

5 September 2011

Nplate[®]▼: DHPC EU

Direct Healthcare Professional Communication on the risk of disease progression to Acute Myelogenous Leukaemia (AML) with romiplostim (Nplate[®]) use in patients with Myelodysplastic Syndrome (MDS)

Dear Healthcare Professional

Summary

- **Available data from a randomised clinical study of patients with thrombocytopenia associated with myelodysplastic syndrome (MDS) has shown an increase in the number of cases of disease progression to acute myelogenous leukaemia (AML) and transient increases in blast cell counts in patients treated with romiplostim (Nplate[®]) compared to placebo.**
- **A positive benefit/risk for Nplate[®] is only established for the treatment of thrombocytopenia associated with chronic immune (idiopathic) thrombocytopenic purpura (ITP), Nplate[®] must not be used in other clinical conditions associated with thrombocytopenia.**
- **The diagnosis of ITP in adults and elderly patients should have been confirmed by the exclusion of other clinical entities presenting with thrombocytopenia. The diagnosis of MDS must be excluded.**
- **A bone marrow aspirate and biopsy should normally have been done before initiating Nplate[®] treatment and over the course of the disease and treatment, particularly in patients over 60 years of age, those with systemic symptoms or abnormal signs, such as increased peripheral blast cells.**

Further information on the safety concern

Romiplostim (Nplate[®]) is indicated for adult chronic immune (idiopathic) thrombocytopenic purpura (ITP) in splenectomised patients who are refractory to other treatments (e.g. corticosteroids, immunoglobulins), and may be considered as second line treatment for adult non-splenectomised patients where surgery is contra-indicated.

On 18 February 2011, the independent Data Monitoring Committee (DMC) for a randomised clinical study of Nplate[®] in myelodysplastic syndrome (MDS) patients with thrombocytopenia recommended to discontinue Nplate[®] in all patients due to the increased risk of progression to acute myelogenous leukaemia (AML).

In this study, there were numerically more subjects in the Nplate[®] arm with disease progression to AML (placebo 2, Nplate[®] 9) and with increases in circulating blasts >10% (placebo 3, Nplate[®] 25). The randomisation was 2:1, Nplate[®]:placebo. Of the cases of MDS disease progression to AML that were observed, patients with RAEB-1 classification of MDS at baseline were more likely to have disease progression to AML compared to lower risk MDS.

In view of the available data from this study, and in agreement with the European Medicines Agency, please remember that Nplate[®] must not be used for the treatment of thrombocytopenia due to MDS or any other cause of thrombocytopenia other than ITP outside of clinical trials. A positive benefit/risk for Nplate[®] is only established for the treatment of thrombocytopenia associated to chronic ITP. The diagnosis of ITP should have been confirmed by the exclusion of other clinical entities presenting with thrombocytopenia. The diagnosis of MDS must be excluded. Furthermore, a bone marrow aspirate and biopsy before initiating Nplate[®] treatment should normally have been done in order to exclude MDS.

The product information for Nplate[®] has been updated with information on the increased risk of progression to AML in MDS patients treated with Nplate[®] (see Annex).

This information has been agreed with the European Medicines Agency and the MHRA.

Reporting of suspected adverse reactions with the use of Nplate[®]

Please report suspected adverse reactions with any medicine or vaccine to the MHRA through the Yellow Card Scheme online at <http://yellowcard.mhra.gov.uk/>

Alternatively, prepaid Yellow Cards for reporting are available:

- upon request by mail: "FREEPOST YELLOW CARD"
- at the back of the British National Formulary (BNF)
- by telephoning the Commission of Human Medicines (CHM) free phone line: 0800-731-6789
- or by electronic download through the MHRA website (<http://yellowcard.mhra.gov.uk/downloads/>)

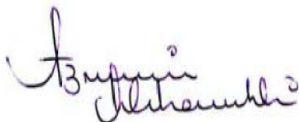
When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset and treatment dates.

Any suspected adverse reactions to romiplostim (Nplate[®]) may also be reported to Amgen Europe B.V. by contacting Amgen UK/Ireland Drug Safety Department directly on 01223 436712.

Communication Information

Should you have any questions or require additional information regarding the use of Nplate[®], please contact Amgen UK/Ireland Medical Information on 01223 436441 or by email to gbinfoline@amgen.com.

Yours sincerely,



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