הודעה על החמרה (מידע בטיחות) בעלון לרופא

(מעודכן 05.2013)

תאריך 08/03/2017

שם תכשיר באנגלית ומספר הרישום Translarna 125 34264-00/01

Translarna 250 34266-00/01

Translarna 1000 34267-00/01

שם בעל הרישום ___מדיסון פארמה בע"מ_____

טופס זה מיועד לפרוט ההחמרות בלבד !

ההחמרות המבוקשות		
טקסט חדש	**טקסט נוכחי**	**פרק בעלון**
Potential interactions with other medicinal products Caution should be exercised when ataluren is co-administered with medicinal products that are ~~substrates or~~ inducers of UGT1A9, or substrates of OAT1, OAT3, or OATP1B3 (see section 4.5).	Potential interactions with other medicinal products Caution should be exercised when ataluren is co-administered with medicinal products that are substrates or inducers of UGT1A9, or substrates of OAT1, OAT3, or OATP1B3 (see section 4.5).	**4.4 Special warnings and precautions for use**
Aminoglycosides Ataluren should not be co-administered with intravenous aminoglycosides, based on cases of decreased renal function observed in a clinical trial in patients with nmCF (see section 4.3). Elevations of serum creatinine occurred in several nmCF patients	Aminoglycosides Ataluren should not be co-administered with intravenous aminoglycosides, based on cases of decreased renal function observed in a clinical trial in patients with nmCF (see section 4.3).	**4.5 Interaction with other medicinal products and other forms of interaction**

treated with ataluren and intravenous aminoglycosides together with other antibiotics for cystic fibrosis exacerbations. The serum creatinine elevations resolved in all cases, with discontinuation of the intravenous aminoglycoside, and either continuation or interruption of Translarna. These findings suggested that co-administration of Translarna and intravenous aminoglycosides may potentiate the nephrotoxic effect of the aminoglycosides. Therefore, if treatment with intravenous aminoglycosides is necessary the treatment with Translarna should be stopped and can be resumed 2 days after administration of the aminoglycoside has ended. The effect of co-administration of ataluren with other nephrotoxic medicinal products is unknown. Dehydration may be a contributing factor in some of these cases. Patients should maintain adequate hydration while taking ataluren. See section 4.4 *Effect of other medicinal products on ataluren pharmacokinetics* Based on *in vitro* studies, ataluren is a substrate of UGT1A9. Co-administration of rifampicin, a strong inducer of metabolic enzymes including UGT1A9, decreased ataluren exposure by 30%. The significance of these findings for humans is unknown. Caution should be exercised when ataluren is co-administered with medicinal products that are inducers of UGT1A9 (e.g. ~~mycophenolate mofetil~~ rifampicin). *Effect of ataluren on pharmacokinetics of other medicinal products* Based on *in vitro* studies, ataluren has the potential to inhibit UGT1A9, organic anion transporter 1 (OAT1), organic anion	Elevations of serum creatinine occurred in several nmCF patients treated with ataluren and intravenous aminoglycosides together with other antibiotics for cystic fibrosis exacerbations. The serum creatinine elevations resolved in all cases, with discontinuation of the intravenous aminoglycoside, and either continuation or interruption of Translarna. These findings suggested that co-administration of Translarna and intravenous aminoglycosides may potentiate the nephrotoxic effect of the aminoglycosides. Therefore, if treatment with intravenous aminoglycosides is necessary the treatment with Translarna should be stopped and can be resumed 2 days after administration of the aminoglycoside has ended. The effect of co-administration of ataluren with other nephrotoxic medicinal products is unknown. Dehydration may be a contributing factor in some of these cases. Patients should maintain adequate hydration while taking ataluren. See section 4.4 *Effect of other medicinal products on ataluren pharmacokinetics* Based on *in vitro* studies, ataluren is a substrate of UGT1A9. Caution should be exercised when ataluren is co-administered with medicinal products that are inducers of UGT1A9 (e.g. mycophenolate mofetil). *Effect of ataluren on pharmacokinetics of other medicinal products* Based on *in vitro* studies, ataluren is an inhibitor of UGT1A9, organic anion transporter 1 (OAT1), organic anion transporter 3	

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<td>transporter 3 (OAT3) and organic anion transporting polypeptide 1B3 (OATP1B3). Co-administration of ataluren with mycophenolate mofetil in healthy subjects did not affect the exposure of its active metabolite, mycophenolic acid (a substrate of UGT1A9). No dose adjustment is required when ataluren is co-administered with medicinal products that are substrates of UGT1A9. Caution should be exercised when ataluren is co-administered with medicinal products that are substrates of ~~UGT1A9,~~ OAT1, OAT3, or OATP1B3 because of the risk of increase concentration of these medicinal products (eg, oseltamivir, aciclovir, ciprofloxacin, captopril, furosemide, bumetanide, valsartan, pravastatin, rosuvastatin, atorvastatin, pitavastatin).</td>
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<td>4.8 Undesirable effects</td>
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Gastrointestinal disorders	Vomiting	Nausea , upper abdominal pain, flatulence, abdominal discomfort, constipation		
Skin and subcutaneous tissue disorders		Rash erythematous		
Musculoskeletal and connective tissue disorders		Pain in extremity musculoskeletal chest pain		
Renal and urinary disorders		Haematuria, enuresis	Change in renal function tests (increased creatinine, blood urea nitrogen, cystatin C)	
General disorders and administration site conditions		Pyrexia, weight decreased		

In a 48-week open-label extension study in patients with nmDMD patients who were ambulant or non-ambulant demonstrated a similar safety profile. Long term safety data is not available

Clinical efficacy and safety The efficacy and safety of Translarna were assessed in 2 randomized,	Clinical efficacy and safety The efficacy and safety of Translarna were assessed in 2 randomized,	**5.1 Pharmacodynamic**

double-blind, placebo-controlled, trials in nmDMD. The primary efficacy endpoint in both trials was change in 6 Minute Walk Distance (6MWD) at Week 48. Other endpoints included in both trials were time to persistent 10% worsening in 6MWD, change in time to run/walk 10 meters at Week 48, change in time to climb 4 stairs at Week 48, and change in time to descend 4 stairs at Week 48. -). Patients were also required to have documented confirmation of the presence of a nonsense mutation in the dystrophin gene as determined by gene sequencing. Study 1 evaluated 174 male patients ages 5 to 20 years. All patients were required to be able to walk ≥75 meters without the need for assistive devices during a screening 6 Minute Walk Test (6MWT). The majority of patients in all treatment groups were Caucasian (90%). Patients were randomised in a 1:1:1 ratio and received ataluren or placebo 3 times per day (morning, midday, and evening) with 57 receiving ataluren 40 mg/kg/day (10-, 10-, 20-mg/kg), 60 receiving ataluren	double-blind, placebo-controlled, trials in nmDMD. The primary efficacy endpoint in both trials was change in 6 Minute Walk Distance (6MWD) at Week 48. Other endpoints included in both trials were time to persistent 10% worsening in 6MWD, change in time to run/walk 10 meters at Week 48, change in time to climb 4 stairs at Week 48, and change in time to descend 4 stairs at Week 48. Study 1 evaluated 174 male patients ages 5 to 20 years. All patients were required to be able to walk ≥75 meters without the need for assistive devices during a screening 6 Minute Walk Test (6MWT.). Patients were also required to have documented confirmation of the presence of a nonsense mutation in the dystrophin gene as determined by gene sequencing. The majority of patients in all treatment groups were Caucasian (90%). Patients were randomised in a 1:1:1 ratio and received ataluren or placebo 3 times per day (morning, midday, and evening) with 57 receiving ataluren 40 mg/kg/day (10-, 10-, 20-mg/kg), 60 receiving ataluren	**properties**

מצ"ב העלון, שבו מסומנות ההחמרות המבוקשות על רקע צהוב.
שינויים שאינם בגדר החמרות סומנו (בעלון) בצבע שונה. יש לסמן רק תוכן מהותי ולא שינויים במיקום הטקסט.

הודעה על החמרה (מידע בטיחות) בעלון לצרכן

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ההחמרות המבוקשות		
פרק בעלון	**טקסט נוכחי**	**טקסט חדש**
1. לפני שימוש בתרופה	• מיקופנולאט מופטיל, פנוברביטל ,ריפמפיצין, אדפוויר, קפטופריל , פורזמיד, מתוטרקסאט, אוסלטמיוויר , אציקלוויר , בומטניד ,ציפרופלוקצסין, פמוטידין , בנזילפניצילין, סיטגליפטין -,פרווסטטין ,רוסווסטטין, אטורווסטטין, פיטווסטטין ,טלמיסרטן,וולסרטן ,אולמסרטן. תכשירים אלה לא נבדקו במתן עם טרנסלרנה, על כן עליך להיות במעקב צמוד של הרופא שלך.	• ~~מיקופנולאט מופטיל~~, פנוברביטל ,ריפמפיצין, אדפוויר, קפטופריל , פורזמיד, מתוטרקסאט, אוסלטמיוויר , אציקלוויר , בומטניד ,ציפרופלוקצסין, פמוטידין , בנזילפניצילין, סיטגליפטין -,פרווסטטין ,רוסווסטטין, אטורווסטטין, פיטווסטטין ,טלמיסרטן,וולסרטן ,אולמסרטן. תכשירים לא נבדקו במתן עם טרנסלרנה, על כן עליך להיות במעקב צמוד של הרופא שלך.

מצ"ב העלון, שבו מסומנות ההחמרות המבוקשות על רקע צהוב.
שינויים שאינם בגדר החמרות סומנו (בעלון) בצבע שונה. יש לסמן רק תוכן מהותי ולא שינויים במיקום הטקסט.