

July 2008

Dear Healthcare Professional

EXJADE® (deferasirox): hepatic failure and need for hepatic monitoring; gastrointestinal haemorrhage and ulceration; and renal tubulopathy

Summary

In agreement with EU regulatory authorities, Novartis wishes to provide you with the following updated safety information regarding Exjade® (deferasirox), which is indicated for the treatment of chronic iron overload due to frequent blood transfusions, or when Desferal® (desferrioxamine) is contraindicated or inadequate:

- **Postmarketing cases of hepatic failure, sometimes fatal, have been reported in patients treated with Exjade. The role of Exjade as a contributing or aggravating factor cannot be excluded. It is recommended that serum transaminases, bilirubin and alkaline phosphatase are checked before the initiation of treatment, every 2 weeks during the first month and monthly thereafter. If there is a persistent and progressive increase in serum transaminase levels that cannot be attributed to other causes, Exjade should be interrupted (see section 4.8 of revised SPC, attached).**
- **Upper gastrointestinal ulceration and haemorrhage have been reported in patients, including children and adolescents, receiving Exjade. Physicians and patients should remain alert for signs and symptoms of gastrointestinal ulceration and haemorrhage during Exjade therapy and promptly initiate additional evaluation and treatment if a serious gastrointestinal adverse event is suspected.**
- **Cases of renal tubulopathy (Fanconi's syndrome) have been reported in patients treated with Exjade. Dose reduction or interruption may be considered if there are abnormalities in levels of tubular markers and/or if clinically indicated.**

The product information (SPC Summary of Product Characteristics) has been updated (see sections 4.4, 4.5 and 4.8). A European Commission decision implementing this change is pending.

Healthcare professionals should report any suspected adverse reactions associated with the use of Exjade (see below).

Further information

The new information follows a review of the available data as part of the periodic safety reviews of the product. Details of the findings are described below:

Hepatic failure:

There have been reports of hepatic failure in patients treated with Exjade, some with a fatal outcome. Most of these reports involved patients with significant comorbidities, including liver cirrhosis and multi-organ failure. However, the role of Exjade as a contributing or aggravating factor cannot be excluded. No patient with normal baseline liver function or without additional life-threatening complications of their underlying disease is reported to have developed hepatic failure.

The Exjade SPC has been updated with monitoring recommendations.

Gastrointestinal haemorrhage and ulceration, and oesophagitis:

There have been reports of GI haemorrhage and upper GI ulceration, sometimes in combination. Some cases were reported in paediatric patients. Some of the patients were taking concomitant medications that are known to predispose to these events (NSAIDs,

corticosteroids, anti-coagulants or oral bisphosphonates) and some had severe pre-existing thrombocytopenia. In addition, a total of seven reasonably well documented cases of oesophagitis have been reported. The following adverse drug reactions have therefore been added to the Exjade SPC: gastrointestinal haemorrhage, gastric ulcer (including multiple ulcers), duodenal ulcer and oesophagitis.

Renal tubulopathy (acquired Fanconi's syndrome):

Acquired Fanconi's syndrome is a condition which is characterised by wasting of glucose, phosphate, uric acid and various ions from the proximal renal tubules. Some patients also have renal tubular acidosis (RTA). Cases of renal tubular disorders and RTA (collectively termed acquired Fanconi's syndrome) have been reported in patients treated with Exjade.

- Since the initial approval in 2006, the SPC for Exjade recommends monthly tests for proteinuria (additional markers of renal tubular function may also be monitored such as glycosuria in non-diabetics; low serum levels of potassium, phosphate, magnesium or urate; phosphaturia; aminoaciduria). The SPC also recommends that dose reduction or interruption may be considered if there are abnormalities in levels of tubular markers and/or if clinically indicated.

Should you have any questions or require additional information regarding the use of Exjade (deferasirox), please contact Medical Information Department, Novartis Pharmaceuticals (UK) Ltd on 01276 6988370.

Call for reporting

Suspected adverse drug reactions should be reported to the Medicines and Healthcare product Regulatory Agency (MHRA) by use of a Yellow card, which is available from MHRA, CHM Freepost, London SW8 5BR, or electronically via www.yellowcard.gov.uk. Adverse events should also be reported to Novartis on 01276 698370.

Yours sincerely



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