

November 9, 2020

Eli Lilly and Company
Attention: Christine Phillips, PhD, RAC
Advisor Global Regulatory Affairs - US
Lilly Corporate Center
Drop Code 2543
Indianapolis, IN 46285

Dear Ms. Phillips:

This letter is in response to Eli Lilly and Company's ("Lilly") request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of bamlanivimab for the treatment of mild to moderate coronavirus disease 2019 (COVID-19), as described in the Scope of Authorization (Section II) of this letter, pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3).

On February 4, 2020, pursuant to Section 564(b)(1)(C) of the Act, the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes COVID-19.¹ On the basis of such determination, the Secretary of HHS on March 27, 2020, declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic, pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 360bbb-3), subject to terms of any authorization issued under that section.²

Bamlanivimab is a neutralizing IgG1 monoclonal antibody that binds to the receptor binding domain of the spike protein of SARS-CoV-2. It is an investigational drug and is not currently approved for any indication.

Based on review of the topline data from the planned interim analysis of Trial J2W-MC-PYAB, also called BLAZE-1 (NCT04427501), an ongoing randomized, double-blind, placebo-controlled, Phase 2 dose finding trial of bamlanivimab monotherapy in outpatients with mild to moderate COVID-19, it is reasonable to believe that bamlanivimab may be effective for the treatment of mild to moderate COVID-19 in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization, and that, when

¹ U.S. Department of Health and Human Services, *Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3*. February 4, 2020.

² U.S. Department of Health and Human Services, *Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3*, 85 FR 18250 (April 1, 2020).

used under the conditions described in this authorization, the known and potential benefits of bamlanivimab when used to treat COVID-19 in such patients outweigh the known and potential risks of such product.

Having concluded that the criteria for issuance of this authorization under Section 564(c) of the Act are met, I am authorizing the emergency use of bamlanivimab for treatment of COVID-19, as described in the Scope of Authorization section of this letter (Section II) and subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of bamlanivimab for the treatment of COVID-19 when administered as described in the Scope of Authorization (Section II) meets the criteria for issuance of an authorization under Section 564(c) of the Act, because:

1. SARS-CoV-2 can cause a serious or life-threatening disease or condition, including severe respiratory illness, to humans infected by this virus;
2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that bamlanivimab may be effective in treating mild to moderate COVID-19 in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization, and that, when used under the conditions described in this authorization, the known and potential benefits of bamlanivimab when used to treat COVID-19 in such patients outweigh the known and potential risks of such product; and
3. There is no adequate, approved, and available alternative to the emergency use of bamlanivimab for the treatment of mild to moderate COVID-19 in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.³

II. Scope of Authorization

I have concluded, pursuant to Section 564(d)(1) of the Act, that the scope of this authorization is limited as follows:

- Distribution of the authorized bamlanivimab will be controlled by the United States (U.S.) Government for use consistent with the terms and conditions of this EUA. Lilly will supply bamlanivimab to authorized distributors⁴, who will distribute to healthcare facilities or healthcare providers as directed by the U.S. Government, in collaboration with state and local government authorities, as needed;

³ No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

⁴ “Authorized Distributor(s)” are identified by Lilly as an entity or entities allowed to distribute authorized bamlanivimab.

- The bamlanivimab covered by this authorization will be used only by healthcare providers in an outpatient setting to treat mild to moderate COVID-19 in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization;
- Bamlanivimab is not authorized for use in the following patient populations⁵:
 - Adults or pediatric patients who are hospitalized due to COVID-19, or
 - Adults or pediatric patients who require oxygen therapy due to COVID-19, or
 - Adults or pediatric patients who require an increase in baseline oxygen flow rate due to COVID-19 in those patients on chronic oxygen therapy due to underlying non-COVID-19-related comorbidity.
- Bamlanivimab may only be administered in settings in which health care providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary.
- The use of bamlanivimab covered by this authorization must be in accordance with the dosing regimens as detailed in the authorized Fact Sheets.

Product Description

Bamlanivimab is a neutralizing IgG1 monoclonal antibody that binds to the receptor binding domain of the spike protein of SARS-CoV-2. Bamlanivimab, injection, 700 mg/20 mL, is a sterile, preservative-free aqueous solution that is to be diluted by using a 250 mL prefilled 0.9% Sodium Chloride Injection infusion solution, withdrawing and discarding 70 mL of 0.9% Sodium Chloride Injection from the infusion bag, and then transferring 20mL of 700mg/20mL bamlanivimab to the 0.9% Sodium Chloride Injection infusion bag. The authorized bamlanivimab includes a vial label and/or carton labeling that is clearly marked for “emergency use authorization”.

Bamlanivimab, injection, 700 mg/20 mL, vials should be stored in unopened vials under refrigerated temperature at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light until time of use. Diluted bamlanivimab infusion solution can be stored for up to 24 hours at refrigerated temperature (2°C to 8°C [36°F to 46°F]) or up to 7 hours at room temperature (20°C to 25°C [68°F to 77°F]) including infusion time.

⁵ Benefit of treatment with bamlanivimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

Bamlanivimab is authorized for emergency use with the following product-specific information required to be made available to healthcare providers and patients/caregivers, respectively, through Lilly's website at www.bamlanivimab.com:

- Fact Sheet for Health Care Providers: Emergency Use Authorization (EUA) of Bamlanivimab
- Fact Sheet for Patients, Parents and Parent/Caregivers: Emergency Use Authorization (EUA) of Bamlanivimab for Coronavirus Disease 2019 (COVID-19)

I have concluded, pursuant to Section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of bamlanivimab, when used for the treatment of COVID-19 and used in accordance with this Scope of Authorization (Section II), outweigh its known and potential risks.

I have concluded, pursuant to Section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that bamlanivimab may be effective for the treatment of COVID-19 when used in accordance with this Scope of Authorization (Section II), pursuant to Section 564(c)(2)(A) of the Act.

Having reviewed the scientific information available to FDA, including the information supporting the conclusions described in Section I above, I have concluded that bamlanivimab (as described in this Scope of Authorization (Section II)) meets the criteria set forth in Section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of your product under an EUA must be consistent with, and may not exceed, the terms of the Authorization, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section III). Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS's determination under Section 564(b)(1)(C) described above and the Secretary of HHS's corresponding declaration under Section 564(b)(1), bamlanivimab is authorized to treat mild to moderate COVID-19 illness in adults and pediatric patients 12 years of age and older weighing at least 40 kg, who are at high risk for progressing to severe COVID-19 illness and/or hospitalization as described in the Scope of Authorization (Section II) under this EUA, despite the fact that it does not meet certain requirements otherwise required by applicable federal law.

III. Conditions of Authorization

Pursuant to Section 564 of the Act, I am establishing the following conditions on this authorization:

Eli Lilly and Company (Lilly) and Authorized Distributors

- A. Lilly and authorized distributor(s) will ensure that the authorized bamlanivimab is distributed, as directed by the U.S. government, and the authorized labeling (i.e., Fact Sheets) will be made available to healthcare facilities and/or healthcare providers consistent with the terms of this letter.

- B. Lilly and authorized distributor(s) will ensure that appropriate storage and cold chain is maintained until the product is delivered to healthcare facilities and/or healthcare providers.
- C. Lilly and authorized distributor(s) will ensure that the terms of this EUA are made available to all relevant stakeholders (e.g., U.S. government agencies, state and local government authorities, authorized distributors, healthcare facilities, healthcare providers) involved in distributing or receiving authorized bamlanivimab. Lilly will provide to all relevant stakeholders a copy of this letter of authorization and communicate any subsequent amendments that might be made to this letter of authorization and its authorized accompanying materials (i.e., Fact Sheets).
- D. Lilly may request changes to this authorization, including to the authorized Fact Sheets for bamlanivimab, that do not alter the analysis of benefits and risks that underlies this authorization and FDA may determine that such changes may be permitted without amendment of this EUA. That determination must be made by joint decision of the Office of Infectious Diseases/Office of New Drugs/Center for Drug Evaluation and Research (CDER), the Counter-Terrorism and Emergency Coordination Staff/Office of the Center Director/CDER, and Office of Counterterrorism and Emerging Threats/Office of the Chief Scientist/Office of the Commissioner.
- E. Lilly will report to FDA serious adverse events and all medication errors associated with the use of the authorized bamlanivimab that are reported to Lilly using either of the following options.

Option 1: Submit reports through the Safety Reporting Portal (SRP) as described on the [FDA SRP](#) web page.

Option 2: Submit reports directly through the Electronic Submissions Gateway (ESG) as described on the [FAERS electronic submissions](#) web page.

Submitted reports under both options should state: “use of bamlanivimab was under an EUA.” For reports submitted under Option 1, include this language at the beginning of the question “Describe Event” for further analysis. For reports submitted under Option 2, include this language at the beginning of the “Case Narrative” field.

- F. All manufacturing facilities will comply with Current Good Manufacturing Practice requirements.
- G. Lilly will retain an independent third party (i.e., not affiliated with Lilly) to conduct a review of the batch records and any underlying data and associated discrepancies of bamlanivimab drug substance manufactured at Lilly Branchburg, NJ.
- For all batches manufactured prior to the effective date of this authorization, these batches can be released while review is ongoing.
 - For all batches manufactured after the effective date of this authorization, the third party review can be performed concurrent to Lilly’s batch release process.

If the independent review finds, prior to release, a discrepancy with significant potential to affect critical quality attributes, the product must not be released unless and until the issue is satisfactorily resolved. Any discrepancies found by the independent review, whether prior to or after release, must be reported to the Agency in a summary report, submitted every 14 calendar days, and include Lilly's corrective and preventive action plans for each discrepancy, including whether market action is required. The plans must include an appropriate evaluation of each discrepancy's potential impact on any released drug substance and associated drug product.

- H. Lilly will retain an independent third-party (i.e., not affiliated with Lilly) to conduct laboratory release testing of bamlanivimab drug substance manufactured at Lilly, Branchburg (excluding bioburden and endotoxin testing). Due to implementation timelines, independent third-party potency testing will commence on February 1, 2021. Until February 1, 2021, the Lilly Indianapolis, IN facility may conduct the equivalent of third-party potency testing. Any discrepancies found by Lilly Indianapolis, IN or the independent laboratory must be reported to the Agency in a summary report, submitted every 14 calendar days, and include Lilly's corrective and preventive action plans for each discrepancy. The plans must include an appropriate evaluation of each discrepancy's potential impact on any released drug substance and associated drug product.
- I. Lilly will submit information to the Agency within three working days of receipt of any information concerning any batch of bamlanivimab (whether the batch is distributed or not), as follows: (1) information concerning any incident that causes the drug product or its labeling to be mistaken for, or applied to, another article; and (2) information concerning any bacteriological or microscopic contamination, or any significant chemical, physical, or other change in deterioration in the drug product, or any failure of one or more batches of the drug product to meet the established specifications. Lilly will include in its notification to the Agency whether the batch, or batches, in question will be recalled. If FDA requests that these, or any other batches, at any time, be recalled, Lilly must recall them.
- J. Lilly will not implement any changes to the description of the product, manufacturing process, facilities and equipment, and elements of the associated control strategy that assure process performance and quality of the authorized product without notification to and concurrence by the Agency.
- K. Lilly will manufacture and test bamlanivimab per the process and methods, including in-process sampling and testing and finishing product testing (release and stability) to meet all specifications as detailed in Lilly's EUA request.
- L. Lilly will list bamlanivimab with a unique product NDC under the marketing category of Unapproved Drug- Other. Further, the listing will include each establishment where manufacturing is performed for the drug and the type of operation performed at each such establishment.

- M. Through a process of inventory control, Lilly and authorized distributor(s) will maintain records regarding distribution of the authorized bamlanivimab (i.e., lot numbers, quantity, receiving site, receipt date).
- N. Lilly and authorized distributor(s) will make available to FDA upon request any records maintained in connection with this EUA.

Healthcare Facilities to Whom the Authorized Bamlanivimab Is Distributed and Healthcare Providers Administering the Authorized Bamlanivimab

- O. Healthcare facilities and healthcare providers will ensure that they are aware of the letter of authorization, and the terms herein, and that the authorized Fact Sheets are made available to healthcare providers and to patients and caregivers, respectively, through appropriate means, prior to administration of bamlanivimab.
- P. Healthcare facilities and healthcare providers receiving bamlanivimab will track serious adverse events that are considered to be potentially attributable to bamlanivimab use and must report these to FDA in accordance with the Fact Sheet for Healthcare Providers. Complete and submit a MedWatch form (www.fda.gov/medwatch/report.htm), or Complete and submit FDA Form 3500 (health professional) by fax (1-800-FDA-0178) (these forms can be found via link above). Call [1-800-FDA-1088](tel:1-800-FDA-1088) for questions. Submitted reports should state, “use of bamlanivimab was under an EUA” at the beginning of the question “Describe Event” for further analysis.
- Q. Healthcare facilities and healthcare providers will ensure that appropriate storage and cold chain is maintained until the product is administered consistent with the terms of this letter.
- R. Through a process of inventory control, healthcare facilities will maintain records regarding the dispensed authorized bamlanivimab (i.e., lot numbers, quantity, receiving site, receipt date), product storage, and maintain patient information (e.g., patient name, age, disease manifestation, number of doses administered per patient, other drugs administered).
- S. Healthcare facilities will ensure that any records associated with this EUA are maintained until notified by Lilly and/or FDA. Such records will be made available to Lilly, HHS, and FDA for inspection upon request.

Conditions Related to Printed Matter, Advertising and Promotion

- T. All descriptive printed matter, as well as advertising and promotional material, relating to the use of the bamlanivimab under this authorization shall be consistent with the authorized labeling, as well as the terms set forth in this EUA and the applicable requirements set forth in the Act and FDA regulations.
- U. No descriptive printed matter, as well as advertising or promotional material, relating to the use of bamlanivimab may represent or suggest that such products are safe or effective when used for the treatment of mild to moderate COVID-19 in adults and pediatric patients with

positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

V. All descriptive printed matter, as well as advertising and promotional material, relating to the use of the bamlanivimab clearly and conspicuously shall state that:

- the bamlanivimab has not been approved, but has been authorized for emergency use by FDA, to treat mild to moderate COVID-19 in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.
- the bamlanivimab is authorized for the treatment of mild to moderate COVID-19 in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of the bamlanivimab under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

IV. Duration of Authorization

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products during the COVID-19 pandemic is terminated under Section 564(b)(2) of the Act or the EUA is revoked under Section 564(g) of the Act.

Sincerely,

--/s/--

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration