



Lilly Bamlanivimab and Etesevimab Together Antibody Playbook

ELI LILLY AND COMPANY | MARCH 2021

For the Emergency Use Authorization of bamlanivimab and etesevimab together for the treatment of COVID-19

The Secretary of the Department of Health and Human Services has declared a public health emergency that justifies the emergency use of bamlanivimab and etesevimab together to treat coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 infection. In response, the US Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) for the unapproved products, bamlanivimab and etesevimab administered together, for the treatment of COVID-19.

- Bamlanivimab and etesevimab together have not been approved, but have been authorized for emergency use by FDA, to treat mild to moderate COVID-19 in adults, and also 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 together are authorized for the treatment of mild to moderate COVID-19 in adults, and also 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 only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of bamlanivimab and etesevimab together under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

The FDA issued this EUA, requested by Eli Lilly and Company and based on their submitted data. Find more information in the [FDA Letter of Authorization](#). Healthcare providers should review the [Fact Sheet for Healthcare Providers](#) for important information on the authorized use of bamlanivimab and etesevimab together and mandatory requirements of the EUA.

This document was developed by Eli Lilly and Company as a resource for health programs to respond to the COVID-19 pandemic using bamlanivimab and etesevimab antibody treatment. **The recommendations in this document apply only to bamlanivimab and etesevimab when administered together.**

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EXECUTIVE SUMMARY

The world is currently in the midst of a global pandemic. As a global pharmaceutical company, we feel a responsibility to do our part to relieve the burden COVID-19 has placed on countries, communities and families around the world.

Clinical trials have shown that monoclonal antibodies may be effective in treating COVID-19. Lilly in partnership with AbCellera, Junshi Biosciences and IMCAS has developed monoclonal antibodies called bamlanivimab and etesevimab. Bamlanivimab and etesevimab are recombinant neutralizing human IgG1 monoclonal antibodies directed against the spike protein of SARS-CoV-2. They are designed to block viral attachment and entry into human cells, thus neutralizing the virus.

This Playbook provides information for state, territorial and local public health programs to plan and operationalize a response to COVID-19 using bamlanivimab and etesevimab together. The sections of this document cover specific areas of COVID-19 antibody program planning and implementation, as well as links to resources to assist with those efforts. The sections described in this Playbook may also overlap with routine monoclonal antibody treatment and infusion program activities. This Playbook represents guidance based on Lilly's Clinical Trial experience in monoclonal antibody treatments and should not supersede local recommendations for infusion sites of care. Please defer to local guidelines.

Healthcare providers should review the [Fact Sheet](#) for information on the authorized use of bamlanivimab and etesevimab together and mandatory requirements of the EUA.

In addition, the Playbook includes information regarding planning and implementation based on varying infusion sites of care, such as:

- Existing hospital or community-based infusion sites of care
- Existing clinical space (e.g., primary care practices affiliated with hospital systems, urgent care locations, emergency departments, surgery centers, dialysis centers, plasma centers, respiratory clinics and other healthcare delivery entities approved to administer infusion therapies)
- Long term care facilities

We expect most infusion treatments will be administered in one of these aforementioned sites of care, but other infusion sites of care may also be considered. **This Playbook provides information that may or may not be applicable to certain spaces depending on existing capabilities.**

SECTION 01

Population for Antibody Treatment and Regulatory Notices

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POPULATION FOR ANTIBODY TREATMENT & REGULATORY NOTICES

This EUA is for the use of the unapproved products, bamlanivimab and etesevimab, to be administered together for the treatment of mild to moderate COVID-19 in adults, and also 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.

Limitations of Authorized Use

- Bamlanivimab and etesevimab 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 has not been studied in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab and etesevimab, may be associated with worse clinical outcomes with COVID-19 hospitalized patients requiring high flow oxygen or mechanical ventilation.

For more information, reference the [Fact Sheet for Healthcare Providers](#).

Antiviral Resistance

Circulating SARS-CoV-2 viral variants may be associated with resistance to monoclonal antibodies. Healthcare providers should review the Antiviral Resistance information in Section 15 of the [Fact Sheet for Healthcare Providers](#) for details regarding specific variants and resistance, and refer to the [CDC website](#) as well as information from state and local health authorities regarding reports of viral variants of importance in their region to guide treatment decisions.

Patient Selection

High risk 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.

Bamlanivimab and etesevimab must be administered together after dilution by intravenous (IV) infusion only.

Bamlanivimab and etesevimab together 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 the ability to activate the emergency medical system (EMS), as necessary.

Health care providers must submit a report on all medication errors and **ALL SERIOUS ADVERSE EVENTS** potentially related to bamlanivimab and etesevimab together. See Sections 8 and 9 of the Full EUA Prescribing Information for reporting instructions below.

The authorized dosage is 700 mg bamlanivimab and 1,400 mg etesevimab administered together as a single intravenous (IV) infusion as soon as possible after positive viral test for SARS-CoV-2 and within ten days of symptom onset.

Rationale for Authorized Dose

- The dosage of 700 mg bamlanivimab and 1,400 mg etesevimab together was selected based on analyses of available data incorporating the following factors:
 - Available clinical data demonstrate that a dosage of 700 mg bamlanivimab and 1,400 mg etesevimab administered together has similar clinical effect 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 together reduced COVID-19 related hospitalizations and deaths in addition to significantly reducing viral load relative to placebo.
 - Bamlanivimab and etesevimab 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 PK/PD modeling, the authorized dosage of 700 mg bamlanivimab and 1,400 mg etesevimab is expected to have similar clinical effect to a dosage of 2,800 mg bamlanivimab and 2,800 mg etesevimab.

Preparation and Administration

- The authorized dosage is 700 mg bamlanivimab and 1,400 mg etesevimab administered together as a single intravenous (IV) infusion as soon as possible after positive viral test for SARS-CoV-2 and within ten days of symptom onset.
- Bamlanivimab and etesevimab are both available as solutions in separate vials and must be administered with dilution in 0.9% Sodium Chloride Injection. Vial labels and cartons may state that the product must be diluted before use. The information in the [Fact Sheet](#) regarding preparation of material supersedes the carton and container labeling.
- To prepare the dose you will need 1 vial of bamlanivimab and 2 vials of etesevimab.
- Administer bamlanivimab and etesevimab together via intravenous (IV) infusion over 21-70 minutes via pump or gravity (see Table 1 and Table 2).
- Clinically monitor patients during administration and observe patients for at least 1 hour after infusion is complete.
- Patients treated with bamlanivimab and etesevimab together should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect “high touch” surfaces, and frequent handwashing) according to CDC guidelines.

For full Preparation and Administration information, please see **Section 3: Infusion Site of Care Recommendations**.

The authorized dosage may be updated as additional data from clinical trials becomes available.

For information on clinical trials that are testing the use of bamlanivimab and etesevimab together in COVID-19, please see www.clinicaltrials.gov.

†Patients with **mild** COVID-19 illness may exhibit a variety of signs and symptoms (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell). They do not have shortness of breath, dyspnea on exertion, or abnormal imaging.

Moderate COVID-19 illness is defined as evidence of lower respiratory disease during clinical assessment or imaging, with SpO₂ ≥94% on room air at sea level.

Source: National Institutes of Health

Mandatory Requirements for Bamlanivimab and Etesevimab Administration Together Under Emergency Use Authorization

In order to mitigate the risks of using these unapproved products under the EUA and to optimize the potential benefit of bamlanivimab and etesevimab to be administered together, the following items are required. Use of bamlanivimab and etesevimab together under this EUA is limited to the following (all requirements **must** be met):

1. Treatment of mild to moderate COVID-19 in adults, and also 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.

Limitations of Authorized Use

- Bamlanivimab and etesevimab 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 has not been studied in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab and etesevimab, may be associated with worse clinical outcomes with COVID-19 hospitalized patients requiring high flow oxygen or mechanical ventilation.
2. As the healthcare provider, communicate to your patient or parent/caregiver, as age appropriate, information consistent with the [Fact Sheet for Patients, Parents and Caregivers](#) prior to the patient receiving bamlanivimab and etesevimab together. Healthcare providers (to the extent practicable given the circumstances of the emergency) must document in the patient's medical record that the patient/caregiver has been:
 - a. Given the [Fact Sheet for Patients, Parents and Caregivers](#),
 - b. Informed of alternatives to receiving authorized bamlanivimab and etesevimab together, and
 - c. Informed that bamlanivimab and etesevimab are unapproved drugs that are authorized for use together under this Emergency Use Authorization.
 3. Patients with known hypersensitivity to any ingredient of bamlanivimab or etesevimab must not receive bamlanivimab and etesevimab together.
 4. The prescribing health care provider and/or the provider's designee are/is responsible for mandatory reporting of all medication errors and serious adverse events* potentially related to bamlanivimab and etesevimab treatment within 7 calendar days from the onset of the event. The reports should include unique identifiers and the words "Bamlanivimab and etesevimab treatment under Emergency Use Authorization (EUA)" in the description section of the report.

Submit adverse event reports to FDA MedWatch 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 it 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
- Submitted reports should include in the field name, “Describe Event, Problem, or Product Use/Medication Error” the statement “Bamlanivimab and etesevimab treatment under Emergency Use Authorization (EUA)”

***Serious Adverse Events are defined as:**

- death;
 - a life-threatening adverse event;
 - inpatient hospitalization or prolongation of existing hospitalization;
 - a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
 - a congenital anomaly/birth defect;
 - a medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability or congenital anomaly.
5. The prescribing health care provider and/or the provider’s designee are/is to provide mandatory responses to requests from FDA for information about adverse events and medication errors following receipt of bamlanivimab and etesevimab together.
6. Other Reporting Requirements
- Healthcare facilities and providers must report therapeutics information and utilization data through HHS Protect, Teletracking or National Healthcare Safety Network (NHSN) as directed by the U.S. Department of Health and Human Services.
 - **In addition, please provide a copy of all FDA MedWatch forms to:**
Eli Lilly and Company, Global Patient Safety
Fax: 1-317-277-0853
E-mail: mailindata_gsmtindy@lilly.com
Or call Eli Lilly and Company at 1-855-LillyC19 (1-855-545-5921) to report adverse events.

Approved Available Alternatives

There is no adequate, approved and available alternative to bamlanivimab and etesevimab to be administered together for patients who have mild to moderate COVID-19 who are at high risk for progressing to severe COVID-19 and/or hospitalization. Additional information on COVID-19 treatments can be found at <https://www.cdc.gov/coronavirus/2019-ncov/index.html>. The health care provider should visit <https://clinicaltrials.gov/> to determine whether the patient may be eligible for enrollment in a clinical trial.

Authority for Issuance of the EUA

The Secretary of the Department of Health and Human Services (HHS) has declared a public health emergency that justifies the emergency use of drugs and biological products during the COVID-19 pandemic. FDA has issued this EUA, requested by Eli Lilly and Company for the unapproved products, bamlanivimab and etesevimab together for the treatment of mild to moderate COVID-19 in adults, and also 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.¹ As a health care provider, you must comply with the mandatory requirements of the EUA (see above).

Although limited scientific information is available, based on the totality of the scientific evidence available to date, it is reasonable to believe that bamlanivimab and etesevimab together may be effective for the treatment of mild to moderate COVID-19 in certain high-risk patients as specified in this Fact Sheet. You may be contacted and asked to provide information to help with the assessment of the use of the product during this emergency.

This EUA for bamlanivimab and etesevimab together will end when the Secretary determines that the circumstances justifying the EUA no longer exist or when there is a change in the approval status of the product such that an EUA is no longer needed.

Contact Information

For additional information visit www.BAMandETE.com

If you have questions, please contact 1-855-LillyC19 (1-855-545-5921)

¹ The health care provider should visit clinicaltrials.gov to determine whether there is an active clinical trial for the product in this disease/condition and whether enrollment of the patient(s) in a clinical trial is more appropriate than product use under this EUA.

IMPORTANT SAFETY INFORMATION

There are limited clinical data available for bamlanivimab and etesevimab. Serious and unexpected adverse events may occur that have not been previously reported with the use of bamlanivimab and etesevimab together.

Hypersensitivity Including Anaphylaxis and Infusion-Related Reactions

Serious hypersensitivity reactions, including anaphylaxis, have been observed with administration of bamlanivimab with and without etesevimab. If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive therapy.

Infusion-related reactions have been observed with administration of bamlanivimab and etesevimab together. These reactions may be severe or life threatening.

Signs and symptoms of infusion-related reactions may include:

- fever, difficulty breathing, reduced oxygen saturation, chills, fatigue, arrhythmia (e.g. atrial fibrillation, sinus tachycardia, bradycardia), chest pain or discomfort, weakness, altered mental status, nausea, headache, bronchospasm, hypotension, hypertension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, dizziness, and diaphoresis.

If an infusion-related reaction occurs, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care.

Clinical Worsening After Bamlanivimab Administration

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.

Limitations of Benefit and Potential Risk in Patients with Severe COVID-19

Treatment with bamlanivimab and etesevimab has not been studied 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.

Limitations of Authorized Use

- Bamlanivimab and etesevimab 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 has not been studied in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab and etesevimab, may be associated with worse clinical outcomes with COVID-19 hospitalized patients requiring high flow oxygen or mechanical ventilation.

Adverse Events

Based on Phase 2 data from BLAZE-1, nausea was the most commonly reported adverse event, reported by 4% of subjects in both bamlanivimab and etesevimab treatment and placebo groups. Pruritus and pyrexia were more frequently reported from subjects treated with both bamlanivimab and etesevimab (2% and 1%) compared to placebo (1% and 0%, respectively).

Based on Phase 3 data from BLAZE-1, the most common adverse events were nausea, dizziness, and rash. These events each occurred in 1% of subjects treated with bamlanivimab and etesevimab and in 1% of placebo subjects.

Use in Specific Populations

Pregnancy

There are insufficient data to evaluate a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Bamlanivimab and etesevimab should only be used during pregnancy if the potential benefit outweighs the potential risk for the mother and the fetus.

Breastfeeding

There are no available data on the presence of bamlanivimab or etesevimab in human or animal milk, the effects on the breastfed infant, or the effects on milk production. Breastfeeding individuals with COVID-19 should follow practices according to clinical guidelines to avoid exposing the infant to COVID-19.

SECTION 02

Scaling Operations

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SCALING OPERATIONS

The time duration to administer a 700 mg / 20 mL dose of bamlanivimab and a 1,400 mg / 40 mL dose of etesevimab together is 21-70 minutes at the appropriate infusion rate for both infusion pumps and gravity infusion. Treatment also requires a post-infusion observation period. It is clinically recommended to monitor patients during administration and observe patients for at least 1 hour after infusion is complete. Sites of care should follow local recommendations when determining appropriate observation periods. If patients will occupy chairs for infusion during this period, rather than a post-treatment monitoring area, planning must account for this time as well.

The number of chairs for infusion can be scaled along with the hours of operation to determine the size of the infusion site of care. Infusion sites of care should take into account time for patient intake, IV preparation, infusion and post-infusion observation when determining potential capacity. For example, in Lilly's monoclonal antibody clinical trial settings, Lilly found a single infusion could take between 126–205 minutes to complete from patient intake to discharge. See Appendix A for more information.

The above values could be used to determine a rough approximation of the number of facilities that may be needed per region. A region can easily modify the number based on changing the capacity assumptions with the various facilities. Depending on the dispersion of the population in a region, the region may choose to size some facilities larger than others.

SECTION 03

Infusion Site of Care Recommendations

INFUSION SITE OF CARE RECOMMENDATIONS

Preparation, Storage and Handling

Prepare infusions using aseptic technique, in a manner consistent with local laws, regulations, guidelines and policies for outpatient infusion.

- Use aseptic technique and applicable good clinical practice for intravenous solution preparation of bamlanivimab and etesevimab together.
- Only use materials which are listed as compatible with bamlanivimab and etesevimab for preparation and administration of the infusion solutions (see “**Compatible Materials**” section below).
- Gather the materials for infusion:
 - Polyvinyl chloride (PVC) or polyethylene (PE)-lined PVC infusion set
 - Use of an in-line or add-on 0.20/0.22 micron polyethersulfone (PES) filter is strongly recommended.

Bamlanivimab and etesevimab have no known incompatibilities with traditional medical supplies and equipment. Infusion sites of care may determine based on medical best practices what supplies and equipment to use when administering bamlanivimab and etesevimab together, including add-on filter devices.

- Use new, sterile syringes and needles to prepare each dosing solution of bamlanivimab and etesevimab together.
- Refrigerate bamlanivimab and etesevimab drug products when not in use (2° to 8° C or 36° to 46° F).
- Bamlanivimab and etesevimab should be free of any visible particulate matter. Obtain new vial(s) and/or IV bags if the drug product contains any visible particulate matter.
- All medication must be stored, inventoried and destroyed according to applicable regulations.
- Bamlanivimab and etesevimab are administered together by intravenous (IV) infusion either using an infusion pump or gravity infusion. Consider use of a rate control or infusion rate monitoring device if using gravity infusion. Tubing with an integrated rate flow regulator can also be considered if an infusion pump is not available.
- The IV solutions are intended for immediate patient administration. If immediate administration is not possible, store diluted bamlanivimab and etesevimab infusion solutions for up to 24 hours at refrigerated temperature (2° C to 8° C [36° F to 46° F]) and up to 7 hours at room temperature (20° C to 25° C [68° F to 77° F]) including transportation and infusion time. If refrigerated, allow the infusion solutions to equilibrate to room temperature for approximately 20 minutes prior to administration. The hold time includes preparation, solution hold, infusion and flush.

Compatible Materials

Individual infusion sites of care should follow best medical practices when determining materials to use. Procurement of materials from a specific vendor or vendors is not required. If alternate materials are used, the compatibility of these materials should be confirmed with that vendor. Bamlanivimab and etesevimab have no known incompatibilities with conventional medical supplies and equipment. During clinical trials, Lilly has used the following materials:

- Polypropylene syringes
- Stainless steel needles
- Polyvinyl chloride (PVC) IV bags with or without DEHP
- Polyvinyl chloride (PVC) infusion sets with or without DEHP containing an in-line polyethersulfone (PES)* filter (Please see footnote.)

Storage

Bamlanivimab is preservative-free. Discard unused portion.

Etesevimab is preservative-free. Discard unused portion.

Store unopened vials in a refrigerator at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light.

DO NOT FREEZE, SHAKE, OR EXPOSE TO DIRECT LIGHT.

Solution in vial requires dilution prior to administration. The prepared infusion solution is intended to be used immediately. If immediate administration is not possible, store diluted infusion solution in the refrigerator at 2°C to 8°C (36°F to 46°F) for up to 24 hours and at room temperature (20°C to 25°C [68°F to 77°F]) and for up to 7 hours, including transportation and infusion time. If refrigerated, allow the infusion solution to equilibrate to room temperature prior to administration.

Preparation and Administration

Preparation

Bamlanivimab and etesevimab solution for infusion should be prepared by a qualified healthcare professional using aseptic technique.

The 700 mg dose of bamlanivimab and 1,400 mg dose of etesevimab MUST BE prepared using 0.9% Sodium Chloride.

- [Preparation of 700 mg dose of bamlanivimab and 1400 mg dose of etesevimab together for IV infusion](#)
- [Administration of a dose of 700 mg of bamlanivimab and 1400 mg dose of etesevimab together in an IV infusion](#)
- Gather the materials for preparation:
 - Polyvinyl chloride (PVC) or polyethylene (PE)-lined PVC, sterile prefilled infusion bag. Choose one of the following:
 - Prefilled 50, 100, 150 or 250 mL infusion bag containing 0.9% Sodium Chloride Injection.
 - One vial of bamlanivimab (700 mg/20 mL) and two vials of etesevimab (700 mg/20 mL).
- Bamlanivimab and etesevimab are supplied in individual single-dose vials but are administered together using a single infusion bag.

*If alternate materials are used, the compatibility of these materials should be confirmed with that vendor. Bamlanivimab and etesevimab have no known incompatibilities with conventional medical supplies and equipment.

- Remove 1 bamlanivimab vial and 2 etesevimab vials from refrigerated storage and allow to equilibrate to room temperature for approximately 20 minutes before preparation. **Do not expose to direct heat. Do not shake the vials.**
- Inspect both bamlanivimab and etesevimab vials visually for particulate matter and discoloration.
 - Bamlanivimab and etesevimab are clear to opalescent and colorless to slightly yellow to slightly brown solutions.
- Withdraw 20 mL from one bamlanivimab vial and 40 mL from two etesevimab vials and inject all 60 mL into a prefilled infusion bag of 0.9% Sodium Chloride (see Table 1 or Table 2).
- Discard any product remaining in the vials.
- Gently invert the bag by hand approximately 10 times to mix. **Do not shake.**
- These products are preservative-free and therefore, the diluted infusion solution should be administered immediately.
 - If immediate administration is not possible, store the diluted infusion solution for up to 24 hours at refrigerated temperature (2°C to 8°C [36°F to 46°F]) and up to 7 hours at room temperature (20°C to 25°C [68°F to 77°F]) including infusion time. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 20 minutes prior to administration.

Administration

Bamlanivimab and etesevimab infusion solution should be administered by a qualified healthcare professional.

- Gather the materials for infusion:
 - Polyvinyl chloride (PVC) or polyethylene (PE)-lined PVC infusion set
 - Use of an in-line or add-on 0.2/0.22 micron polyethersulfone (PES) filter is strongly recommended.
- Attach the infusion set to the IV bag.
- Prime the infusion set.
- Administer the entire infusion solution in the bag via pump or gravity according to the size of infusion bag used (**see Table 1 for patients weighing ≥ 50 kg or Table 2 for patients weighing < 50 kg**). Due to potential overfill of pre-filled saline bags, the entire infusion solution in the bag should be administered to avoid underdosage.
- The prepared infusion solution should not be administered simultaneously with any other medication. The compatibility of bamlanivimab and etesevimab injection with IV solutions and medications other than 0.9% Sodium Chloride Injection is not known.
- Once infusion is complete, **flush the tubing with 0.9% Sodium Chloride** to ensure delivery of the required dose.
- Clinically monitor patients during administration and observe patients for at least 1 hour after infusion is complete.
- If the infusion must be discontinued due to an infusion reaction, discard any unused product.
- The use of closed system transfer devices (CSTDs), elastomeric pumps, and pneumatic transport with bamlanivimab has not been studied.

Table 1: Recommended Dilution and Administration Instructions for Bamlanivimab and Etesevimab Together for IV Infusion^a in Patients Weighing 50 kg or More

Drug ^a : Add 20 mL of bamlanivimab (1 vial) and 40 mL of etesevimab (2 vials) for a total of 60 mL to a prefilled infusion bag and administer as instructed below		
Size of Prefilled 0.9% Sodium Chloride Infusion Bag	Maximum Infusion Rate	Minimum Infusion Time
50 mL	310 mL/hr	21 minutes
100 mL	310 mL/hr	31 minutes
150 mL	310 mL/hr	41 minutes
250 mL	310 mL/hr	60 minutes

^a 700 mg of bamlanivimab and 1,400 mg of etesevimab are added to the same infusion bag and administered together as a single intravenous infusion.

Table 2: Recommended Dilution and Administration Instructions for Bamlanivimab and Etesevimab Together for IV Infusion^a in Patients Weighing **Less Than 50 kg**

Drug ^a : Add 20 mL of bamlanivimab (1 vial) and 40 mL of etesevimab (2 vials) for a total of 60 mL to a prefilled infusion bag and administer as instructed below		
Size of Prefilled 0.9% Sodium Chloride Infusion Bag	Maximum Infusion Rate	Minimum Infusion Time
50 mL	310 mL/hr	21 minutes
100 mL	310 mL/hr	31 minutes
150 mL	310 mL/hr	41 minutes
250 mL ^b	266 mL/hr	70 minutes

^a 700 mg of bamlanivimab and 1,400 mg of etesevimab are added to the same infusion bag and administered together as a single intravenous infusion.

^b The minimum infusion time for patients weighing less than 50 kg who are administered bamlanivimab and etesevimab using the 250 mL prefilled 0.9% Sodium Chloride infusion bag must be extended to at least 70 minutes to ensure safe use (endotoxin load).

Calculating Drip Rate for Gravity Infusion

For gravity infusions, please use the following formula to calculate drip rate:

Drip Rate Formula

$$\frac{\text{Volume to be infused (in mL)} \times \text{Drop factor (see tubing package)}}{\text{Total infusion time (in minutes)}} = \text{Drip rate (in drops/min)}$$

For additional information, please see [Fact Sheet for Healthcare Providers](#).

Note: After the appropriate infusion volume has been administered, flush the tubing with 0.9% Sodium Chloride as per infusion site of care recommendations or with sufficient volume to flush residual volume from tubing to ensure the patient receives the entire dose. Discard unused product.

SECTION 04

Recommended Infusion Site of Care Resources and Equipment Considerations

STAFFING RECOMMENDATIONS

Staffing recommendations may vary by state. Follow your local recommendations when determining the staff needed for your infusion site of care. Based on Lilly’s clinical trial experience, the following roles should be considered to ensure the safest care environment for patients receiving antibody infusion of bamlanivimab and etesevimab together.

Infusion sites of care should have appropriately trained medical staff to administer infusion treatments and identify and manage potential adverse reactions. It is recommended that participants who experience a systemic hypersensitivity reaction be treated per the local standard of care.

IV admixture should be prepared in a dedicated area with a working sink available. Depending on their role in the infusion unit, all individuals may be trained to wear PPE.

Role	Recommendations
Patient intake	Person with basic administrative skills
Drug infusion preparation	Healthcare professional trained in IV admixture preparation (such as a nurse, pharmacist, pharmacy tech)
Infusion: start IV	Healthcare professional trained to start an IV
Infusion: administer infusion	Healthcare professional trained in administering IV infusion
Infusion monitoring	Healthcare professional trained in: <ul style="list-style-type: none"> • assessing infusion-related reactions • treating infusion-related reactions • vital sign monitoring
Post-infusion observation	Healthcare professional trained in: <ul style="list-style-type: none"> • assessing infusion-related reactions • treating infusion-related reactions • vital sign monitoring • providing post-infusion education for the patient
Patient release	Person with basic administrative skills
Waste removal and cleaning	Person trained in COVID-19 cleaning and disinfection

Notes:

- At least one healthcare professional should have Advanced Cardiovascular Life Support (ACLS) or Basic Life Support (BLS) certification or equivalent.
- At least one healthcare professional should be able to respond to medical emergency (e.g., severe infusion reaction); any specific certifications based on state and healthcare facility regulations and policies.
- The same healthcare professional may perform more than one role.
- State or country recommendations may dictate specific qualifications for some roles.

INFUSION SITE OF CARE MATERIALS

Equipment recommendations may vary by state. Follow your local recommendations when determining the equipment needed for your infusion site of care. Based on Lilly's clinical trial experience, the following equipment should be considered to ensure the safest care environment for patients receiving bamlanivimab and etesevimab antibody infusion.

Additional recommended equipment and emergency medical supplies can be found in Appendix B.

Below are recommended non-consumable materials which are needed in an infusion site of care:

- Infusion pumps (if available)
- Infusion pump bracket for IV pole (if available)
- Chairs for infusion
- Mobile IV poles
- Emergency medical management equipment and backboard, including a reaction management kit (see Appendix B)
- Chairside table
- Locking refrigerator with temperature monitoring capability
- Transilluminator (vein finder)
- Vital sign monitoring equipment (see Appendix B)

Below are recommended consumable items which are needed in an infusion site of care:

Consumable Items Recommended supplies are based on Lilly's clinical trial experience.

PPE	Infusion supplies*	General supplies
Gloves Gowns Eye and face protection (e.g., goggles, safety glasses, face shields) NIOSH-certified, disposable N95 filter facepiece respirators or better	IV and catheters* 0.20/0.22µm filter 50, 100, 150 or 250 mL 0.9% Sodium Chloride PVC or PE-lined PVC IV bags Prefilled 0.9% Sodium Chloride syringes Appropriately sized syringes Alcohol wipes 2x2 gauze pads Adhesive bandages Tegaderm™ bio-occlusive dressing Absorbent underpads (blue pads) Extension set tubing Sterile needles - stainless steel 18ga IV administration sets (tubing) Sharps containers Transpore™ tape	Biohazard disposal bag Disposable disinfecting wipes Thermometer probe covers (if required) 70% alcohol wipes Paper towels Trash bins and liners Infusion Reaction Kit (See Appendix B)

Listed supplies are reflective of quantities/volumes used in Lilly clinical trials. Infusion sites of care may substitute alternate quantities and volumes as needed based on best medical practices and local recommendations.

*24 g catheter is sufficient.

SECTION 05

Considerations for Residents of Long Term Care Facilities

CONSIDERATIONS FOR RESIDENTS OF LONG TERM CARE FACILITIES

The COVID-19 pandemic presents unique challenges to long-term care facilities. Residents of long term care facilities account for only 5% of US cases but nearly 34% of US deaths from COVID-19†. It is critical that available treatments, such as bamlanivimab and etesevimab, are accessible to these facilities and the residents they care for. Below, find information about receiving infusion treatments, reimbursement and unique considerations for long term care facilities administering bamlanivimab and etesevimab together.

†Numbers accurate as of March 2021. Source: [Kaiser Family Foundation](#)

Receiving Infusion Treatments

Long term care pharmacy providers will typically receive infusion treatments from a long term care pharmacy, hospital pharmacy network or contract pharmacy network.

Long Term Care Recommended Resources and Equipment Considerations

Long term care facilities may need to take unique equipment considerations into account. In addition to resources and equipment recommendations outlined in other parts of this Playbook (See Section 5 and Appendix B), long term care facilities should consider the following:

- Needles (18 gauge may be incompatible with this population)
- Pharmacy/transportation considerations

SECTION 06

Education and Awareness

Lilly

COMBATING COVID-19

Attacking the coronavirus will require a diverse set of approaches, including both vaccines and treatments, such as antibodies.

Q. What's the difference between vaccines and monoclonal antibody drugs?

A. While there are some similarities, here's how they are different:

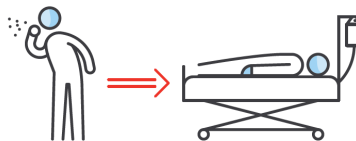
- Monoclonal antibody drugs, like bamlanivimab and etesevimab, provide passive immunity by giving the body antibodies to protect itself. Vaccines provide active immunity by helping the body make its own antibodies to protect itself.
- Monoclonal antibody drugs are designed to start working faster than vaccines, while protection provided by vaccines will generally last longer.
- Generally, scientists are able to develop antibody treatments faster than they are able to develop vaccines.

Developing any approach against COVID-19 involves assessing key factors:



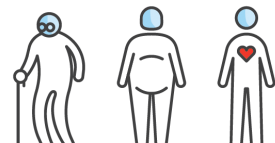
Viral exposure

A vaccine will not help an already-infected patient



Stage of disease

When to apply the medicine to prevent the infection or treat the disease

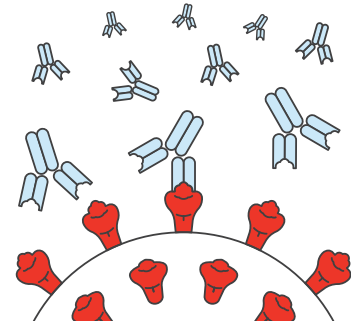


At-risk populations

Factors linked to worse outcomes (e.g., age, concurrent diseases)

NEUTRALIZING ANTIBODIES AS POTENTIAL TREATMENTS

Identified and characterized using various methods, including from the blood of COVID-19 survivors, neutralizing antibodies target the viral spike protein that SARS-CoV-2 uses to gain entry into host cells. Neutralizing antibodies, therefore, are specifically designed to treat COVID-19.



Q. What are antibodies?

A. Antibodies are naturally made in our bodies to fight infection.

- Whenever the immune system meets a new foreign substance in the body, it makes new antibodies that attack the foreign substance. So the next time that substance shows up, the immune system can produce the same antibodies to help the body fight it off before it can make a person sick. These types of naturally occurring antibodies provide active immunity.
- Vaccines work in a similar way, helping the body make antibodies to attack specific foreign substances and providing active immunity in the body.
- Antibody drugs are different. They are man-made antibodies that are given directly through an infusion or injection rather than prompting the body to make the antibodies for itself. This type of immunity is called passive immunity.

Find more information about monoclonal antibody drugs and vaccines from the CDC, State Health Departments, and the following resources:

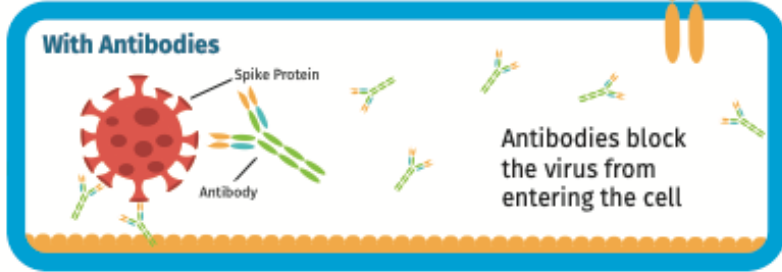
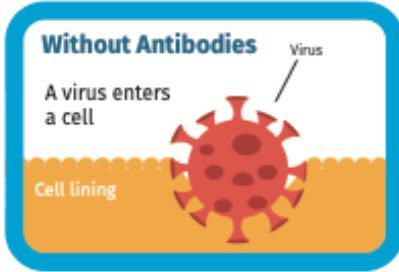
- [CombatCOVID.HHS.gov](https://www.combatcovid.gov)
- [Coronavirus Prevention Network](#)
- [National Infusion Center Association](#)
- [Fact Sheet for Healthcare Providers](#)
- [Fact Sheet for Patients, Parents and Caregivers \(English\)](#)
- [Fact Sheet for Patients, Parents and Caregivers \(Spanish\)](#)
- [FDA Authorization Letter](#)

Monoclonal Antibodies

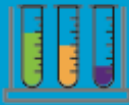


What are antibodies?

Antibodies are naturally made in our bodies to fight infection.



What are **MONOCLONAL ANTIBODIES**?



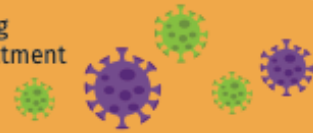
Monoclonal antibodies (**mAbs**) are antibodies developed in a laboratory to help our bodies fight infection.

Nearly
100

mAbs are FDA approved to treat health conditions including cancers and autoimmune diseases.



mAbs are also being studied for the treatment and prevention of COVID-19.



How are mAbs administered?



mAbs are given through intravenous infusion (i.e., through a vein) or injection.

OR



How often infusions or injections of mAbs are needed depends on the specific mAbs.

What are common side effects of mAbs?



Allergic reactions



Flu-like symptoms



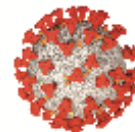
Nausea & vomiting



Diarrhea



Low blood pressure



COVID-19
Prevention Network

PreventCOVID.org

ama-assn.org cancer.org mayoclinic.org medicinenet.com nature.com synabs.be uptodate.com

APPENDIX A

Lilly Monoclonal Antibody Clinical Trial Modeling Information

Lilly

LILLY MONOCLONAL ANTIBODY CLINICAL TRIAL MODELING INFORMATION

Assuming the infusion site of care setup details provided below, this information can be used to model the estimated number of infusions (patients) an infusion site of care can serve, depending on its capacity.

Each infusion site of care will vary in terms of the amount of chairs for infusion, staffing considerations, work day length and more. The information provided here is meant as a general guide based upon Lilly’s clinical trial experience. In some cases, ideal criteria are included, such as for observation time. In other instances, such as the patient education and intake time, there are estimated ranges shown, with “+” or “-” conditions in parentheses.

Infusion Timing		
Criteria	Details	Additional Notes
Patient education and intake time	30 min (+/- 15 min)	Patient education and intake may occur outside of the infusion chair, such as at the prescriber’s location, and patient education and intake time may vary per patient.
IV prep time	30 min	This step usually does not take place until the patient is in the chair for infusion and vascular access has been obtained.
Infusion time	21 – 70 min	Infusion time should be a minimum of 21–70 minutes, although more time may be necessary.
Observation time*	60 min	It is clinically recommended to monitor patients during infusion and observe patients for at least 1 hour after infusion is complete, although more time may be necessary. Sites of care should follow local recommendations when determining appropriate observation periods.
TOTAL TIME	126 – 205 min	This represents the estimated total time from patient education through observation of the patient.

*It is recommended that infusion sites of care have a protocol in place for patients who refuse to stay for post-infusion observation. For example, this may include an AMA form, release of responsibility waiver, etc.

APPENDIX B

Basic Equipment Recommendations

Lilly

BASIC EQUIPMENT RECOMMENDATIONS

Equipment recommendations may vary from state to state. Follow your local recommendations when determining the equipment needed for your infusion center. Based on Lilly’s clinical trial experience, the following equipment should be considered to ensure the safest care environment for patients receiving antibody infusion of bamlanivimab and etesevimab together.

Basic Equipment Recommendations	
Drug preparation	<ul style="list-style-type: none"> Locked refrigerator with min/max temp monitoring Prep table / area 18ga needles Appropriate sized syringes 50, 100, 150 or 250 mL 0.9% Sodium Chloride PVC or PE-lined PVC IV bags Sterile alcohol prep pads PPE gloves all sizes PPE face shields or goggles (only if prepared in a COVID-19 unit) PPE N95 masks (only if prepared in a COVID-19 unit) Sharps containers Drug transport bags if using mobile pharmacy Alcohol sanitizing wipes Step-by-step instruction sheet (with images)
Patient intake and release	<ul style="list-style-type: none"> Signage with patient instructions Phone for intake worker Schedule or list of appointments Office supplies (e.g. pens, stapler, scissors, paper clips, etc.) Clipboard with patient intake and monitoring sheet Patient intake and monitoring form Check-in table Chair(s) for check-in staff Bleach sanitizing wipes Hand sanitizer PPE gloves all sizes PPE face shields or goggles PPE N95 masks PPE gowns

Basic Equipment Recommendations

Infusion area supplies

- Chairs for infusion
- Chairside table
- IV poles
- IV pump (or gravity feed)
- Vital signs monitoring equipment (BP, HR, Resp Rate, Temp, O2 Sat)
- Supply cart or other storage cabinet
- Hand sanitizer
- Hand soap
- Biohazard trash can
- Bleach wipes (cleaning non-electronic equipment)
- Alcohol wipes (cleaning electronic equipment)
- Medical emergency supplies (See next slide)
- Sterile alcohol prep pads
- IV catheters
- IV extension tubing
- Tourniquet
- PVC infusion sets
- 0.20/0.22µm filter
- Gauze pads
- Adhesive bandages
- 0.9% Sodium Chloride flush syringes
- Bio-occlusive dressing
- Tape
- 50 mL saline bag or 20 mL syringe to flush the tubing following infusion
- PPE gloves all sizes
- PPE face shields or goggles
- PPE N95 masks
- PPE gowns

Observation area

- Vital signs monitoring equipment (BP, HR, Resp Rate, Temp, O2 Sat)
- Table for staff
- Chairs for patients and staff
- Bleach sanitizing wipes
- Hand sanitizer
- PPE gloves all sizes
- PPE face shields or goggles
- PPE N95 masks
- PPE gowns

MEDICAL EMERGENCY SUPPLIES AND MEDICATIONS

Emergency medical management equipment should contain the following items:

**Some medications listed below should only be administered by a healthcare provider with ACLS training*

	Essential	Recommended
Medications	<ul style="list-style-type: none"> Albuterol inhaler Diphenhydramine injection Epinephrine 0.1 mg/mL (1 mg/10 mL) OR epinephrine auto-injector 0.3 mg Solu-Medrol injection 	<ul style="list-style-type: none"> Adenosine injection Atropine sulfate Chewable ASA Dextrose 50% injection Insta glucose Nitroglycerine Ondansetron injection Sodium bicarbonate injection
IV supplies	<ul style="list-style-type: none"> 0.9% Sodium Chloride flush (10 mL) 0.9% Sodium Chloride bag (500 mL) 	<ul style="list-style-type: none"> IV admin set IV start kit IV catheter Non-DEHP cath/extension set 5% dextrose bag
Airway		<ul style="list-style-type: none"> Nasopharyngeal/oral airway suction Barrier mask for CPR Ambu bag Oxygen and airway equipment
Emergency medical management	<p>Infusion sites of care should have a standard operating procedure in place instructing site of care staff how emergency events should be managed, including appropriate contacts (911, physician, etc.), ACLS protocol and any follow-up activities.</p>	