

## הודעה על החמרה (מידע בטיחות)

תאריך: 13.05.2012

שם תכשיר באנגלית: Amiodacore tablets

מספר רישום: 052072351700

שם בעל הרישום: CTS chemical industries ltd

השינויים בעלון מסומנים על רקע צהוב

**בעלון לרופא**

פרטים על השינויים המבוקש/ים		
טקסט חדש	טקסט נוכחי	פרק בעלון
<p>Cardiac effects</p> <ul style="list-style-type: none"> <li>• An ECG must be performed before starting treatment <b>and serum potassium measurement. Monitoring of ECG is recommended during treatment .</b></li> <li>• Slowing of heart rate may be accentuated in elderly patients .</li> <li>• The electrocardiogram is modified under amiodarone. This "amiodaronic" modification consists of a prolongation in QT reflecting a repolarisation prolongation, possibly with the appearance of a U <b>wave and deformed T-waves;</b> this is a sign of therapeutic impregnation and not of toxicity.</li> <li>• <b>Too high a dosage may lead to severe bradycardia and conduction disturbances with the appearance of an idioventricular rhythm, particularly in elderly patients or during digitalis therapy. In these circumstances, Amiodacore treatment should be withdrawn. If necessary beta-adrenostimulants or glucagon may be given. Because of the long half-life of amiodarone, if bradycardia is severe and symptomatic the insertion of pacemaker should be considered .</b></li> <li>• <b>Amiodacore is not contra-indicated in patients with latent or manifest heart failure but caution should be exercised as, occasionally, existing heart failure may be worsened. In such cases, Amiodacore may be used with other appropriate therapies .</b></li> <li>• <b>Amiodarone may increase the</b></li> </ul>	<p>Cardiac effects</p> <ul style="list-style-type: none"> <li>• An ECG must be performed before starting treatment .</li> <li>• Slowing of heart rate may be accentuated in elderly patients .</li> <li>• The electrocardiogram is modified under amiodarone. This "amiodaronic" modification consists of a prolongation in QT reflecting a repolarisation prolongation, possibly with the appearance of a U; this is a sign of therapeutic impregnation and not of toxicity.</li> </ul>	<p><b>Precautions</b></p>

<p><b>defibrillation threshold and/or pacing threshold in patients with an implantable cardioverter defibrillator or a pacemaker, which may adversely affect the efficacy of the device. Regular tests are recommended to ensure the proper function of the device after initiation of treatment or change in posology .</b></p> <p><b>Pulmonary signs</b>  <b>Patients should be carefully evaluated clinically and consideration given to chest X-rays before starting therapy. During treatment, if pulmonary toxicity is suspected, this should be repeated and associated with lung function testing including, where possible, measurement of transfer factor. Initial radiological changes may be difficult to distinguish from pulmonary venous congestion. Pulmonary toxicity has usually been reversible following early withdrawal of amiodarone therapy, with or without corticosteroid. Clinical symptoms often resolve within a few weeks followed by slower radiological and lung function improvement. Some patients can deteriorate despite discontinuing amiodarone .</b></p> <p><b>Hepatic signs</b>  <b>• Amiodarone may be associated with a variety of hepatic effects, including cirrhosis, hepatitis, jaundice and hepatic failure. Some fatalities have been reported, mainly following long-term therapy, although rarely they have occurred soon after starting treatment particularly after Amiodarone intravenous .</b>  <b>• At the beginning of therapy, elevation of serum transaminases which can be in isolation may occur. These may return to normal with dose reduction, or sometimes spontaneously. Isolated cases of acute liver disorders with elevated serum transaminases and/or jaundice may occur; in such cases treatment should be discontinued.</b></p> <p><b>Neuromuscular signs</b>  <b>Both these conditions may be severe, although recovery usually occurs within several months after amiodarone withdrawal, but may sometimes be incomplete .</b></p>		
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<p>-Combination with medicinal products liable to induce torsades de pointes :</p> <ul style="list-style-type: none"> <li>• class Ia antiarrhythmics (quinidine, hydroquinidine, disopyramide)</li> <li>• class III antiarrhythmics (sotalol, dofetilide, ibutilide)</li> <li>• Intravenous erythromycin, <b>co-trimoxazole or pentamidine injection.</b></li> <li>• <b>Some anti-psychotics (Chlorpromazine, Thioridazine, Fluphenazine, Pimozide, Haloperidol, Amisulpiride and Sertindole)</b></li> <li>• <b>Lithium and anti-depressants (Doxepin, Maprotiline and Amitriptyline)</b></li> <li>• <b>Certain antihistamines (Terfenadine, Astemizole and Mizolastine)</b></li> <li>• <b>Anti-malarials (Quinine, Mefloquine, Chloroquine and Halofantrine)</b></li> <li>• Moxifloxacin.</li> </ul>	<p>-combination with medicinal products liable to induce torsades de pointes :</p> <ul style="list-style-type: none"> <li>• class Ia antiarrhythmics (quinidine, hydroquinidine, disopyramide)</li> <li>• class III antiarrhythmics (sotalol, dofetilide, ibutilide)</li> <li>• other medicinal products, such as bepridil, cisapride, diphemanil, erythromycin IV, mizolastine, moxifloxacin, spiramycin IV, vincamine IV, (see 4.5 Interactions with other medicinal products and other forms of interaction )</li> <li>• sultopride</li> </ul>	<p><b>Contraindications</b></p>
<p>Thyroid signs: <b>Very rare: syndrome of inappropriate antidiuretic hormone secretion (SIADH)</b></p> <p>Hepatic signs : -Very rare: chronic liver damage during prolonged treatment <b>(sometimes fetal)</b></p> <p>Cardiac effects : <b>Onset or worsening of arrhythmia, sometimes followed by cardiac arrest.</b></p> <p>Effects on the reproductive system: <b>epididymo-orchitis, impotence</b></p> <p>Effects on the blood and lymphatic system: <b>haemolytic anemia, aplastic anaemia.</b></p> <p>Immune system disorder: <b>Angioedema (there have been some reports of angioedema although exact frequencies are not known)</b></p>	<p>Hepatic signs : -Very rare: chronic liver damage during prolonged treatment</p>	<p><b>Adverse events</b></p>
<p><b>In cases of hypokalaemia, corrective action should be taken and QT interval monitored. In case of torsades de pointes antiarrhythmic agents should be given; pacing may be instituted and IV magnesium may be used</b></p> <p><b>+Fluoroquinolones</b> There have been rare reports of QTc interval prolongation, with or without torsades de pointes, in patients taking amiodarone with fluoroquinolones. Concomitant use of amiodarone with fluoroquinolones should be avoided.</p> <p><b>+Stimulant laxatives</b></p>		<p><b>Drug Interactions</b></p>

<p><b>May cause hypokalaemia, thus increasing the risk of torsades de pointes; other type of laxatives should be used.</b></p> <p><b>+Grapefruit juice</b> Inhibits cytochrome P450 3A4 and may increase the plasma concentration of amiodarone, grapefruit should be avoided during treatment with amiodarone .</p> <p><b>+ Flecainide</b> Given the flecainide is mainly metabolized by CYP 2D6, by inhibiting this isoenzyme, amiodarone may increase flecainide plasma levels; it is advised to reduce the flecainide dose by 50% and to monitor the patient closely for adverse effects. Monitoring of flecainide plasma is strongly recommended in such circumstances .</p> <p><b>+Other drugs metabolized by CYP450 3A4</b> Co- administered with amiodarone, an inhibitor of CYP 3A4, this may result in a higher level of their plasma concentration, which may lead to possible increase in their toxicity. Examples of such drugs: sildenafil, fentanyl, midazolam, triazolam, dihydroergotamine and ergotamine.</p>		
<p><b>The ability to drive or to operate machinery may be impaired in patients with clinical symptoms of amiodarone-induced eye disorders.</b></p>	Not applicable	<p><b>Effects on ability to drive and use machines</b></p>
<p><b>gastric lavage may be employed to reduce absorption in addition to general supportive measures</b></p>		<p><b>Overdose</b></p>

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פרטים על השינויים המבוקשים		
פרק בעלון	טקסט נוכחי	טקסט חדש
מתי אין להשתמש בתכשיר	<p>• אין להשתמש בצירוף עם תרופות הניתנות בהזרקה שעלולות לגרום להפרעות קצב, כגון: erythromycin IV, spiramycin IV, vincamicin IV,</p> <p>Co-trimoxazole or Pentamidine injection</p> <p>• אין להשתמש בתרופה בשילוב עם תרופות אנטי-פסיכוטיות, כגון: Chlorpromazine, Thioridazine, Fluphenazine, Pimozide, Haloperidol, Amisulpiride, Sertindole</p> <p>• אין להשתמש בתרופה בשילוב עם ליתיום או עם תרופות נוגדות דיכאון, כגון: Terfenadine, Astemizole, Mizolastine</p> <p>• אין להשתמש בתרופה בשילוב עם תרופה לטיפול במלריה, כגון: Quinone, Mefloquine, Chloroquine, Halofantrine</p>	<p>• אין להשתמש בצירוף עם תרופות הניתנות בהזרקה שעלולות לגרום להפרעות קצב, כגון: erythromycin IV, spiramycin IV, vincamicin IV</p>
תגובות בין תרופתיות		<p>• פלורוקווינולון, תרופות משלשלות, מיץ אשכוליות, פליקיניד.</p>
תופעות לוואי		<p>• אין אונות, אנגיואדמה- בצקות בצוואר ובפנים, אנמיה</p>
תופעות לוואי הדורשות התייחסות מיוחדת		<p>• השימוש בתרופה זו עלול לפגום בראיה ועל כן מחייב זהירות בנהיגה ברכב, בהפעלת מכונות מסוכנות.</p>

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