treated with potassium citrate:

Group 1 comprised of 19 patients, 10 with renal tubular acidosis and 9 with chronic diarrhea syndrome. Group 2 comprised of 37 patients, 5 with uric acid stones alone, 6 with uric acid and calcium stones, and 3 with type I absorptive hyperparathyroidism, 3 with type II absorptive hyperparathyroidism and 4 with hyperoxaluria. Group 3 comprised of 15 patients with history of relapsing on other therapy and Group 4 comprised of 18 patients, 9 with type I absorptive hyperparathyroidism and calcium stones, 7 with type II absorptive hyperparathyroidism and calcium stones, 2 with hyperoxaluric calcium oxalate nephrolithiasis, 4 with uric acid lithiasis accompanied by calcium stones and 2 with hypouricosuria and hypercalcemia accompanied by calcium stones. The dose of potassium citrate ranged from 20 to 60 mEq per day in 2 to 3 divided doses, administered orally 3 to 5 meals/day. Patients were followed in an outpatient setting every 4 months during treatment and were studied over a period from 1 to 4.33 years. A three-year retrospective pre-study history for stone passage or removal was obtained and corroborated by medical records. Concurrent therapy (with thiazide or allopurinol) was allowed if patients failed hypocalciuria, hyperuricosuria, or hypercalcemia. Group 2 was treated with potassium calcium alone.

In all groups, treatment that included potassium citrate was associated with a sustained increase in urinary citrate excretion from subnormal values to normal values (400 to 700 mEq/d), and a sustained increase in urinary pH from 5.6 to 6.0 to approximately 6.3. The stone formation rate was reduced in all groups as shown in Table 1.

Table 1. Effect of Potassium Citrate Extended-release Tablets in Patients With Calcium Oxalate Nephrolithiasis

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>On Treatment</th>
<th>Remission*</th>
<th>Any Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (n=15)</td>
<td>1.2 ± 2</td>
<td>0.4 ± 1.5</td>
<td>89%</td>
<td>97%</td>
</tr>
<tr>
<td>II (n=37)</td>
<td>1.2 ± 2</td>
<td>0.4 ± 1.5</td>
<td>89%</td>
<td>97%</td>
</tr>
<tr>
<td>III (n=15)</td>
<td>4.2 ± 7</td>
<td>0.7 ± 2</td>
<td>67%</td>
<td>100%</td>
</tr>
<tr>
<td>Total (n=67)</td>
<td>4.3 ± 15</td>
<td>0.6 ± 2</td>
<td>80%</td>
<td>98%</td>
</tr>
</tbody>
</table>

* Remission defined as “the percentage of patients remaining free of new formed stones during treatment.”

14.3 Uric acid lithiasis with or without calcium stones

A parallel non-randomized, non-placebo controlled clinical study with eighteen adult patients with uric acid lithiasis participated in the study. Six patients formed only uric acid stones, and the remaining 12 patients formed mixed stones containing both uric acid and calcium salts or formed both uric acid stones (without calcium salts) and calcium stones (without uric acid) on separate occasions. Eleven of the 15 patients received potassium citrate alone. Six of the 7 other patients also received allopurinol for hyperuricemia with gouty arthritis, symptomatic hyperuricosuria, or hypercalcemia. One patient also received hydroxychloroquine because of unclassified hyperparathyroidism. The main inclusion criteria was a history of stone passage or surgical removal of stones during the 3 years prior to initiation of potassium citrate therapy. All patients received potassium citrate dosage of 30-80 mg/kg daily in 2 to 3 divided doses and were followed every four months for up to three to five years. While on potassium citrate treatment, urinary pH rose significantly from a low value of 5.3 to 6.3 within normal limits (6.2 to 6.5). Urinary citrate which was low before treatment rose to the high normal range and only one stone was formed in the entire group of 15 patients.

15 REFERENCES


16 HOW SUPPLIED/STORAGE AND HANDLING

Potassium Citrate Extended-release Tablets 5 mEq are uncoated, tan to yellowish in color, elliptical shaped, debossed with “K” in white ink, and have an average weight of approximately 0.25 mg. Potassium Citrate Extended-release Tablets 10 mEq are uncoated, tan to yellowish in color, modified ball shaped, debossed with “K” in white ink, and have an average weight of approximately 0.5 mg.

Store in a tight container.

17 PATIENT COUNSELING INFORMATION

17.1 Administration of Drug

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

Tell patients to take this medicine only as directed. The important information is that the patient also take both diuretics and digital preparations.

Tell patients to check with the doctor if there is trouble swallowing tablets 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.

18 MANUFACTURER

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