LITHOS® Dissolve 21mEq

Tripotassium citrate and trimagnesium citrate in sachets

(14mEq Potassium - 7mEq Magnesium - 21mEq Citrate ions)

Calcium stones: Supersaturation of urine with insoluble calcium salts is the single most important determinant of lithogenesis. When concentration of calcium complexes in urine exceeds their solubility the excess salt formed is unable to dissolve. This phenomenon is called urine supersaturation. The excess insoluble salt thus formed, can precipitate giving rise to calcium oxalate and calcium phosphate crystals. Crystals can gradually aggregate and finally form urinary stones[1]. 75-80% of urinary stones are composed of calcium oxalate and calcium phosphate salts. **ESWL:** Most of the residual stone fragments after lithotripsy have an average size that allows for passage through the urinary tract and their gradual elimination with the urine. Nevertheless, the residual stone fragments are not immediately eliminated: at discharge, up to 85-96% of the patients with calcium stones[2, 3] and up to 92% of the patients with infectious stones[4] have been reported as having fragments less than 5mm in size. Residual stone fragments (stone fragments remaining in the urinary tract more than 3 months after lithotripsy) may act as nidus for recurrent stone growth, can acutely dislodge and cause significant obstruction with pain or they may be the source of persistent infection. The risk of recurrence of urinary stones due to residual stone fragments is widely recognized through a large number of clinical trials. Several studies have shown that medical treatment of residual stone fragments after lithotripsy can prevent recurrence of urolithiasis. **Citrate ions and calcium stones:** Citrate ions are generally regarded as potent inhibitors of calcium urolithiasis[1, 5]. Citrates act through several mechanisms of action: they form water soluble complexes with urinary calcium ions, thus preventing the supersaturation of urine with insoluble calcium oxalate and calcium phosphate complexes. Citrates inhibit the aggregation and growth of calcium oxalate and calcium phosphate crystals, through electrostatic repulsion of oxalate and phosphate anions on the surface of the crystals. Results from several clinical trials(Table 1) support the benefits of the treatment with citrates in patients undergoing lithotripsy. Citrates can increase the clearance rate of residual stone fragments and prevent the formation of new stones. The total daily dose of citrates administered in the setting of clinical trials was 40 to 80mEq. **Magnesium ions and calcium stones:** Magnesium ions are generally regarded as potent inhibitors of calcium urolithiasis. Magnesium ions reduce urine supersaturation with calcium oxalate, through formation of water soluble magnesium oxalate and inhibits calcium phosphate and brushite crystal formation. **Citrate ions and dissolution of uric acid stones:** Uric acid stones form in urine usually of low pH and reduced volume. Hyperuricosuria (excretion of uric acid in the urine >750mg/day), low pH and low urine volume are the critical elements for the formation of uric acid stones. Alkalization of urine is mandatory[1] for the dissolution of uric acid stones. The pH should be increased to a level above 6.5 and the general recommendation is to achieve a pH in the range 6.5-7.0. According to the International Guidelines[1, 5] potassium citrate and magnesium citrate are the most appropriate and effective alkalinizing agents for the dissolution of uric acid stones. For the dissolution of uric acid stones it is recommended (Guidelines[1, 5] Level of Evidence: 1 and Grade of Recommendation: A) the use of 40-80mEq of citrates per day, divided in 2-3 doses.

What is LITHOS® Dissolve and what it contains: **LITHOS® Dissolve** is a food supplement that contains tripotassium citrate and trimagnesium citrate. **LITHOS® Dissolve** does not contain sodium. **Qualitative and quantitative composition:** Each sachet of **LITHOS® Dissolve** contains 14mEq of potassium ions, 7mEq magnesium ions and 21mEq citrate ions. Active ingredients: tripotassium citrate (1514mg) and trimagnesium citrate (581mg). Sweeteners: sorbitol and ace K. Acidification agent: citric acid. Coloring agent: concentrated extract of red potato (*Solanum tuberosum L.*). Antiagglomeration agent: silicon dioxide. **Indicated use:** **(1) LITHOS® Dissolve** is indicated for the clearance of residual stone fragments and the prevention of new stone formation after lithotripsy. **(2) LITHOS® Dissolve** is indicated for the dissolution of uric acid stones. (3) **LITHOS® Dissolve** is indicated for the treatment of distal renal tubular acidosis. **Dosage:** The dosage range of **LITHOS® Dissolve** is 40 to 80mEq per day. The total daily dose should be divided in two (morning and evening) or three (morning-afternoon-and evening) equal doses. **Administration:** **LITHOS® Dissolve** should be administered during or within 30 minutes after each meal. The content of each sachet is dissolved in a small quantity of water. The resulting solution is clear, pink colored, with a pleasant cranberry flavor. For the dissolution of uric acid stones the pH of the urine must be adjusted between 6,5 and 7,0 and regularly monitored to remain within this range (6.5-7.0) with the enclosed pH strips (pH range of the strips: 5,0-9,0). During the treatment period for dissolution of uric acid stones it is necessary to consume adequate quantity of water. **Contraindications and Precautions:** **LITHOS® Dissolve** 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® Dissolve** should not be administered together with potassium-sparing diuretics (amiloride/Frumil®, spironolactone/Aldactone®, eplerenone/Inspra®). **Adverse reactions:** During treatment with **LITHOS® Dissolve** 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® Dissolve** can cause fetal harm when administered to pregnant women or can affect reproduction capacity. should be given to pregnant women only if clearly needed. **Caution:** Do not exceed the highest recommended daily dose. Not suitable for diabetics. 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. **Packaging:** Carton box containing 60 sachets of **LITHOS® Dissolve** weighing 3,85gr each.

Table 1 Studies of the benefits of citrates after ESWL			% of patients without residual fragments after ESWL that remained free of stones		% of patients with residual fragments after ESWL that remained free of stones	
Study	Number of patients	Length of treatment	Treatment with citrates	Hygienic measures only	Treatment with citrates	Hygienic measures only
1	70	12 μήνες			74%	32%
2	80	43,2 μήνες	89,5%	50%	63,9%	23,1%
3	110	12 μήνες	100%	71,5%	87,5%	55,5%
4	44	24,4 μήνες			81,8%	27,2%
5	76	12 μήνες	92,3%	57,7%		

Studies of Table 1: **(1).** Cicerello E et al, *J Urol* **1994**, 16, 149-152. **(2).** Fine JK et al, *J Urol* **1995**, 153, 27-33. **(3).** Soygur T et al, *J Endourol* **2002**, 16, 149-152. **(4).** Sarica K et al, *J Endourol* **2006**, 20, 875-879. **(5).** Lojanapiwat B et al, *Int Braz J Urol* **2011**, 37, 611-616.

Literature **(1).** Tiselius H-G et al, Guidelines on urolithiasis. *European Association of Urology Update* **2008**. **(2).** Drach GW et al, *J Urol* **1986**, 135, 1127–1133. **(3).** Lingeman JE et al, *J Urol* **1986**, 135, 1134–1137. **(4).** Beck EM et al, *J Urol* **1991**, 145, 6–10. **(5).** Turk C et al, Guidelines on Urolithiasis. *European Association of Urology Update* **2013**.