AMGEN
International Regulatory Affairs

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Nplate: DHCP EU

Nplate® (romiplostim) - Revised Dose Adjustment in ITP patients and warnings for use in ITP patients with hepatic impairment

Dear Healthcare Professional

Summary

- **Portal venous thrombosis has been identified in patients with thrombocytopenia associated with hepatic insufficiency that were treated with thrombopoietin (TPO) agonists.**

- **Platelet count thresholds at which romiplostim dose should be reduced and interrupted have been lowered to >150x10^9/L for two consecutive weeks and >250x10^9/L, respectively in order to minimise the risk of thrombotic/thromboembolic events.**

- **Romiplostim should not be used in patients with moderate to severe hepatic impairment (Child-Pugh score ≥ 7) unless the expected benefit outweighs the identified risk of portal venous thrombosis in patients with thrombocytopenia associated to hepatic insufficiency treated with TPO agonists.**

This information has been endorsed by the European Medicines Agency.

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.

Splanchnic thromboembolic events have been detected in patients with hepatic impairment that were treated with TPO agonists. Changes to the dosing information of romiplostim have been introduced in order to decrease the platelet count thresholds for dose adjustment. These changes reflect the recommendations for dose adjustment for TPO agonists introduced to minimise the risk of thrombotic/thromboembolic events.

Dose Adjustment

Recommendations:

- Following initiation of Nplate® treatment, platelet counts should be assessed weekly until a stable platelet count (≥ 50 x 10^9/L for at least 4 weeks without dose adjustment) has been achieved (as described in the SmPC). Platelet counts should be assessed monthly thereafter.
- If the platelet count is >150 x 10^9/L for two consecutive weeks (instead of >200 x 10^9/L as previously recommended), then the once weekly dose of Nplate® should be decreased by 1µg/kg.
- If the platelet count is >250 x 10^9/L (instead of >400 x 10^9/L as previously recommended), then treatment should be discontinued and the platelet count should be assessed weekly.
- After the platelet count has fallen to < 150 x 10^9/L, then once weekly treatment with the dose reduced by 1 µg/kg should be resumed.
- Due to the interindividual variable platelet response, in some patients platelet count may abruptly fall below 50 x 10^9/L after dose reduction or treatment discontinuation. In these cases, if clinically appropriate, higher cut-off levels of platelet count for dose reduction (200 x 10^9/L) and treatment interruption (400 x 10^9/L) may be considered according to medical judgement.

Hepatic Impairment

The product information has also been updated with information on the use of romiplostim in patients with hepatic impairment.

Romiplostim has not been studied in patients with hepatic impairment. However, cases of thromboembolic events, including portal vein thrombosis, have been reported in patients with chronic liver disease receiving romiplostim. Romiplostim should be used with caution in this population.

Romiplostim should not be used in patients with moderate to severe hepatic impairment (Child-Pugh score ≥7) unless the expected benefit outweighs the identified risk of portal venous thrombosis in patients with thrombocytopenia associated to hepatic insufficiency treated with TPO agonists.

Please, refer to the SmPC for full details of the new dose adjustment guidance and on use in patients with hepatic impairment (see Annex).

Reporting of suspected adverse reactions with the use of Nplate®

Any suspected adverse reactions should be reported in accordance with your national reporting system or alternatively to Amgen Europe B.V. by contacting Amgen UK/Ireland Drug Safety department directly on 00 44 1223 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 0044 1223 436441 or by email to gbinfoline@amgen.com.

Yours Sincerely,

Dr Azmina Khanbhai
Acting Medical Director, UK & Ireland