U.S. FOOD & DRUG ADMINISTRATION

Frequently Asked Questions on the Emergency Use Authorization for Bamlanivimab

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 bamlanivimab, manufactured by Eli Lilly and Company (Lilly), for emergency use for the treatment of mild to moderate COVID-19 in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

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 ≥85th 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 is 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.

A benefit of treatment with bamlanivimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

Q. Is bamlanivimab a monoclonal antibody? What is a monoclonal antibody?
A. Yes, bamlanivimab is a monoclonal antibody. 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 is designed to block viral attachment and entry into human cells, thus neutralizing the virus.

Q. When should bamlanivimab be administered to a patient?
A. It is recommended that bamlanivimab be administered as soon as possible after positive viral test for SARS-CoV-2 and within 10 days of symptom onset. Bamlanivimab is administered as a single dose of 700 mg via IV infusion. More information about administration is available in the Health Care Provider Fact Sheet.

Q. Where are infusions of bamlanivimab 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 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 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. Is bamlanivimab approved by the FDA to treat COVID-19?
A. No. Bamlanivimab is an investigational drug. It is not currently FDA-approved to treat any diseases or conditions, including COVID-19.

However, upon issuance of the EUA, bamlanivimab is authorized for emergency use for the treatment of mild to moderate COVID-19 in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

Q. Does the EUA permit the use of bamlanivimab as authorized in patients hospitalized *for reasons other* than COVID-19?
A: Bamlanivimab is 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, 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 is 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 might benefit patients with COVID-19?
A. The data supporting this EUA are based on an interim analysis from Part A of the BLAZE-1 clinical trial that occurred after all enrolled patients completed at least Day 29 of the trial.

BLAZE-1 Part A was a randomized, double-blind, placebo-controlled clinical trial studying bamlanivimab for the treatment of ambulatory patients with mild to moderate COVID-19. BLAZE-1 enrolled adult patients who were not hospitalized and had 1 or more mild or moderate COVID-19 symptoms. Treatment was initiated within 3 days of obtaining the first positive clinical sample for SARS-CoV-2 viral infection determination. Patients were treated with a single infusion of bamlanivimab (at doses of 700 mg [N=101], 2800 mg [N=107], or 7000 mg [N=101]) or placebo [N=156]).

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. Among patients who were at high risk for disease progression, hospitalizations and emergency room visits occurred in 3% of bamlanivimab-treated patients compared to 10% in placebo-treated patients. The primary endpoint was change in viral load from baseline to Day 11 for bamlanivimab versus placebo. Most patients, including those receiving placebo, effectively cleared the virus by Day 11. The effects on viral load and on reduction in hospitalizations and ER visits, and the safety profile, were similar in patients receiving any of the three bamlanivimab doses.

Based on the totality of the scientific evidence available, FDA determined that it is reasonable to believe that bamlanivimab may be effective for the treatment of mild to moderate COVID-19 in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

Q. Why was the EUA issued for bamlanivimab 700mg dose, and not a higher dose (2800 mg)?
A. A Phase 2 trial (BLAZE-1) evaluated bamlanivimab over a dose range of 1 to 10 times the authorized dose (700 to 7000 mg) of bamlanivimab in patients with mild to moderate COVID-19. A flat exposure-response relationship for efficacy was identified for bamlanivimab within this dose range, based on viral load and clinical outcomes. This means that no meaningful differences were seen between doses with respect to key endpoints. The effects on viral load and on reduction in hospitalizations and ER visits, and the safety profile, were similar in patients receiving any of the three bamlanivimab doses.

See Sections 14.2 and 18.1 of bamlanivimab's Health Care Provider Fact Sheet for additional information.

Q. Are there clinical trials underway evaluating bamlanivimab for COVID-19?
A. Yes. Clinical trials remain ongoing to study bamlanivimab for investigational uses.

Q. Was the bamlanivimab arm of a clinical trial (ACTIV-3) terminated?
A. Yes. The National Institute of Allergy and Infectious Diseases (NIAID)-sponsored ACTIV-3 clinical trial is a platform trial designed to test the safety and efficacy of various investigational agents, including bamlanivimab, for the treatment of patients ***hospitalized*** with COVID-19. The trial was paused on October 13, 2020, by the independent Data Safety Monitoring Board (DSMB). On October 26, 2020, it was announced that no additional patients in ACTIV-3 would receive bamlanivimab. This recommendation was based on trial data suggesting that bamlanivimab is unlikely to help ***hospitalized*** COVID-19 patients recover from a more advanced stage of disease.

The population being studied in the ACTIV-3 trial is different than the population authorized to use bamlanivimab under the EUA. The EUA authorizes emergency use for the treatment of mild to moderate COVID-19 in ***non-hospitalized*** adult and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization, while the ACTIV-3 trial studied ***hospitalized*** patients with COVID-19. This EUA request was based on the interim results from Lilly's BLAZE-1 clinical trial that includes non-hospitalized patients. The EUA limits the authorized use of bamlanivimab. Bamlanivimab is 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. Monoclonal antibodies, such as bamlanivimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

Q. Are there side effects of bamlanivimab?
A. Over 850 participants in clinical trials have been treated with a single dose of bamlanivimab 700 mg or higher in clinical trials. Across this total safety database, one anaphylaxis reaction and one serious infusion-related reaction have been reported during infusion of bamlanivimab. The infusions were stopped. Both reactions required treatment, one required epinephrine. Both events resolved.

In BLAZE-1, there were no serious infusion-related reactions. The most commonly reported (in 2-4% of subjects) adverse events during these trials were nausea, diarrhea, dizziness, headache, pruritus, and vomiting. Clinical studies evaluating the safety of bamlanivimab are ongoing, so it is possible all of the risks in using the drug to treat COVID-19 are not known at this time.

Q. How can bamlanivimab be obtained for use under the EUA?
A. HHS will review case counts and severity of outbreaks across the U.S. and make allocations accordingly to state and territorial health departments. State and territorial health departments will allocate to healthcare facilities. AmeriSource Bergen will distribute bamlanivimab for the U.S. Government.

Q. Will there be adequate supply of bamlanivimab for all patients covered under the EUA to receive the drug?
A. HHS recently announced that the Biomedical Advanced Research and Development Authority (BARDA), part of the HHS Office of the Assistant Secretary for Preparedness and Response, collaborated with the DoD Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense and Army Contracting Command to purchase 300,000 doses of bamlanivimab from Lilly over the next two months. Under the agreement, the federal government can purchase up to 650,000 additional doses through the end of June 2021. FDA is closely monitoring Lilly's efforts to increase the supply of bamlanivimab so all patients who need it and are within the scope of the authorization can receive the drug if appropriate.

Q: Bamlanivimab is authorized for the treatment of mild to moderate COVID-19 in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40 kg, 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 to report all medication errors and serious adverse events considered to be potentially related to bamlanivimab 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 occurring during bamlanivimab treatment is required.

Q. Does the EUA authorize bamlanivimab to be used to prevent COVID-19?
A. No. Use of bamlanivimab 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 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. 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.