Emergency Use Authorization (EUA) for Bamlanivimab 700mg IV and Etesevimab 1400 mg IV administered together

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	February 25, 2021
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)
Integrated Review Completion Date	February 9, 2021
Proprietary Name	n/a
Established Name/Other names used during development	Bamlanivimab (BAM, LY3819253, LY-CoV555) and Etesevimab (ETE, LY3832479, LY-CoV016)
Dosage Forms/Strengths	Bamlanivimab - 700mg IV Etesevimab – 1400mg IV

Therapeutic Class	SARS-CoV-2 spike protein directed human IgG1κ monoclonal antibodies (mAbs)
Intended Use or Need for EUA	Mild to moderate COVID-19
Intended Population(s)	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 illness and/or hospitalization

Emergency Use Authorization (EUA) 94 authorizes the emergency use of bamlanivimab and etesevimab administered together for the treatment of mild to moderate coronavirus disease 2019 (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. This memorandum provides a brief summary of the changes to the Letter of Authorization for EUA 94.

Under section 564(g) of the Federal Food, Drug & Cosmetic Act, the Agency must periodically review the circumstances and appropriateness of an EUA. The Agency may revise an EUA, for example, if circumstances warrant revision to protect the public health or safety.

On February 9, 2021, FDA issued the Letter of Authorization (LOA) for EUA 94, which included a condition to the authorization requiring Lilly to submit instructional and educational materials to the Agency for review and concurrence prior to initial dissemination of such materials, or when making revisions to instructional and educational materials previously authorized. Upon further consideration, FDA believes that making instructional and educational materials available in an expedient manner, when such materials are necessary to meet public health needs and on condition that these materials are consistent with the terms and conditions of the authorization, including authorized labeling, will facilitate the appropriate use of the authorized bamlanivimab and etesevimab. Section 564 of the FD&C Act, including condition E as revised below, details mechanisms by which FDA may address any disseminated instructional or educational materials that are inconsistent with the terms and conditions of the authorization, including the authorized labeling.

As such, FDA is revising condition E, as detailed below, to no longer require prior Agency review and concurrence of instructional and educational materials, or revisions to instructional and educational materials previously 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 the 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.

SARS-CoV-2 is evolving as it spreads through the human population, resulting in the emergence of multiple variants. A new virus variant of SARS-CoV-2 has one or more mutations that differentiate it from the original Wuhan isolate (Wuhan-Hu1) or predominant virus variants already circulating in the general population. Variants of SARS-CoV-2 are identified by genomic sequences that contain mutation(s) in the RNA genome, which could result in amino acid substitutions, insertions, and/or deletions in viral proteins. Mutations in genomic regions encoding for viral proteins that are targeted by therapeutics are of particular concern as the mutations may result in resistance to these therapies. Consequently, FDA is revising the LOA to include two new conditions on the monitoring and assessment of emerging global viral variants, as follows:

P. 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.

Q. 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.

Regulatory Conclusion:

Consistent with section 564(g) of the FD&C Act, FDA will be re-issuing the Letter of Authorization for EUA 94, dated February 9, 2021, in its entirety to include the revisions detailed above. These revisions, among other things, revise the process for the development and dissemination of instructional and educational materials and facilitate the Agency's evaluation of any emerging global viral variants, including the assessment and potential impact on the authorized bamlanivimab and etesevimab.

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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