הודעה על החמרה (מידע בטיחות) בעלון לרופא

תאריך 13.11.2012

שם תכשיר באנגלית ומספר הרישום Tracleer 62.5mg (125 57 30487 00)

Tracleer 125mg (125 58 30488 00)

שם בעל הרישום Neopharm Ltd.

טופס זה מיועד לפרוט ההחמרות בלבד !

ההחמרות המבוקשות

טקסט חדש	טקסט נוכחי	פרק בעלון
Children - Pulmonary arterial hypertension: ~~Based on available data the recommended target dose of bosentan in pediatric patients is 2 mg/kg. The following dosing regimen was used in study AC-052-356~~ [BREATHE-3]: Safety and efficacy in patients under the age of 12 years have not been substantially documented. The following dosing regimen was used in study AC-052-356 (BREATHE-3): ראה טבלה מס' 1 בסוף טבלת ההחמרות. This study was primarily designed to assess pharmacokinetics in children. The number of patients studied in each dose group was insufficient to establish the optimal dosing regimen in patients under the age of 12 years. The pharmacokinetic findings showed that systemic exposure was lower than in adults with pulmonary hypertension which may provide sub-optimal effect on pulmonary vasculature. However the safety of higher doses has not been established in children. There is no experience in children below 3 years.	*Children* - Pulmonary arterial hypertension: Safety and efficacy in patients under the age of 12 years have not been substantially documented. The following dosing regimen was used in study AC-052-356 (BREATHE-3): ראה טבלה מס' 1 בסוף טבלת ההחמרות. This study was primarily designed to assess pharmacokinetics in children. The number of patients studied in each dose group was insufficient to establish the optimal dosing regimen in patients under the age of 12 years. The pharmacokinetic findings showed that systemic exposure was lower than in adults with pulmonary hypertension which may provide sub-optimal effect on pulmonary vasculature. However the safety of higher doses has not been established in children. There is no experience in children below 3 years.	**4. CLINICAL PARTICULARS** **4.2 Posology and method of administration** ***Special populations***

... Hepatic impairment In patients with mildly impaired liver function (Child-Pugh class A) no relevant changes in the pharmacokinetics have been observed. The steady state AUC of bosentan was 9% higher and the AUC of the active metabolite, Ro 48-5033, was 33% higher in patients with mild hepatic impairment than in healthy volunteers. The impact of moderately impaired liver function (Child-Pugh class B) on the pharmacokinetics of bosentan and its primary metabolite Ro 48-5033 was investigated in a study including 5 patients with pulmonary hypertension associated with portal hypertension and Child-Pugh class B hepatic impairment, and 3 patients with pulmonary arterial hypertension from other causes and normal liver function. In the patients with Child-Pugh class B liver impairment, the mean (95% CI) steady-state AUC of bosentan was 360 (212-613) ng.h/mL, i.e., 4.7 times higher, and the mean (95% CI) AUC of the active metabolite Ro 48-5033 was 106 (58.4-192) ng.h/mL, i.e., 12.4 times higher than in thepatients with normal liver function (bosentan: mean [95% CI] AUC : 76.1 [9.07-638] ng.h/mL; Ro 48- 5033: mean [95% CI] AUC 8.57 [1.28-57.2] ng.h/ml). Though the number of patients included was limited and with high variability, these data indicate a marked increase in the exposure to bosentan and its primary metabolite Ro 48-5033 in patients with moderate liver function impairment (Child-Pugh class B). The pharmacokinetics of bosentan have not been studied in patients	... Hepatic impairment In patients with mildly impaired liver function (Child-Pugh class A) no relevant changes in the pharmacokinetics have been observed. The steady state AUC of bosentan was 9% higher and the AUC of the active metabolite, Ro 48-5033, was 33% higher in patients with mild hepatic impairment than in healthy volunteers.	**5. PHARMACOLOGICAL PROPERTIES** **5.2 Pharmacokinetic properties**

with Child-Pugh class ~~B or~~ C hepatic impairment. ~~and~~ Tracleer is contra-indicated in ~~this patient population~~ patients with moderate to severe hepatic impairment, i.e., Child-Pugh class B or C (see section 4.3).	The pharmacokinetics of bosentan have not been studied in patients with Child-Pugh class B or C hepatic impairment and Tracleer is contra-indicated in this patient population (see section 4.3).	

<u>טבלה מס' 1</u>

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

Body Weight (kg)	Initiation Dose (4 weeks)	Maintenance Dose
$10 \leq \times \leq 20$	31.25 mg once daily	31.25 mg twice daily
$20 < \times \leq 40$	31.25 mg twice daily	62.5 mg twice daily
> 40	62.5 mg twice daily	125 mg twice daily