הודעה על החמרה (מידע בטיחות)

תאריך: **10.06.2012**

שם התכשיר באנגלית: **Herceptin® Vials 440 mg**

מספרי רישום: **113 91 29676**

שם בעל הרישום: **רוש פרמצבטיקה (ישראל) בע"מ**

ההחמרות בעלון מסומנות על רקע צהוב

בעלון לרופא

פרטים על השינוי/ים המבוקש/ים		
פרק בעלון	**טקסט נוכחי**	**טקסט חדש**
4.4 **Special warningsand precautions for use**	Herceptin and anthracyclines should not be used currently in combination except in a well-controlled clinical trial setting with cardiac monitoring. Patients who have previously received anthracyclines are also at risk of cardiotoxicity with Herceptin treatment, although the risk is lower than with concurrent use of Herceptin and anthracyclines.Because the half-life of Herceptin is approximately 4-5 weeks Herceptin may persist in the circulation for up to 20-25 weeks after stopping Herceptin treatment. Patients who receive anthracyclines after stopping Herceptin may possibly be at increased risk of cardiotoxicity. If possible, physicians should avoid anthracycline-based therapy for up to 25 weeks after stopping Herceptin. If anthracyclines are used, the patient's cardiac function should be monitored carefully.	.Because the half-life of Herceptin is approximately 4-5 weeks Herceptin may persist in the circulation for up to 20-25 weeks after stopping Herceptin treatment. Patients who receive anthracyclines after stopping Herceptin may possibly be at increased risk of cardiotoxicity. If possible, physicians should avoid anthracycline-based therapy for up to 25 weeks after stopping Herceptin. If anthracyclines are used, the patient's cardiac function should be monitored carefully. Metastatic breast cancer Herceptin and anthracyclines should not be given concurrently in combination in the metastatic breast cancer setting. Patients with metastatic breast cancer who have previously received anthracyclines are also at risk of cardiotoxicity with Herceptin treatment, although the risk is lower than with concurrent use of Herceptin and anthracyclines. Early breast cancer (EBC) For patients with early breast cancer, cardiac assessments, as performed at baseline, should be repeated every 3 months during treatment and every 6 months following discontinuation of treatment until 24 months from the last administration

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of Herceptin. In patients who receive anthracycline containing chemotherapy further monitoring is recommended, and should occur yearly up to 5 years from the last administration of Herceptin, or longer if a continuous decrease of LVEF is observed. <u>Adjuvant treatment</u> Herceptin and anthracyclines should not be given concurrently in combination in the adjuvant treatment setting. In patients with EBC an increase in the incidence of symptomatic and asymptomatic cardiac events was observed when Herceptin was administered after anthracycline-containing chemotherapy compared to administration with a non-anthracycline regimen of docetaxel and carboplatin and was more marked when Herceptin was administered concurrently with taxanes than when administered sequentially to taxanes. Regardless of the regimen used, most symptomatic cardiac events occurred within the first 18 months. In one of the 3 pivotal studies conducted in which a median follow-up of 5.5 years was available (BCIRG006) a continuous increase in the cumulative rate of symptomatic cardiac or LVEF events was observed in patients who were administered Herceptin concurrently with a taxanefollowing anthracycline therapy up to 2.37% compared to approximately 1% in the two comparator arms (anthracycline plus cyclophosphamide followed by taxane and taxane, carboplatin and Herceptin). <u>Neoadjuvant-adjuvant treatment</u> In patients with early breast cancer eligible for neoadjuvant-adjuvant treatment, Herceptin should only be used concurrently with anthracyclines in chemotherapy-naive patients and only with low-dose		**4.4** **Special warnings and precautions for use**

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anthracycline regimens (maximum cumulative doses: doxorubicin 180 mg/m^2 or epirubicin 360 mg/m^2). If patients have been treated concurrently with low-dose anthracyclines and Herceptin in the neoadjuvant setting, no additional cytotoxic chemotherapy should be given after surgery. Experience of concurrent administration of trastuzumab with low dose anthracycline regimens is currently limited. Only few patients in the NOAH trial were > 65 years of age. Therefore, clinical experience in this age group is limited, and therefore neoadjuvant-adjuvant treatment is not recommended for patients older than 65 years. *Pulmonary events* Risk factors associated with interstitial lung disease include prior or concomitant therapy with other anti-neoplastic therapies known to be associated with it such as taxanes, gemcitabine, vinorelbine and radiation therapy.		**4.4** **Special warnings and precautions for use**

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In the post-marketing setting, cases of foetal renal growth and/or function impairment in association with oligohydramnios, some associated with fatal pulmonary hypoplasia,or skeletal abnormalities of the foetus**,** have been reported in pregnant women receiving Herceptin. Women of childbearing potential should be advised to use effective contraception during treatment with Herceptin and for at least 6 months after treatment has concluded. Women who become pregnant should be advised of the possibility of harm to the foetus. If a pregnant woman is treated with Herceptin, close monitoring by a multidisciplinary team is desirable.	In the post-marketing setting, cases of oligohydramnios, some associated with fatal pulmonary hypoplasia, or skeletal abnormalities of the foetus**,** have been reported in pregnant women receiving Herceptin. Women of childbearing potential should be advised to use effective contraception during treatment with Herceptin and for at least 6 months after treatment has concluded. Women who become pregnant should be advised of the possibility of harm to the foetus. If a pregnant woman is treated with Herceptin, close monitoring by a multidisciplinary team is desirable.	**4.6 Fertility, pregnancy and lactation**
Eye disorders ConjunctivitisVery Common Lacrimation increased Very Common Cardiac disorders Ejection fraction decreased* Very Common Respiratory, thoracic and mediastinal disorders Cough Very Common Epistaxis Very Common Rhinorrhoea Very Common *Haematotoxicity* Febrile neutropenia occured very commonly. Commonly occurring adverse reactions included anaemia, leukopenia, thrombocytopenia and neutropenia. The frequency of occurrence of hypoprothrombinemia is not known. The risk of neutropenia may be slightly increased when trastuzumab is administered with docetaxelfollowing anthracycline therapy.	Eye disorders Lacrimation increased Common Cardiac disorders Ejection fraction decreased Common Respiratory, thoracic and mediastinal disorders Cough Common Epistaxis Common Rhinorrhoea Common *Haematotoxicity* Febrile neutropenia occured very commonly. Commonly occurring adverse reactions included anaemia, leukopenia, thrombocytopenia and neutropenia. The frequency of occurrence of hypoprothrombinemia is not known.	**4.8 Undesirable Effects**

חתימת רוקחת ממונה