NOVARTIS

ספטמבר 2012

רופא/ה נכבד/ה, רוקח/ת נכבד/ה,

הנדון: Exjade 125, 250, 500 mg, dispersible tablets
אקסג'ייד טבליות מסיסות 125, 250, 500 מ"ג

התכשיר שבנדון רשום בישראל להתוויה הבאה:
Exjade is indicated for the treatment of chronic iron overload due to blood transfusions (transfusional hemosiderosis) in adult and pediatric patients (aged 2 years and over).

המרכיב הפעיל: Exjade 125 mg, 250 mg and 500 mg contain Deferasirox 125 mg, 250 mg and 500 mg, respectively.

באוגוסט 2012 עודכן העלון לרופא של התכשיר, כדלקמן (קו תחתי משמעו תוספת טקסט, ~~קו חוצה~~ משמעו מחיקת טקסט):

עלון לרופא:

תיקונים בסעיף

Dosage and administration

...
The decision to administer iron chelation therapy should take into account the risk-benefit ratio for the individual patient.
~~**General target population:**~~
Starting dose
...
Dose adjustment~~Maintenance dose~~
...
If serum ferritin is below 500 microgram/L at several consecutive determinations, treatment should be interrupted (see section 6 Warnings and Precautions).
...
As with other iron chelator treatment, the risk of toxicity of EXJADE may be increased when inappropriately high doses are given in patients with a low iron burden or with serum ferritin levels that are only slightly elevated (see section 6 Warnings and precautions).
...
Special populations:
Patients with renal impairment
...
Serum creatinine should be monitored monthly in all patients and if necessary daily doses can be reduced by 10 mg/kg (see section 6 Warnings and precautions**)**.
...
Pediatric patients
However, the initial dose should be the same as in adults, followed by individual titration. Changes in weight of pediatric patients over time must be taken into account when calculating the dose.
...
Method of administration
Exjade must be taken once daily on an empty stomach at least 30 minutes before food, preferably at the same time each day. The tablets are dispersed by stirring in a glass of water or non-carbonated (still) apple or orange juice (100–200 ml) until a fine dispersion is obtained. After the dispersion has been swallowed, any residue must be re~~dispersed~~-suspended in a small volume of water or juice and swallowed.

תיקונים בסעיף

Pregnancy and breast-feeding
There have been no controlled clinical studies of the use of deferasirox during pregnancy. Studies in animals have shown some reproductive toxicity at maternally toxic doses (see ~~Pre~~Non-clinical safety data).

עדכונים ותוספות בסעיף

Adverse drug reactions
Summary of the safety profile
The adverse effects most frequently reported during long-term treatment with Exjade in adult and paediatric patients include gastrointestinal disturbances in about 26% of patients (mainly nausea, vomiting, diarrhoea or abdominal pain) and skin rash in about 7% of patients. These reactions are dose-dependent, mostly mild to moderate, generally transient and mostly resolve even if treatment is continued.~~.~~
...
Elevations ~~in~~of liver transaminases were reported in about 2% of patients. The~~y~~se were not dose-dependent and most of the patients in question already had elevated transaminase levels prior to treatment with Exjade.~~.~~ Elevations of transaminases greater

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than 10 times the upper limit of the normal range, suggestive of hepatitis, were uncommon (0.3%). There have been post-marketing reports of hepatic failure with Exjade. Most cases of hepatic failure involved patients with significant co-morbidities including liver cirrhosis and multi-organ failure, and fatal outcomes were reported in some cases.

...

Tabulated summary of adverse drug reactions from clinical trials

Table 1 Adverse drug reactions reported in clinical studies

Psychiatric disorders	
Uncommon:	anxiety, sleep ~~disturbances~~disorders
Gastrointestinal disorders	
Uncommon:	gastrointestinal hemorrhage, gastric ulcer (including multiple ulcers), duodenal ulcer, gastritis~~, pharyngitis~~
Rare:	~~o~~esophagitis
Hepatobiliary disorders	
Common:	~~elevated~~ transaminases increased
General disorders and administration site conditions	
Uncommon:	~~fever~~Ppyrexia, edema, fatigue

...

Listing of Adverse drug reactions from post-marketing spontaneous reports

...

Table 2 Adverse drug reactions derived from spontaneous reports

Renal and urinary disorders	
	Cases of acute renal failure (mostly serum creatinine increased ≥ 2x upper limit of normal, and usually reversible after treatment interruption), some with fatal outcome have been described , tubulointerstitial nephritis

...

~~Blood and lymphatic system disorders~~

There have been post-marketing reports (both spontaneous and from clinical trials) of cytopenias including neutropenia, thrombocytopenia, aggravated aneimia and pancytopenia in patients treated with Exjade. Most of these patients had pre-existing h~~a~~ematological disorders that are frequently associated with bone marrow failure (see Warnings and Precautions). The relationship of these episodes to treatment with Exjade is uncertain.

תיקון בסעיף

Clinical pharmacology

Pharmacokinetics (PK)

...

Linearity / non-linearity

תיקון בסעיף

Pharmaceutical information

...

Special precautions for storage

Do not store above~~Store below~~ 30°C.

Store in the original package. Protect from moisture.

Exjade must be kept~~Keep all medicines~~ out of the reach and sight of children.

העלון לרופא נשלח למאגר התרופות שבאתר משרד הבריאות, וניתן לקבלו מודפס על-ידי פניה לבעל הרישום.

בברכה,

רוני דוידוביץ'
רוקחת ממונה

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