

NM Outpatient Protocol:
Emergency Use of Bamlanivimab for Treating Mild to Moderate Coronavirus Disease 2019 (COVID-19)

BACKGROUND

Bamlanivimab (LY-CoV555) is an investigational human immunoglobulin G-1 (IgG1 variant) monoclonal antibody that has been authorized under an FDA Emergency Use Authorization (EUA) for the treatment of mild to moderate coronavirus disease 2019 (COVID-19). Bamlanivimab is for use only in non-hospitalized adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12 years and older weighing at least 40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization. See **Appendix 1** for high-risk details.

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.

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 in hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

Efficacy: The potential efficacy of bamlanivimab is based on interim data from one Phase 2 trial (BLAZE-1) of 465 ambulatory (non-hospitalized) adults with mild to moderate COVID-19 symptoms. More details on this can be found in Section 18 CLINICAL TRIAL RESULTS AND SUPPORTING DATA FOR EUA, within the [FACT SHEET FOR HEALTH CARE PROVIDERS: EMERGENCY USE AUTHORIZATION \(EUA\) OF BAMLANIVIMAB](#).

OBJECTIVE

This protocol is intended to guide health providers in the therapeutic use of bamlanivimab once a patient has been judged to be medically eligible for the treatment. Use must be in strict accordance with the following elements of the EUA labeling for bamlanivimab. Under this protocol, bamlanivimab treatment may be ordered by NM nurses and pharmacists through Epic after this explicit order, “bamlanivimab per protocol” is made by any NM-authorized prescriber: physicians (MDs or DOs) or advance practice providers (APPs).

DOSAGE AND ADMINISTRATION

Dosage

Bamlanivimab should be administered as soon as possible after positive viral test for SARS-CoV-2 and within 10 days of symptom onset. The dosage of bamlanivimab in adults and pediatric patients 12 years of age and older weighing at least 40 kg is a single intravenous (IV) infusion of 700 mg bamlanivimab administered over at least 60 minutes. The 700mg dose is provided in a prepared IV solution with a final volume of 200 mL. **(NOTES: Dose form and storage is detailed in Appendix 2. Dose preparation is detailed in Appendix 3. For special dose adjustment information see Appendix 4.)**

Administration

Bamlanivimab solution should be administered by a qualified healthcare professional.

- Gather the recommended materials for infusion:
 - Polyvinylchloride (PVC) infusion set containing a 0.20/0.22 micron in-line polyethersulfone (PES) filter.
- Attach the infusion set to the IV bag.
- Prime the infusion set.
- Administer the infusion solution via pump or gravity over at least 60 minutes (see **Table 1**).
- Once infusion is complete, flush the infusion line to ensure delivery of the required dose.
- Discard unused product.

- Clinically monitor patients during infusion and observe patients for at least 1 hour after infusion is complete.

Monitoring

- Clinically monitor patients during the 60-minute infusion and observe patients for at least 1 hour after the infusion is complete.
- **Hypersensitivity including anaphylaxis and infusion-related reactions:** There is a potential for serious hypersensitivity reaction, including anaphylaxis, with administration of bamlanivimab. Signs and symptoms of infusion related reactions may include fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, dizziness.
- **If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive care.** (please see Reporting Requirements and/or Appendix 5 for additional details)

Safety

Contraindications: known hypersensitivity to any ingredient of bamlanivimab.

Adverse reactions: The most commonly reported adverse event in the Blaze 1 was nausea. Other possible side effects of bamlanivimab include anaphylaxis and infusion-related reactions, diarrhea, dizziness, headache, itching and vomiting. More details on this can be found in the Overall Safety Summary, Section 6.1 Clinical Trials Experience, within the [FACT SHEET FOR HEALTH CARE PROVIDERS: EMERGENCY USE AUTHORIZATION \(EUA\) OF BAMLANIVIMAB](#). Due to the limited number of patients who received bamlanivimab under controlled study conditions, the full range of possible adverse reactions, along with their frequency and severity remain uncertain. This emphasizes the importance of reporting reactions, as described in the following section.

Managing Anaphylaxis and Infusion-related reactions: The Epic order panel includes medications that may be administered for significant infusion reactions or hypersensitivity reactions including anaphylaxis.

Reporting Requirements

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 treatment within 7 calendar days from the onset of the event. See **Appendix 5** for details.

INFORMATION FOR PATIENTS, PARENTS, OR CAREGIVERS

Healthcare providers must communicate to each patient or parent/caregiver, as age appropriate, information consistent with the "Fact Sheet for Patients, Parents and Caregivers" (and provide a copy of the Fact Sheet) prior to the patient receiving bamlanivimab:

- [English Fact Sheet for Patients, Parents and Caregivers on Emergency Use Authorization \(EUA\) of Bamlanivimab for Coronavirus Disease 2019 \(COVID-19\). November, 2020.](#)
- [Spanish Fact Sheet for Patients, Parents and Caregivers on Emergency Use Authorization \(EUA\) of Bamlanivimab for Coronavirus Disease 2019 \(COVID-19\). November, 2020.](#)

Furthermore, 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
- c) Informed that bamlanivimab is an unapproved drug that is authorized for use under this Emergency Use Authorization.

This will be documented in the Epic Referral Order (b & c) and the Epic Order Panel/Therapy Plan (a)

NM-SPECIFIC RESOURCES

- For assistance specific to managing the care of a patient who is receiving or has received bamlanivimab, the prescribing health provider of record must be contacted.
- Medication Errors or adverse events associated with this medication should be entered as a NETS report as per standard procedure.

REFERENCES

- [FACT SHEET FOR HEALTH CARE PROVIDERS: EMERGENCY USE AUTHORIZATION \(EUA\) OF BAMLANIVIMAB](#). Note: This includes approved labeling for EUA use. November, 2020.
- [FDA letter. Emergency Use Authorization \(EUA\) for emergency use of bamlanivimab for the treatment of mild to moderate coronavirus disease 2019 \(COVID-19\)](#). November, 2020.

APPENDIX 1 Patients at High Risk of Progressing to Severe COVID-19 and/or Hospitalization

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
 - o cardiovascular disease, OR
 - o hypertension, OR
 - o chronic obstructive pulmonary disease/other chronic respiratory disease.
- Are 12 – 17 years of age AND have
 - o BMI ≥ 85 th percentile for their age and gender based on [CDC growth charts](#), OR
 - o sickle cell disease, OR
 - o congenital or acquired heart disease, OR
 - o neurodevelopmental disorders, for example, cerebral palsy, OR
 - o a medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19), OR
 - o asthma, reactive airway or other chronic respiratory disease that requires daily medication for control.

APPENDIX 2 Dose Form and Storage

Bamlanivimab injection, 700 mg/20 mL (35 mg/mL), is a sterile, preservative-free clear to slightly opalescent and colorless to slightly yellow to slightly brown solution supplied as one single-dose vial per carton.

Bamlanivimab 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 bamlanivimab infusion solution in the refrigerator at 2°C to 8°C (36°F to 46°F) for up to 24 hours or at

room temperature (20°C to 25°C [68°F to 77°F]) for up to 7 hours, including infusion time. If refrigerated, allow the infusion solution to equilibrate to room temperature prior to administration.

APPENDIX 3 Dose Preparation

Bamlanivimab infusion solution should be prepared by a qualified healthcare professional using aseptic technique:

- Remove bamlanivimab vial from refrigerated storage and allow to equilibrate to room temperature for approximately 20 minutes before preparation. **Do not expose to direct heat.**
- Inspect bamlanivimab visually for particulate matter and discoloration.
 - Bamlanivimab is a clear to slightly opalescent and colorless to slightly yellow to slightly brown solution.
- Gently invert vial by hand approximately 10 times. **Do not shake.**
- Dilute bamlanivimab using a 250 mL prefilled 0.9% Sodium Chloride Injection bag for intravenous infusion according to **Table 1.**
 - Withdraw and discard required volume of 0.9% Sodium Chloride Injection from the infusion bag.
 - Withdraw required volume of bamlanivimab from the vial using an appropriately sized syringe.
 - Transfer bamlanivimab to the 0.9% Sodium Chloride Injection infusion bag.
 - Discard any product remaining in the vial.
- Gently invert IV bag by hand approximately 10 times to mix. **Do not shake.**
- This product is preservative-free and therefore, the diluted infusion solution should be administered immediately. If immediate administration is not possible, store the diluted bamlanivimab infusion solution for up to 24 hours at refrigerated temperature (2°C to 8°C [36°F to 46°F]) or 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.

Table 1: Recommended Dilution and Administration Instructions for Bamlanivimab

Treatment	Dose/Volume of Bamlanivimab (# of vials)	Volume of 0.9% sodium chloride to Discard from a 250 mL IV bag	Total Final Volume for Infusion	Minimum Infusion Rate	Minimum Infusion Time
Bamlanivimab	700 mg/20 mL (1 vial)	70 mL	200 mL	200 mL/hr	60 minutes

APPENDIX 4 Dosage Adjustment in Specific Populations

- **Pregnancy or Lactation:** No dosage adjustment is recommended in pregnant or lactating women.
- **Pediatric Use:** No dosage adjustment is recommended in pediatric patients who weigh at least 40 kg. Bamlanivimab is not authorized for patients weighing less than 40 kg.

- Note: The safety and effectiveness have not been assessed in pediatric patients. The recommended dosing regimen is expected to result in comparable serum exposures of bamlanivimab in patients 12 years of age and older and weighing at least 40 kg as observed in adults, based on PK modeling
- **Geriatric Use:** No dosage adjustment is recommended in geriatric patients.
 - Note: Of the 309 patients receiving bamlanivimab in BLAZE-1, 11% were 65 years of age and older and 3% were 75 years of age and older. Based on population PK analyses, there is no difference in PK in geriatric patients compared to younger patients.
- **Renal Impairment:** No dosage adjustment is recommended in patients with renal impairment.
 - Note: Bamlanivimab is not eliminated intact in the urine, thus renal impairment is not expected to affect the exposure of bamlanivimab.
- **Hepatic Impairment:** No dosage adjustment is recommended in patients with mild hepatic impairment. Bamlanivimab has not been studied in patients with moderate or severe hepatic impairment.
 - Note: Based on population PK analysis, patients with mild hepatic impairment had approximately 20% higher clearance than patients with normal hepatic function. This effect is statistically significant, but not clinically meaningful.

APPENDIX 5 Reporting Requirements – *All suspected adverse events and medication errors MUST be recorded in the NETS system. These events will be reviewed centrally and will be reported when appropriate by the review team utilizing the process outlined below.*

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 treatment within 7 calendar days from the onset of the event.

*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.

The reports should include unique identifiers and the words “Bamlanivimab 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
- By using a postage-paid Form FDA 3500 (available at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf>) and returning 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 treatment under Emergency Use Authorization (EUA)”

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.

OTHER REPORTING REQUIREMENTS

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.

Also refer to the [EUA labeling](#), section **8 ADVERSE REACTIONS AND MEDICATION ERRORS REPORTING REQUIREMENTS AND INSTRUCTIONS**