**Important Safety Information on LARTRUVO (olaratumab) –
New clinical trial information important to prescribing decisions**

2019/01/29

Audience
Healthcare professionals including oncologists, oncology nurses, oncology pharmacists, and other healthcare professionals providing oncology care to cancer patients, including those working in hospitals, cancer centres, oncology clinics, and pharmacies.

Key messages

- **The global, Phase III study (ANNOUNCE) of LARTRUVO used in combination with doxorubicin did not confirm the clinical benefit in prolonging lives of patients with advanced or metastatic soft tissue sarcoma compared to doxorubicin alone.**
- **Based on the information available so far, no new safety concerns were identified during the study.**
- **Patients who currently are receiving LARTRUVO should discuss with their physician whether to continue their course of therapy.**
- **LARTRUVO should not be initiated in new patients outside of an investigational setting. Enrolment in the LillyPlus™ Patient Support Program is now closed for patients who have not yet initiated therapy with LARTRUVO.**
- **Health Canada is currently working with the manufacturer to determine the appropriate next steps.**

What is the issue?
The ANNOUNCE trial, a global, randomized, placebo-controlled Phase III study 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 to doxorubicin alone, a standard of care treatment.

Products affected
LARTRUVO (olaratumab) solution for injection, 10 mg/mL (19 mL and 50 mL vials), intravenous infusion.

Background information
In Canada, LARTRUVO has been issued marketing authorization with conditions based on the promising evidence of an overall survival benefit demonstrated in a Phase II study. Continued authorization was contingent on verification of clinical benefit in a confirmatory Phase III study. LARTRUVO has been authorized, in combination with doxorubicin, for the treatment of adult patients with advanced soft tissue sarcoma (STS) not amenable to curative treatment with radiotherapy or surgery and for whom treatment with an anthracycline-containing regimen is appropriate. In Canada, as of January 28, 2019, there are approximately 180 patients undergoing treatment with LARTRUVO.

The ANNOUNCE trial, a global, randomized, placebo-controlled Phase III study 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 to doxorubicin, a standard of care treatment.

Specifically, the study did not meet the primary endpoints to prolong survival in the overall population (hazard ratio [HR]: 1.05; Median 20.4 vs. 19.7 months for LARTRUVO + doxorubicin and doxorubicin, respectively) or in the leiomyosarcoma (LMS) sub-population (HR: 0.95; Median 21.6 vs. 21.9 months for LARTRUVO + doxorubicin and doxorubicin, respectively). There was also a shortening in progression free survival in the LARTRUVO plus doxorubicin arm (median 5.4 months for Lartruvo plus doxorubicin versus 6.8 months for doxorubicin), which was one of the secondary objectives of the study. Based on the information available so far, no new safety concerns were identified during the study.

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.

Information for consumers
LARTRUVO is a cancer medicine used together with doxorubicin (another cancer medicine) to treat soft tissue sarcoma (a cancer of muscles, fat or other tissues) when treatment with radiation or surgery are not options. To receive LARTRUVO, doxorubicin must be an appropriate treatment option.

A new study showed that LARTRUVO in combination with doxorubicin is not more effective at prolonging patients' lives than doxorubicin alone. Patients should discuss any questions or concerns about this information with their healthcare professional.

Patients should also inform their healthcare professional if they are experiencing any side effects while receiving LARTRUVO treatment.

Information for healthcare professionals

- Patients who currently are receiving LARTRUVO should discuss with their physician whether to continue their course of therapy.
- No new patients should start LARTRUVO treatment outside of an investigational setting.
- Effective immediately, enrollment in the LillyPlus™ Patient Support Program (PSP) is closed for patients who have not yet initiated therapy with LARTRUVO.
- Patients already enrolled in the LillyPlus™ PSP and receiving treatment with LARTRUVO will continue to receive the same services currently provided, should they decide to remain on therapy.

Action taken by Health Canada

Health Canada is communicating this important safety information to healthcare professionals and Canadians via the Recalls and Safety Alerts Database on the Healthy Canadians Web Site (www.healthycanadians.gc.ca/recall-alert-rappel-avis/index-eng.php). This communication update will be further distributed through the MedEffect™ e-Notice email notification system. Health Canada is currently working with the manufacturer to determine the appropriate next steps.

Report health or safety concerns

Managing marketed health product-related side effects depends on health care professionals and consumers reporting them. Any case of lack of efficacy or other serious or unexpected side effects in patients receiving LARTRUVO (olaratumab) should be reported to Eli Lilly Canada Inc. or Health Canada.

Eli Lilly Canada Inc.
3650 Danforth Avenue
Toronto, Ontario M1N 2E8
Toll free: 1-888-545-5972

To correct your mailing address or fax number, contact Eli Lilly Canada Inc.

You can report any suspected adverse reactions associated with the use of health products to Health Canada by:

- Calling toll-free at 1-866-234-2345; or
- Visiting MedEffect Canada's Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax.

For other health product inquiries related to this communication, contact Health Canada at:

Marketed Health Products Directorate
E-mail: mhpd_dpsc.public@hc-sc.gc.ca
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