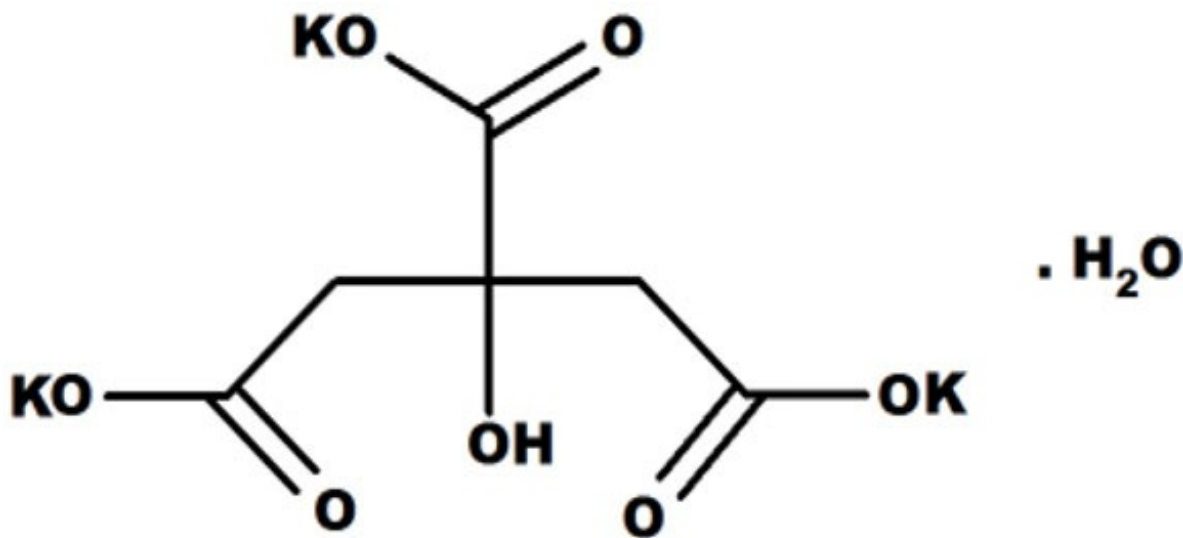


POTASSIUM CITRATE - potassium citrate tablet, extended release
Physicians Total Care, Inc.

POTASSIUM CITRATE EXTENDED-RELEASE TABLETS USP
5 mEq (540 mg) and 10 mEq (1080 mg)
Rx only

DESCRIPTION

Potassium citrate USP is a citrate salt of potassium and has the chemical name 1,2,3-Propanetricarboxylic acid, 2-hydroxy-, tripotassium salt, monohydrate. Its molecular formula is $K_3C_6H_5O_7 \cdot H_2O$, and its structural formula is: M.W. 324.41



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

Potassium citrate extended-release tablets USP are supplied as wax matrix tablets, containing 5 mEq (540 mg) potassium citrate or 10 mEq (1080 mg) potassium citrate, for oral administration. In addition, potassium citrate extended-release tablets USP contain the inactive ingredients carnauba wax, magnesium stearate and stearic acid.

CLINICAL PHARMACOLOGY

When potassium citrate 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 ultrafilterable serum citrate. Thus, potassium citrate 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, potassium citrate increases urinary potassium by approximately the amount contained in the medication. In some patients, potassium citrate causes a transient reduction in urinary calcium.

The changes induced by potassium citrate produce a 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 (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.

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 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 potassium citrate dosage. Following long-term treatment, potassium citrate 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 diarrheal syndrome where urinary citrate may be very low (<100 mg/day), potassium citrate may be relatively ineffective in raising urinary citrate. A higher dose of potassium citrate may therefore be required to produce a satisfactory citraturic response. In patients with renal tubular acidosis in whom urinary pH may be high, potassium citrate produces a relatively small rise in urinary pH.

INDICATIONS AND USAGE

Potassium citrate extended-release tablets are indicated for the management of renal tubular acidosis (RTA) with calcium stones, hypocitraturic calcium oxalate nephrolithiasis of any etiology, and uric acid lithiasis with or without calcium stones.

CONTRAINDICATIONS

Potassium citrate extended-release tablets are contraindicated in patients with hyperkalemia (or who have conditions predisposing 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).

Potassium citrate extended-release tablets are 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, esophageal compression, intestinal obstruction or stricture or those taking anticholinergic medication. Because of its ulcerogenic potential, potassium citrate extended-release tablets should not be given to patients with peptic ulcer disease.

Potassium citrate extended-release tablets are 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 potassium citrate extended-release tablets to increase urinary citrate may be attenuated by bacterial enzymatic degradation of citrate. Moreover, the rise in urinary pH resulting from potassium citrate therapy might promote further bacterial growth.

Potassium citrate extended-release tablets are 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.

WARNINGS

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.

INTERACTION WITH 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.

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 gastro-intestinal bleeding, potassium citrate should be discontinued immediately and the possibility of bowel perforation or obstruction investigated.

PRECAUTIONS

Information For Patients:

Physicians should consider reminding the patient of the following:

- To take each dose without crushing, chewing or sucking the tablet.
- To take this medicine only as directed. This is especially important if the patient is also taking both diuretics and digitalis preparations.
- To check with physician if there is trouble swallowing tablets or if the tablet seems to stick in the throat.
- To check with the doctor at once if tarry stools or other evidence of gastrointestinal bleeding is noticed.

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 acidosis.

Drug Interactions: POTASSIUM-SPARING DIURETICS: See WARNINGS section.

DRUGS THAT SLOW GASTROINTESTINAL TRANSIT TIME (such as anticholinergics) can be expected to increase the gastrointestinal irritation produced by potassium salts. (see

CONTRAINDICATIONS section).

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term carcinogenicity studies in animals have not been performed.

Pregnancy Category C: Animal reproduction studies have not been conducted with potassium citrate. 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.

Nursing Mothers: 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.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

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. (see also

CONTRAINDICATIONS, WARNINGS

OVERDOSAGE

The administration of potassium salts to persons without predisposing conditions for hyperkalemia (see **CONTRAINDICATIONS**) 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: (1) elimination of potassium-rich foods, medications containing potassium, and of potassium-sparing diuretics, (2) intravenous administration of 300-500 ml/hr of 10% dextrose 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, hemodialysis or peritoneal dialysis.

In treating hyperkalemia, it should be recalled that in patients who have been stabilized on digitalis, too rapid a lowering of the serum potassium concentration can produce digitalis toxicity.

DOSAGE AND ADMINISTRATION

Treatment with potassium citrate extended-release tablets 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 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 (20 mEq three times/day or 15 mEq four times/day with meals or within 30 minutes after meals or bedtime snack). In patients with mild-moderate hypocitraturia (>150 mg/day), potassium citrate extended-release tablets should be initiated at a dosage of 30 mEq/day (10 mEq three times/day with meals). 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 potassium citrate extended-release tablets 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. Treatment should be discontinued if there is hyperkalemia, a significant rise in serum creatinine, or a significant fall in blood hematocrit or hemoglobin.

HOW SUPPLIED

Potassium citrate extended-release tablets USP 10 mEq (1080 mg) are pale yellow, capsule shaped compressed tablets debossed cor 149 on one side and other side is plain. They are supplied as follows:

Bottles of 30 (NDC 54868-5644-1)

Bottles of 90 (NDC 54868-5644-0)

Store at 20°C to 25°C (68°F to 77°F).excursions permitted to 15 to 30°C(59 to 86°F) [see USP Controlled Room Temperature].

Store in a tight container as defined in the USP.

Keep this and all drugs out of the reach of children.

Manufactured by:
Corepharma LLC
Middlesex, NJ 08846

Distributed by:
Rising Pharmaceuticals, Inc
Allendale, NJ 07401

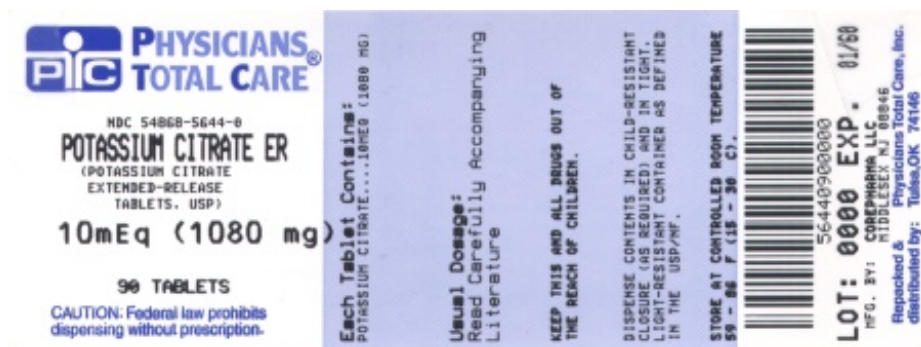
MF # 718
May 2009



Relabeling and Repackaging by:
Physicians Total Care, Inc.
Tulsa, OK 74146

PRINCIPAL DISPLAY PANEL

Potassium citrate extended-release tablets USP 10 mEq (1080 mg)



POTASSIUM CITRATE

potassium citrate tablet, extended release

Product Information

| | | | |
|-------------------------|-------------------------|--------------------|-------------------------------|
| Product Type | HUMAN PRESCRIPTION DRUG | Item Code (Source) | NDC:54868-5644(NDC:64980-138) |
| Route of Administration | ORAL | | |

Active Ingredient/Active Moiety

| Ingredient Name | Basis of Strength | Strength |
|---|-------------------|----------|
| POTASSIUM CITRATE (UNII: EE90ONI6FF) (POTASSIUM CATION - UNII:295O53K152) | POTASSIUM CITRATE | 1080 mg |

Inactive Ingredients

| Ingredient Name | Strength |
|---------------------------------------|----------|
| CARNAUBA WAX (UNII: R12CBM0EIZ) | |
| MAGNESIUM STEARATE (UNII: 70097M6I30) | |
| STEARIC ACID (UNII: 4ELV7Z65AP) | |

Product Characteristics

| | | | |
|----------|----------------------|--------------|----------|
| Color | yellow (Pale yellow) | Score | no score |
| Shape | CAPSULE | Size | 19mm |
| Flavor | | Imprint Code | cor;149 |
| Contains | | | |

Packaging

| # | Item Code | Package Description | Marketing Start Date | Marketing End Date |
|---|------------------|-------------------------|----------------------|--------------------|
| 1 | NDC:54868-5644-0 | 90 in 1 BOTTLE, PLASTIC | | |
| 2 | NDC:54868-5644-1 | 30 in 1 BOTTLE, PLASTIC | | |

Marketing Information

| Marketing Category | Application Number or Monograph Citation | Marketing Start Date | Marketing End Date |
|--------------------|--|----------------------|--------------------|
| ANDA | ANDA077440 | 07/24/2006 | |

Labeler - Physicians Total Care, Inc. (194123980)

Establishment

| Name | Address | ID/FEI | Business Operations |
|-----------------------------|----------------|---------------|----------------------------|
| Physicians Total Care, Inc. | | 194123980 | relabel, repack |

Revised: 2/2010

Physicians Total Care, Inc.