

Emergency Use Authorization (EUA) for bamlanivimab 700 mg and etesevimab 1,400 IV
Center for Drug Evaluation and Research (CDER) Memorandum

Identifying Information

Application Type (EUA or Pre-EUA) If EUA, designate whether pre-event or intra-event EUA request.	EUA
EUA Application Number(s)	94
Date of Memorandum	January 24, 2021 Correct date: January 24, 2022
Sponsor (entity requesting EUA or pre-EUA consideration), point of contact, address, phone number, fax number, email address	Eli Lilly and Company: Christine Phillips, PhD, RAC Advisor, Global Regulatory Affairs - NA Mobile: (b) (6) Email: phillips_christine_ann@lilly.com
Manufacturer	Eli Lilly and Company
OND Division / Office	Division of Antivirals (DAV)/Office of Infectious Diseases (OID)
Proprietary Name	n/a
Established Name/Other names used during development	bamlanivimab (LY3819253, LY-CoV555) and etesevimab (LY3832479, LY-CoV016)
Dosage Forms/Strengths	Bamlanivimab 700 mg and etesevimab 1400 mg IV
Therapeutic Class	SARS-CoV-2 spike protein directed human IgG1k monoclonal antibody (mAb)
Intended Use or Need for EUA	Treatment of mild to moderate coronavirus disease 2019 (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. 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, and are:

	<ul style="list-style-type: none"> • not fully vaccinated or who are not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination (for example, individuals with immunocompromising conditions including those taking immunosuppressive medications) and <ul style="list-style-type: none"> ○ have been exposed to an individual infected with SARS-CoV-2 consistent with close contact criteria per Centers for Disease Control and Prevention (CDC) 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).
Intended Population(s)	Adults and pediatric patients, including neonates

Rationale and Revisions to EUA Fact Sheets

Brief Summary of Key Relevant Regulatory Actions for EUA 94

The EUA for bamlanivimab and etesevimab administered together was initially authorized on February 9, 2021. In the months following initial authorization, there was an emergence and substantial increase in viral variants (Gamma (P.1) and Beta (B.1.351)) of SARS-CoV-2 that are resistant to bamlanivimab and etesevimab. Based on this information, on August 27, 2021, FDA revised the EUA to include a Limitation on Authorized Use that provided that “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 exceeds 5%.” At that time, there were other authorized monoclonal antibody therapies that were expected to be fully active against the P.1 and B.1.351 variants, and other circulating variants, and were available for use and distribution. As part of the August 27, 2021 revision, the Fact Sheet for Health Care Providers was also revised to inform health care providers about these other therapeutic options as follows:

There are other authorized monoclonal antibody treatments available and healthcare providers should choose an authorized therapeutic option with activity against circulating variants in their state. Variant frequency data for states and jurisdictions can be accessed on the following CDC website: <https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variant-proportions.html>

Circumstances have changed significantly since August 2021. The first confirmed U.S. case of Omicron (B.1.1.529) was identified in December 2021 and the Omicron variant has subsequently become the dominant circulating variant across the U.S.¹ On December 22, 2021, the Fact Sheet for Health Care Providers was revised in Section 15 to provide pseudotyped virus data from the Omicron variant that showed reduced susceptibility to bamlanivimab and

¹ Refer to Figure 1 below.

etesevimab administered together, rendering the drugs, when used according to the terms and conditions of the authorization at the time, unlikely to have activity against the Omicron variant.²

Concurrently, the authorization for bamlanivimab and etesevimab, including the authorized Fact Sheet for Healthcare Providers, was also revised to remove the Limitation of Authorized Use related to the specified 5% of the combined frequency of variants as described above.

Despite any uncertainty about the frequency of the Omicron variant, data from the Centers for Disease Control (CDC) indicated that the frequency exceeded the 5% threshold in the majority of US states, territories and jurisdictions, and as such, the Limitation of Authorized Use including the 5% threshold as described above would have resulted in bamlanivimab and etesevimab not being authorized at a time when the Delta variant was still in high circulation throughout the United States. Bamlanivimab and etesevimab are expected to retain activity against the Delta variant (see [EUA Memorandum dated 12/22/2021](#)).

Recommendation to Revise EUA 094

Consistent with section 564(g) of the Federal Food, Drug & Cosmetic Act, the Agency will periodically review the appropriateness and circumstances of each EUA. This provision further states, among other things, that the Secretary may revise an EUA if circumstances exist that make such revision appropriate to protect the public health or safety.

At the time of this review, the most recent surveillance data from actual sequencing on the CDC's website indicate that Omicron accounted for 89.1% (95%CI 86.1-91.7%) of the SARS-CoV-2 sequences nationally for the week ending January 1, 2022. CDC also uses available data to estimate the proportions of circulating variants in a model, called Nowcast, to enable timely public health action. Currently, Nowcast is our best tool to predict the prevalence of Omicron in real time. For the week ending January 15, 2022, Nowcast predicts that the frequency of the Omicron variant was 99.5% nationally, with a 95% prediction interval of 99.3-99.7% (see Figure 1 below).³ All HHS regions⁴ of the U.S. have point estimates above 95% for the Omicron variant.⁵

² Source (accessed 1/22/2022): <https://www.fda.gov/media/155150/download>

³ Source (accessed on 1/22/2022): https://covid.cdc.gov/covid-data-tracker/?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fcases-updates%2Fvariant-proportions.html#variant-proportions

⁴ See <https://www.hhs.gov/about/agencies/iea/regional-offices/index.html>

⁵ Source (accessed on 1/22/2022): https://covid.cdc.gov/covid-data-tracker/?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fcases-updates%2Fvariant-proportions.html#variant-proportions



Figure 1: CDC Nowcast data ending the Week of January 15, 2022 source <https://covid.cdc.gov/covid-data-tracker/#variant-proportions> (accessed 01/22/2022)

Based on the above, the Division of Antivirals and Office of Infectious Diseases recommends adding the following new limitations on the authorized use of bamlanivimab and etesevimab administered together for treatment of COVID-19 or as post-exposure prophylaxis for prevention of COVID-19, respectively:

Treatment

Bamlanivimab and etesevimab administered together are **not** authorized for treatment of mild to moderate COVID-19 in geographic regions where infection is likely to have been caused by a non-susceptible SARS-CoV-2 variant based on available information including variant susceptibility to these drugs and regional variant frequency.

Post-exposure prophylaxis

Bamlanivimab and etesevimab are **not** authorized for post-exposure prophylaxis of COVID-19 in geographic regions where exposure is likely to have been to a non-

susceptible SARS-CoV-2 variant based on available information including variant susceptibility to these drugs and regional variant frequency.

Currently, there are no authorized or available point-of-care tests to accurately determine the SARS-CoV-2 variant that a patient is infected with; therefore, all therapy decisions are empiric and regional epidemiology is important to guide appropriate therapy choices. FDA will monitor conditions to determine whether use in a geographic region is consistent with this scope of authorization, referring to available information, including information on variant susceptibility (see, e.g., section 15 of authorized Fact Sheet for Health Care Providers), and CDC regional variant frequency data available at: <https://covid.cdc.gov/covid-data-tracker/#variant-proportions>. FDA's determination and any updates will be available at: <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs>. The Limitations of Authorized Use proposed above will ensure that, based on available information including variant susceptibility to bamlanivimab and etesevimab and regional variant frequency, any patient or individual receiving these drugs consistent with the terms and conditions of the authorization will likely benefit from the therapy.

Additionally, on January 19, 2022, the NIH COVID-19 Treatment Guidelines Panel updated their recommendations to address the fact that Omicron is the dominant SARS-CoV-2 variant in the U.S. stating: "Because the anti-SARS-CoV-2 monoclonal antibodies (mAbs) bamlanivimab plus etesevimab and casirivimab plus imdevimab are predicted to have markedly reduced activities against this VOC, and because real-time testing to identify rare, non-Omicron variants is not routinely available, the Panel **recommends against** the use of these anti-SARS-CoV-2 mAbs **(AIII)**."⁶

The Agency recognizes that bamlanivimab and etesevimab may retain activity against other SARS-CoV-2 variants and that future circulating SARS-CoV-2 variants and the susceptibility patterns of our available countermeasures may shift. It's also important to underscore that the known and potential benefits of bamlanivimab and etesevimab administered together when used to treat a patient with mild-to-moderate COVID-19 that is likely caused by a susceptible variant to this therapy, or when used as post-exposure prophylaxis of COVID-19 in an individual likely exposed to a susceptible variant to this therapy, consistent with the terms and conditions of the authorization, outweigh the known and potential risks of the products.

Moreover, the conditions to the authorization for bamlanivimab and etesevimab administered together include requirements for monitoring and testing the authorized products against any global SARS-CoV-2 variant(s) of interest. Such requirements are essential to the Agency's continued understanding of bamlanivimab and etesevimab under this EUA.

Regulatory Conclusion and Associated Actions:

Based on the above, the Division of Antivirals and Office of Infectious Diseases believes that revision to the EUA for bamlanivimab and etesevimab administered together as described above is appropriate to protect the public health or safety.

⁶ Source (accessed 1/21/2022) [What's New | COVID-19 Treatment Guidelines \(nih.gov\)](#)

Consistent with the above, and concurrent with the revision to this EUA, FDA will also communicate publicly on the FDA website that bamlanivimab and etesevimab are not authorized for use in any U.S. region at this time.

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/

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