Louisiana Department of Health
Protocol- Monoclonal Antibodies for Treatment of COVID-19
Bamlanivimab and Etesevimab
Revised 10/01/2021

GENERAL REQUIREMENTS

1. Review and be familiar with the most current revision of the **Fact Sheet for Health Care Providers for the EUA of Bamlanivimab and Etesevimab**, available at http://pi.lilly.com/eua/bam-and-ete-eua-factsheet-hcp.pdf.
2. Verify that the individual meets the FDA EUA criteria for administration of Bamlanivimab and Etesevimab.
3. Review and be familiar with personal protective equipment (PPE) required for providing Bamlanivimab and Etesevimab to qualifying patients.
4. Review and follow the "Intravenous Infusion Preparation and Administration Instructions" outlined in this Protocol for qualifying patients receiving intravenous infusion.
5. Review and follow the "Subcutaneous Injection Preparation and Administration Instructions" outlined in this Protocol for qualifying patients receiving subcutaneous injections.
6. Inform each patient, or parent or legal guardian if the patient is under 18 years of age or incapable of consenting, that Bamlanivimab and Etesevimab is not approved by the FDA but has received emergency use authorization from the FDA for (1) the treatment of mild to moderate COVID-19 in adult 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 progression to severe COVID-19, including hospitalization or death and (2) for post-exposure prophylaxis of COVID-19 in adult and pediatric individuals (12 years of age and older weighing at least 40 kg) who are at high risk for progression to severe COVID-19, including hospitalization or death. Provide to the patient, or parent or legal guardian if the patient is under 18 years of age or incapable of consenting, the most current revision of the **Fact Sheet for Patients, Parents and Caregivers for the EUA of Bamlanivimab and Etesevimab**, available at https://www.regeneron.com/downloads/treatment-covid19-eua-fact-sheet-for-patient.pdf, prior to administering the drug.
7. Receive informed written consent for use of Bamlanivimab and Etesevimab for treatment of COVID-19 or post-exposure prophylaxis from the patient, or parent or legal guardian if the patient is under 18 years of age or incapable of consenting.
8. Submit a report on all medication errors and all serious adverse events potentially related to Bamlanivimab and Etesevimab.
9. Advise all patients, or parents or legal guardians if the patient is under 18 years of age or incapable of consenting, to continue to self-isolate and use infection control measures.

Patient Selection for Treatment and Post-Exposure Prophylaxis

This section provides essential information on the unapproved products bamlanivimab and etesevimab administered together in adults and pediatric patients (12 years of age and older weighing at least 40 kg) who are at high risk for progression to severe COVID-19, including hospitalization or death for:

- Treatment of mild to moderate COVID-19 in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing *[see Limitations of AuthorizedUse (1.1)]*.
- Post-exposure prophylaxis of COVID-19 in high risk individuals who are:
    - not fully vaccinated[1] **or** who are not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination (for example, individuals with immunocompromising conditions including those takingimmunosuppressive medications[2]) **and**
        - have been exposed to an individual infected with SARS-CoV-2consistent with close contact criteria per Centers for Disease Control and Prevention (CDC)[3] **or**
        - who are at high risk of exposure to an individual infected with SARS-CoV-2 because of occurrence of SARS-CoV-2 infection in other individuals in the same institutional setting (for example, nursing homes, prisons) *[see Limitations of Authorized Use (1.2)]*.

---

1 Individuals are considered to be fully vaccinated 2 weeks after their second vaccine dose in a 2-dose series (such as the Pfizer or Moderna vaccines), or 2 weeks after a single-dose vaccine (such as Johnson &Johnson's Janssen vaccine). See this website for more details: https://www.cdc.gov/coronavirus/2019- ncov/vaccines/fully-vaccinated.html#vaccinated.

2 See this website for more details: https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html.

3 Close contact with an infected individual is defined as: being within 6 feet for a total of 15 minutes or more,providing care at home to someone who is sick, having direct physical contact with the person (hugging or kissing, for example), sharing eating or drinking utensils, or being exposed to respiratory droplets from an infected person (sneezing or coughing, for example). See this website for additional details: https://www.cdc.gov/coronavirus/2019-ncov/if-you-are-sick/quarantine.html.

Criteria for Identifying High Risk Individuals

The following medical conditions or other factors may place adults and pediatric patients(12 years of age and older weighing at least 40 kg) at higher risk for progression to severe COVID-19:

- Older age (for example age ≥65 years of age)
- Obesity or being overweight (for example, adults with BMI >25 kg/m^2, or if age 12-17, have BMI ≥85th percentile for their age and gender based on CDC growthcharts, https://www.cdc.gov/growthcharts/clinical_charts.htm)
- Pregnancy
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease or immunosuppressive treatment
- Cardiovascular disease (including congenital heart disease) or hypertension
- Chronic lung diseases (for example, chronic obstructive pulmonary disease,asthma [moderate-to-severe], interstitial lung disease, cystic fibrosis and pulmonary hypertension)
- Sickle cell disease
- Neurodevelopmental disorders (for example, cerebral palsy) or other conditions that confer medical complexity (for example, genetic or metabolic syndromes andsevere congenital anomalies)
- Having a medical-related technological dependence (for example, tracheostomy,gastrostomy, or positive pressure ventilation (not related to COVID-19))

Other medical conditions or factors (for example, race or ethnicity) may also place individual patients at high risk for progression to severe COVID-19 and authorization of bamlanivimab and etesevimab under the EUA is not limited to the medical conditions orfactors listed above. For additional information on medical conditions and factors associated with increased risk for progression to severe COVID-19, see the CDC website: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people- with-medical-conditions.html. Healthcare providers should consider the benefit-risk for an individual patient.

Dosage

Treatment:

The dosage in adults and pediatric patients (12 years of age and older weighing at least40 kg) is bamlanivimab 700 mg and etesevimab 1,400 mg administered together as soon as possible after positive results of direct SARS-CoV-2 viral testing and within 10 days of symptom onset.

Post-Exposure Prophylaxis:

The dosage in adults and pediatric individuals (12 years of age and

older weighing at least 40 kg) is 700 mg bamlanivimab and 1,400 mg etesevimab administered togetheras soon as possible following exposure to SARS-CoV-2.

Dosage Adjustment in Specific Populations
No dosage adjustment is recommended based on age, sex, race, body weight, renal ormild hepatic impairment, during pregnancy or while lactating, or for disease severity or inflammation *[see Full EUA Prescribing Information, Use in Specific Populations (11)]*.

Preparation and Administration

Preparation
Bamlanivimab and etesevimab solution for infusion should be prepared by a qualifiedhealthcare professional using aseptic technique:

- Gather the materials for preparation:
  - Polyvinyl chloride (PVC) or polyethylene (PE)-lined PVC, sterile prefilledinfusion bag. Choose one of the following sizes:
    - Prefilled 50 mL, 100 mL, 150 mL, or 250 mL infusion bag containing 0.9% Sodium Chloride Injection (see **Table 1** and**Table 2**).
  - 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 areadministered together using a single infusion bag.
- Remove 1 bamlanivimab vial and 2 etesevimab vials from refrigerated storage and allow to equilibrate to room temperature for approximately 20 minutes beforepreparation. **Do not expose to direct heat. Do not shake the vials.**
- Inspect both bamlanivimab and etesevimab vials visually for particulate matterand discoloration.
  - Bamlanivimab and etesevimab are clear to opalescent and colorless toslightly yellow to slightly brown solutions.
- Withdraw 20 mL from one bamlanivimab vial and 40 mL from two etesevimabvials and inject all 60 mL into a prefilled infusion bag containing 0.9% SodiumChloride (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 solutionshould 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 toequilibrate to room temperature for approximately 20 minutes prior to administration.

Administration

Bamlanivimab and etesevimab infusion solution should be administered by a qualifiedhealthcare 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 isstrongly 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 tothe 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 prefilled saline bags, the entire infusion solution in the bag should be administered to avoid underdosage.
- The prepared infusion solution should not be administered simultaneously withany 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 toensure delivery of the required dose.
- Clinically monitor patients during administration and observe patients for at least1 hour after infusion is complete.
- If the infusion must be discontinued due to an infusion reaction, discard anyunused product.
- The use of closed system transfer devices (CSTDs), elastomeric pumps, andpneumatic transport with bamlanivimab has not been studied.

Table 1: Recommended Dilution and Administration Instructions for Bamlanivimab and Etesevimab 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 totalof 60 mL to a prefilled infusion bag and administer as instructed below		
Size of Prefilled 0.9% Sodium Chloride InfusionBag	**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 for IV Infusion 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 60 mL to an 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 together 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).

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, shake, or expose to direct light.

Warnings

There are limited clinical data available for bamlanivimab and etesevimab. Serious and unexpected adverse events may occur that have not been previously reported with 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 and 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, occurring during the infusion and up to 24 hours after theinfusion, 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, vasovagal reactions (e.g., pre-syncope, syncope), dizziness and diaphoresis.

Consider slowing or stopping the infusion and administer appropriate medications and/orsupportive care if an infusion-related reaction occurs.

Hypersensitivity reactions occurring more than 24 hours after the infusion have alsobeen reported with the use of bamlanivimab and etesevimab under Emergency UseAuthorization.

Clinical Worsening After Bamlanivimab and Etesevimab Administration
Clinical worsening of COVID-19 after administration of bamlanivimab and etesevimabtogether 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 and etesevimab use or were due to progression of COVID-19.

Limitations of Benefit and Potential for 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 tohospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation. Therefore, bamlanivimab and etesevimab are not authorized for use in patients *[see Limitations of Authorized Use (1.1)]*:

- 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 relatedcomorbidity.

Side Effects
Adverse events have been reported with bamlanivimab and etesevimab

[see Full EUAPrescribing Information, Overall Safety Summary (6.1)].

Additional adverse events associated with bamlanivimab and etesevimab, some ofwhich may be serious, may become apparent with more widespread use.