הודעה על החמרה (מידע בטיחות) בעלון לרופא

(מעודכן 05.2013)

תאריך 11/2016

שם תכשיר באנגלית ומספר הרישום

Giotrif 20mg film coated tablets	**151 47 33984**
Giotrif 30mg film coated tablets	**151 48 33986**
Giotrif 40mg film coated tablets	**151 49 33987**
Giotrif 50mg film coated tablets	**151 50 33988**

שם בעל הרישום בורינגר אינגלהיים ישראל בע"מ

טופס זה מיועד לפרוט ההחמרות בלבד !

ההחמרות המבוקשות

טקסט חדש	טקסט נוכחי	פרק בעלון
Skin related adverse events …. Bullous, blistering and exfoliative skin conditions have been reported including rare cases suggestive of Stevens-Johnson syndrome and toxic epidermal necrolysis. …. Severe hepatic impairment Hepatic failure, including fatalities, has been reported during treatment with this medicinal product in less than 1% of patients. In these patients, confounding factors have included pre-existing liver disease and/or comorbidities associated with progression of underlying malignancy. Periodic liver function testing is recommended in patients with pre-existing liver disease. In the pivotal trials Grade 3 alanine aminotransferase (ALT) and aspartate aminotransferase (AST) elevations were observed	Skin related adverse events …. Bullous, blistering and exfoliative skin conditions have been reported including rare cases suggestive of Stevens-Johnson syndrome. …. Severe hepatic impairment Hepatic failure, including fatalities, has been reported during treatment with this medicinal product in less than 1% of patients. In these patients, confounding factors have included pre-existing liver disease and/or comorbidities associated with progression of underlying malignancy. Periodic liver function testing is recommended in patients with	**4.4 Special warnings and precautions for use**

ההחמרות המבוקשות		
טקסט חדש	**טקסט נוכחי**	**פרק בעלון**
in 2.4% (LUX-Lung-3) and 1.6% (LUX-Lung 8) of patients with normal baseline liver tests treated with 40 mg/day. In LUX-Lung-3 Grade 3 ALT/AST elevations ~~and~~ were about 3.5 fold higher in patients with abnormal baseline liver tests. There were no Grade 3 ALT/AST elevations in patients with abnormal baseline liver tests in LUX-Lung 8 (see section 4.8). Dose interruption may become necessary in patients who experience worsening of liver function (see section 4.2). In patients who develop severe hepatic impairment while taking GIOTRIF, treatment should be discontinued.	pre-existing liver disease. Grade 3 alanine aminotransferase (ALT) and aspartate aminotransferase (AST) elevations were observed in 2.4% of patients with normal baseline liver tests treated with 40 mg/day and were about 3.5 fold higher in patients with abnormal baseline liver tests (see section 4.8). Dose interruption may become necessary in patients who experience worsening of liver function (see section 4.2). In patients who develop severe hepatic impairment while taking GIOTRIF, treatment should be discontinued.	
4.8 Undesirable effects Summary of the safety profile …. In patients treated with once daily GIOTRIF 40 mg, dose reductions due to ADRs occurred in 57% of the patients in the LUX-Lung 3 trial and in 25% of the patients in the LUX-Lung 8 trial. Discontinuation due to ADRs diarrhoea and rash/acne was 1.3% and 0% in LUX-Lung 3 and 3.8% and 2.0% in LUX-Lung 8, respectively. **…** Bullous, blistering and exfoliative skin conditions have been reported including rare cases suggestive of Stevens-Johnson syndrome and toxic epidermal necrolysis although in these cases there were potential alternative aetiologies (see section 4.4). …… Table 2: Summary of ADRs per frequency	**4.8 Undesirable effects** Summary of the safety profile …. In patients treated with once daily GIOTRIF 40 mg, dose reductions due to ADRs occurred in 57% of the patients. Discontinuation due to ADRs diarrhoea and rash/acne was 1.3% and 0% respectively. **…** Bullous, blistering and exfoliative skin conditions have been reported including rare cases suggestive of Stevens-Johnson syndrome although in these cases there were potential alternative	**Adverse events**

מעוצב:שמאל, אחרי: 91.0- ס"מ, מרווח בין שורות: מרובה 51.1 שו, ללא בקרת שורות מיותמות, אל תשנה רווח בין טקסט לטיני לאסיאתי, אל תשנה רווח בין טקסט אסיאתי למספרים

ההחמרות המבוקשות		
טקסט חדש	**טקסט נוכחי**	**פרק בעלון**
category: - Pancreatitis was added as uncommon (≥1/1,000 to < 1/100) gastrointestinal disorder - Stevens-Johnson Syndrome and toxic epidermal necrolysis were added as rare (≥1/10,000 to <1/1,000) skin and subcutaneous tissue disorder. **....**	aetiologies (see section 4.4).	

ההחמרות המבוקשות		
טקסט חדש	טקסט נוכחי	פרק בעלון

Table 4: Very common ADRs in trial LUX-Lung 7

	GIOTRIF (40 mg/day) N=160			**Gefitinib** N=159		
NCI-CTC Grade	Any Grade	3	4	Any Grade	3	4
MedDRA Preferred Term	%	%	%	%	%	%
Infections and infestations						
Paronychia[1]	57.5	1.9	0	17.0	0.6	0
Cystitis[2]	11.3	1.3	0	7.5	1.3	0.6
Metabolism and nutrition disorders						
Decreased appetite	27.5	1.3	0	24.5	1.9	0
Hypokalaemia[3]	10.6	2.5	1.3	5.7	1.3	0
Respiratory, thoracic and mediastinal disorders						
Rhinorrhoea[4]	19.4	0	0	7.5	0	0
Epistaxis	18.1	0	0	8.8	0	0
Gastrointestinal disorders						
Diarrhoea	90.6	13.8	0.6	64.2	3.1	0
Stomatitis[5]	64.4	4.4	0	27.0	0	0
Nausea	25.6	1.3	0	27.7	1.3	0
Vomiting	19.4	0.6	0	13.8	2.5	0
Dyspepsia	10.0	0	0	8.2	0	0
Hepatobiliary disorders						
Alanine aminotransferase increased	11.3	0	0	27.7	8.8	0.6
Skin and subcutaneous tissue disorders						
Rash[6]	80.0	7.5	0	67.9	3.1	0

ההחמרות המבוקשות						
טקסט חדש	טקסט נוכחי			פרק בעלון		
Dry skin	32.5	0	0	39.6	0	0
Pruritus[7]	25.6	0	0	25.2	0	0
Dermatitis acneiform[8]	23.8	1.9	0	32.1	0.6	0
General disorders and administration site conditions						
Pyrexia	13.8	0	0	6.3	0	0
Investigations						
Weight decreased	10.0	0.6	0	5.7	0.6	0

Table 5: Very common ADRs in trial LUX-Lung 8*

	GIOTRIF (40 mg/day) N=392			**Erlotinib** N=395		
NCI-CTC Grade	Any Grade	3	4	Any Grade	3	4
MedDRA Preferred Term	%	%	%	%	%	%
Infections and infestations						
Paronychia[1]	11.0	0.5	0	5.1	0.3	0
Metabolism and nutrition disorders						
Decreased appetite	24.7	3.1	0	26.1	2.0	0
Gastrointestinal disorders						
Diarrhoea	74.7	9.9	0.8	41.3	3.0	0.3
Stomatitis[2]	30.1	4.1	0	10.6	0.5	0
Nausea	20.7	1.5	0	16.2	1.0	0.3
Skin and subcutaneous tissue disorders						
Rash[3]	60.7	5.4	0	56.7	8.1	0
Dermatitis acneiform[4]	14.0	1.3	0	18.0	2.5	0

ההחמרות המבוקשות		
פרק בעלון	**טקסט נוכחי**	**טקסט חדש**
4.8 Undesirable effects	---	function test abnormalities (including ed ALT and AST) were observed in ts receiving GIOTRIF 40 mg. These elevations were mainly transient and did not lead to discontinuation. Grade 2 ALT elevations occurred in 1% and Grade 3 elevations occurred in 0.8% of patients treated with GIOTRIF (see section 4.4).

מעוצב:משמאל לימין, אחרי: -91.0 ס"מ

טבלה מעוצבת

הודעה על החמרה (מידע בטיחות) בעלון לצרכן

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ההחמרות המבוקשות		
פרק בעלון	**טקסט נוכחי**	**טקסט חדש**
תופעות לוואי:	-----	תופעות לוואי שכיחות מאוד (עשויות להופיע בקרב יותר ממשתמש אחד מתוך 10): • יובש וגירודים בעור תופעות לוואי שאינן שכיחות (עשויות להופיע עד למשתמש אחד מתוך 100): • דלקת בלבלב תופעות לוואי נדירות (עשויות להופיע עד למשתמש אחד מתוך 1,000): • מצב חמור של שלפוחיות בעור או קילוף של העור (עלול לרמז על תסמונת סטיבנס-ג'ונסון ונמק אפידרמי רעלני (toxic epidermal necrolysis).