# הודעה על החמרה ( מידע בטיחות) בעלון לרופא

**תאריך 01.02.2015**

**שם תכשיר באנגלית ומספר הרישום:**

 **TAXOTERE 20mg/ml 144 44 33092 \_**

**שם בעל הרישום: סאנופי-אוונטיס ישראל בע"מ**

**המידע שהוסף מסומן בצהוב. הסעיפים שעודכנו כוללים מידע נוסף שאינו מופיע כאן. מידע מלא ניתן למצוא בעלון המלא.**

טופס זה מיועד לפרוט ההחמרות בלבד !

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| **ההחמרות המבוקשות** |
| **פרק בעלון** | **טקסט נוכחי** | **טקסט חדש** |
| **blackbox****4.4** **Special Warnings and Special Precautions for Use** |  | **The incidence of treatment-related mortality associated with TAXOTERE therapy is increased in patients with abnormal liver function, in patients receiving higher doses, and in patients with non-small cell lung carcinoma and a history of prior treatment with platinum based chemotherapy who receive TAXOTERE as a single agent at a dose of 100 mg/m2****Patients with elevations of bilirubin or abnormalities of transaminase concurrent****with alkaline phosphatase are at increased risk for the development of grade 4 neutropenia, febrile neutropenia, infections, severe thrombocytopenia, severe stomatitis, severe skin toxicity, and toxic death. Patients with isolated elevations of transaminase >1.5 × ULN also had a higher rate of febrile neutropenia grade 4 but did not have an increased incidence of toxic death. Bilirubin, AST or ALT, and alkaline phosphatase values should be obtained prior to each cycle of docetaxel therapy.**TAXOTERE® THERAPY SHOULD NOT BE GIVEN TO PATIENTS WITH NEUTROPHIL COUNTS OF LESS THAN 1,500 CELLS/MM3. IN ORDER TO MONITOR THE OCCURRENCE OF NEUTROPENIA, WHICH MAY BE SEVERE AND RESULT IN INFECTION, IT IS RECOMMENDED THAT FREQUENT BLOOD CELL COUNTS BE PERFORMED ON ALL PATIENTS RECEIVING TAXOTERE®.~~SEVERE HYPERSENSITIVITY REACTIONS RESULTING IN IMMEDIATE DISCONTINUATIONS OCCURRED IN 0.4% (5 OF 1260) OF PATIENTS. TAXOTERE~~~~®~~ ~~MUST NOT BE GIVEN TO PATIENTS WHO HAVE A HISTORY OF SEVERE HYPERSENSITIVITY REACTIONS TO TAXOTERE~~~~®~~ ~~OR TO OTHER DRUGS FORMULATED WITH POLYSORBATE 80.~~**Severe hypersensitivity reactions characterized by generalized rash/erythema, hypotension and/or bronchospasm, or very rarely fatal anaphylaxis , have been reported in patients who received a 3-day dexamethasone premedication. Hypersensitivity reactions require immediate discontinuation of the TAXOTERE infusion and administration of appropriate therapy. TAXOTERE must not be given to patients who have a history of severe hypersensitivity reactions to TAXOTERE or to other drugs formulated with polysorbate 80****Severe fluid retention occurred in 6.5% (6/92) of patients despite use of a 3-day****dexamethasone premedication regimen. It was characterized by one or more of the following events : poorly tolerated peripheral edema, generalized edema, pleural effusion requiring urgent drainage, dyspnea at rest, cardiac tamponade, or pronounced abdominal distention (due to ascites )***Ethanol*This product contains ethanol.Harmful for those suffering from alcoholism. To be taken into account in pregnant or breast-feeding women, children and high-risk groups such as patients with liver disease, or epilepsy. The amount of alcohol in this medicinal product may alter the effects of other medicinal products. The amount of alcohol in this medicinal product may impair the patients ability to drive or use machines.**///////////////////////////////****Patients with liver impairment****//////////////////////////////**The amount of ethanol in Taxotere should be taken into account when given to patients with hepatic impairment (see below “Excipients”).**//////////////////////////////****Hypersensitivity reactions**Patients should be observed closely for hypersensitivity reactions especially during the first and second infusions. Severe hypersensitivity reactions characterized by generalized rash/erythema, hypotension and/or bronchospasm, or very rarely fatal anaphylaxis, have been reported in patients premedicated with 3 days of corticosteroids. Hypersensitivity reactions may occur within a few minutes following the initiation of the infusion of docetaxel, thus facilities for the treatment of hypotension and bronchospasm should be available. If hypersensitivity reactions occur, minor symptoms such as flushing or localised cutaneous reactions do not require interruption of therapy. However, severe reactions, such as severe hypotension, bronchospasm or generalised rash/erythema require immediate discontinuation of docetaxel and appropriate therapy. Patients who have developed severe hypersensitivity reactions should not be re-challenged with docetaxel**Fluid retention**Patients with severe fluid retention such as pleural effusion, pericardial effusion and ascites should be monitored closely.Severe fluid retention has been reported following docetaxel therapy. Patients should be premedicated with oral corticosteroids prior to each docetaxel administration to reduce the incidence and severity of fluid retention. Patients with pre-existing effusions should be closely monitored from the first dose for the possible exacerbation of the effusions.When fluid retention occurs, peripheral edema usually starts in the lower extremities and may become generalized with a median weight gain of 2 kg.Among 92 breast cancer patients premedicated with 3-day corticosteroids, moderate fluid retention occurred in 27.2% and severe fluid retention in 6.5%. The median cumulative dose to onset of moderate or severe fluid retention was 819 mg/m2. Nine of 92 patients (9.8%) of patients discontinued treatment due to fluid retention: 4 patients discontinued with severe fluid retention; the remaining 5 had mild or moderate fluid retention. The median cumulative dose to treatment discontinuation due to fluid retention was 1021 mg/m2. Fluid retention was completely, but sometimes slowly, reversible with a median of 16 weeks from the last infusion of docetaxel to resolution (range: 0 to 42+ weeks). Patients developing peripheral edema may be treated with standard measures, e.g., salt restriction, oral diuretic(s).**Respiratory disorders** Acute respiratory distress syndrome, interstitial pneumonia/pneumonitis, interstitial lung disease, pulmonary fibrosis and respiratory failure have been reported and may be associated with fatal outcome. Cases of radiation pneumonitis have been reported in patients receiving concomitant radiotherapy. If new or worsening pulmonary symptoms develop, patients should be closely monitored, promptly investigated, and appropriately treated. Interruption of docetaxel therapy is recommended until diagnosis is available. Early use of supportive care measures may help improve the condition. The benefit of resuming docetaxel treatment must be carefully evaluated.***Interactions***The concomitant use of Taxotere with strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin, indinavir, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin and voriconazole) should be avoided (see Section 4.5).**//////////////////////////////***Excipients***//////////////////////////////**The amount of ethanol in Taxotere may by harmful for those suffering from alcoholism and should also ~~To~~ be taken into account in pregnant or breast-feeding women, in children and in high-risk groups such as patients with liver disease, or epilepsy.Consideration should be given to possible effects on the central nervous system.The amount of alcohol in this medicinal product may alter the effects of other medicinal products.The amount of alcohol in this medicinal product may impair the patients ability to drive or use machines. |
| **4.5****Interaction with Other Medicaments and Other Forms of Interaction** |  | **//////////////////////////////**In case of combination with CYP3A4 inhibitors, the occurrence of Taxotere adverse reactions may increase, as a result of reduced metabolism. If the concomitant use of a strong CYP3A4 inhibitor (e.g., ketoconazole, itraconazole, clarithromycin, indinavir, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin and voriconazole) cannot be avoided, a close clinical surveillance is warranted and a dose-adjustment of Taxotere may be suitable during the treatment with the strong CYP3A4 inhibitor (see section 4.4). In a pharmacokinetic study with 7 patients, the co-administration of docetaxel with the strong CYP3A4 inhibitor ketoconazole leads to a significant decrease in docetaxel clearance by 49%.**//////////////////////////////**~~Clinical cases consistent with an increase in docetaxel toxicity were reported when it was combined with ritonavir. The mechanism behind this interaction is a CYP3A4 inhibition, the main isoenzyme involved in docetaxel metabolism by ritonavir. Based on extrapolation from a pharmacokinetic study with ketoconazole in 7 patients, consider a 50% docetaxel dose reduction if patients require co-administration of a strong CYP3A4 inhibitor such as azole antifungals, ritonavir and some macrolides (clarithromycin, telithromycin).~~**//////////////////////////////** |
| **4.7** **Effects on ability to drive and use machines** |  | ~~No studies on the effects on the ability to drive and use machines have been performed.~~The amount of ethanol in Taxotere may impair the ability to drive or use machines (see section 4.4). |