Date: 30th October 2013

Document reference number Nivestim CLS-MT 2013

Direct Health Care Professional communication

Filgrastim (Nivestim) is associated with a risk of capillary leak syndrome in patients with cancer and in healthy donors.

Dear Healthcare Professional,

Hospira UK Limited - UK, in agreement with the European Medicines Agency and the Malta Medicines Authority, would like to inform you about an adverse effect of capillary leak syndrome (CLS) associated with filgrastim.

Summary

- **CLS has been reported in recipients of filgrastim including patients undergoing chemotherapy and a healthy donor undergoing peripheral blood progenitor cell mobilisation.**
- **Episodes vary in severity and frequency and may be fatal. CLS is characterised by hypotension, hypoalbuminaemia, oedema and haemoconcentration.**
- **Healthcare professionals should closely monitor for CLS symptoms in patients and healthy donors receiving filgrastim. Standard symptomatic treatment should be given immediately if symptoms occur (this may include intensive care).**
- **Patients and healthy donors should be advised to contact their doctor immediately if they develop symptoms (often with rapid onset) such as generalised body swelling, puffiness (which may be associated with passing water less frequently), difficulty breathing, abdominal swelling and tiredness.**
- **The benefits of treatment with filgrastim continue to outweigh any risks in the approved indications.**

Further information on the safety concern

CLS has been reported in patients with cancer undergoing chemotherapy and a healthy donor undergoing peripheral blood progenitor cell mobilisation who were receiving granulocyte colony-stimulating factor (G-CSF) products including filgrastim. Reports have generally involved people with advanced malignant diseases, sepsis, those taking multiple chemotherapy medications or those undergoing aphaeresis. The mechanism of CLS remains unclear.

No reports of CLS have been reported with Nivestim during the period since launch in 2010 to the current date. This safety concern communication is based on the post-marketing experience with the reference product (Neupogen®).

For Neupogen® (filgrastim), 34 post-marketing reports of CLS were received world-wide between April 1991 and August 2012. Of these, one case concerned a healthy donor undergoing stem cell mobilisation and apheresis. In 12 cases, there was a positive de-challenge with supportive treatment or corticosteroids. In the majority of cases, the CLS symptoms occurred after the first dose of filgrastim treatment. In 2 cases the symptoms occurred after the first dose with a positive re-challenge during the second dose. Six cases had a fatal outcome from CLS.

The total number of CLS reports expressed above have been seen in over 8.5 million patients exposed to Neupogen® (filgrastim) in the post-marketing setting.

Call for reporting

Healthcare professionals should report any adverse reactions suspected to be associated with the use of filgrastim products to
ADR Reporting
The Medicines Authority
Post-Licensing Directorate
203 Level 3, Rue D'Argens
GŻR-1368 Gżira
Website: www.medicinesauthority.gov.mt
e-mail: postlicensing.medicinesauthority@gov.mt

Additionally, any such information may be reported to Drugsales Ltd on Tel: +356 21 419 070/1/2 or email safety@drugsalesltd.com

Company contact point

Should you have any questions or require additional information regarding the use of Nivestim, please contact Medical Information on Tel: + 44 (0) 1926 820820

Sincerely,

Adrian Busuttil B.Pharm (Hons)
Responsible Person/Regulatory Affairs officer
Drugsales Ltd obo Hospira UK Limited UK