



Federal response to COVID-19: Monoclonal Antibody Playbook

Outpatient administration playbook version 2.2

25 FEB 2021

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Product specific supplements to this playbook will also be made available by manufacturers

Introduction

EUA Playbook Audience

This playbook is intended to support sites interested in administering COVID-19 treatment under EUA including:

- Existing hospital or community-based infusion centers
- Existing clinical space (e.g. urgent care, emergency depts)
- Ad hoc new infusion sites (e.g. "hospitals without walls")
- Long-term care facilities or home infusions with infusion delivery capability

Initial version of playbook focused on:

- Monoclonal antibody treatment
- Delivery via infusion
- Outpatient setting

This playbook will continue to evolve as other treatments and administration methods become available. We hope this playbook will be used to help healthcare facilities to implement monoclonal antibody treatment in an outpatient setting for those with COVID-19.

Context of mAbs outpatient administration playbook

Proven **operationally challenging** to run monoclonal antibodies clinical trials in **outpatient setting** for variety of reasons

Recent EUAs have been granted for Eli Lilly and Regeneron only **for outpatient setting**

Few sites likely to have experience with this type of procedure in an outpatient setting with COVID-19 patients

Scope of this playbook

Goal of playbook to articulate what is needed for outpatient administration to potential Tx sites:

- **Supplies likely required** for administration and potential challenges in procurement
- **Personnel needed** for infusions
- **Space and logistics** needed to safely treat COVID-19 patients and protect others
- **Drug administration** process
- **Reimbursement** process
- **Reporting** process

Elements currently out of scope

- Process for site **engagement with state health departments** on ordering or reporting
- **Mechanisms for communication with United States Government** on allocation or distribution

To be addressed in future versions of the playbook

Overview of therapeutic

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

mAbs likely to be most effective when **given early in infection**

Product delivered via **single administration (e.g., IV infusion)**

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

- Early evidence from Eli Lilly mAb **showed potential to reduce hospitalization** for infected people if given early in infection in BLAZE-1 clinical trial
- Early evidence from Regeneron mAb cocktail data showed potential to decrease **viral load** and **reduced medical visits** in infected people if given early in the Outpatient 2067 clinical trial

**mAbs
products now
available
under EUA
therefore...**

Administration site **does not need to be a clinical trial site** to administer product

Informed consent is not needed to administer products under EUA

No clinical data reporting required beyond established mechanisms for tracking and reporting serious adverse events; teletracking data reporting required on utilization of product

Treatment eligibility

Products granted EUA for **mild to moderate COVID-19 cases** early in infection, who are at **high risk for progressing to severe COVID-19 and/or hospitalization**; with following criteria

- Confirmation via **positive PCR or antigen test**
- Treatment **as soon as possible** following positive viral test and **within 10 days of symptom onset**
- Patient symptomatic but **not yet progressed to require hospitalization or oxygen therapy**

Treatment recommended just for **high-risk adult and pediatric patients 12 years and older >40 kgs** – high-risk defined as patients who meet at least one of following criteria:

- | | |
|---|---|
| <ul style="list-style-type: none">• ave BMI ≥ 35• Have chronic kidney disease• Have diabetes• Have immunosuppressive disease• Are currently receiving immunosuppressive treatment• Are ≥ 65 years of age | <ul style="list-style-type: none">• Are 12-17 years of age AND have<ul style="list-style-type: none">- BMI $\geq 85^{\text{th}}$ percentile for age/gender based on CDC growth charts, OR- Sickle cell disease, OR- Congenital or acquired heart disease, OR- Neurodevelopmental disorders, OR- A medical-related technological dependence, OR- Asthma, reactive airway or other chronic resp. disease that requires daily meds/control |
| <ul style="list-style-type: none">• Are ≥ 55 years of age AND have<ul style="list-style-type: none">- Cardiovascular disease, OR- Hypertension, OR- Chronic obstructive pulmonary disease (or others) | |

Please reference EUA factsheets for specific treatment guidelines and detailed definitions of high-risk patients

**For your awareness
(e.g. for patients not eligible for treatment under EUA):**

Monoclonal antibodies **under evaluation** for additional indications

Participation encouraged in clinical trials to assess additional drugs and indications

Clinical trial information available at

<http://www.riseabovecovid.org>

Lilly clinical trials:

<https://blaze2study.com/>
<https://trials.lillytrialguide.com/en-US/>

Regeneron clinical trials:

<https://www.regeneron.com/covid19>

EUA summary: Eli Lilly Bamlanivimab

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved product bamlanivimab for the treatment of mild to moderate coronavirus disease 2019 (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 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 when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation

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

For additional information— please reference EUA factsheet

Key caveats

The EUA is for the use of the **unapproved product** bamlanivimab to treat COVID-19

Bamlanivimab is an **investigational drug** that has not been approved by the FDA for any use; and should not be considered the standard of care for treatment of patients with COVID-19

It is **not yet known** if bamlanivimab is **safe and effective** for the treatment of COVID-19

This use is authorized **only for the duration of the declaration** that circumstances exist justifying the authorization of the emergency use, unless the authorization is terminated or revoked sooner

Health care providers must submit a report on **all medication errors and ALL SERIOUS ADVERSE EVENTS** related to bamlanivimab

EUA summary: Regeneron (casirivimab/imdevimab)

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved products casirivimab/imdevimab to be administered **together** for the treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adults 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 progressing to severe COVID-19 and/or hospitalization

Casirivimab/Imdevimab 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

Benefit of treatment with casirivimab/imdevimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as casirivimab/imdevimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation

Casirivimab/imdevimab 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

For additional information— please reference EUA factsheet and [RegeneronEUA.com](https://www.fda.gov/oc/ohrt/eua-casirivimab-imdevimab)

Key caveats

The EUA is for the use of the **unapproved products** casirivimab/imdevimab to treat COVID-19

Casirivimab/imdevimab are **investigational drugs** that have not been approved by the FDA for any use; and should not be considered the standard of care for treatment of patients with COVID-19

It is **not yet known** if casirivimab/imdevimab are **safe and effective** for the treatment of COVID-19

This use is authorized **only for the duration of the declaration** that circumstances exist justifying the authorization of the emergency use, unless the authorization is terminated or revoked sooner

Health care providers must submit a report on **all medication errors and ALL SERIOUS ADVERSE EVENTS** related to casirivimab/imdevimab

EUA summary: Eli Lilly (bamlanivimab/ etesevimab)

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved products bamlanivimab/ etesevimab to be administered **together** for the treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adults 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 progressing to severe COVID-19 and/or hospitalization

Bamlanivimab/ 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

Benefit of treatment with bamlanivimab/ etesevimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab/ etesevimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation

Bamlanivimab/ etesevimab 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

For additional information— please reference EUA factsheet

Key caveats

The EUA is for the use of the **unapproved products** bamlanivimab/ etesevimab to treat COVID-19

Bamlanivimab/ etesevimab are **investigational drugs** that have not been approved by the FDA for any use; and should not be considered the standard of care for treatment of patients with COVID-19

It is **not yet known** if bamlanivimab/ etesevimab are **safe and effective** for the treatment of COVID-19

This use is authorized **only for the duration of the declaration** that circumstances exist justifying the authorization of the emergency use, unless the authorization is terminated or revoked sooner

Health care providers must submit a report on **all medication errors and ALL SERIOUS ADVERSE EVENTS** related to bamlanivimab/ etesevimab



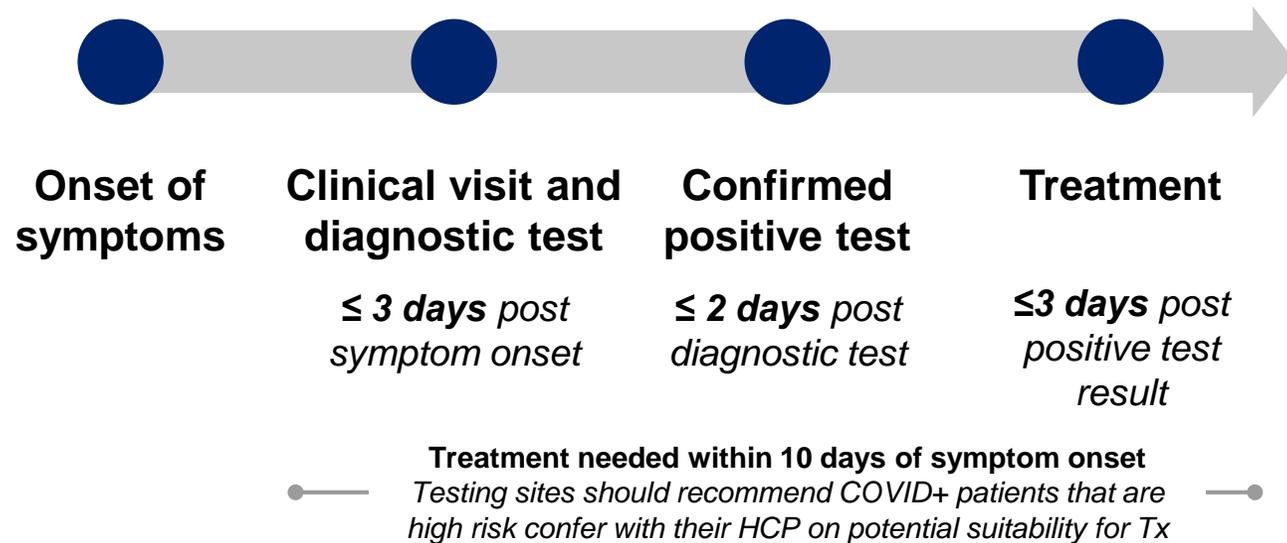
Based on what we have learned to date - early administration of treatment needs **fast testing turnaround** and **patient scheduling**

Planning required for **"Test and treat"** or **"Test and refer"** models

Overview

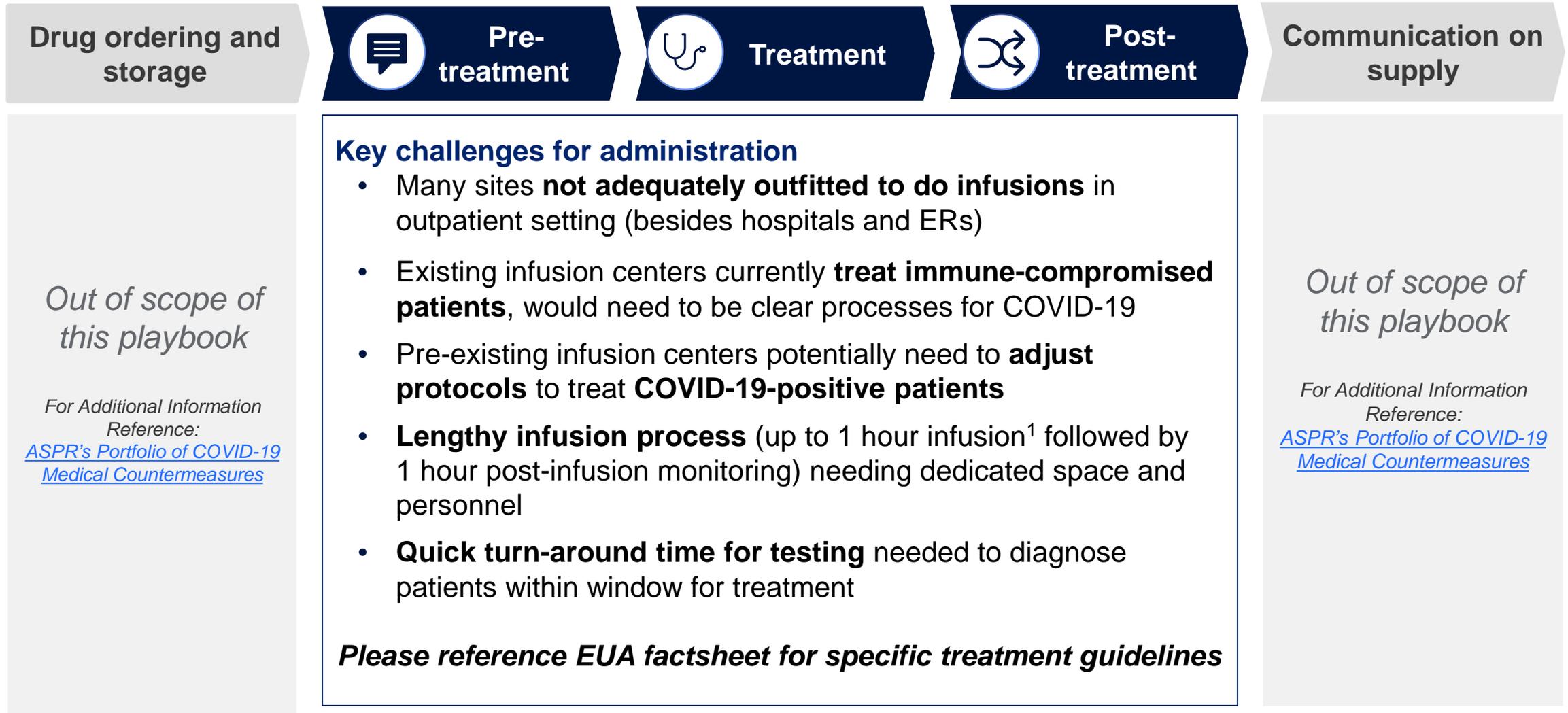
- Treatment likely most beneficial to patients if given **early in symptom progression**
- EUA requires administration of **treatment as soon as possible** after confirmed positive test result and within **10 days of symptom onset**
- Strong **partnership and communication** between patients and HCP to get right treatment to right patients at right time
- Fast testing turnaround needed, to efficiently **identify positive tests** and **schedule for treatment**

Example of timeline which would fulfill EUA requirements



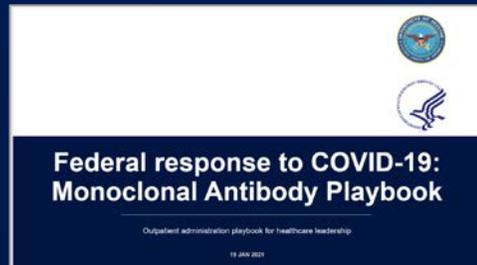
Please reference EUA factsheet for specific treatment guidelines including recommended treatment window

Key challenges to overcome to allow for successful administration of mAb in outpatient setting



1. Contingent on product dilution, reference EUA fact sheet for dilution and infusion timing

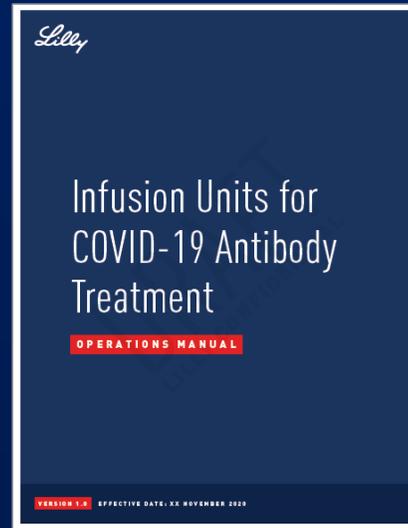
Playbook resources for hospital administrators and leadership



Federal response playbook for Healthcare administrators

Objective to summarize requirements to administer monoclonal antibodies for healthcare facilities interested in administering the product

[This document](#)

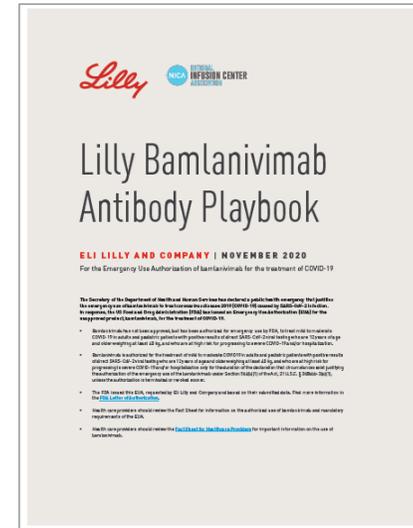


Eli Lilly Infusion Units for COVID-19 Antibody Treatment

Objective to provide recommendations for establishing infusion units to treat COVID-19 patients in diverse settings

[Infusion units for COVID-19 Antibody treatment link](#)

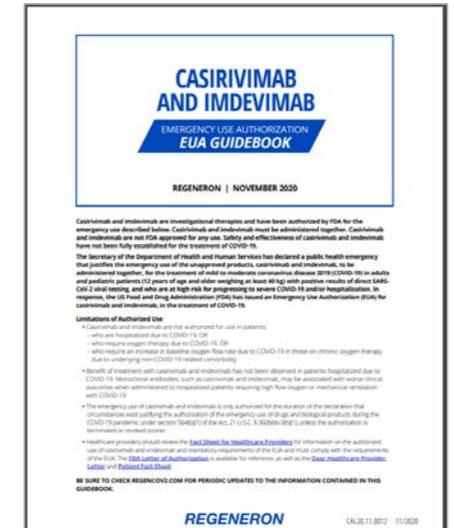
Playbook resources for healthcare providers administering mAbs



[Eli Lilly Bamlanivimab Antibody Playbook](#)

Objective to help sites of care operationalize a Bamlanivimab antibody response to COVID-19 across varying infusion sites of care

<https://www.covid19.lilly.com/assets/pdf/bamlanivimab/lilly-antibodies-playbook.pdf>



[Regeneron EUA guidebook](#)

Provides additional detail on administration requirements for Regeneron mAbs product

<https://www.regeneroneua.com/Content/pdf/treatment-covid19-eua-guidebook.pdf>

**Please note...
EUA
guidelines
continue to
evolve**

**Please reference EUA fact-
sheets for latest treatment
guidelines and information**

FDA continues to update
dilution requirements and
infusion times based on latest
clinical information

Comprehensive checklist overview

Plan of action to administer monoclonal antibodies under outpatient EUA



Confirm your site wants to participate

- Review needs** for treatment in outpatient settings
- Ensure site prepared** to meet needs for treatment or willing to make required investments
- Confirm site leadership supportive** of participation
 - Including senior clinical leadership (e.g., Chief Medical Officer)
- Approval of product for use by the hospital's **Pharmacy and Therapeutics Committee** (or equivalent committee)
- Coordinate with State Chief Medical Officers** to confirm participation



Prepare your site and staff for outpatient mAbs administration

- Ensure **sufficient supply** of needed materials for treatment
 - Infusion supplies, resuscitation equipment, etc.
- Develop **staffing and personnel** plan to support treatment
- Allocate **needed facilities and equipment** to support administration
- Ensure existing **infection prevention plan** sufficient
 - Adjust existing plan if needed to safely manage patient flow
 - Consider potential security requirements if needed
- Review **drug administration needs** with staff
- Inquire with hospital leadership about **reimbursement process**
- Prepare for **adverse events data tracking process**



Develop procedures to identify and treat patients in timely manner

- Prepare for scheduling and routing of referrals** from testing center or other HCPs to treatment
- Ensure hospital staff and doctors are **aware of outpatient treatment** availability
- Ensure **patient privacy** (HIPAA compliant) **maintained during** process
- Communicate to patient that EUA issued for investigational treatment but **does not constitute research** on behalf of the hospital

Readiness checklist: Administration of outpatient mAbs under EUA



Allocate **dedicated space** and develop plan to **manage patient flow**

- Clear process for patients that are coming to clinical site including scheduling requirements
- Admission process for COVID-19 positive patients designed to minimize risk of spread per facility requirements / directions / guidelines'
- Dedicated room available for treatment



Ensure **dedicated source of supplies**; which may be difficult to procure

- Needed infusion components obtained
 - Example: IV kits, infusion chair, IV pole, vital sign monitoring equipment, emergency medications



Assign **sufficient personnel** to meet expected demand

- Sufficient staffing plans in place for Nurse/IV tech, Physician, Pharmacist or other licensed medical professional
 - Likely need dedicated team to treat patients



Prepare for **drug administration** process

- Pre-visit: Clear treatment and monitoring plan developed for during infusion
- Treatment: 1-hour treatment² and 1-hour post-treatment observation
 - Emergency protocol defined for addressing potential infusion reactions or complications
- Post-treatment: Clear process for patient follow-up defined using telemedicine as possible



Ensure **process for reimbursement** in place (non-drug administrative costs)



Prepare for **reporting needs** for adverse events and record keeping

² Contingent on product dilution, reference EUA fact sheet for dilution and infusion timing.

Activity 1: Define facilities and patient visit logistics



**Site will need
dedicated outpatient
COVID-19 treatment
space**

Dedicated COVID-19 patient area with needed infusion supplies

- Some sites using COVID-19 waiting rooms for monitoring post infusion
- Rededication of existing clinical space acceptable under CMS Hospital Without Walls Initiative

Immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the **ability to activate the EMS**, as necessary

*Select recommendations for outpatient setting, for more information reference [CDC guidelines](https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html)
<https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html>*



Alternate site of care allowances and needs

As part of **CMS Hospital Without Walls initiative**, hospitals can **provide services** outside of standard hospital settings

- **Other healthcare facilities** (e.g., urgent care clinics, doctors' offices etc)
- **Remote locations or sites** not normally considered healthcare facilities, (e.g., patient home via telemedicine, hotels, community site, temporary tents)
- **Nursing home or home health services** also likely to be acceptable sites of administration

Alternate site of care will need **same core capabilities and supplies** as typical site of administration

- Facility and patient flow needs (page 15 and 17)
- Supplies needed on site (e.g., rescue medication, infusion supplies, etc – page 23)

Please reference CMS Hospitals Without Walls waivers and guidance for detailed information about program



Important to manage patient flow in a healthcare setting

- Have patient **wait to enter the site** until pre-scheduled time for treatment
- Ensure patient **wearing a mask or face covering** before entering the building
- Escort patient **directly to room, limit transport and movement of the patient outside of the room**
- Keep the **door closed** while patient in infusion room
- Medical and support personnel entering room need to **wear sufficient PPE** based on CDC guidelines
- Room should undergo **appropriate cleaning and surface disinfection** before it is returned to routine use

Select recommendations for outpatient setting, for more information reference [CDC guidelines](https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html)
<https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html>



Pharmacy needs

Note pharmacy does not need to be onsite, product can be prepared bedside by any qualified medical professional

Infusion preparation process:

- Prepare sterile infusions in a manner consistent with local laws, regulations, guidelines and policies
- Obtain new vial(s) and/or IV bags if the drug product contains any visible particulate matter

Needs for space to prepare mAb drug:

- Dedicated preparation area with sufficient capacity onsite or nearby

Acceptable equipment for mAb drug storage:

- Functional pharmacy sink
- Refrigerated storage (2-8° C)
- Temperature monitoring system with back-up
- Alarm system for notification to authorized personnel of temperature deviations/excursions in place

Please see EUA manufacturer fact sheet for drug-specific requirements



Testing needs

Outpatient monoclonal antibody product likely to need administration early in symptom progression

- Treatment should be administered as soon as possible following positive test result, and within 10 days of symptom onset

Fast turn-around testing capabilities key to identify patients and treat within this window

- On-site point-of-care rapid testing or PCR tests ideal to provide quick diagnosis and treat patients on the same day
- Alternatives include partnership with off-site testing facility nearby with reliable and quick turnaround and robust patient tracking and reporting mechanism
 - Accelerated testing results turnaround likely recommended to allow for infusion early in disease progression

Please reference EUA factsheet for detailed treatment guidelines including recommended treatment window

Distribution – Direct ordering for all three mAb products

- HHS/ASPR continues to **manage the distribution of mAb products under EUA** as stated in the FDA Letters of Authorization
- Given the **current supply of product**, bamlanivimab, casirivimab / imdevimab, and bamlanivimab / etesevimab can be requested **via direct ordering for all sites** (no further allocations to states are currently planned)
- Direct orders for casirivimab / imdevimab and bamlanivimab / etesevimab **are limited to 48 patient courses per site/per week**, though sites with higher utilization can request additional courses
- **Questions** regarding the direct order process:
HHS: COVID19Therapeutics@hhs.gov
ABC: C19therapies@amerisourcebergen.com



Overview of Direct Order Process for COVID-19 Therapeutics

Purpose:
The United States Government (USG) is responsible for the allocation and distribution of monoclonal antibody (mAb) therapeutics for the treatment of COVID-19 as per the Emergency Use Authorizations (EUA) issued by the U.S. Food and Drug Administration (FDA). The USG has developed a process for sites to directly order from the distributor, AmerisourceBergen (ABC).

Process overview:

- Sites (based on classes of trade), are able to order bamlanivimab (Lilly) and/or casirivimab/imdevimab (Regeneron) monoclonal antibodies for their facilities at the link listed below
- Sites will be required to:
 - Provide ABC with a board of pharmacy license or physician letter of authorization
 - Attest to their designated class of trade and that they will administer the authorized product according to the terms of the FDA issued EUA
 - Provide utilization data via either TeleTracking or NHSN
- Sites can order product based on established minimum amounts; subsequent orders are subject to a maximum amount based on previous orders and utilization
- State departments of health will be informed of therapies ordered within their jurisdictions for awareness.

Information on [direct order process](#) available at phe.gov –

<https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Documents/Overview%20of%20direct%20order%20process%20Fact%20Sheet-508.pdf>



High level guidance on product shipping and storage

Product will be **shipped refrigerated (2-8° C)** to your location by USG distribution partners

Product should be **stored refrigerated (2-8° C)** before use

Target **shelf-life for product ~10 months at minimum**, follow guidance from manufacturer on expiration dates and product turnover

Prepared IV solutions are **intended for immediate patient administration**. If not used immediately:

- Solutions may be held at refrigerated conditions for example
 - Eli Lilly **no more than 24 hours**
 - Regeneron **no more than 36 hours**
- Solutions may be held at ambient light and room temperature conditions (including preparation, solution hold, infusion and flush) for example
 - Eli Lilly **no more than 7 hours**
 - Regeneron **no more than 5 hours**

Please adhere to all guidelines for storage and use provided by manufacturer of EUA product

Activity 2: Ensure sufficient supplies

Site supplies needed: Standard infusion supplies are needed but several components have been difficult to source

Sites interested in providing outpatient infusions of mAbs to COVID+ patients should:

1. **Confirm sufficient supplies of infusion materials**
2. **Proactively ensure items with long-lead times are sourced for your site**

Ensure supplies sufficient to cover mAbs treatment in addition to day-to-day operations needs

List of suggested supplies (not exhaustive)

PPE

- Gloves
- Gowns
- Eye and face protection (e.g. goggles, safety glasses, face shields)
- NIOSH-certified, disposable N95 filter facepiece respirators or better

Infusion supplies

- Infusion chairs – *recommended only*
- IV pole
- IV administration sets
 - *PVC infusion set with/without DEHP containing 0.2 or 0.22 micron polyethersulfone (PES) in-line filter*
- IV and catheters
- 3mL saline syringes
- Appropriately sized syringes
- Alcohol wipes
- 2x2 gauze pads
- Adhesive bandages
- Tegaderm bio-occlusive dressing
- Absorbent underpads (blue pads)
- Extension set tubing
- Needles – stainless steel 18ga
- Sharps containers
- Transpore tape
- Transilluminator (vein finder)

General supplies

- Infusion Reaction Kit
- Vital signs equipment
- Crash cart or Emergency Medical Management Equipment and Backboard
- Refrigerator
 - *Optional to store prepared solution onsite*
- Privacy screens
- Biohazard disposal bag
- Disposable disinfecting wipes
- Thermometer probe covers (*if required*)
- 70% alcohol wipes
- Paper towels
- Trash bins and liners

Please reference EUA factsheet for final requirements

Activity 3: Develop plan for staffing and personnel

Treating patients needs support of...

HCP



Prescribe monoclonal antibody to patient, answer questions and **respond in case of emergency**

- Infectious disease or general HCP
- HCP will need to be on site or available telehealth or phone for treatment
- At least 1 provider nurse or C onsite 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

**Pharmacist
or other HCP**



Prepare the infusion, answer questions and support with monoclonal antibody storage

- Pharmacy does not need to be physically located at the site of infusion
- Note the infusion can be prepared by any qualified medical professional

Nurses



Administer patient infusion (up to 1 hr) and monitor patient wellbeing (1 hr)

- May require 2 nurses to start infusion, nurse practitioner to oversee larger infusion unit (if needed)
- Experienced phlebotomist needed as often difficult to find vein in patients (often high BMI and dehydrated)

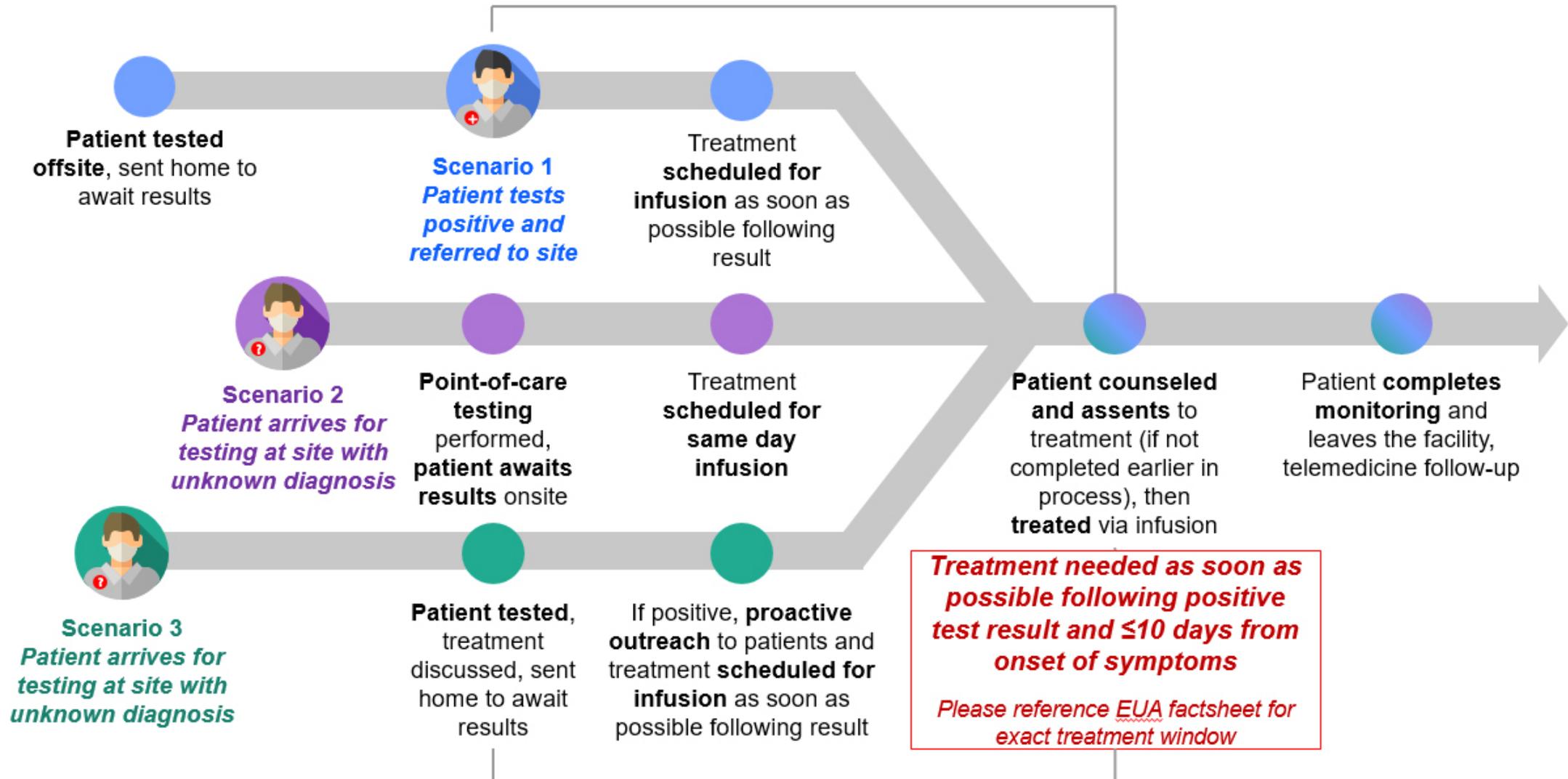
Please reference EUA factsheet for specific treatment guidelines

Needed roles and responsibilities for site

Role	Needed skills/profile
Patient intake	Scheduling and administrative skills
Drug preparation	Pharmacist, pharmacy technician, or nurse or other HCP trained in IV preparation
Infusion: Start IV	Nurse or other alternate healthcare team member trained to begin an IV
Infusion: Administer infusion	Nurse or other alternate healthcare team member trained in administering an IV
Infusion monitoring	Nurse or other alternate healthcare team member trained in vital sign monitoring
Post infusion observation	Nurse or other alternate healthcare team member trained in vital sign monitoring
Patient release	Administrative skills, or nurse or other alternate healthcare team member as required
Cleaning	Person trained in COVID cleaning / disinfection

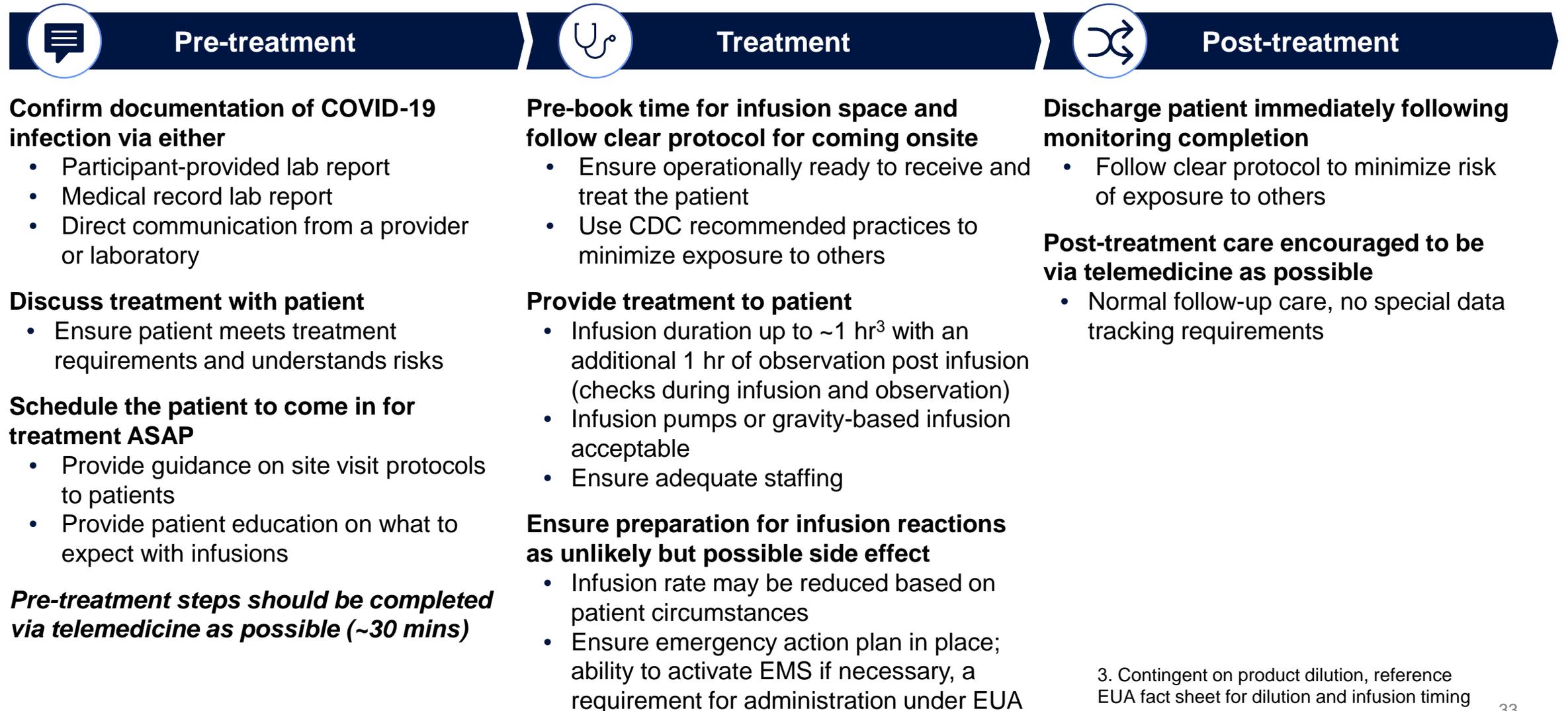
Activity 4: Review drug administration process

Three potential treatment pathways for symptomatic COVID-19 patients to receive care



Patient flow for outpatient mAbs product

Scenario 1: Confirmed positive patient referred for treatment

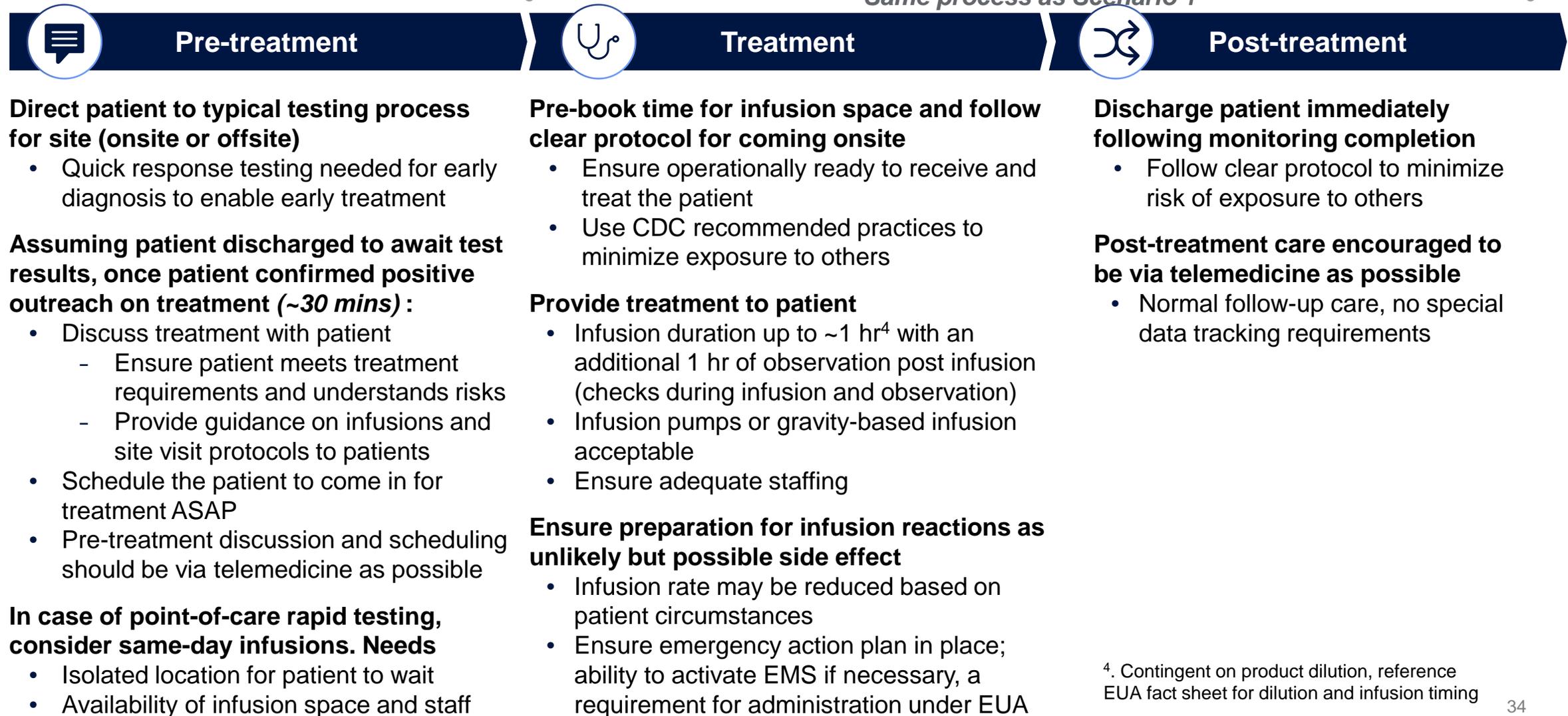


3. Contingent on product dilution, reference EUA fact sheet for dilution and infusion timing

Patient flow for outpatient mAbs product

Scenario 2 and 3: Patient arrives for testing at site with unknown diagnosis

Same process as Scenario 1



⁴. Contingent on product dilution, reference EUA fact sheet for dilution and infusion timing

General Guidelines for Regeneron and Lilly mAbs

Product	Eli Lilly Bamlanivimab	Eli Lilly Bamlanivimab & Etesevimab	Regeneron Casirivimab (Regn 10933) & Imdevimab (Regn 10987)
Start	<ul style="list-style-type: none"> Begin with 50 mL, 100 mL, 150 mL, or 250 mL normal saline bag 	<ul style="list-style-type: none"> Begin with 50 mL, 100 mL, 150 mL, or 250 mL normal saline bag 	<ul style="list-style-type: none"> Begin with 250 ml normal saline bag
Add	<ul style="list-style-type: none"> 20 ml bamlanivimab 	<ul style="list-style-type: none"> 20 mL bamlanivimab 40 mL etesevimab <p><i>Note: not all 50mL & 100mL saline bags will allow addition of 60mL of bam / ete – please ensure bag allows for mixing</i></p>	<ul style="list-style-type: none"> 10 ml of casirivimab (Regn10933) 10 ml of imdevimab (Regn 10987)
Final Volume in IV Bag	<ul style="list-style-type: none"> 70 mL, 120 mL, 170 mL, or 270 mL 	<ul style="list-style-type: none"> 110 mL, 160 mL, 210 mL, or 310 mL 	<ul style="list-style-type: none"> 270 mL

Notes for Regeneron: CASIRIVIMAB AND IMDEVIMAB MUST BE ADMINISTERED TOGETHER AFTER DILUTION BY INTRAVENOUS (IV) INFUSION ONLY.

Regeneron cocktail casirivimab & imdevimab are available in the following size vials: 2.5 ml vial 120 mg/ml AND 11.1 ml vial 120 mg/ml

Notes for Eli Lilly: BAMLANIVIMAB MAY BE ADMINISTERED AS COCKTAIL WITH ETESEVIMAB OR AS MONO THERAPY ALONE. ETESEVIMAB MUST BE ADMINISTERED TOGETHER WITH BAMLANIVIMAB AFTER DILUTION BY INTRAVENOUS (IV) INFUSION ONLY.

Detailed product preparation guidelines for Regeneron and Lilly mAbs

Product	Eli Lilly	Eli Lilly Combo	Regeneron			
Vials provided	<ul style="list-style-type: none"> One - 20 mL vial of Bamlanivimab 	<ul style="list-style-type: none"> One - 20 mL vial of Bamlanivimab Two – 20 mL vial of Etesevimab 	<ul style="list-style-type: none"> One -11.1 mL vial Casirivimab (Regn10933) One - 11.1 mL vial Imdevimab (Regn10987) 	<ul style="list-style-type: none"> One - 11.1 mL vial Casirivimab (Regn10933) Four - 2.5 mL vials Imdevimab (Regn10987) 	<ul style="list-style-type: none"> Four - 2.5 mL vials Casirivimab (Regn10933) Four - 2.5 mL vials Imdevimab (Regn10987) 	<ul style="list-style-type: none"> Four - 2.5 mL vials Casirivimab (Regn10933) One - 11.1 mL vial Imdevimab (Regn10987)
Initial 0.9% saline bag required	<ul style="list-style-type: none"> 50 mL, 100 mL, 150 mL, or 250 mL 	<ul style="list-style-type: none"> 50 mL, 100 mL, 150 mL, or 250 mL 	<ul style="list-style-type: none"> 250 mL 	<ul style="list-style-type: none"> 250 mL 	<ul style="list-style-type: none"> 250 mL 	<ul style="list-style-type: none"> 250 mL
Required saline to remove from bag	<ul style="list-style-type: none"> N/A 	<ul style="list-style-type: none"> N/A 	<ul style="list-style-type: none"> N/A 	<ul style="list-style-type: none"> N/A 	<ul style="list-style-type: none"> N/A 	<ul style="list-style-type: none"> N/A
Volume product to withdraw from vial(s) and dilute in bag	<ul style="list-style-type: none"> 20 mL Bamlanivimab from 1x 20mL vial 	<ul style="list-style-type: none"> 20 mL Bamlanivimab from 1x 20mL vial 40 mL Etesevimab from 2x 20mL vial 	<ul style="list-style-type: none"> 10 mL Casirivimab from 1x 11.1 mL vial 10 mL Imdevimab from 1x 11.1 mL vial 	<ul style="list-style-type: none"> 10 mL Casirivimab from 1x 11.1 mL vial 10 mL Imdevimab from 4x 2.5 mL vial 	<ul style="list-style-type: none"> 10 mL Casirivimab from 4x 2.5 mL vial 10 mL Imdevimab from 4x 2.5 mL vial 	<ul style="list-style-type: none"> 10 mL Casirivimab from 4x 2.5 mL vial 10 mL Imdevimab from 1x 11.1 mL vial
Final volume of product in IV bag	<ul style="list-style-type: none"> 70 mL, 120 mL, 170 mL, or 270 mL 	<ul style="list-style-type: none"> 110 mL, 160 mL, 210 mL, or 310 mL 	<ul style="list-style-type: none"> 270 mL 	<ul style="list-style-type: none"> 270 mL 	<ul style="list-style-type: none"> 270 mL 	<ul style="list-style-type: none"> 270 mL

Dose packs for REGEN-COV casirivimab and imdevimab

New packaging presentation of casirivimab and imdevimab containing one treatment dose of REGEN-COV available beginning in February 2021

Each REGEN-COV Dose Pack is delivered in a plastic bag and contains:

- **Sufficient number of vials** of casirivimab (REGN10933) and imdevimab (REGN10987) to prepare one treatment dose – since both casirivimab and imdevimab are available in different sizes, REGEN-COV Dose Packs may contain **2, 5 or 8 vials**
- **A 1-page Information Sheet**
- A sticker on bag with name REGEN-COV and the NDC based on the combination of cartons contained within the dose pack

In addition to REGEN-COV Dose Packs, single cartons of casirivimab and imdevimab will still be in distribution – see *next page for examples*

	<p>NDC 61755-035-02 Combination of 2 vials</p> <p> 1 vial of casirivimab 11.1 mL</p> <p>AND</p> <p> 1 vial of imdevimab 11.1 mL</p>		<p>NDC 61755-037-05 Combination of 5 vials</p> <p> 1 vial of casirivimab 11.1 mL</p> <p>AND</p> <p> 4 vials of imdevimab 2.5 mL</p>
	<p>NDC 61755-036-08 Combination of 8 vials</p> <p> 4 vials of casirivimab 2.5 mL</p> <p>AND</p> <p> 4 vials of imdevimab 2.5 mL</p>		<p>NDC 61755-038-05 Combination of 5 vials</p> <p> 4 vials of casirivimab 2.5 mL</p> <p>AND</p> <p> 1 vial of imdevimab 11.1 mL</p>

REGEN-COV Requires 10ml of Casirivimab AND 10 ml of Imdevimab

Casirivimab	Imdevimab
 <p>casirivimab (Regn10933) Use a single 11.1ml vial Only use 10ml Discard the remaining 1.1ml</p>	 <p>imdevimab (Regn10987) Use a single 11.1 ml vial Only use 10ml Discard the remaining 1.1ml</p>
 <p>casirivimab (Regn10933) Use a single 11.1ml vial Only use 10ml Discard the remaining 1.1ml</p>	 <p>imdevimab (Regn10987) Use four 2.5 ml vials = 120mg/ml</p>
 <p>casirivimab (Regn10933) Use four 2.5 ml vials = 10ml</p>	 <p>imdevimab (Regn10987) Use a single 11.1 ml vial Only use 10ml Discard the remaining 1.1ml</p>
 <p>casirivimab (Regn10933) Use four 2.5 ml vials = 10ml</p>	 <p>imdevimab (Regn10987) Use four 2.5 ml vials = 10ml</p>

Note: Variation in carton and labeling may be encountered – refer to [playbook for other variations](https://www.regeneroneua.com/Content/pdf/treatment-covid19-eua-guide-book.pdf) <https://www.regeneroneua.com/Content/pdf/treatment-covid19-eua-guide-book.pdf>

Activity 5: Prepare for reimbursement and ordering

Reimbursement process for mAbs therapeutic under EUA

Connect with state or territory health authority on appropriate ordering procedures to receive mAbs product

Under initial phase of treatment (likely through 2020), **drug cost likely to be paid by US government** under advanced purchase agreements

Confirm internally with your site administration on reimbursement for **non-drug costs** (e.g., infusion services, pharmacy)

Please **reference CMS resources** for more information

- **Provider toolkit**: <https://www.cms.gov/covidvax>
- **COVID FAQs**:
<https://www.cms.gov/files/document/03092020-covid-19-faqs-508.pdf>

CMS: Coverage of Monoclonal Antibody Products to Treat COVID-19

Medicare

Site of Care ¹	Payable by Medicare	Expected Patient Cost-Sharing
Inpatient Hospital 		No patient cost-sharing
Outpatient Hospital or "Hospital without Walls ² " 		No patient cost-sharing
Outpatient Physician Office/Infusion Center 		No patient cost-sharing ³
Nursing Home (See third bullet in Key Facts on CMS enforcement discretion) 		No patient cost-sharing
Home 		No patient cost-sharing

¹Services must be furnished within the scope of the product's FDA authorization or approval and within the provider's scope of practice.

²Under the Hospital Without Walls initiative, hospitals can provide hospital services in other healthcare facilities and sites that would not otherwise be considered to be part of a healthcare facility; or can set up temporary expansion sites to help address the urgent need to increase capacity to care for patients.

³Cost-sharing may apply to Medicare beneficiaries when they receive care from a provider that doesn't participate in Medicare.

⁴Certain monoclonal antibody products to treat COVID-19 have been authorized under Food and Drug Administration Emergency Use Authorizations since November 10, 2020. More information including the level II HCPCS codes for the administration/ infusion and post administration monitoring of these products can be found online in the Program Instruction.

Expected Payment to Providers: Key Facts

- Medicare payment for monoclonal antibody products to treat COVID-19 is *similar across sites of care*, with some small differences.
- Medicare *pays for the administration* of monoclonal antibody products to treat COVID-19. For example, Medicare will pay a national average of approximately \$310 for the administration of certain monoclonal antibody products⁴.
- CMS will exercise *enforcement discretion* to allow Medicare-enrolled immunizers working within their scope of practice and subject to applicable state law to *bill directly and receive direct reimbursement from the Medicare program for administering monoclonal antibody treatments* to Medicare Part A Skilled Nursing Facility residents
- Medicare will pay the provider for these monoclonal antibody products *when they are purchased by the provider*. Medicare won't pay if the product is given to the provider for free by, for example, a government entity.
- When purchased by the provider, Medicare payment is typically at *reasonable cost or at 95% of the Average Wholesale Price* (an amount determined by the manufacturer). These payment amounts vary depending on *which type of provider is supplying the product*. Original Medicare will pay for these products for beneficiaries enrolled in Medicare Advantage.
- For more specific information about Medicare payments to providers for these monoclonal antibody products, please see these [Frequently Asked Questions](#).

[Additional information](https://www.cms.gov/files/document/covid-infographic-coverage-monoclonal-antibody-products-treat-covid-19.pdf) can be found at <https://www.cms.gov/files/document/covid-infographic-coverage-monoclonal-antibody-products-treat-covid-19.pdf>

CMS billing codes

Eli Lilly product codes

Q0239:

- Long descriptor: Injection, bamlanivimab-xxxx, 700 mg
- Short descriptor: bamlanivimab-xxxx

M0239:

- Long Descriptor: intravenous infusion, bamlanivimab-xxxx, includes infusion and post administration monitoring
- Short Descriptor: bamlanivimab-xxxx infusion

Regeneron product codes

Q0243:

- Long descriptor: Injection, casirivimab and imdevimab, 2400 mg
- Short descriptor: casirivimab and imdevimab

M0243:

- Long Descriptor: intravenous infusion, casirivimab and imdevimab includes infusion and post administration monitoring
- Short Descriptor: casirivimab and imdevimab infusion

Please reference <https://www.cms.gov/medicare/covid-19/monoclonal-antibody-covid-19-infusion> for [additional information](#)

Activity 6: Reporting process

Reporting needs

Sites receiving monoclonal antibody will follow established mechanisms for tracking and reporting **serious adverse events**

- Events that are potentially attributable to monoclonal antibody use must be reported to the FDA
 - Refer to the Fact Sheet for Healthcare Providers as part of EUA for guidance
 - Complete and submit a MedWatch form or complete and fax FDA Form 3500 to report

Site must **maintain records** regarding use of the monoclonal antibody by patients

- **Inventory information:** e.g., lot numbers, quantity, receiving site, receipt date, product storage
- **Patient information:** e.g., patient name, age, disease manifestation, number of doses administered per patient, other drugs administered

USG will track product delivery through the commercial distributor and CMS systems

Ensure that any records associated with this EUA are **maintained for inspection** upon request



Thank you!