Important Safety Information
Bamlanivimab – Potential Risk of Treatment Failure Due to Circulation of Resistant SARS-CoV-2 Variants

2021/04/28

Audience
Healthcare professionals including infectious disease physicians, internal medicine physicians, pharmacists, hospital pharmacy departments, chiefs of medicine in hospitals, intensive care unit and emergency room physicians.

Key messages

- **A potential risk of treatment failure of bamlanivimab against certain severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants was identified through global surveillance. Bamlanivimab is expected to retain neutralizing activity against the United Kingdom (UK) origin B.1.1.7 variant.**
- **Healthcare professionals are advised that:**
  - **Bamlanivimab, in in vitro assays, exhibited reduced activity against SARS-CoV-2 variants with the E484K (e.g., South Africa or Brazil origin) and L452R (e.g., California origin) mutations.**
  - **Local epidemiology of variants should be taken into consideration before empiric use of bamlanivimab as single monoclonal antibody therapy. Bamlanivimab should be used only in regions where there is a known or confirmed low prevalence of lineages containing E484K and/or L452R SARS-CoV-2 variants.**
  - **Patients treated with bamlanivimab should be monitored for coronavirus disease 2019 (COVID-19) signs and symptoms of infection and provided additional confirmation or treatment of disease where required.**
- **The Canadian Product Monograph (CPM) for bamlanivimab was updated to include new information concerning SARS-CoV-2 variants of concern, and is now available in French and English on Health Canada's Drug Product Database, at www.bamlanivimabHCPinfo.com or www.lilly.ca.**

What is the issue?
Bamlanivimab was authorized for use in relation to the COVID-19 pandemic, in accordance with the Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19. The CPM for bamlanivimab was updated on 14 April 2021 with information concerning SARS-CoV-2 variants of concern.

Products affected
Bamlanivimab for injection, anti-SARS-CoV-2 spike protein monoclonal antibody, solution for infusion, 700 mg/20 mL (35 mg/mL), single-dose vial, DIN 02508176.

Background information
Bamlanivimab is indicated for the treatment of adults and pediatric patients (12 years of age or older and weighing 40 kg or more) with mild to moderate COVID-19, who are at high risk of progressing to severe COVID-19 illness and/or hospitalization.

Bamlanivimab should not be used in patients hospitalized with severe COVID-19 respiratory disease as benefit of treatment has not been observed in this setting. Bamlanivimab, a monoclonal antibody, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

Certain circulating SARS-CoV-2 viral variants may be associated with resistance to bamlanivimab.

Evaluation of susceptibility of variants identified through global surveillance in subjects treated with bamlanivimab is ongoing.

Antiviral activity of bamlanivimab against SARS-CoV-2 variants was evaluated using in vitro pseudovirus assays.
Pseudovirus harboring the concurrent spike substitutions, present in the B.1.351 variant lineage (K417N + E484K + N501Y) first identified in South Africa, the P.1 variant lineage (K417T + E484K + N501Y) first identified in Brazil, B.1.427/B.1.429 variant lineage (L452R) first identified in California, and E484K containing B.1.526 variant lineage first identified in New York, exhibited reduced susceptibility to bamlanivimab. Bamlanivimab retained activity against pseudovirus expressing del69-70 + N501Y spike substitutions found in the UK origin B.1.1.7 variant lineage.

Information for healthcare professionals
There is a potential risk of treatment failure with bamlanivimab due to resistant SARS-CoV-2 variants.

Healthcare professionals are advised that:

- The in vitro pseudovirus results indicate there will likely be limited or no clinical benefits with the use of bamlanivimab against SARS-CoV-2 viruses that contain the E484K mutation and/or the L452R mutation. Bamlanivimab is expected to retain clinical benefit against the UK origin B.1.1.7 variant.
- Local epidemiology of variants should be taken into consideration before empiric use of bamlanivimab as single monoclonal antibody therapy. Bamlanivimab should be used only in regions where there is known or confirmed low prevalence of lineages containing E484K (e.g., South Africa or Brazil origin) and/or L452R (e.g., California origin) SARS-CoV-2 variants, and if other monoclonal antibodies that retain neutralization activity across variants are not available.

- Patients treated with bamlanivimab should be monitored for COVID-19 signs and symptoms of infection and provided additional confirmation or treatment of disease where required.
- For further details regarding variants of concern, healthcare professionals should consult the CPM for bamlanivimab. Updated information was included in the *Indications*, *Warnings and Precautions*, and *Microbiology* (*Antiviral Resistance*) sections.

The updated CPM is available in French and English on Health Canada's Drug Product Database, at www.bamlanivimabHCPinfo.com or www.lilly.ca.

For any questions, contact Eli Lilly Canada Inc. directly at 1-888-545-5972.

Action taken by Health Canada
Health Canada, in collaboration with Eli Lilly Canada Inc., has updated the *Indication* section of the CPM for bamlanivimab to include a limitation statement related to resistance of certain circulating SARS-CoV-2 viral variants to bamlanivimab. In addition, *Warnings and Precautions* and *Microbiology* sections, as well as the title page of the CPM, have also been updated with information concerning SARS-CoV-2 variants of concern.

Health Canada has worked with Eli Lilly Canada Inc. to prepare this alert for bamlanivimab. 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. This communication will be further distributed through the MedEffect™ e-Notice email notification system, as well as through social media channels, including LinkedIn and Twitter.

Report health or safety concerns
Managing marketed health product-related side effects depends on healthcare professionals and consumers reporting them. Any side effects in patients receiving bamlanivimab should be reported to Eli Lilly Canada Inc., or to Health Canada.

Eli Lilly Canada Inc.
P.O. Box 73, Exchange Tower
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Toronto, Ontario M5X 1B1
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 (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) 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:

Biologic and Radiopharmaceutical Drugs Directorate
E-mail: hc.brdd.dgo.enquiries.sc@canada.ca

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