

White Paper:

Operationalizing the delivery of Bamlanivimab infusions in an FQHC

Overview:

On Nov 9, 2020, the FDA issued an Emergency Use Authorization to Eli Lilly and Company for the investigational monoclonal antibody (mAb) treatment bamlanivimab. This EUA allows health care providers to administer bamlanivimab to non-hospitalized patients with confirmed COVID-19 who are experiencing mild to moderate symptoms and are at high-risk for severe symptoms and hospitalization.

The Department of Health and Human Services (HHS), the Office of the Assistant Secretary for Preparedness and Response (ASPR), Eli Lilly and Company, and AmerisourceBergen (the distributor of the drug), have been working with state and territorial health departments to distribute bamlanivimab to local health care facilities.

St. John's Well Child and Family Center was identified as a site for drug allocation and distribution. At the time of this assignment, St. John's did not have experience with infusion medications in any of its 17 outpatient clinic settings. As such, the medical and operations staff had to quickly design and execute on a safe and efficacious plan to deliver the medication to patients in need.

The logistics of mAb administration are difficult for several reasons:

- Patient eligibility is narrow, so screening correctly is important.
- It must be given intravenously, and many outpatient clinics do not have the ability to give infusions on site.
- People in the early stages of COVID-19 are at their most contagious, so risk-mitigation is critical.
- Prepared IV admixture is stable for just 7 hours at room temperature or 24 hours under refrigeration (including infusion time).
- Both infusion and post-treatment monitoring demand significant time, so close attention to operations is needed to get the workflow just right.
- Serious side effects may occur.

These logistical hurdles are enormous, and not easy to get right. To assist other outpatient clinic systems that are interested in a similar effort, we have put together this white paper to disseminate the lessons from our experience.

In this white paper, we will consider the following questions:

1. What are monoclonal antibodies?
2. What are the eligibility criteria for patients to receive bamlanivimab?
3. What licensing considerations need to be undertaken in setting up an infusion center?

4. What are the structural requirements, equipment provisions and staffing needs of an infusion clinic?
5. How is bamlanivimab shipped and prepared?
6. What reporting requirements exist for serious adverse events related to bamlanivimab?
7. What Electronic Health Record changes were needed to support the workflow?

The content in the following resource is meant to be used as a general guideline. St. John's Well Child and Family Center is not responsible for damage resulting from the use of this material.

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1. What are monoclonal antibodies?

Monoclonal antibodies (mAbs) directly neutralize the COVID-19 virus and are intended to prevent progression of disease.

These mAbs are likely to be most effective when given early in infection.

Product is delivered via a single IV infusion treatment.

Early evidence appears to suggest promise of mAb products in outpatient settings -

- Early evidence from Eli Lilly – bamlanivimab – showed potential to reduce hospitalization rates or emergency room visits for infected people within 28 days after treatment if given early in infection (the phase 2 BLAZE-1 clinical trial).
- Early evidence from Regeneron data showed potential to reduce viral load and alleviate symptoms compared to placebo through Day 7 in seronegative patients.

2. What are the eligibility criteria for patients to receive bamlanivimab?

Per the FDA, 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-10 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity

Per the EUA, Bamlanivimab is used for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older, weighing at least 40kg) 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.

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.

St. John’s operationalized patient selection through our inclusion and exclusion criteria:

Inclusion criteria:

- 12 or older age group
- Weigh at least 40 kg
- Positive COVID PCR
- Within 10 days of symptom onset
- Meets high risk criteria (listed above)

Exclusion criteria:

- Currently hospitalized due to COVID-19
- Require oxygen therapy due to COVID-19
- Require an increase in baseline oxygen flow rate due to COVID-10 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity
- Currently pregnant or breast-feeding (institutional policy based on lack of data/ literature on the safety of the medication and difficulty of intervention in case of adverse side effects in this population in an outpatient setting)

3. What licensing considerations need to be undertaken in setting up an infusion center?

California law allows nurses to administer, but not furnish, medications and therapeutic agents ordered by and within the licensed practice of a physician. PAs and NPs also may administer, furnish and order drugs in limited circumstances – under physician supervision and pursuant to standardized procedures or protocols developed with their supervising physicians.

Per FTCA regulations, as the proposed infusion center would be incorporated into our existing clinic apparatus, we did not need to apply for additional licensing. Received similar feedback from the pharmacy board.

4. What are the structural requirements, equipment provisions and staffing needs of an infusion clinic?

In considering clinic selection, we prioritized the following characteristics:

- Infusion rooms equipped with comfortable chairs.
 - o We ended up using a dental clinic with excess capacity, with reclining chairs.
- The infusion room has to have a sink.

- Separate room for staff where they can consume food and drinks.

The infusion itself takes an hour, followed by observation for allergic or adverse reactions for another hour. Between patient intake, preparation of the infusion, starting the infusion, and cleaning the room post-infusion, we allocated 3 patients per chair over an 8-hour shift.

Equipment:

PPE	Infusion	Supplies
<ul style="list-style-type: none"> • Negative pressure air filters for each room • Head cap • Face shield • N-95 or KN-95 mask • Gown • Gloves • Shoe covers • PPE-disposing containers (regular and biohazard) <p>All these for both patients and staff</p>	<ul style="list-style-type: none"> • Infusion pump • (can use gravity infusion) • IV needle and IV starter kit • Vitals machine • Normal Saline infusion bags • Polyvinylchloride infusion set containing 0.20/0.22 micron inline polyethersulfone filter • Syringes- 20 ml and 2ml syringes • Saline swabs, gauze pieces • Antiseptic lotions 	<ul style="list-style-type: none"> • Comfortable chair for the patient • Sharps containers • water bottles for staff and patients • Refrigerator • Crash cart • Cameras with remote monitoring • TV for each room • Emergency calling bell for the patients • 3 working computers at staff room and 3 working phones. (One of them with DID for patients to call the center)

Medications:

- Ondansetron ODT 4 mg
- Ondansetron 4 mg IV for nausea
- Diphenhydramine 25 mg IV
- Albuterol inhaler
- Solu-Medrol injection
- 0.9% Sodium chloride flush (10 mL)
- 0.9% Sodium Chloride bag (500 mL)
- Epinephrine 0.3 mg IM
- Bamlanivimab 700 mg in 0.9% NaCl
- Famotidine
- Clonidine and
- Hydralazine

Staffing:

- One MD on site in a supervisory role
- NP or PA
- RN
- Medical Assistant
- Care-coordinator
- Custodial crew to clean the rooms after each infusion
- Pharmacist for medication management (not on-site)
- IT support
- Infusion therapy specialist/ trainer as needed

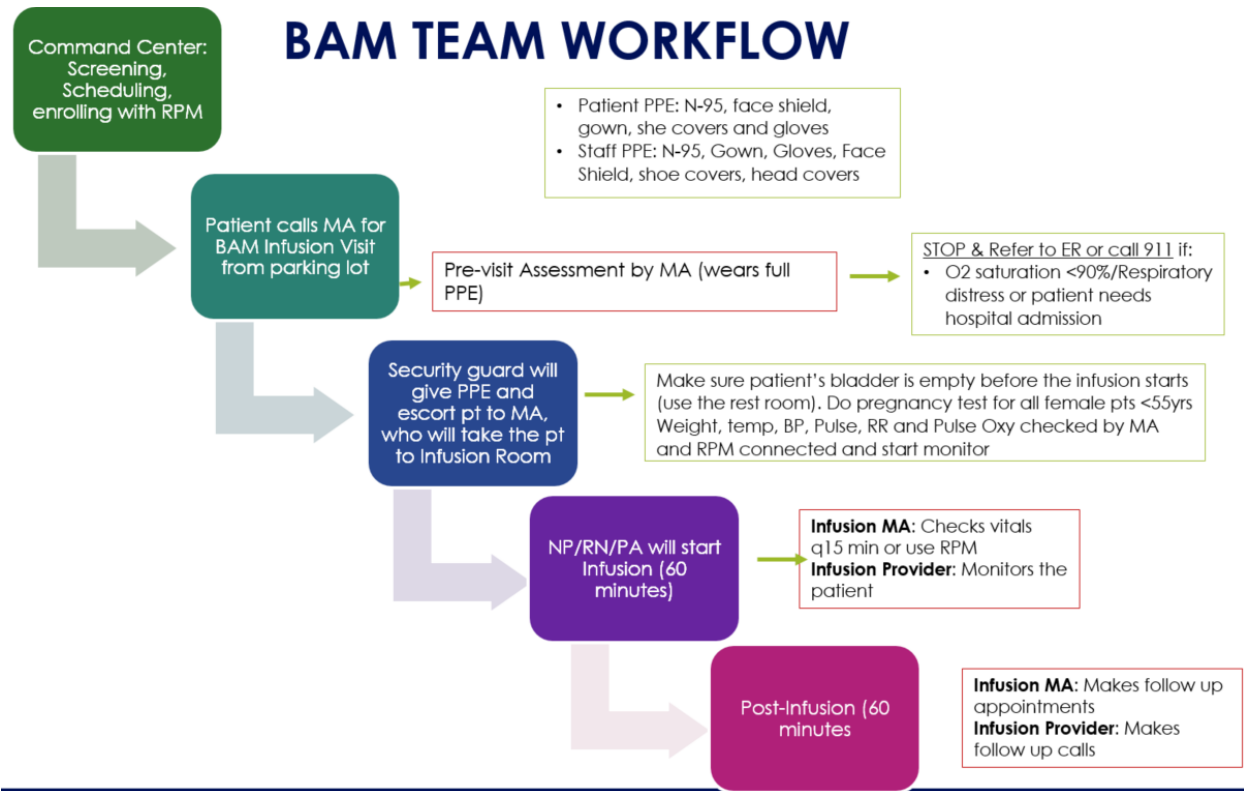
Roles and Responsibilities, organized by workflow:

Roles	Responsibilities
Referring center & clinicians	Screening and refer the patient for infusion
Care Coordinator	Scheduling, patient pre-infusion checklist review. Document emergency contact. Make referral for Remote Patient Monitors (RPM)
Medical Assistant	Confirm appointment the day before and the day of appointment
Medical Assistant	Patient check-in, pregnancy test, prepare PPE tests
NP/ PA/RN with IV experience	Prepare drug, start and administer the IV infusion
RN (NP or PA in the RN absence)	Maintain medication logs and patient lists
Medical Assistant	Monitor vitals q15 min and document
NP or MA + RN	Post-infusion observation
MD/DO	On-site infusion supervision
RN/ NP/ PA and notify MD/DO	Treatment for adverse reaction
Medical Assistant	Discharge patient with RPM (Pulse Oximeter and thermometer) equipment, makes an appointment with NP/PA for follow ups
NP/PA	Follow up next day & in 3 days by phone call Report any adverse events to Medwatch

Bamlanivimab Team workflow:

We clinically monitor patients during the infusion and observe patients for at least 1 hour after infusion is complete.

We advise patients post-infusion to 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. We also send them home with Remote monitoring devices we used during the infusion.



We provide patients with contact information to the clinic hotline for adverse reactions. We operationalized a workflow to ensure that an NP or PA calls the patient the day after infusion to check on them. We also provide education to the patient about calling 911 if they develop severe shortness of breath, high fever, chest pain, extreme fatigue, or other side effects.

5. How is bamlanivimab shipped and prepared?

Bamlanivimab is supplied as one single-dose 20-ml vial per carton. There are 50-100 cartons delivered per case based on order.

Unopened vials must be stored at refrigerated temperatures (2°C–8°C / 36°F–46°F) until use. Vials should not be frozen, shook, or exposed to direct light.

Per FDA guidance, Bamlanivimab solution for infusion should be prepared by a qualified healthcare professional using aseptic technique:

- Remove one bamlanivimab vial (700 mg/20 mL) 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 vial.**
- Inspect bamlanivimab visually for particulate matter and discoloration.
 - o Bamlanivimab is a clear-to-opalescent and colorless to slightly yellow-to-slightly brown solution.
- Withdraw Bamlanivimab from one 20 mL vial and inject into the infusion bag containing 250 mL prefilled 0.9% Sodium Chloride Injection (see **the table below**).
- 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]) 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.

Per manufacturer, there is no dosage adjustment based on age, sex, race, body weight, renal or mild hepatic impairment, during pregnancy or while lactating, or for disease severity or inflammation.

As stated previously, St. John's policy has been to defer on administering this to pregnant or breast-feeding patients due to limited experience treating this population with bamlanivimab and the nature of our standing out-patient setting.

6. What reporting requirements exist for serious adverse events related to bamlanivimab?

As part of the EUA, FDA is requiring health care providers who prescribe bamlanivimab to report-

- all medication errors and serious adverse events considered to be potentially related to bamlanivimab
- Through FDA's MedWatch [Adverse Event](#) Reporting program.
 - Providers can complete and submit the report [online](#) or
 - download and complete the [form](#), then submit it via fax at 1-800-FDA-0178.
- This requirement is outlined in the EUA's health care provider [Fact Sheet](#).
- FDA MedWatch forms should also be provided to Lilly Global Patient Safety Fax: 1-317-277-0853 or E-mail: mailindata_gsmtindy@lilly.com

To operationalize adherence to best practices, reporting requirements, and managing adverse reactions, we ensured that the following documents were always present on site and on the Electronic Health Record:

- Emergency Contacts
- FDA-Approved Fact Sheet in both English and Spanish
- COVID Infusion Referral Workflows
- Policies and procedures on infusion and managing anaphylaxis
- Reporting Documents
- Patient and Medication Logs (Sharepoint)

7. What Electronic Health Record changes were needed to support the workflow?

We created an infusion referral template for the referring providers to use. This template includes all the indications, contraindications, and verbal consent and understanding of the patient about the EUA status of the drug.

We also created another template for Infusion center that includes indications for infusion, drug information and it's EUA status, explanation of side effects, emergency contact verification, pregnancy test, documentation of breast feeding if any. We also added assessments for the Covid transfusion along with the codes as below. We printed copies of the FDA fact sheet attestation for patients in both English and Spanish, and also saved them in patient letters to give to the patient before transfusion.

Per CMS, we used the following Medicare Part B codes for payment:

Code	CPT Short Descriptor	Labeler Name	Vaccine/Procedure Name	Payment Allowance
Q0239	bamlanivimab -xxxx	Eli Lilly	Injection, bamlanivimab, 700 mg	\$0.010*
M0239	bamlanivimab -xxxx infusion	Eli Lilly	Intravenous infusion, bamlanivimab-xxxx, includes infusion and post administration monitoring	\$309.600* **

**For providers and suppliers with payments that are geographically adjusted by the methodology used by the Medicare Physician Fee Schedule (MPFS), files with the geographically adjusted payment rates for monoclonal antibody administration are included in the “Additional Resources” section. Certain settings utilize other payment methodologies.

In summary:

- Confirm clinic leadership supportive of participation
- Prepare your site and staff for outpatient mAbs administration, by developing staffing plan and workflows
- Ensure sufficient supply of needed materials for treatment
- Develop workflows to refer the patients using proper inclusion and exclusion criteria and using appropriate indications
- Educate the patient before infusion, and follow-up post-infusion and provide appropriate support system.
- Use Remote Patient Monitoring devices to monitor the patients, post-follow up if available.