

December 3, 2021

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

RE: Emergency Use Authorization 094

Dear Ms. Phillips:

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 coronavirus disease 2019 (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

On February 9, 2021, the Food and Drug Administration (FDA or Agency) issued an Emergency Use Authorization (EUA) for emergency use of bamlanivimab and etesevimab administered together for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization. Bamlanivimab and etesevimab are neutralizing IgG1 monoclonal antibodies that bind to distinct but overlapping epitopes within the receptor binding domain of the spike protein of SARS-CoV-2. They are both investigational drugs and are not currently approved for any indication.

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).

FDA subsequently reissued the Letter of Authorization on the following dates: February 25, 2021,³ August 27, 2021,⁴ and September 16, 2021.⁵

On December 3, 2021, again having concluded that revising this EUA is appropriate to protect the public health or safety under section 564(g)(2) of the Act, FDA is reissuing the September 16, 2021 letter in its entirety, to also authorize bamlanivimab and etesevimab administered together for emergency use as treatment for COVID-19 and as post-exposure prophylaxis of COVID-19 in certain younger pediatric individuals, including neonates, not covered under prior authorizations.

To support the emergency use of bamlanivimab and etesevimab, which were originally authorized to be administered together for the treatment of mild-to-moderate COVID-19 in certain adults and pediatric patients (12 years of age and older weighing at least 40 kg), FDA reviewed data from the Phase 2/3 BLAZE-1 trial (NCT04427501), a randomized, double-blind, placebo-controlled clinical trial, and the Phase 2 BLAZE-4 trial (NCT04634409), a randomized, double-blind, placebo-controlled clinical trial. Expansion of this authorization to also include younger pediatric patients, including neonates, is supported by FDA's review of pharmacokinetic and clinical data from the Phase 3 portion of the BLAZE-1 trial (NCT04427501), clinical data from the BLAZE-1 (NCT04427501) and BLAZE-4 (NCT04497987) clinical trials, and the Agency's understanding of the similar course of COVID-19 disease across the authorized patient populations. Based on the totality of scientific evidence available, including these data, it is reasonable to believe that bamlanivimab and etesevimab administered together may be effective for the treatment of mild to moderate COVID-19 in adults and pediatric patients, including neonates, with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death, and that, when used under the conditions described in this authorization, the known and potential benefits of bamlanivimab and etesevimab administered together outweigh the known and potential risks of such products.

Additionally, to support the emergency use of bamlanivimab and etesevimab, which were originally authorized to be administered together for post-exposure prophylaxis of COVID-19 in certain adults and pediatric individuals (12 years of age and older weighing at least 40 kg), FDA reviewed the topline analysis of data from BLAZE-2 Part 1 (also known as Trial J2X-MC-PYAD; NCT04497987), a Phase 3 randomized, double-blind, placebo-controlled trial evaluating bamlanivimab alone for prevention of COVID-19 in residents and staff of skilled nursing

³ FDA revised the condition on instructional and educational materials. New conditions were also incorporated on the establishment of a process for monitoring genomic databases for the emergence of global viral variants of SARS-CoV-2 and the assessment, if requested by FDA, of the activity of the authorized bamlanivimab and etesevimab against any global SARS-CoV-2 variant(s) of interest.

⁴ FDA revised the authorized use for bamlanivimab and etesevimab administered together clarifying the meaning of "severe COVID-19" and further limited the use of bamlanivimab and etesevimab by authorizing bamlanivimab and etesevimab administered together only in those states, territories, and US jurisdictions in which the combined frequency of variants resistant to bamlanivimab and etesevimab administered together is less than or equal to 5%. Revisions were also incorporated to the conditions on compliance with cGMPs, product quality reporting, requests for CMC (chemistry, manufacturing and controls) changes to this authorization, the provision of samples of the authorized bamlanivimab and etesevimab to HHS, upon request, and the conditions on advertising and promotion.

⁵ FDA reissued the EUA to authorize bamlanivimab and etesevimab administered together for emergency use as post-exposure prophylaxis for COVID-19 in certain adults and pediatric individuals (12 years of age and older weighing at least 40 kg).

facilities following a confirmed reported case of SARS-CoV-2 infection at the facility. Expansion of this authorization to also include younger pediatric patients, including neonates, is supported by the Agency’s review of pharmacokinetic data and its understanding of the mechanism of action for bamlanivimab and etesevimab administered together and the expectation that bamlanivimab and etesevimab administered together will provide a similar clinical benefit in younger pediatric patients, including neonates, as compared to adults. Based on the totality of scientific evidence available, including these data, it is reasonable to believe that bamlanivimab and etesevimab administered together may be effective for use as post-exposure prophylaxis of COVID-19 in adults and pediatric individuals, including neonates, who are at high risk for progression to severe COVID-19, including hospitalization or death, as described in the Scope of Authorization (Section II), and that, when used under such conditions, the known and potential benefits of bamlanivimab and etesevimab 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 and etesevimab administered together for treatment and as post-exposure prophylaxis 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 and etesevimab administered together for treatment and as post-exposure prophylaxis 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 the following:
 - Bamlanivimab and etesevimab administered together may be effective for the treatment of mild to moderate COVID-19 in adults and pediatric patients, including neonates, with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death, as further described in the Scope of Authorization (Section II)
 - Bamlanivimab and etesevimab administered together may be effective for use as post-exposure prophylaxis in certain adults and pediatric individuals, including neonates, who are at high risk for progression to severe COVID-19, including hospitalization or death, as further described in the Scope of Authorization (Section II)

And that, when used under the conditions described in the Scope of Authorization (Section II), the known and potential benefits of bamlanivimab and etesevimab administered together outweigh the known and potential risks of such products; and

3. There is no adequate, approved, and available alternative to the emergency use of bamlanivimab and etesevimab administered together for treatment and as post-exposure prophylaxis of COVID-19, as described in the Scope of Authorization (Section II).⁶

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 and etesevimab 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 and etesevimab to authorized distributors⁷, 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;

Treatment of COVID-19

- Bamlanivimab and etesevimab covered by this authorization will be administered together only by healthcare providers to treat mild to moderate COVID-19 in adults and pediatric patients, including neonates, with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death;
- Bamlanivimab and etesevimab may only be administered together;
- Bamlanivimab and etesevimab are authorized for use **only** in states, territories, and U.S. jurisdictions in which the combined frequency of variants resistant to bamlanivimab and etesevimab administered together is less than or equal to 5%, as determined by FDA.⁸ A list of states, territories and U.S. jurisdictions in which

⁶ No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

⁷ “Authorized Distributor(s)” are identified by Lilly as an entity or entities allowed to distribute authorized bamlanivimab and etesevimab to be administered together.

⁸ FDA will make this determination considering current variant frequency data (available at: <https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variant-proportions.html>), trends in variant frequency over time, the precision of the estimates and information regarding emerging variants of concern. FDA will update the list of states, territories, and US jurisdictions in which bamlanivimab and etesevimab are and are not currently authorized as new data and information becomes available. Healthcare providers should refer to the FDA website regularly for updates.

bamlanivimab and etesevimab are and are not⁹ currently authorized is available on FDA’s website at: <https://www.fda.gov/media/151719/download>;

- Bamlanivimab and etesevimab are **not** authorized for use in patients 2 years of age and older who are hospitalized due to COVID-19¹⁰;
- Bamlanivimab and etesevimab are **not** authorized for use in patients, regardless of age, who:
 - require oxygen therapy and/or respiratory support due to COVID-19; or
 - require an increase in baseline oxygen flow rate and/or respiratory support due to COVID-19 and are on chronic oxygen therapy and/or respiratory support due to underlying non-COVID-19 related comorbidity.
- Bamlanivimab and etesevimab may only be administered together 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 and etesevimab covered by this authorization must be in accordance with the authorized Fact Sheets.

Post-Exposure Prophylaxis of COVID-19

- Bamlanivimab and etesevimab administered together may only be used in adult and pediatric individuals, including neonates, for post-exposure prophylaxis of COVID-19 in individuals who are at high risk for progression to severe COVID-19, including hospitalization or death, and are:
 - not fully vaccinated¹¹ **or** who are not expected to mount an adequate immune

⁹ Bamlanivimab and etesevimab are not authorized for use in states, territories, and U.S. jurisdictions in which the combined frequency of variants resistant to bamlanivimab and etesevimab administered together exceeds 5%. New orders will not be fulfilled and product will not be shipped to states, territories, and US jurisdictions where bamlanivimab and etesevimab administered together are not authorized. Supplies of bamlanivimab and etesevimab that are already in distribution in a state, territory, or U.S. jurisdiction in which the product is not currently authorized may remain in distribution and be held for future use if the combined frequency of variants resistant to bamlanivimab and etesevimab administered together in that state, territory or U.S. jurisdiction become less than or equal to 5%.

¹⁰ Treatment with bamlanivimab and etesevimab has not been studied in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab and etesevimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation. However, the reasons for hospital admission may be different and the threshold for hospital admission may be lower for neonates, young infants and toddlers with COVID-19 compared to older children and adults. This authorization covers young children (i.e., birth to 2 years of age) who are hospitalized with mild to moderate COVID-19 at the time of treatment to receive bamlanivimab and etesevimab.

¹¹ Individuals are considered to be fully vaccinated 2 weeks after their second vaccine dose in a 2-dose series (such as the Pfizer or Moderna vaccines), or 2 weeks after a single-dose vaccine (such as the Johnson & Johnson/ Janssen vaccine). See this website for more details: <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/fully-vaccinated.html#vaccinated>.

response to complete SARS-CoV-2 vaccination (for example, individuals with immunocompromising conditions including those taking immunosuppressive medications¹²) **and**

- have been exposed to an individual infected with SARS-CoV-2 consistent with close contact criteria per Centers for Disease Control and Prevention (CDC)¹³ **or**
 - who are at high risk of exposure to an individual infected with SARS-CoV-2 because of occurrence of SARS-CoV-2 infection in other individuals in the same institutional setting (for example, nursing homes, prisons).
- Bamlanivimab and etesevimab may only be administered together;
 - Bamlanivimab and etesevimab are authorized for use **only** in states, territories, and U.S. jurisdictions in which the combined frequency of variants resistant to bamlanivimab and etesevimab administered together is less than or equal to 5%, as determined by FDA.¹⁴ A list of states, territories and U.S. jurisdictions in which bamlanivimab and etesevimab are and are not¹⁵ currently authorized is available on FDA's website at: <https://www.fda.gov/media/151719/download>;
 - Bamlanivimab and etesevimab 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 EMS, as necessary.
 - The use of bamlanivimab and etesevimab covered by this authorization must be in accordance with the authorized Fact Sheets.
 - Post-exposure prophylaxis with bamlanivimab and etesevimab administered together is **not** intended to be a substitute for vaccination against COVID-19.
 - Bamlanivimab and etesevimab administered together is **not** authorized for pre-exposure prophylaxis for prevention of COVID-19.

¹² See this website for more details: <https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html>

¹³ Close contact with an infected individual is defined as: being within 6 feet for a total of 15 minutes or more, providing care at home to someone who is sick, having direct physical contact with the person (hugging or kissing, for example), sharing eating or drinking utensils, or being exposed to respiratory droplets from an infected person (sneezing or coughing, for example). See this website for additional details: <https://www.cdc.gov/coronavirus/2019-ncov/if-you-are-sick/quarantine.html>

¹⁴ Supra at Note 8.

¹⁵ Supra at Note 9.

Product Description

Bamlanivimab and etesevimab are neutralizing IgG1 monoclonal antibodies that bind to distinct but overlapping epitopes within the receptor binding domain of the spike protein of SARS-CoV-2. Bamlanivimab injection, 700 mg/20 mL, and etesevimab, 700 mg/20 mL, are sterile, preservative-free clear to opalescent and colorless to slightly yellow to slightly brown solutions to be diluted prior to infusion. One vial of bamlanivimab (20 mL) and two vials of etesevimab (40 mL) are to be added to a prefilled 0.9% sodium chloride infusion bag as described in the healthcare provider fact sheet. The authorized bamlanivimab includes a vial label and/or carton labeling that is clearly marked “For use under Emergency Use Authorization (EUA)”. The authorized etesevimab includes a vial label and/or carton labeling that is clearly marked “For use under Emergency Use Authorization (EUA)” and “MUST ADMINISTER WITH BAMLANIVIMAB.”

Bamlanivimab, injection, 700 mg/20 mL, and etesevimab, injection, 700mg/20 mL 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 and etesevimab infusion solution can be stored for up to 24 hours at refrigerated temperature (2°C to 8°C [36°F to 46°F]) and up to 7 hours at room temperature (20°C to 25°C [68°F to 77°F]) including infusion time.

Bamlanivimab and etesevimab are authorized for emergency use as described in the Scope of Authorization (Section II) with the following product-specific information required to be made available to healthcare providers and patients, parents, and caregivers, respectively, through Lilly’s website at www.LillyAntibody.com:

- Fact Sheet for Health Care Providers: Emergency Use Authorization (EUA) of Bamlanivimab and Etesevimab
- Fact Sheet for Patients, Parents and Caregivers: Emergency Use Authorization (EUA) of Bamlanivimab and Etesevimab for Coronavirus Disease 2019 (COVID-19)
- Bamlanivimab and Etesevimab Authorized States, Territories and US Jurisdictions

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 and etesevimab administered together, when used for treatment and as post-exposure prophylaxis of COVID-19 as described in 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 and etesevimab administered together may be effective for treatment and as post-exposure prophylaxis 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 and etesevimab (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 and etesevimab administered together are authorized for treatment and as post-exposure prophylaxis of COVID-19 as described in this 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 and etesevimab are 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 and etesevimab. 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 and etesevimab. Any request for changes to this EUA must be submitted to the Office of Infectious Diseases/Office of New Drugs/Center for Drug Evaluation and Research. Such changes require appropriate authorization prior to implementation.¹⁶

¹⁶ The following types of revisions may be authorized without reissuing this letter: (1) changes to the authorized labeling; (2) non-substantive editorial corrections to this letter; (3) new types of authorized labeling, including new fact sheets; (4) new carton/container labels; (5) expiration dating extensions; (6) changes to manufacturing processes, including tests or other authorized components of manufacturing; (7) new conditions of authorization to require data collection or study; (8) new strengths of the authorized product, new product sources (e.g., of active pharmaceutical ingredient) or of product components. For changes to the authorization, including the authorized

- E. Lilly may develop and disseminate instructional and educational materials (e.g., materials providing information on product administration and/or patient monitoring) that are consistent with the authorized emergency use of bamlanivimab and etesevimab as described in this Letter of Authorization and authorized labeling, without FDA’s review and concurrence, when necessary to meet public health needs. Any instructional and educational materials that are inconsistent with the authorized labeling of bamlanivimab and etesevimab are prohibited. Should the Agency become aware of any instructional or educational materials that are inconsistent with the authorized labeling of bamlanivimab and etesevimab, the Agency will require Lilly to cease distribution of such instructional or educational materials.
- F. Lilly will report to FDA serious adverse events and all medication errors associated with the use of the authorized bamlanivimab and etesevimab 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: “bamlanivimab and etesevimab use for COVID-19 under Emergency Use Authorization (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.

- G. All manufacturing, packaging, and testing sites for both drug substance and drug product will comply with current good manufacturing practice requirements of Section 501(a)(2)(B) of the Act.
- H. 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

labeling, of the type listed in (3), (6), (7), or (8), review and concurrence is required from the Counter-Terrorism and Emergency Coordination Staff/Office of the Center Director/CDER and the Office of Counterterrorism and Emerging Threats/Office of the Chief Scientist.

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.

- I. 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). Any discrepancies found by 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.
- J. Lilly will submit information to the Agency within three working days of receipt of any information concerning significant quality problems with batches (whether distributed or undistributed) of drug product of bamlanivimab and etesevimab that includes the following:
 - Information concerning any incident that causes the drug product or its labeling to be mistaken for, or applied to, another article; or
 - Information concerning any microbiological contamination, or any significant chemical, physical, or other change or deterioration in the distributed drug product, or any failure of one or more distributed batches of the product to meet the established specifications.

If a significant quality problem affects unreleased product and may also impact product(s) previously released and distributed, then information should be submitted for all potentially impacted lots.

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.

If not included in its initial notification, Lilly must submit information confirming that Lilly has identified the root cause of the significant quality problems and taken corrective action, and provide a justification confirming that the corrective action is appropriate. Lilly must submit this information as soon as possible but no later than 45 calendar days from the initial notification.

- K. Lilly will manufacture bamlanivimab and etesevimab to meet all quality standards and per the manufacturing process and control strategy as detailed in Lilly's EUA request. 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 as described under condition D.

- L. Lilly will individually list bamlanivimab and etesevimab with a unique product NDC under the marketing category of Unapproved Drug- Other. Further, each 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 and etesevimab (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.
- O. Lilly will establish a process for monitoring genomic database(s) for the emergence of global viral variants of SARS-CoV-2. A summary of Lilly's process should be submitted to the Agency as soon as practicable, but no later than 30 calendar days of the issuance of this letter, and within 30 calendar days of any material changes to such process. Lilly will provide reports to the Agency on a monthly basis summarizing any findings as a result of its monitoring activities and, as needed, any follow-up assessments planned or conducted.
- P. FDA may require Lilly to assess the activity of the authorized bamlanivimab and etesevimab against any global SARS-CoV-2 variant(s) of interest (e.g., variants that are prevalent or becoming prevalent that harbor substitutions in the target protein or in protein(s) that interact with the target protein). Lilly will perform the required assessment in a manner and timeframe agreed upon by Lilly and the Agency. Lilly will submit to FDA a preliminary summary report immediately upon completion of its assessment followed by a detailed study report within 30 calendar days of study completion. Lilly will submit any relevant proposal(s) to revise the authorized labeling based on the results of its assessment, as may be necessary or appropriate based on the foregoing assessment.
- Q. Lilly shall provide samples as requested of the authorized bamlanivimab and etesevimab to the HHS for evaluation of activity against emerging global viral variants of SARS-CoV-2, including specific amino acid substitution(s) of interest (e.g., variants that are highly prevalent or that harbor substitutions in the target protein) within 5 business days of any request made by HHS. Analyses performed with the supplied quantity of authorized bamlanivimab and etesevimab may include, but are not limited to, cell culture potency assays, protein binding assays, cell culture variant assays (pseudotyped virus-like particles and/or authentic virus), and *in vivo* efficacy assays.

Healthcare Facilities to Whom the Authorized Bamlanivimab and Etesevimab Are Distributed and Healthcare Providers Administering the Authorized Bamlanivimab and Etesevimab

- R. 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 and etesevimab as described in the Scope of Authorization (Section II) under this EUA.

- S. Healthcare facilities and healthcare providers receiving bamlanivimab and etesevimab will track serious adverse events and all medication errors that are considered to be potentially attributable to the use of bamlanivimab and etesevimab under this authorization 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, “bamlanivimab and etesevimab use for COVID-19 under Emergency Use Authorization (EUA)” at the beginning of the question “Describe Event” for further analysis.
- T. Healthcare facilities and healthcare providers will ensure that appropriate storage and cold chain is maintained until the products are administered consistent with the terms of this letter.
- U. Through a process of inventory control, healthcare facilities will maintain records regarding the dispensed authorized bamlanivimab and etesevimab (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).
- V. 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.
- W. Healthcare facilities and providers will report therapeutics information and utilization data as directed by HHS.

Conditions Related to Printed Matter, Advertising and Promotion

- X. All descriptive printed matter, advertising, and promotional materials relating to the use of bamlanivimab and etesevimab under this authorization shall be consistent with the authorized labeling, as well as the terms set forth in this EUA, and meet the requirements set forth in Section 502(a) and (n) of the Act, as applicable, and FDA implementing regulations. References to “approved labeling”, “permitted labeling” or similar terms in these requirements shall be understood to refer to the authorized labeling for the use of bamlanivimab and etesevimab under this authorization. In addition, such materials shall:
 - Be tailored to the intended audience.
 - Not take the form of reminder advertisements, as that term is described in 21 CFR 202.1(e)(2)(i), 21 CFR 200.200 and 21 CFR 201.100(f).

- Present the same risk information relating to the major side effects and contraindications concurrently in the audio and visual parts of the presentation for advertising and promotional materials in audio-visual format.
- Be accompanied by the authorized labeling, if the promotional materials are not subject to Section 502(n) of the Act.
- Be submitted to FDA accompanied by Form FDA-2253 at the time of initial dissemination or first use.

If the Agency notifies Lilly that any descriptive printed matter, advertising or promotional materials do not meet the terms set forth in conditions X-Z of this EUA, Lilly must cease distribution of such descriptive printed matter, advertising, or promotional materials in accordance with the Agency's notification. Furthermore, as part of its notification, the Agency may also require Lilly to issue corrective communication(s).

- Y. No descriptive printed matter, advertising, or promotional materials relating to the use of bamlanivimab and etesevimab under this authorization may represent or suggest that bamlanivimab and etesevimab administered together is safe or effective when used for the treatment or as post-exposure prophylaxis of COVID-19.
- Z. All descriptive printed matter, advertising, and promotional material, relating to the use of bamlanivimab and etesevimab under this authorization clearly and conspicuously shall state that:
- Bamlanivimab and etesevimab have not been approved, but have been authorized for emergency use by FDA under an EUA, for treatment and as post-exposure prophylaxis of COVID-19 in certain adults and pediatric individuals, including neonates, with high risk for progression to severe COVID-19, including hospitalization or death, and
 - The emergency use of bamlanivimab and etesevimab is only authorized for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products during the COVID-19 pandemic under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization 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,



Digitally signed by Jacqueline
A. O'shaughnessy -S
Date: 2021.12.03 12:44:40
-05'00'

Jacqueline A. O'Shaughnessy, Ph.D.
Acting Chief Scientist
Food and Drug Administration

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

ALICIA MORUF
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