

# הודעה על החמרה (מידע בטיחות)

תאריך: **28 בדצמבר 2015**

שם תכשיר באנגלית: **URSOFALK 500 Tablets**

מספר רישום: **150 68 33832**

שם בעל הרישום: **מעבדות רפא בע"מ**

השינויים המשמעותיים (שעל פי רוב מהווים גם החמרה) מסומנים בצבע. **צהוב**=הוספה, **ירוק**=מחיקה.

## בעלון לרופא

טקסט חדש	פרק בעלון
<p>...</p> <p>In patients with PBC, in rare cases the clinical symptoms may worsen at the beginning of treatment, e.g. the itching may increase. In this case the dose of Ursofalk 500mg tablets should be reduced to half a tablet Ursofalk 500mg tablets or one Ursofalk 250mg capsule daily and then gradually increased again as described in section 4.2.</p> <p>...</p>	<p><b>4.4 Special warnings and precautions for use</b></p>
<p>Ursofalk 500mg tablets should not be administered concomitantly with colestyramine, colestipol or antacids containing aluminium hydroxide and/or smectite (aluminium oxide), because these preparations bind ursodeoxycholic acid in the intestine and thereby inhibit its absorption and efficacy. Should the use of a preparation containing one of these substances be necessary, it must be taken at least 2 hours before or after Ursofalk 500mg tablets.</p> <p>Ursofalk 500mg tablets can <b>affect increase</b> the absorption of ciclosporin from the intestine. In patients receiving ciclosporin treatment, blood concentrations of this substance should therefore be checked by the physician and the ciclosporin dose adjusted if necessary.</p> <p>In isolated cases, Ursofalk 500mg tablets can reduce the absorption of ciprofloxacin.</p> <p><b>In a clinical study in healthy volunteers concomitant use of UDCA (500 mg/day) and rosuvastatin (20 mg/day) resulted in slightly elevated plasma levels of rosuvastatin. The clinical relevance of this interaction also with regard to other statins is unknown.</b></p> <p>Ursodeoxycholic acid has been shown to reduce peak plasma concentrations (<math>C_{max}</math>) and area under the curve (AUC) of the calcium antagonist nitrendipine <b>in healthy volunteers. Close monitoring of the outcome of concurrent use of nitrendipine and UDCA is recommended. An increase of the dose of nitrendipine may be necessary.</b></p> <p>An interaction with a reduction of the therapeutic effects of dapsone was also reported.</p> <p>These observations, together with in-vitro findings could indicate a potential for ursodeoxycholic acid to induce cytochrome P450 3A enzymes. Induction has, however, not been observed in a well-designed interaction study with budesonide, which is a known cytochrome P450 3A substrate.</p> <p><b>Oestrogenic hormones and blood cholesterol lowering agents, such as clofibrate, increase hepatic cholesterol secretion and may therefore encourage biliary lithiasis, which is a counter-effect to UDCA in some cases.</b></p>	<p><b>4.5 Interaction with other medicinal products and other forms of interaction</b></p>
<p>Animal studies did not show an influence of UDCA on fertility (see section 5.3). Human data on fertility effects following treatment with UDCA are not available.</p> <p>There are no or limited data <del>on</del> from the use of ursodeoxycholic acid in pregnant women, <b>particularly in the first trimester of pregnancy.</b> Studies in animals have shown reproductive toxicity during the early phase of gestation (see section 5.3). Ursofalk 500mg tablets must not be used during pregnancy unless clearly necessary. Women of childbearing potential should be treated only if they use reliable contraception.</p>	<p><b>4.6 Fertility, pregnancy and lactation</b></p>

<p>Non-hormonal or low oestrogen oral contraceptive measures are recommended. <b>The possibility of a pregnancy must be excluded before beginning treatment.</b></p> <p>According to few documented cases of breast feeding women, milk levels of ursodeoxycholic acid are very low and probably no adverse reactions are to be expected in breastfed infants.</p>	
<p><del>No effects on ability to drive and use machines have been observed.</del>  <b>Ursofalk 500mg tablets have no or negligible influence on the ability to drive and use machines.</b></p>	<b>4.7 Effects on ability to drive and use machines</b>
<p>...  <i>Gastrointestinal disorders:</i>  In clinical trials, reports of <b>soft pasty</b> stools or diarrhoea during ursodeoxycholic acid therapy were common.  Very rarely, severe right upper abdominal pain has occurred during the treatment of primary biliary cirrhosis.  ...</p>	<b>4.8 Undesirable effects</b>
<p>...  <b>Additional information on special populations:</b>  Long term high dose UDCA therapy (28-30 mg/kg/day) used in patients with primary sclerosing cholangitis was associated with higher rates of serious adverse events.</p>	<b>4.9 Overdose</b>

### **בעלון לצרכן**

<b>טקסט חדש (כולל סימון השינויים המשמעותיים לעומת הטקסט הקיים)</b>	<b>פרק בעלון</b>
<p>...</p> <ul style="list-style-type: none"> <li>• רזובסטטין (להורדת כולסטרול) - אורסופאלק עלול להשפיע על פעילות התרופה.</li> <li>• גלולות למניעת הריון ותרופות מסוימות להורדת כולסטרול ושומנים בדם כגון קלופיברט: במקרים מסוימים תרופות אלו עלולות להשפיע על הפעילות של אורסופאלק. יש להתייעץ על כך עם הרופא.</li> </ul>	<b>תגובות אפשריות עם תרופות אחרות שנלקחות במקביל</b>