Lilly Bamlanivimab Antibody Playbook

ELI LILLY AND COMPANY | NOVEMBER 2020

For the Emergency Use Authorization of bamlanivimab 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 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 product, bamlanivimab, for the treatment of COVID-19.

- Bamlanivimab has not been approved, but has been authorized for emergency use by FDA, to treat 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.
- Bamlanivimab is authorized for the treatment of mild to moderate COVID19 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 only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of the bamlanivimab 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**.
- Health care providers should review the Fact Sheet for information on the authorized use of bamlanivimab and mandatory requirements of the EUA.
- Health care providers should review the **Fact Sheet for Healthcare Providers** for important information on the use of bamlanivimab.

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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 AbCellara has developed a monoclonal antibody called bamlanivimab. Bamlanivimab is a recombinant neutralizing human IgG1 monoclonal antibody directed against the spike protein of SARS-CoV-2. It is designed to block viral attachment and entry into human cells, thus neutralizing the virus.

NATIONAL INFUSION CENTER ASSOCIATION

This Antibody Playbook provides information for state, territorial and local public health programs to plan and operationalize a bamlanivimab antibody response to COVID-19. 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 and National Infusion Center Association (NICA) experience in monoclonal antibody treatments and should not supersede local requirements for infusion sites of care. Please defer to local guidelines.

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 health care delivery entities approved to administer infusion therapies)

We expect most infusion treatments will be administered in one of these aforementioned infusion 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

POPULATION FOR ANTIBODY TREATMENT

This EUA is for the use of the unapproved product bamlanivimab 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 and older weighing at least 40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

Limitations of Benefit in Patients with Severe COVID-19

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. Therefore, 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.

For more information, reference the **Fact Sheet for Healthcare Providers**.

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 ≥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.

Bamlanivimab must be administered by intravenous (IV) infusion.

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 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. See Sections 8 and 9 of the Fact Sheet for Healthcare Providers for reporting instructions below.

- The authorized dosage for bamlanivimab is a single intravenous (IV) infusion of 700 mg administered as soon as possible after positive viral test for SARS-CoV-2 and within 10 days of symptom onset.
- Bamlanivimab is available as concentrated solution and must be diluted prior to administration.
- Administer bamlanivimab 700 mg via IV infusion over at least 60 minutes via pump or gravity.
- Clinically monitor patients during infusion and observe patients for at least 1 hour after infusion is complete.
- Patients treated with bamlanivimab 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.

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 in COVID-19, please see **www.clinicaltrials.gov**.

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†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 Administration Under Emergency Use Authorization

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

1. 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.

2. Healthcare providers must communicate to patients or parents/caregivers, as age appropriate, information consistent with the **Fact Sheet for Patients, Parents and Caregivers** prior to the patient receiving bamlanivimab. 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.

3. Patients with known hypersensitivity to any ingredient of bamlanivimab must not receive bamlanivimab.

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* occurring within 7 calendar days from the onset of the event. 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
        - 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 treatment under Emergency Use Authorization (EUA)"

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.

***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.

IMPORTANT SAFETY INFORMATION

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

Hypersensitivity Including Anaphylaxis and Infusion-Related Reactions

There is a potential for serious hypersensitivity reaction, including anaphylaxis with administration of bamlanivimab. 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. 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 an infusion-related reaction occurs, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care.

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

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. See Limitations of Authorized Use.

Adverse Events

Adverse events reported in at least 1% of BLAZE-1 clinical trial participants on bamlanivimab 700 mg and placebo were Nausea (3% vs 4%), Diarrhea (1% vs 5%), Dizziness (3% vs 2%), Headache (3% vs 2%), Pruritus (2% vs 1%) and Vomiting (1% vs 3%).

Use in Specific Populations

Pregnancy

There are insufficient data on the use of bamlanivimab during pregnancy. Bamlanivimab 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 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.

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SECTION 02

SUPPLY AND SCALE OF EFFORT

SUPPLY AND SCALE OF EFFORT

Product Allocation and Supply

Lilly has committed to manufacturing up to 1,000,000 vials of bamlanivimab in 2020, with 100,000 doses available to ship within days of authorization.

Additionally, Lilly has reached an agreement with the U.S. government to supply 300,000 vials within the first two months after Emergency Use Authorization (EUA) with the option to purchase an additional 650,000 vials through June 2021.

Bamlamivimab will be allocated to each state by the Federal Government. Upon EUA, the Federal Government will begin allocating to states immediately and thereafter on a weekly basis. Weekly allocations to state and territorial health departments will be proportionally based on confirmed hospitalizations and COVID-19 cases in each state and territory over the previous seven days, based on data hospitals and state health departments enter into the HHS Protect data collection platform. State Health Authorities will then allocate to individual sites of care within their jurisdiction. If you would like more information about the allocation process or would like to be considered for product allocation, please contact your state health department directly.

Scaling Operations

The time duration to administer a 700mg/20mL dose of bamlanivimab is 60 minutes at the infusion rate of 200mL/hr (20mL bamlanivimab/180mL 0.9% sodium chloride) for both infusion pumps and gravity infusion. Treatment also requires a post-infusion observation period. It is clinically recommended to monitor patients during infusion and observe patients for at least 1 hour after infusion is complete. Sites of care should follow local requirements 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 165–225 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 infusion sites of care that may be needed per region. A region can easily modify the number based on changing the capacity assumptions with the various infusion sites of care. Depending on the dispersion of the population in a region, the region may choose to size some infusion sites of care larger than others.

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SECTION 03

ALLOCATION AND ORDERING

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- **How can the product be ordered?** State health departments will allocate an amount of the product to infusion sites of care. AmerisourceBergen, the contracted distributor, will contact these infusion sites of care directly. They may accept (in part or in full) or decline the allocated product. The receipt of the product requires an account with AmerisourceBergen. Infusion sites of care that would like to be considered for product allocation should contact their state health departments directly.

- **When can orders be placed?** Infusion sites of care cannot order product from their wholesaler(s). AmerisourceBergen will proactively contact infusion sites of care that have received State Health Department allocations to confirm acceptance of the allocation. Product allocations will occur on a weekly basis after the initial allocation, and quantities may fluctuate depending on highest medical need.

- **Where can orders be shipped?** Orders will be shipped via UPS overnight to infusion sites of care that have received state health department allocations and that accepted product upon being contacted by AmerisourceBergen customer service.

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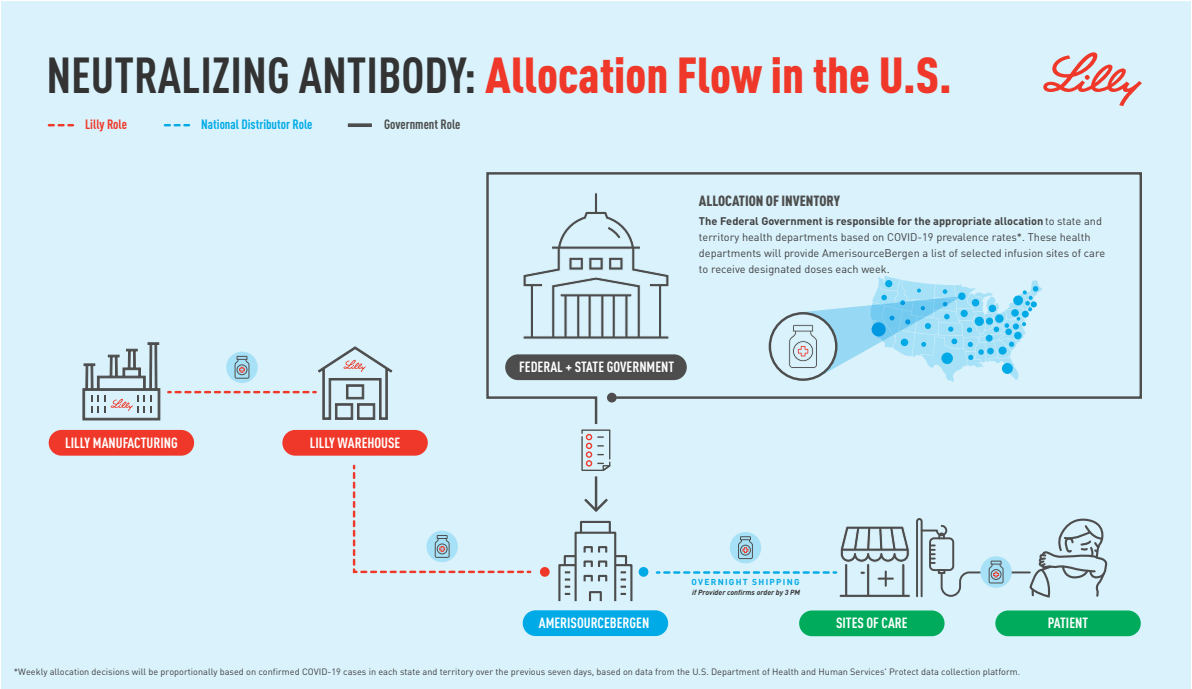
Flow of Allocated Product

Below is a depiction of the basic flow of allocated product. Through a government allocation program, the Federal Government, in partnership with state health departments, will provide the contracted distributor, AmerisourceBergen, with a list of infusion sites of care approved for a product allocation on a periodic basis. The distributor will then contact the approved infusion sites of care, confirm they would like to receive the allocated amount of product and then ship the product.



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SECTION 04

INFUSION SITE OF CARE REQUIREMENTS

INFUSION SITE OF CARE REQUIREMENTS

Preparation, Storage and Handling

Prepare sterile infusions in a manner consistent with local laws, regulations, guidelines and policies and with National Infusion Center Association (NICA) standards for outpatient infusion.*

National Infusion Center Association Parenteral Medication Preparation Guidelines

According to NICA standards, prepared product is intended for immediate administration to an individual patient. Administration of parenteral medications should begin immediately, ideally within one hour of beginning preparation. If extenuating circumstances preclude immediate administration, manufacturer guidelines regarding stability and storage must be followed; however, storage should not exceed 4 hours unless the product was prepared in accordance with United States Pharmacopeia (USP) General Chapter 797 pharmacy standards for compounding sterile products.

- Use aseptic technique and applicable good clinical practice for intravenous solution preparations of bamlanivimab in accordance with NICA standards.
- Only use materials which are listed as compatible with bamlanivimab for preparation and administration of the infusion solutions (see **Compatible Materials** section below).
- Gather the recommended materials for infusion:
    - Polyvinylchloride (PVC) infusion set containing a 0.20/0.22 micron filter.
- Use new, sterile syringes and needles to prepare each dosing solution of bamlanivimab.
- Refrigerate bamlanivimab drug product when not in use at 2°C to 8°C (36°F to 46°F).
- Bamlanivimab 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 is administered 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 (and the solution has been prepared according to USP 797 guidelines), 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. The hold time includes preparation, solution hold, infusion and flush. Any solution which exceeds these time period requirements and/or is not compounded according to USP 797 guidelines MUST BE DISCARDED and a fresh solution MUST BE PREPARED.

Find more information on National Infusion Center Association (NICA) standards for outpatient infusion.

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. Bamalanivimab has no known incompatibilities with conventional medical supplies and equipment. During clinical trials, Lilly has used the following materials:

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

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.

Preparation and Administration

- **The 700 mg dose MUST BE prepared using 0.9% sodium chloride.**
    - Preparation of 700 mg dose of bamlanivimab for IV infusion*
    - Administration of a dose of 700 mg of bamlanivimab in an IV infusion*

    **Applicable state/local/federal agencies, regulatory bodies, and industry standards (e.g. USP 797, NICA Standards for In-Office Infusion).*
- Bamlanivimab solution for infusion should be prepared by a qualified health care professional using aseptic technique.
- Refer to section on **Preparation Summary Table for 700mg Dose of Bamlanivimab Solution for Intravenous Infusion** for additional dose preparation information.
- Remove ONE (1) vial of bamlanivimab injection, 700mg/20mL (drug product) from refrigerated storange at 2°C to 8°C (36°F to 46°F), and equilibrate the vial to room temperature, not exceeding 30°C or 86°F for approximately 20 minutes (or no longer cool to the touch). **Do not expose to direct heat.**
- **Do not shake** or vigorously agitate the vial. Visually inspect the vial for the presence of any visible particulate matter and discoloration. Bamlanivimab is a clear to slightly opalescent and colorless to slightly yellow to slightly brown solution. If visible particulate matter is observed, appropriately discard the vial, obtain a new vial, and restart the preparation, beginning at the prior step.
- Prepare the IV solution using the following approach using aseptic technique.
    - The IV solution can be prepared using a filled 250mL IV bag. Using a syringe with an 18-gauge needle, withdraw a total of **70mL** of 0.9% sodium chloride from the IV bag and discard that volume, leaving **180mL** in the IV bag.
    - Using a new, sterile syringe with an 18-gauge needle, withdraw **20mL** of bamlanivimab from the prepared vial and inject the contents into the prepared IV bag, so that the combined total volume is **200mL**.
- Gently invert the prepared IV bag by hand approximately 10 times to ensure homogeneity of the contents. **Do not shake** or vigorously agitate the prepared bag. Avoid foaming. Visually inspect the bag after preparation. The contents of the bag should be free of any visible particulate matter. Obtain new vial(s) and re-prepare the dose if visible particulate matter is observed.

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

- Attach an infusion set containing a 0.20/0.22 µm filter to the IV bag.
- Prime the infusion set and adjust for a **flow rate of 200mL/hr** for both infusion pumps and gravity infusion. Administer the infusion solution over **60 minutes**.

Infusion sites of care can use the following chart to calculate a 60 minute drip rate when administering via gravity infusion.

60 Minute Drip Rate for Gravity Infusion

VTBI (mL)	Duration (min)	Drip factor (drops per milliliter)	Drops per minute	Drops per 15 seconds
200	60	10 gtt/mL	33 gtt/min	8 drops per 15 seconds
200	60	12 gtt/mL	40 gtt/min	10 drops per 15 seconds
200	60	15 gtt/mL	50 gtt/min	13 drops per 15 seconds
200	60	20 gtt/mL	67 gtt/min	17 drops per 15 seconds
200	60	60 gtt/mL	200 gtt/min	50 drops per 15 seconds

- At the discretion of the infusion site of care medical staff, the proposed infusion rate may be reduced and the corresponding infusion time increased for infusion reactions or patient circumstances.
- This product is preservative-free and therefore, the diluted infusion solution should be administered immediately. If immediate administration is not possible (and the solution has been prepared according to USP 797 guidelines), 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. The hold time includes preparation, solution hold, infusion and flush. Any solution which exceeds these time period requirements and/or is not compounded according to USP 797 guidelines MUST BE DISCARDED and a fresh solution MUST BE PREPARED.
- After the entire infusion volume of **200mL has been administered**, flush the infusion line as per infusion site of care requirements or with sufficient volume to flush residual volume from tubing to ensure patient receives entire dose. Discard unused product.
- For additional information, please see **Fact Sheet for Healthcare Providers**.

Preparation Summary Table for 700mg Dose of Bamlanivimab Solution for Intravenous Infusion

Bamlanivimab dose	700mg
Volume of bamlanivimab drug product (and # of vials) needed	20mL (1 vial)
Volume of 0.9% sodium chloride to discard from 250mL IV bag	70mL
Nominal bamlanivimab dosing solution concentration	3.5mg/mL
Total infusion volume prepared and administered	200mL
Infusion rate[1]	200mL/hr.
Infusion time[1]	60 min.

[1]At the discretion of the infusion site of care medical staff, the proposed infusion rate may be reduced and the corresponding infusion time increased for infusion reactions or patient circumstances.

Note: Upon completion of intravenous infusion, the infusion line should be flushed as per infusion site of care requirements or with approximately 25mL of 0.9% sodium chloride with the flush volume administered to the patient to ensure delivery of the required dose.

SECTION 5

RECOMMENDED INFUSION SITE OF CARE RESOURCES AND EQUIPMENT CONSIDERATIONS

STAFFING RECOMMENDATIONS

Staffing requirements may vary by state. Follow your local requirements 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 bamlanivimab antibody infusion.

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.

Role	Recommendations
Patient intake	Person with basic administrative skills
Drug infusion preparation	Health care professional trained in IV admixture preparation (such as a nurse, pharmacist, pharmacy tech)
Infusion: start IV	Health care professional trained to start an IV
Infusion: administer infusion	Health care professional trained in administering IV infusion
Infusion monitoring	Healthcare professional trained in: • assessing infusion-related reactions • treating infusion-related reactions • vital sign monitoring
Post-infusion observation	Healthcare professional trained in: • assessing infusion-related reactions • treating infusion-related reactions • vital sign monitoring • providing discharge 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 health care professional should have Advanced Cardiovascular Life Support (ACLS) or Basic Life Support (BLS) certification or equivalent.
- The same health care professional may perform more than one role.
- State or county requirements may dictate specific qualifications for some roles.

INFUSION SITE OF CARE MATERIALS

Equipment requirements may vary by state. Follow your local requirements 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 infusion site of care environment for patients receiving bamlanivimab 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)
- Privacy screens
- 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 250mL PVC IV bags (infusion prep), if required 250mL 0.9% sodium chloride (infusion prep) Pre-filled saline 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 requirements.

**24g catheter is sufficient

SECTION 06

EDUCATION AND AWARENESS

EDUCATION AND AWARENESS

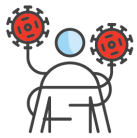
Attacking the coronavirus will require a diverse set of approaches, including both vaccines and treatments, such as antibodies.

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

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

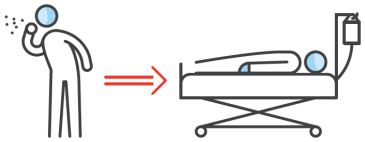
- Monoclonal antibody drugs, like bamlanivimab, provide passive immunity by giving the body antibodies to protect itself. Vaccines provide active immunity by helping the body make its own antibodies to protect itself.
- Monoclonal antibody drugs are designed to start working faster than vaccines, while 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:



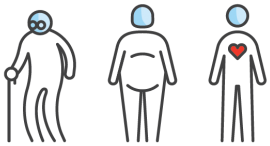
Viral exposure

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

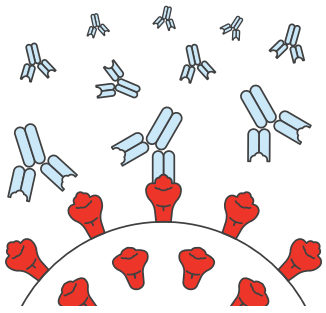


At-risk populations

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. 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:

- www.coronaviruspreventionnetwork.org
- www.infusioncenter.org/
- Fact Sheet for Healthcare Providers
- Fact Sheet for Patients, Parents and Caregivers (English)
- Fact Sheet for Patients, Parents and Caregivers (Spanish)
- FDA Letter of Authorization

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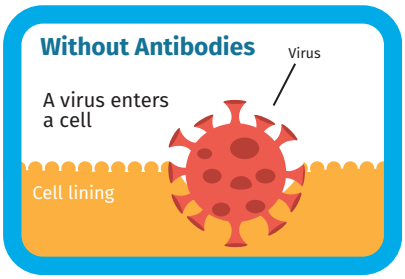
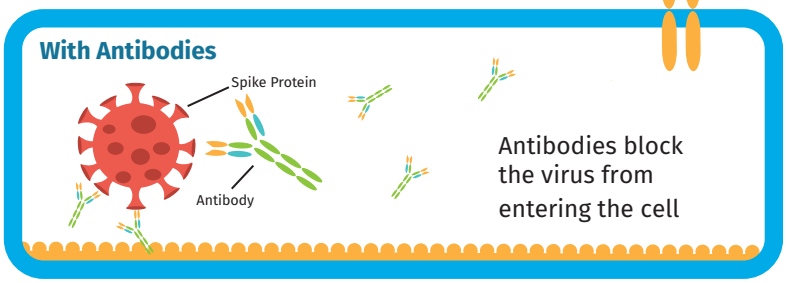
Monoclonal Antibodies

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 Symtoms | Nausea & Vomiting | Diarrhea | Low blood pressure

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

COVID-19 Prevention Network
PreventCOVID.org

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APPENDIX A

LILLY MONOCLONAL ANTIBODY CLINICAL TRIAL MODELING INFORMATION

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 consent and intake time, there are estimated ranges shown, with "+" or "-" conditions in parentheses.

Infusion Timing

Criteria	Details	Additional Notes
Consent and intake time	30 min (+/- 15 min)	Consent and intake may occur outside of the infusion chair, such as at the prescriber's location, and consent 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	60 min (+30 min)	Infusion time should be a minimum of 60 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 requirements when determining appropriate observation periods.
TOTAL TIME	**165–225 min**	**This represents the estimated total time from consent 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.

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APPENDIX B

BASIC EQUIPMENT RECOMMENDATIONS

BASIC EQUIPMENT RECOMMENDATIONS

Equipment requirements may vary by state. Follow your local requirements 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 bamlanivimab antibody infusion.

Basic Equipment Recommendations

Drug preparation	Locked refrigerator with min/max temp monitoring Prep table or area 18ga needles Appropriate sized syringes 250mL PVC IV bags (infusion prep), if required 250mL 0.9% sodium chloride Sterile alcohol prep pads PPE gloves all sizes PPE face shields or goggles PPE N95 masks Sharps containers Drug transport bags (if using mobile pharmacy) Alcohol sanitizing wipes Step-by-step instruction sheet (with images)
Patient intake and release	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

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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, 02 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 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 50mL 0.9% sodium chloride bags 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, 02 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

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MEDICAL EMERGENCY SUPPLIES AND MEDICATIONS

Emergency medical management equipment should contain the following items:

Some medications listed below should only be administered by HCP with ACLS training

	Essential	Recommended
Medications	Albuterol inhaler Diphenhydramine injection Epinephrine 0.1 mg/mL (1 mg/10mL) OR epinephrine auto-injector 0.3 mg Solu-Medrol injection	Adenosine injection Atropine sulfate Chewable ASA Dextrose 50% injection Insta glucose Nitroglycerine Ondansetron injection Sodium bicarb injection
IV supplies	0.9% Sodium chloride flush (10mL) 0.9% Sodium chloride bag (500mL)	IV admin set IV start kit IV catheter Non-DEHP cath/extension set 5% dextrose bag
Airway	Barrier mask for CPR Ambu Bag	Nasopharyngeal/oral airway suction
Emergency medical management	Infusion sites of care should have a standard operating procedure in place instructing infusion site of care staff how emergency events should be managed, including appropriate contacts (911, physician, etc.), ACLS protocol and any follow-up activities.	