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Direct Healthcare Professional Communication

07 May 2019

LARTRUVO®▼(olaratumab): withdrawal of the EU marketing authorisation due to lack of therapeutic efficacy

Dear Healthcare Professional,

Eli Lilly and Company in agreement with the European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency (MHRA) would like to inform you of the following:

Summary

- The required phase 3 study (ANNOUNCE) of olaratumab in combination with doxorubicin in patients with advanced or metastatic soft tissue sarcoma did not show a clinical benefit of olaratumab.
- As a consequence, **the benefit-risk balance of olaratumab is negative** and the marketing authorisation in the EU will be withdrawn.
- No new patients should be started on olaratumab.
- For patients currently on treatment with olaratumab, alternative treatment options should be considered as available stock will expire by April 2020.
- No new safety concerns were identified during the study.

Background information

Olaratumab was authorised in the European Union in November 2016 to treat advanced soft tissue sarcoma. At time of its approval, data on the effects of olaratumab were limited due to the small number of patients included in the main study that supported authorisation. The medicine was therefore granted a marketing authorisation on condition that the company provided additional data from the ANNOUNCE study in order to confirm the efficacy and safety of the medicine.

The ANNOUNCE study did not show clinical benefit of olaratumab in combination with doxorubicin compared with doxorubicin, a standard of care treatment for advanced soft tissue sarcoma. Specifically, the study (comprising of 509 randomised patients, 258 in the investigational arm and 251 in the control arm) did not meet the primary endpoint to prolong overall survival in the study (hazard ratio 1.05, [95% CI: 0.841, 1.303]; median overall survival 20.4 months for olaratumab plus doxorubicin group vs. 19.8 months for doxorubicin group).

Overall survival was also not prolonged in the subpopulation (comprising of 234 randomised patients, 119 in the investigational arm and 115 in the control arm) of patients with leiomyosarcoma (hazard ratio 0.95, [95% CI: 0.690, 1.312]; median overall survival 21.6 months for olaratumab plus doxorubicin group vs. 21.9 months for doxorubicin group).

There was no clinical benefit for key secondary efficacy endpoints, including median progression-free survival in the overall population (hazard ratio 1.23, [95% CI: 1.009, 1.502]; median progression-free survival 5.4 months for olaratumab plus doxorubicin group vs. 6.8 months for doxorubicin group). No new safety concerns were identified.

Because this study did not confirm clinical benefit, the conditional marketing authorisation for olaratumab will be withdrawn.

Call for reporting

Lartruvo▼ is subject to additional monitoring. This will allow quick identification of new safety information.
Please report ANY suspected adverse drug reactions (ADRs) to new drugs and vaccines identified by the black triangle▼ to the MHRA through the Yellow Card Scheme.

It is easiest and quickest to report ADRs online via the Yellow Cards website - https://yellowcard.mhra.gov.uk/ or via the Yellow Card app available from the Apple App Store or Google Play Store.

Alternatively, prepaid Yellow Cards for reporting are available:

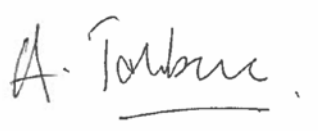
- by writing to FREEPOST YELLOW CARD (no other address details necessary)
- by emailing yellowcard@mhra.gov.uk
- at the back of the British National Formulary (BNF)
- by telephoning the Commission on Human Medicines (CHM) free phone line: 0800-731-6789 or
- by downloading and printing a form from the Yellow Card website (see link above)

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

Company Contact Point

Please do not hesitate to contact Eli Lilly and Company Limited at: +44 1256 315000 for further clarification of your questions.

Yours sincerely,



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