הודעה על החמרה (מידע בטיחות) בעלון לרופא

תאריך **06.2014**

שם תכשיר באנגלית **JEVTANA**

מספר רישום 145-23-33286-

שם בעל הרישום **Sanofi-Aventis Israel ltd**

פרטים על השינוי/ים המבוקש/ים		
פרק בעלון	**טקסט נוכחי**	**טקסט חדש**
2.5 Instructions for Preparation		**מצוין רק המידע שהתווסף ומהווה החמרה. למידע מלא עבור סעיף זה יש לבדוק את העלון לרופא.** Read this **entire** section carefully before mixing and diluting. JEVTANA requires **two** dilutions prior to administration. Please follow the preparation instructions provided below, as improper preparation may lead to overdose (see Overdosage (10))

מצוין רק המידע שהתווסף ומהווה החמרה. למידע מלא עבור סעיף זה יש לבדוק את העלון לרופא. **5.3 Gastrointestinal Symptoms** **……..** Gastrointestinal (GI) hemorrhage and perforation, ileus, enterocolitis, neutropenic enterocolitis, including fatal outcome, have been reported in patients treated with Jevtana (see adverse reactions (6.2)). Risk may be increased with neutropenia, age, steroid use, concomitant use of NSAIDs, anti-platelet therapy or anti-coagulants, and patients with a prior history of pelvic radiotherapy, adhesions, ulceration and GI bleeding**……..**		**5. WARNINGS AND PRECAUTIONS**
מצוין רק המידע שהתווסף ומהווה החמרה. למידע מלא עבור סעיף זה יש לבדוק את העלון לרופא. 6.2 Post -marketing experience The following adverse reactions have been identified from clinical trials and/or post-marketing surveillance. Because they are reported from a population of unknown size, precise estimates of frequency cannot be made. ***Gastrointestinal:*** gastritis, intestinal obstruction		**6. ADVERSE REACTIONS**
מצוין רק המידע שהתווסף ומהווה החמרה. למידע מלא עבור סעיף זה יש לבדוק את העלון לרופא. **7.1 Drugs That May Increase Cabazitaxel Plasma Concentrations:….** **CYP3A4 Inhibitors**: **If co-administration with a strong CYP3A inhibitor cannot be avoided, close monitoring for toxicity and a cabazitaxel dose reduction should be considered** (see sections 8.7 and 11.3)...		**7. DRUG INTERACTIONS**
מצוין רק המידע שהתווסף ומהווה החמרה. למידע מלא עבור סעיף זה יש לבדוק את העלון לרופא. 8.7 ***Concomitant drug use*** Concomitant drugs that are strong CYP3A inducers or strong CYP3A inhibitors should be avoided (see Sections 7 and Section 11.3). However, if patients require co-administration of a strong CYP3A inhibitor, a 25% cabazitaxel dose reduction should be considered (see Sections 7.1 and Section 11.3).		**8. USE IN SPECIFIC POPULATIONS**
מצוין רק המידע שהתווסף ומהווה החמרה. למידע מלא עבור סעיף זה יש לבדוק את העלון לרופא. There is no known antidote for JEVTANA overdose. Overdose has resulted from improper preparation. Please read the entire section *Dosage and Administration (2)* carefully before mixing or diluting. Complications of overdose include exacerbation of adverse reactions such as bone marrow suppression and gastrointestinal disorders. Overdose has led to fatal outcome		9. **OVERDOSAGE**

מצוין רק המידע שהשתנה ומהווה החמרה. למידע מלא עבור סעיף זה יש לבדוק את העלון לרופא Metabolism Cabazitaxel is extensively metabolized in the liver (> 95%), mainly by the CYP3A4/5 isoenzyme (80% to 90%), and to a lesser extent by CYP2C8. Cabazitaxel is the main circulating moiety in human plasma. Seven metabolites were detected in plasma (including the 3 active metabolites issued from O-demethylation), with the main one accounting for 5% of cabazitaxel exposure. Around 20 metabolites of cabazitaxel are excreted into human urine and feces. Based on *in vitro* studies, the potential for cabazitaxel to inhibit drugs that are substrates of other CYP isoenzymes (1A2,-2B6,-2C9, -2C8, -2C19, -2E1, -2D6, and CYP3A4/5) is low. In addition, cabazitaxel did not induce CYP isozymes (-1A,-2C and -3A) *in vitro*. A drug interaction study in 11 patients with advanced cancers has shown that cabazitaxel (25 mg/m^2 administered as a single 1-hour infusion) did not modify the plasma levels of midazolam, a probe substrate of CYP3A. Therefore, cabazitaxel is not an inhibitor of CYP3A in vivo. ……. Drug interactions Cabazitaxel is mainly metabolized by CYP3A. Repeated administration of ketoconazole (400 mg once daily), a strong CYP3A inhibitor, resulted in a 20% decrease in cabazitaxel clearance corresponding to a 25% increase in AUC. Concomitant administration of aprepitant, a moderate CYP3A inhibitor, had no effect on cabazitaxel clearance or exposure. Repeated administration of rifampin (600 mg once daily), a strong CYP3A inducer, resulted in an increase in cabazitazel clearance of 21% corresponding to a decrease in AUC of 17%.		**11.3** **Pharmacokinetics**