הודעה על החמרה (מידע בטיחות) בעלון לרופא
(מעודכן 3102.50)

תאריך 9.7.2013

שם תכשיר באנגלית ומספר הרישום Tykerb 139 23 31609

שם בעל הרישום : GlaxoSmithKline (ISRAEL) Ltd

טופס זה מיועד לפרוט ההחמרות בלבד !

ההחמרות המבוקשות		
טקסט חדש	**טקסט נוכחי**	**פרק בעלון**
Interstitial lung disease / pneumonitis Tykerb should be discontinued in patients who experience pulmonary symptoms which are NCI CTCAE grade 3 or greater (see section 4.4).	*Interstitial lung disease/pneumonitis (see Warnings and Precautions and Adverse Reactions)* Lapatinib should be discontinued in patients who experience pulmonary symptoms indicative of interstitial lung disease/pneumonitis which are NCI CTCAE grade 3 or greater.	**Posology and method of administration**
Renal impairment No dose adjustment is necessary in patients with mild to moderate renal impairment. Caution is advised in patients with severe renal impairment as there is no experience of Tykerb in this population	**Renal Impairment** There is no experience of lapatinib in patients with severe renal impairment, however, patients with renal impairment are unlikely to require dose modification of lapatinib given that less than 2% of an administered dose (lapatinib and metabolites) is eliminated by the kidneys	**Posology and method of administration**
Cardiac toxicity Lapatinib has not been evaluated in patients with symptomatic cardiac failure. Caution should be taken if Tykerb is to be administered to patients with conditions that could impair left ventricular function (including co-administration with potentially cardiotoxic medicinal products). Evaluation of cardiac function, including LVEF determination, should be conducted for all patients prior to initiation of treatment with Tykerb to ensure that the patient has a baseline LVEF that is within the institutions normal limits. LVEF should continue to be evaluated during treatment with Tykerb to ensure that LVEF does not decline to an unacceptable level (see section 4.2). In some cases, LVEF decrease may be severe and lead to cardiac failure…	*Cardiac toxicity* Lapatinib has been associated with reports of decreases in left ventricular ejection fraction [LVEF] (see *Adverse Reactions*). Caution should be taken if lapatinib is to be administered to patients with conditions that could impair left ventricular function. LVEF should be evaluated in all patients prior to initiation of treatment with lapatinib to ensure that the patient has a baseline LVEF that is within the institutions normal limits. LVEF should continue to be evaluated during treatment with lapatinib to ensure that LVEF does not decline to an unacceptable level…	**Special Warnings and Special Precautions for Use** **Special Warnings and Special Precautions for Use**

…There has been no dedicated study to assess the potential for lapatinib to prolong the QT interval. A small, concentration dependent increase in QTc interval was observed in an uncontrolled, open-label dose-escalation study of lapatinib in advanced cancer patients, such that an effect on QT interval cannot be ruled out. Caution should be taken if Tykerb is administered to patients with conditions that could result in prolongation of QTc (including hypokalemia, hypomagnesemia, congenital long QT syndrome, or co-administration of other medicinal product known to cause QT prolongation). Hypokalemia or hypomagnesemia should be corrected prior to treatment. Electrocardiograms with QT measurement should be considered prior to administration of Tykerb and throughout treatment.		
Interstitial lung disease and pneumonitis … Patients should be monitored for symptoms of pulmonary toxicity (dyspnoea, cough, fever) and treatment discontinued in patients who experience symptoms which are NCI CTCAE grade 3 or greater. Pulmonary toxicity may be severe and lead to respiratory failure. Fatal cases have been reported, causality of the deaths is uncertain.	*Interstitial lung disease and pneumonitis* Lapatinib has been associated with reports of interstitial lung disease and pneumonitis (see *Adverse Reactions*). Patients should be monitored for pulmonary symptoms indicative of interstitial lung disease/pneumonitis (see *Dosage and Administration*).	**Special Warnings and Special Precautions for Use**
Hepatotoxicity …At the initiation of treatment, patients should be advised of the potential for hepatotoxicity… Patients who carry the HLA alleles DQA1*02:01 and DRB1*07:01 have increased risk of Tykerb-associated hepatotoxicity… …Caution is advised if Tykerb is prescribed to patients with severe renal impairment	-	**Special Warnings and Special Precautions for Use** **Special Warnings and Special Precautions for Use**
Nervous system disorders Very common: Headache†	**Nervous system disorders** Common: Headache.	**Adverse events**
Vascular disorders Very common: Hot flush†	-	**Adverse events**
Respiratory, thoracic and mediastinal disorders Very common: Epistaxis†, cough†, dyspnoea†.	**Respiratory, thoracic and mediastinal disorders** Very common: Epistaxis†	**Adverse events**
Gastrointestinal disorders Common Diarrohea… Constipation†	**Gastrointestinal disorders** Common Diarrohea…	**Adverse events**
Hepatobiliary disorders Common: Hyperbilirubinaemia, hepatotoxicity (see section 4.4).	**Hepatobiliary disorders**	**Adverse events**

	Uncommon	Hyperbilirubinaemia, hepatotoxicity (see section 4.4).	
Skin and subcutaneous tissue disorders Very common: rash…pruritus†	**Skin and subcutaneous tissue disorders** Very common: rash		**Adverse events**
Musculoskeletal and connective tissue disorders Very common: Pain in extremity*†, back pain*†, arthralgia†.	**Musculoskeletal and connective tissue disorders** Very common: Pain in extremity*, back pain*		**Adverse events**
General disorders and administration site conditions Very common: Fatigue, mucosal inflammation*, asthenia†.	**General disorders and administration site conditions** Very common: Fatigue, mucosal inflammation*		**Adverse events**
Rash Rash occurred in approximately 28 % of patients who received lapatinib in combination with capecitabine, in 45 % of patients who received lapatinib in combination with letrozole. Rash was generally low grade and did not result in discontinuation of treatment with lapatinib. Prescribing physicians are advised to perform a skin examination prior to treatment and regularly during treatment. Patients experiencing skin reactions should be encouraged to avoid exposure to sunlight and apply broad spectrum sunscreens with a Sun Protection Factor (SPF) ≥ 30. If a skin reaction occurs a full body examination should be performed at every visit until one month after resolution. Patients with extensive or persistent skin reactions should be referred to a dermatologist.	Diarrhoea and rash were generally low grade and did not result in discontinuation of treatment with lapatinib. Diarrhoea responds well to proactive management (see *Warnings and Precautions*). Rash was transient in the majority of cases.		**Adverse events**

** These adverse reactions were observed when lapatinib was administered in combination with capecitabine.*

†These adverse reactions were observed when lapatinib was administered in combination with letrozole.

מצ"ב העלון, שבו מסומנות ההחמרות המבוקשות על רקע צהוב.

שינויים שאינם בגדר החמרות סומנו (בעלון) בצבע ירוק.

הודעה על החמרה (מידע בטיחות) בעלון לצרכן
(מעודכן 3102.50)

תאריך 11.7.2013

שם תכשיר באנגלית ומספר הרישום Tykerb 139 23 31609

שם בעל הרישום GlaxoSmithKline (ISRAEL) Ltd

טופס זה מיועד לפרוט ההחמרות בלבד !

ההחמרות המבוקשות		
פרק בעלון	**טקסט נוכחי**	**טקסט חדש**
אין להשתמש בתרופה מבלי להיוועץ ברופא לפני התחלת הטיפול:	**אין להשתמש בתרופה מבלי להיוועץ ברופא לפני התחלת הטיפול:** אם הינך בהריון, מתכננת הריון או מיניקה. אם הנך סובל או סבלת בעבר מליקוי בתפקוד : הלב ו/או כלי הדם, הכבד. אם הנך סובל מבעיות בנשימה או בריאות.	בנוסף, לפני שאתה לוקח טייקרב הרופא שלך צריך לדעת אם יש לך : • מחלת ריאות • דלקת של הריאה • **בעיות כלשהן בכבד** • **בעיות כלשהן בכליות** • שלשול **הריון והנקה** ...לא ידוע אם טייקרב עוברת לחלב אם. אל תניקי במהלך תקופת הטיפול בטייקרב.
תופעות לוואי:		תופעות לוואי נוספות **תופעות לוואי נפוצות מאוד** : • גלי חום

מצ"ב העלון, שבו מסומנות ההחמרות המבוקשות על רקע צהוב.
שינויים שאינם בגדר החמרות סומנו (בעלון) בצבע ירוק.

.....