

LITHOS[®] Prevent 10,5mEq

Tripotassium citrate and trimagnesium citrate in prolonged release tablets

(7mEq Potassium - 3,5mEq Magnesium - 10,5mEq Citrate ions)

Citrates in the prevention of calcium urolithiasis: A meta-analysis of 21 clinical trials that involved more than 1000 patients has shown that preventive treatment with citrate ions resulted in reduction of calcium stone recurrence ranging from 47% up to 100%⁽¹⁾. **Hypocitraturia:** When the metabolic disorder is severe hypocitraturia (urine citrate <150mg/day) the recommended^(2, 3) average daily dose of citrates is 60mEq divided in 2-3 equal doses. In case of moderate hypocitraturia (urine citrate >150mg/day) the recommended^(2, 3) dose of citrates is 20-30mEq daily divided in 2-3 equal doses. **Hypercalciuria:** Hypercalciuria is defined as daily (24h) calcium excretion in urine >300mg for men and >250mg in women while on unrestricted diet. When calcium excretion is 200-320mg/day while the patient is on dietary calcium restriction the recommended^(2, 3) daily dose of citrate is 20-60mEq divided in 2-3 equal doses. In case of severe hypercalciuria (calcium excretion >320mg/day while the patient is on dietary calcium restriction) not adequately responding to sole citrate therapy, it is recommended^(2, 3) combined therapy with citrate and a diuretic.

For the prevention of calcium urolithiasis and regardless of the underlying metabolic disorder, it is recommended (Guidelines^(2, 3) Level of Evidence: 1 & Grade of Recommendation: A) treatment with 20-60mEq potassium and magnesium citrate daily, divided in 2-3 equal doses.

Citrates in the prevention of uric acid urolithiasis: Uric acid stones form in urine supersaturated with uric acid usually of low pH and reduced volume. According to the Guidelines of EAU (European Association of Urology)^(2, 3) potassium and magnesium citrate are the most appropriate and effective treatments for the prevention of recurrence of uric acid stones. For the prevention of recurrence of uric acid stones it is recommended (Guidelines^(2, 3) Level of Evidence: 2 & Grade of Recommendation: B) treatment with 20-60mEq potassium and magnesium citrate daily, divided in 2-3 equal doses.

What is LITHOS[®] Prevent and what it contains: LITHOS[®] Prevent is a food supplement that contains tripotassium citrate and trimagnesium citrate. LITHOS[®] Prevent does not contain sodium. **Qualitative and quantitative composition:** Each prolonged release tablet of LITHOS[®] Prevent contains 7mEq of potassium ions, 3,5mEq magnesium ions and 10,5mEq citrate ions. Active ingredients: tripotassium citrate (757mg), trimagnesium citrate (358mg). Inactive ingredients: magnesium stearate, hydrogenated vegetable oil, stearic acid, microcrystalline cellulose. Coating agents: propylmethyl cellulose, ethyl cellulose, chlorophyllin copper complexes, SiO₂, talc. Technology used in tablets: The tablets of LITHOS[®] Prevent are manufactured by making use of prolonged release technology. Prolonged release technology ensures consistent and around the clock release of citrates in the urine.

Indicated use: (1) LITHOS[®] Prevent is indicated for restoring normal levels of urine citrate in case of **hypocitraturia** that predisposes to calcium urolithiasis. (2) LITHOS[®] Prevent is indicated for restoring normal levels of urine calcium in case of **hypercalciuria** that predisposes to calcium urolithiasis. (3) LITHOS[®] Prevent is a useful nutritional supplement in case of diet poor in citrate consumption. (4) LITHOS[®] Prevent is a useful nutritional supplement in case of diet rich in purines or proteins consumption. Both purines and proteins give rise to increased levels of uric acid that acidifies the urine. LITHOS[®] Prevent can restore urine pH in the normal range and prevent the recurrence of uric acid stones. (5) LITHOS[®] Prevent is useful after ESWL for the long term prevention of recurrence of urolithiasis. (6) LITHOS[®] Prevent is indicated for the treatment of distal renal tubular acidosis.

Dosage: The dosage range of LITHOS[®] Prevent is 20-60mEq per day. Dosage should be adjusted according to the necessary mEq of citrates. The total daily dose should be divided in two (morning and evening) or three (morning-afternoon-and evening) equal doses. **Administration:** LITHOS[®] Prevent should be administered during or within 30 minutes after each meal. **Treatment objectives:** correction of the underlying metabolic disorders in order to prevent recurrence of urolithiasis. LITHOS[®] Prevent can restore normal levels of urine citrate (normal levels: daily excretion of citrate >320mg and as close as possible to the average normal level, i.e. 640mg). LITHOS[®] Prevent can restore normal levels of urine calcium (normal levels: daily excretion of calcium <200mg) or to restore normal levels of urine pH in case of hyperuricosuria. The efficacy of the treatment should be evaluated every 4 months by measuring urine levels of citrate or calcium or by measuring urine pH depending on the underlying metabolic disorder.

Contraindications and Precautions: LITHOS[®] Prevent is contraindicated to patients with (or with conditions predisposing to) hyperkalemia or hypermagnesemia. Such conditions include chronic heart or renal failure, uncontrolled diabetes mellitus, acute dehydration (e.g. due to diarrhea or strenuous physical exercise in unconditioned individuals). LITHOS[®] Prevent should not be administered together with potassium-sparing diuretics (amilofide/Frumil[®], spironolactone/Aldactone[®], eplerenone/Inspra[®]). **Adverse reactions:** During treatment with LITHOS[®] Prevent some patients may develop minor gastrointestinal complaints such as abdominal discomfort, loose bowel movements or diarrhea. These may be alleviated by taking the dose with meals or snacks or by reducing the dose. **Pregnancy:** Category C. There are no human or animal studies whether LITHOS[®] Prevent can cause fetal harm when administered to pregnant women or can affect reproduction capacity. LITHOS[®] Prevent should be given to pregnant women only if clearly needed. **Caution:** Do not exceed the highest recommended daily dose. Keep out of children's reach. Store at room temperature (15-30°C). Avoid contact of the product with water, heat radiators or its direct exposure to sunlight. Do not use the product beyond the expiration date indicated on the back of the outer package. **Package:** Plastic tube containing 100 prolonged release tablets of LITHOS[®] Prevent.

Notification Number to Reg Authorities:

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Distribution for Romania:

Literature: (1). Mattle D. et al, *Urol Res* 2005, 33, 73-79. (2). Tiselius H-G et al, Guidelines on urolithiasis. *European Association of Urology Update* 2008. (3). Turk C et al, Guidelines on urolithiasis. *European Association of Urology Update* 2013.