

Frequently Asked Questions on the Emergency Use Authorization for Bamlanivimab and Etesevimab

Q. What is an Emergency Use Authorization (EUA)?

A: Under section 564 of the Federal Food, Drug & Cosmetic Act, the FDA may, pursuant to a declaration by the HHS Secretary based on one of four types of determinations, authorize an unapproved product or unapproved uses of an approved product for emergency use. In issuing an EUA, the FDA must determine, among other things, that the product may be effective in diagnosing, treating, or preventing a serious or life-threatening disease or condition caused by a chemical, biological, radiological, or nuclear agent; that the known and potential benefits, when used to treat, diagnose or prevent such disease or condition, outweigh the known and potential risks for the product; and that there are no adequate, approved, and available alternatives. Emergency use authorization is NOT the same as FDA approval or licensure.

Q. What does this EUA authorize?

A. The [EUA](#) authorizes Eli Lilly and Company's (Lilly's) bamlanivimab and etesevimab, administered together, for emergency use 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.

While bamlanivimab may currently be administered alone under a separate [EUA](#), etesevimab is not authorized for use alone and must be administered with bamlanivimab.

Q. How is high risk defined under the EUA?

A. High risk for progressing to severe COVID-19 and/or hospitalization is defined as patients who meet at least one of the following criteria:

- Have a body mass index (BMI) ≥ 35
- Have chronic kidney disease
- Have diabetes
- Have immunosuppressive disease
- Are currently receiving immunosuppressive treatment
- Are ≥ 65 years of age
- Are ≥ 55 years of age AND have
 - cardiovascular disease, or
 - hypertension, or
 - chronic obstructive pulmonary disease/other chronic respiratory disease.
- Are 12 – 17 years of age AND have
 - BMI ≥ 85 th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm, or
 - sickle cell disease, or
 - congenital or acquired heart disease, or
 - neurodevelopmental disorders, for example, cerebral palsy, or
 - a medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19), or
 - asthma, reactive airway or other chronic respiratory disease that requires daily medication for control.

Q. Are there limitations of the authorized use under this EUA?

A. Yes. Bamlanivimab and etesevimab administered together are not authorized for use in patients:

- who are hospitalized due to COVID-19, or
- who require oxygen therapy due to COVID-19, or
- who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.

Treatment with bamlanivimab and etesevimab, administered together, has not been shown to provide benefit 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.

Q. Are bamlanivimab and etesevimab monoclonal antibodies? What is a monoclonal antibody?

A. Yes, bamlanivimab and etesevimab are monoclonal antibodies. Monoclonal antibodies are laboratory-produced molecules engineered to serve as substitute antibodies that can restore, enhance or mimic the immune system's attack on pathogens. Bamlanivimab and etesevimab are designed to block viral attachment and entry into human cells, thus neutralizing the virus.

Q. When should bamlanivimab and etesevimab be administered to a patient?

A. It is recommended that bamlanivimab and etesevimab be administered as soon as possible after positive viral test for SARS-CoV-2 and within 10 days of symptom onset. Bamlanivimab (700 mg) and etesevimab (1,400 mg) are administered together as a single intravenous infusion. More information about administration is available in the [Fact Sheet for Health Care Providers](#).

Q. Where are infusions of bamlanivimab and etesevimab available?

A. The following websites contain information regarding access to monoclonal antibody treatments for COVID-19:

- HHS Protect Public Data Hub – Therapeutics Distribution: <https://protect-public.hhs.gov/pages/therapeutics-distribution>
- National Infusion Center Association (NICA): <https://covid.infusioncenter.org/>

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 have the ability to activate the emergency medical system (EMS), if necessary. Please speak with your doctor or contact your local or state public health department for more information.

Q. Are bamlanivimab and etesevimab approved by the FDA to treat COVID-19?

A. No. Bamlanivimab and etesevimab are investigational drugs. They are not currently FDA-approved to treat any diseases or conditions, including COVID-19.

Q. Does the EUA permit the use of bamlanivimab and etesevimab as authorized in patients hospitalized for reasons other than COVID-19?

A. Bamlanivimab and etesevimab, administered together, are authorized for emergency use 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. If a patient is hospitalized *for reasons other than COVID-19*, such as for an elective orthopedic procedure, and the patient reports mild to moderate

symptoms of COVID-19, confirmed with positive results of a direct SARS-CoV-2 viral test, then it may be appropriate for treatment with bamlanivimab and etesevimab, administered together, if the patient is also at high risk for progressing to severe COVID-19 and/or hospitalization and the terms and conditions of the authorization are met, as detailed in the [Fact Sheet for Health Care Providers](#).

Bamlanivimab and etesevimab, administered together, are not authorized for use in patients:

- who are hospitalized *due to* COVID-19, or
- who require oxygen therapy *due to* COVID-19, or who require an increase in baseline oxygen flow rate *due to* COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.

Q. Are there data showing bamlanivimab and etesevimab, administered together, might benefit patients with COVID-19?

A. Yes. The strongest evidence supporting the issuance of this EUA for bamlanivimab and etesevimab, administered together, comes from the phase 3 portion of a randomized, double-blind, placebo-controlled clinical trial (BLAZE-1) in 1,035 non-hospitalized adults with mild to moderate COVID-19 symptoms who were at high risk for progressing to severe COVID-19. Of these patients, 518 received a single infusion of bamlanivimab 2,800 mg and etesevimab 2,800 mg together and 517 received placebo. The primary endpoint was COVID-19 related hospitalizations or death by any cause during 29 days of follow-up. Hospitalization or death occurred in 36 (7%) patients who received placebo compared to 11 (2%) patients treated with bamlanivimab 2,800 mg and etesevimab 2,800 mg administered together ($p < 0.001$), a 70% reduction. All deaths ($n = 10$, 2%) occurred in the placebo group. Thus, all-cause mortality was significantly lower in the bamlanivimab 2,800 mg and etesevimab 2,800 mg group than the placebo group ($p < 0.001$). In addition, patients that received bamlanivimab 2,800 mg and etesevimab 2,800 mg together had a faster time to symptom resolution in the clinical trial.

The authorized dose of bamlanivimab 700 mg and etesevimab 1,400 mg, administered together, in addition to bamlanivimab 2,800 mg and etesevimab 2,800 mg, administered together, was studied in another randomized, double-blind, placebo-controlled clinical trial (BLAZE-4) in non-hospitalized patients with mild to moderate COVID-19 symptoms, with and without risk factors for progression of COVID-19 disease. Reduction of viral load was comparable for both the authorized dose of bamlanivimab 700 mg and etesevimab 1,400 mg, administered together, and the higher bamlanivimab 2,800 mg and etesevimab 2,800 mg dose, administered together. Based on the similar virological response to treatment in BLAZE-4 (at doses of bamlanivimab 700 mg and etesevimab 1400 mg) to that seen in BLAZE-1 (at doses of bamlanivimab 2800 mg and etesevimab 2800 mg), and the treatment benefit on hospitalization and death in BLAZE-1, as well as supportive pharmacokinetic/pharmacodynamic modeling, the authorized dosage of bamlanivimab 700 mg and etesevimab 1,400 mg, administered together, is expected to have similar clinical effect to a dosage of bamlanivimab 2,800 mg and etesevimab 2,800 mg, administered together.

Q. Why was the EUA issued for the dosage of 700 mg bamlanivimab and 1,400 mg etesevimab, administered together, and not a higher dose of both monoclonal agents (2800 mg)?

A. The dosage of 700 mg bamlanivimab and 1,400 mg etesevimab, administered together, was selected based on analyses of available data incorporating the following factors:

- Available clinical data from trials BLAZE-1 and BLAZE-4 demonstrate that a dosage of 700 mg bamlanivimab and 1,400 mg etesevimab administered together has similar antiviral activity to a

dosage of 2,800 mg bamlanivimab and 2,800 mg etesevimab administered together, which is also supported by in vitro data and pharmacokinetics/pharmacodynamics (PK/PD) modeling.

- A dosage of 2,800 mg bamlanivimab and 2,800 mg etesevimab administered together reduced COVID-19 related hospitalizations and deaths in addition to significantly reducing viral load relative to placebo.
- Bamlanivimab and etesevimab administered together resulted in fewer treatment-emergent variants relative to bamlanivimab alone.

Based on analyses of the available pre-clinical, clinical, and virologic data, as well as supportive data from pharmacokinetic/pharmacodynamic modeling, the authorized dosage of 700 mg bamlanivimab and 1,400 mg etesevimab, administered together, is expected to have similar clinical effect to a dosage of 2,800 mg bamlanivimab and 2,800 mg etesevimab, administered together.

See Sections 14.2, 15, and 18.1 of the [Fact Sheet for Health Care Providers](#) for additional information.

Q. Are there clinical trials underway evaluating bamlanivimab and etesevimab for COVID-19?

A. Yes. [Clinical trials](#) remain ongoing to study bamlanivimab and etesevimab for investigational uses.

Q. What is the difference between treatment with bamlanivimab alone and bamlanivimab and etesevimab administered together?

A. Based on the totality of scientific evidence available, both bamlanivimab alone, as well as bamlanivimab and etesevimab administered together, are expected to provide a benefit 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.

A potential difference between bamlanivimab alone and bamlanivimab and etesevimab, administered together, is the difference in the risk for 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 during the clinical trial development program. Although not yet evaluated in clinical trials, treatment with 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. It is recommended that sites use the monoclonal antibody product that is available.

The authorization of bamlanivimab alone, which occurred on November 9, 2020, was primarily based on data from the phase 2 portion of BLAZE-1, a randomized, double-blind, placebo-controlled trial that enrolled patients with mild to moderate COVID-19, with and without risk factors for disease progression. While viral load was used to define the primary endpoint in this phase 2 trial, the most important evidence that bamlanivimab may be effective came from the predefined secondary endpoint of COVID-19-related hospitalizations or emergency room visits within 28 days after treatment. A lower proportion of bamlanivimab-treated subjects progressed to COVID-19-related hospitalization or emergency room visits compared to placebo-treated subjects.

The authorization of bamlanivimab and etesevimab administered together was primarily based upon clinical outcomes data from the phase 2/3 BLAZE-1 trial. In the phase 2 portion of the trial, which enrolled patients with mild to moderate COVID-19 with and without risk factors for disease progression,

a lower incidence of hospitalizations and emergency room visits was seen in patients who were administered bamlanivimab and etesevimab together compared to those who received placebo. The rates of hospitalization and emergency room visits were comparable in individuals given bamlanivimab alone compared to bamlanivimab and etesevimab administered together.

The phase 3 portion of the trial exclusively enrolled patients with mild to moderate COVID-19 symptoms who were at high risk for disease progression and compared bamlanivimab and etesevimab administration together to placebo. The primary endpoint was COVID-19 related hospitalizations or death by any cause during 29 days of follow-up. Hospitalization or death occurred in 36 (7%) patients who received placebo compared to 11 (2%) patients treated with bamlanivimab 2,800 mg and etesevimab 2,800 mg administered together, a 70% reduction. In this high-risk patient population, all 10 deaths (2%) deaths occurred in the placebo group. Thus, all-cause death was significantly lower in the bamlanivimab and etesevimab arm than in the placebo arm.

Q. Are there side effects of bamlanivimab and etesevimab?

A. Over 1,500 non-hospitalized subjects have received bamlanivimab and etesevimab administered together in clinical trials at doses of bamlanivimab 700 mg and etesevimab 1,400 mg or higher. Bamlanivimab and etesevimab at the authorized doses of 700 mg and 1,400 mg have been administered together to approximately 770 subjects.

Serious hypersensitivity reactions, including anaphylaxis, have been observed with administration of bamlanivimab with and without etesevimab. Infusion-related reactions have been observed with administration of bamlanivimab and etesevimab. These reactions may be severe or life threatening.

Based on reporting of adverse events that occurred after administration of bamlanivimab alone under EUA, clinical worsening of COVID-19 after administration of bamlanivimab has been reported and may include signs or symptoms of fever, hypoxia or increased respiratory difficulty, arrhythmia (e.g., atrial fibrillation, sinus tachycardia, bradycardia), fatigue, and altered mental status. Some of these events required hospitalization. It is not known if these events were related to bamlanivimab use or were due to progression of COVID-19.

Nausea, dizziness, and rash were the most commonly reported adverse events after administration of bamlanivimab and etesevimab together.

Q. Will there be adequate supply of bamlanivimab and etesevimab for all patients covered under the EUAs to receive the drugs?

A. At this time there is adequate supply to ensure any patient covered under this [authorization](#) or the bamlanivimab [EUA](#) may receive bamlanivimab alone or bamlanivimab and etesevimab administered together.

Q. Are bamlanivimab and etesevimab co-packaged?

A. At this time, bamlanivimab is not co-packaged with etesevimab under this EUA. While these products are not co-packaged, etesevimab cannot be used alone and must be administered with bamlanivimab.

Q. Bamlanivimab and etesevimab administered together are authorized 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. What does direct SARS-CoV-2 viral testing mean?

A: Direct SARS-CoV-2 viral tests diagnose active COVID-19 infection. Direct SARS-CoV-2 viral tests include two types of diagnostic tests for COVID-19:

- Molecular tests, such as RT-PCR tests, that detect the virus's genetic material
- Antigen tests that detect specific proteins from the virus.

Antibody tests should not be used to diagnose COVID-19 and are not direct SARS-CoV-2 viral tests. Antibody tests look for antibodies made by the immune system in response to the SARS-CoV-2 virus.

Q. Are there reporting requirements for healthcare facilities and providers as part of the EUA?

A. Yes. As part of the EUA, FDA requires health care providers who prescribe bamlanivimab and etesevimab together to report all medication errors and serious adverse events considered to be potentially related to bamlanivimab and etesevimab through FDA's [MedWatch Adverse Event Reporting](#) program. Providers can complete and submit the report [online](#); or download and complete the [form](#), then submit it via fax at 1-800-FDA-0178. This requirement is outlined in the EUA's health care provider [Fact Sheet](#). FDA MedWatch forms should also be provided to Lilly.

Healthcare facilities and providers must report therapeutics information and utilization data as directed by the U.S. Department of Health and Human Services. Such information and data should be reported through HHS Protect, Teletracking or National Healthcare Safety Network (NHSN).

Q. Do patient outcomes need to be reported under the EUA?

A. No, reporting of patient outcomes is not required under the EUA. However, reporting of all medication errors and serious adverse events considered to be potentially related to bamlanivimab and etesevimab, administered together, occurring during treatment is required.

Q. Does the EUA authorize bamlanivimab and etesevimab, administered together, to be used to prevent COVID-19?

A. No. Use of bamlanivimab and etesevimab, administered together, for the prevention of COVID-19 is not authorized.

Q. Can health care providers share the patient/caregiver Fact Sheet electronically?

A. The letter of authorization for bamlanivimab and etesevimab, administered together, requires that Fact Sheets be made available to [health care providers](#) and to [patients/caregivers](#) "through appropriate means." Electronic delivery of the Fact Sheet is an appropriate means. For example, when the patient requests the Fact Sheet electronically, it can be delivered as a PDF prior to medication administration. Health care providers should confirm receipt of the Fact Sheet with the patient.

Q. Is there likely to be an increased risk of infusion-related reactions with shorter versus longer infusion times?

A. FDA does not anticipate an increased risk of infusion-related reactions with the shorter infusion times or use of different size saline bags for dilution authorized. The preparation and administration instructions, including the shorter durations of infusion with smaller volumes of diluent were based on data evaluated by FDA including product quality data and data from clinical trials.

Q. Can I receive a COVID-19 vaccine if I was treated with a monoclonal antibody for COVID-19?

A. Currently, there are no data on the safety and effectiveness of either the Pfizer-BioNTech, Moderna, or Janssen COVID-19 vaccines in people who received monoclonal antibodies authorized by FDA for emergency use as part of COVID-19 treatment (bamlanivimab, casirivimab and imdevimab, or bamlanivimab and etesevimab). Under the conditions of the emergency use authorization (EUA) for each monoclonal antibody product, patients treated should have had a documented positive test for COVID-19 infection. [Data available to the agency](#) suggests that reinfection with SARS-CoV-2 is uncommon in the 90 days after initial infection. Based upon this low risk of reinfection and the estimated half-life of the monoclonal antibodies, the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices (ACIP) [recommends](#) COVID-19 vaccination be deferred for at least 90 days after treatment with a monoclonal antibody for COVID-19. This is a precautionary measure to avoid interference of monoclonal antibody treatment specifically with vaccine-induced immune responses. Updates to this recommendation may be made as additional information on the interaction between prior monoclonal antibody treatment and vaccine response becomes available.