

April 2010
IE-DHPC-KGF/2010

Palifermin (Kepivance) is now restricted to patients who receive both radiotherapy and chemotherapy as conditioning prior to autologous stem cell transplantation

Dear Healthcare Professional,

In agreement with the European Medicines Agency and the Irish Medicines Board (IMB) please be informed of the following important change to restrict the indication for palifermin and consequential changes to product information.

Summary

- Palifermin should **not** be used in patients who receive myeloablative chemotherapy-only conditioning prior to autologous stem cell transplantation
- When used in patients receiving chemotherapy-only conditioning, palifermin demonstrated a lack of efficacy and a higher frequency of serious adverse events compared with placebo.
- The indication for palifermin has been restricted as follows: palifermin is indicated to decrease the incidence, duration and severity of oral mucositis in patients with haematological malignancies receiving myeloablative **radiochemotherapy** associated with a high incidence of severe mucositis, and requiring autologous haematopoietic stem cell support.

Further information on the restriction of the therapeutic indication

Palifermin (Kepivance) was initially licensed to decrease the incidence, duration and severity of oral mucositis in patients with haematological malignancies receiving myeloblastic therapy associated with a high incidence of severe mucositis and requiring autologous stem cell transplantation.

To address remaining questions raised at the time of licensing of palifermin regarding the appropriate dosing regimen, at the request of the CHMP the MAH conducted a randomised, double-blind study in 281 patients with multiple myeloma, evaluating the efficacy of palifermin 60 µg/kg/day received either before and after conditioning with 200 mg/m² melphalan (pre/post CT); palifermin received only before chemotherapy-conditioning (pre-CT) or placebo.

The two active groups with palifermin did not show a therapeutic benefit in the reduction of frequency or duration of severe oral mucositis, compared with placebo (incidence of oral mucositis: 57.9% placebo; 68.7% pre/post CT; 51.4% pre-CT). Furthermore, palifermin-treated patients experienced more serious adverse events and treatment-related adverse events, as assessed by the investigators, than those in the placebo group. On the basis of these study results, the balance of risks and benefits does not support use of palifermin in patients who receive

myeloablative chemotherapy-only conditioning prior to autologous stem cell transplantation (see Annex for changes to the Summary of Product Characteristics).

The safety section of the product information has also been updated with adverse events that were reported more frequently in the palifermin-treated patients than in placebo-treated patients. Peripheral oedema is now included among very common ($\geq 1/10$) adverse events. Oral paresthesia, eyelid oedema, and lip swelling are now included among common ($\geq 1/100$ to $< 1/10$) adverse events.

The posology section of the product information has also been updated following this study. In the pre/post-CT group, the time interval between the last pre-CT dose of palifermin and the first post-CT dose was four days, which is in line with the dosing regimen recommended at the time of licensing. However, this interval is considered to have been suboptimal and to have contributed to the lack of efficacy observed in this study. The recommended dosing schedule has therefore been changed to recommend that the first post-myeloablative therapy dose should be administered after, but on the same day of haematopoietic stem cell infusion and **more than** four days after the most recent palifermin administration.

The revised product information has been agreed with the EU Competent Authorities.

Call for reporting

Please remember that any suspected adverse reaction following the use of Kepivance should be reported in accordance with the national spontaneous reporting system.

Any suspect adverse reaction following the use of Kepivance should be reported to the Marketing Authorisation Holder at DrugSafety@biovitrum.com or by 00800 386 587 21, or alternatively directly to the Irish Medicines Board, in the usual way (using the yellow card system or online at www.imb.ie).

Communication information

If you have any further questions or require further information, please contact your local Biovitrum representative or contact Biovitrum Medical Information directly at medical.info@biovitrum.com. You may also call our medical information service at **00800 386 58721** (European toll-free number).

If your phone service provider does not support the European toll-free number you may also use the following numbers based on your language preference:

English: +41 61 564 13 28

Please observe that the +41 (Switzerland) number listed above is not toll-free.

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With Kind Regards
Biovitrum AB(publ)



Dr Rein Seensalu
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Annex
Text of the revised Product Information (with changes made visible)

