28 February 2019
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Committee for Medicinal Products for Human Use (CHMP)

Scientific conclusions and grounds for the variation to the terms of the marketing authorisation(s)

Active substance(s): lipegfilgrastim

Procedure No. EMEA/H/C/PSUSA/00010111/201807

Period covered by the PSUR: 26 July 2018 to 25 July 2018

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Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for lipegfilgrastim, the scientific conclusions of the CHMP are as follows:

Cumulatively up to 25 July 2018, a total of 48 case reports of nausea with lipegfilgrastim were identified. Whilst it is understood that most of the cases of nausea occurred in patients who may have been receiving chemotherapy concomitantly, 21 cases of nausea have occurred in patients with no underlying malignancy or concomitant chemotherapy. Nausea is listed as an undesirable effect for the class of G-CSF products. Furthermore, the data reviewed to date provide evidence of a possible causal association between lipegfilgrastim and nausea. Therefore, the proposal to include the undesirable effect of nausea under the frequency 'very common' in the product information for lipegfilgrastim is acceptable.

A cumulative review identified a total 915 reports of musculoskeletal pain symptoms reported with lipegfilgrastim. The majority of the reports (868; 94.86%) were non-serious and 48 reports (5.25%) were serious. It is agreed with the MAH that the percentage of patients who developed musculoskeletal pain assessed as serious is significantly lower than patients whose pain was assessed as non-serious. There are potential confounding factors for musculoskeletal pain such as the underlying malignancy and its complications, concomitant use of chemotherapeutic agents and potentially other unreported medical conditions. However, the available 48 serious cases of musculoskeletal pain provide evidence of a possible causal association with lipegfilgrastim. It is fully agreed with the MAH that the SmPC and Package Leaflet should be updated to include information that serious musculoskeletal pain reactions have been reported with lipegfilgrastim and that some cases have been unresponsive to standard analgesics leading to hospitalisation; and that in some of these cases stronger analgesics such as opioids were required.

The CHMP agrees with the scientific conclusions made by the PRAC.

Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions for lipegfilgrastim the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing lipegfilgrastim is unchanged subject to the proposed changes to the product information.

The CHMP recommends that the terms of the marketing authorisation(s) should be varied.