

09 February 2021

IMPORTANT PRESCRIBING INFORMATION

**Subject: New Treatment Option of Bamlanivimab and Etesevimab Together;
Preventing Medication Errors with Bamlanivimab Alone and
Bamlanivimab and Etesevimab Together**

Dear Health Care Provider:

This notice is to alert you of a new treatment option, bamlanivimab and etesevimab together.

Bamlanivimab alone, as well as bamlanivimab and etesevimab administered together, are authorized 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.

Bamlanivimab and etesevimab are monoclonal antibodies that bind to different but overlapping epitopes of the receptor binding domain of the spike protein of SARS-CoV-2. The main benefit of using bamlanivimab and etesevimab together is to reduce the potential risk of emergent resistant variants. Emergent variants were less frequently detected in patients who received bamlanivimab and etesevimab together compared to patients who received bamlanivimab alone or received placebo in clinical trials. In addition, administration of bamlanivimab and etesevimab together may protect against treatment failure, should a patient be infected with a SARS-CoV-2 viral variant that is resistant to bamlanivimab alone. Supply may be limited in your clinical setting and it is therefore recommended that you use the product that is available to you.

This notice summarizes the differences between bamlanivimab alone and bamlanivimab and etesevimab together with respect to dosage, packaging, preparation, and administration, in order to prevent medication errors. This letter is being provided to you at the request of the U.S Food and Drug Administration (FDA).

- Bamlanivimab is authorized both alone (Emergency Use Authorization [EUA] 90) and together with etesevimab (EUA 94) for the authorized use stated above, in the same patient population.
- Etesevimab is not authorized for use alone; etesevimab is only authorized for use together with bamlanivimab under the EUA 94 issued on 09 February 2021.
- Bamlanivimab and etesevimab are packaged separately. Administration of bamlanivimab 700 mg with etesevimab 1,400 mg requires 1 vial of bamlanivimab and 2 vials of etesevimab. **The contents of all 3 vials must be added into a prefilled infusion bag**

containing 0.9% Sodium Chloride, and then administered via a single intravenous (IV) infusion (Table 1).

- Due to the difference in drug volume added for bamlanivimab alone versus bamlanivimab and etesevimab together, the infusion times are different, and are dependent on the size of the prefilled infusion bag containing 0.9% Sodium Chloride..
- It is important for health care providers to reference the correct fact sheet for detailed instructions on dosage, preparation, and administration of bamlanivimab alone and bamlanivimab and etesevimab together (Table 1).

Table 1 provides a summary highlighting the differences in dosage and presentation between bamlanivimab alone and bamlanivimab and etesevimab together.

Table 1 Summary of Differences in Dosage and Presentation of Bamlanivimab Alone and Bamlanivimab and Etesevimab Administered Together

	bamlanivimab alone (EUA 90)	bamlanivimab and etesevimab administered together (EUA 94)
Concentration per vial	700 mg/20mL bamlanivimab	700 mg/20mL bamlanivimab; 700mg/20mL etesevimab (packaged separately)
Authorized dose	700 mg bamlanivimab	700 mg bamlanivimab and 1,400 mg etesevimab together
Number of vials to prepare a treatment dose	1 vial (20 mL) bamlanivimab	1 vial (20 mL) bamlanivimab and 2 vials (40 mL) etesevimab prepared and administered together (60 mL total)
US Fact Sheet Links with detailed preparation and administration instructions	www.bamlanivimab.com OR https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs	www.BAMandETE.com OR https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs

Emergency Use Authorizations

Bamlanivimab Authorized Use (EUA 90)

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved product bamlanivimab 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.

Bamlanivimab and Etesevimab Authorized Use (EUA 94)

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved products bamlanivimab and etesevimab to be 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.

Bamlanivimab and Etesevimab Are Packaged Separately; However, Etesevimab Must Be Administered with Bamlanivimab

Pictures of the vial and carton labels are included with this letter. Please note that the bamlanivimab vial label has a black background, while the etesevimab vial label has a large red background to assist in differentiation.

When preparing to administer bamlanivimab alone, the current authorized dose is 700 mg. You will need **1** vial of bamlanivimab (700 mg/20 mL) for a single IV dose.

When preparing to administer bamlanivimab and etesevimab together, the current authorized dose is bamlanivimab 700 mg and etesevimab 1,400 mg. You will need **1** vial of bamlanivimab (700 mg/20 mL) and **2** vials of etesevimab (700 mg/20 mL). Contents of all 3 vials (60 mL) are required for a single IV infusion dose.

Health Care Provider Action

Health care providers should consider the following strategies in order to mitigate the risk of a possible medication error:

- Store etesevimab together with bamlanivimab in inventory.
- Create alerts in the electronic health record systems for HCPs that bamlanivimab can be used alone or together with etesevimab, but etesevimab can only be used with bamlanivimab.

Reporting Adverse Events and Medication Errors

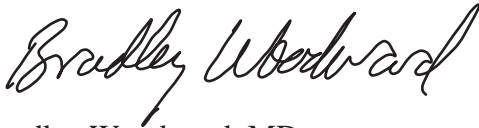
Under the EUA, all serious adverse events and medication errors potentially related to bamlanivimab and etesevimab treatment must be reported within 7 calendar days from the onset of the event. Serious adverse event reports and medication error reports should be submitted to FDA's MedWatch program using one of the following methods:

- Complete and submit the report online: www.fda.gov/medwatch/report.htm, or
- Use a postage-paid Form FDA 3500 (available at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf>) and return by mail (MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787, or by fax (1-800-FDA-0178), or
- Call 1-800-FDA-1088 to request a reporting form.

Health care providers can also report serious adverse events and medication errors when utilizing bamlanivimab and etesevimab to Eli Lilly and Company by calling 1-855-LillyC19 (1-855-545-5921). Copies of the FDA MedWatch forms should be provided to Eli Lilly and Company via fax at 1-317-277-0853 or via email at mailindata_gsmtindy@lilly.com.

Health care providers should direct questions about bamlanivimab and etesevimab packaging and use to Eli Lilly and Company at 1-855-LillyC19 (1-855-545-5921). Additional information on the use of bamlanivimab alone can be found at www.bamlanivimab.com and of bamlanivimab and etesevimab together at www.BAMandETE.com.

Sincerely,

A handwritten signature in black ink that reads "Bradley Woodward". The signature is written in a cursive, flowing style.

Bradley Woodward, MD

Vice President, Global Patient Safety
Eli Lilly and Company

Reference Images of Vial and Carton Labels



YL052IPAM00 Lot/Exp	NDC 0002-7910-01 bamlanivimab injection 700 mg/20 mL (35 mg/mL)	Prescription only Storage: Refrigerate unopened vials at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. Do not freeze or expose to direct heat. Refer to www.bamlanivimabHCPinfo.com for dosage and administration. KEEP OUT OF THE REACH OF CHILDREN Contents: Each mL contains 35 mg bamlanivimab, L-histidine (0.4 mg), L-histidine hydrochloride monohydrate (0.6 mg), sodium chloride (2.9 mg), sucrose (60 mg), polysorbate 80 (0.5 mg), and water for injection. No preservative. No standard of potency. Eli Lilly and Company, Indianapolis, IN 46285, USA
	For Intravenous Infusion Only Must dilute before use Single-Dose Vial: Discard Unused Portion For use under Emergency Use Authorization (EUA). <i>Lilly</i>	(01) 10300027910014



NDC 0002-7950-01 *Lilly*

etesevimab injection
700 mg/20 mL
(35 mg/mL)

For Intravenous Infusion Only
Must dilute before use
Single-Dose Vial: Discard
Unused Portion
For use under Emergency
Use Authorization (EUA).
MUST ADMINISTER WITH BAMLANIVIMAB

YLO5E3IIPAM01
Lot/Exp

Prescription only
Storage: Refrigerate unopened vials at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. Do not freeze or expose to direct heat.
MUST ADMINISTER WITH BAMLANIVIMAB.
Refer to www.etesevimabHCPinfo.com for dosage and administration.
KEEP OUT OF THE REACH OF CHILDREN
Contents: Each mL contains 35 mg etesevimab, L-histidine (1.55 mg), L-histidine hydrochloride monohydrate (2.10 mg), sucrose (80.4 mg), polysorbate 80 (0.5 mg), and water for injection. No preservative. No standard of potency.
Eli Lilly and Company, Indianapolis, IN 46285, USA

(01) 10300027950010