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Direct Healthcare Professional Communication

24th January 2019

LARTRUVO® ▼ (olaratumab): outcome of required post-approval study did not confirm the clinical benefit of olaratumab in the approved indication

Dear Healthcare Professional,

Eli Lilly and Company in agreement with the European Medicines Agency (EMA) and the Maltese Medicines Agency (MMA) would like to inform you of the following:

Summary

- **The global phase 3 study (ANNOUNCE) of Lartruvo in combination with doxorubicin in patients with advanced or metastatic soft tissue sarcoma (STS) did not confirm the clinical benefit of Lartruvo in combination with doxorubicin as compared with doxorubicin, a standard of care treatment.**
- **As a consequence, no new patients should be prescribed Lartruvo.**
- **While further assessment of the study results is ongoing, physicians may consider continuing Lartruvo treatment in patients who experience clinical benefit.**
- **No new safety concerns were identified during the study and the safety profile was comparable between treatment arms.**

Background information

Lartruvo had previously demonstrated an overall survival benefit in soft tissue sarcoma in a US-only randomized phase 2 trial, which led to the accelerated approval by the FDA and conditional marketing authorization by the European Medicines Agency. Continued approval is contingent upon verification of clinical benefit in the confirmatory trial ANNOUNCE.

The ANNOUNCE study did not confirm the clinical benefit of Lartruvo in combination with doxorubicin as compared to doxorubicin, a standard of care treatment. Specifically, the study did not meet the primary endpoints to prolong survival in the overall population (HR: 1.05; Median 20.4 vs. 19.7 months for Lartruvo + doxorubicin and doxorubicin, respectively) or in the leiomyosarcoma (LMS) sub-population

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(HR: 0.95; Median 21.6 vs. 21.9 months for Lartruvo + doxorubicin and doxorubicin, respectively). There was no clinical benefit in key secondary efficacy endpoints (progression-free survival in the overall

population: HR 1.231 p-value 0.042; median 5.42 months vs. 6.77 months for Lartruvo + doxorubicin and doxorubicin, respectively). No new safety concerns were identified and the safety profile was comparable between treatment arms.

As this study did not confirm clinical benefit, Lilly is in the process of reviewing the full results of the ANNOUNCE study and is working with global regulators to determine the appropriate next steps for Lartruvo.

While these discussions are ongoing, patients who are currently receiving Lartruvo may, in consultation with their physician, continue their course of therapy if receiving clinical benefit.

However, the results of the ANNOUNCE study do not support new patients with soft tissue sarcoma starting Lartruvo.

Call for reporting

Healthcare professionals and patients are encouraged to report any adverse events in accordance with the national spontaneous reporting system to the MMA:

Online: http://www.medicinesauthority.gov.mt/adrportal

Company Contact Point

Please do not hesitate to contact Charles de Giorgio Ltd. for further clarification of your questions.

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Yours sincerely,

Eli Lilly Signatory

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