Updates July 30, 2021
Addition of Regeneron Post-Exposure Prophylaxis Indication

Federal Response to COVID-19: Monoclonal Antibody Playbook

Outpatient administration playbook for healthcare leadership

30 JULY 2021

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Introduction

EUA Playbook Audience

This playbook is intended to support sites interested in administering COVID-19 monoclonal antibody (mAb) treatment under EUA including but not limited to:

- 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
- Home infusions

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

Context of mAbs outpatient administration playbook

Initial EUAs were granted for Eli Lilly and Regeneron products in November 2020 only **for outpatient setting**

Expanded eligibility criteria for administration of both Eli Lilly and Regeneron products were released in May 2021 **for outpatient setting**

Monoclonal antibody infusions have been successfully implemented in a variety of outpatient settings

Monoclonal antibody administration has been expanded to include subcutaneous administration of the REGEN-COV product as of June 2021

Indication for REGEN-COV updated to include Post-exposure prophylaxis as of July 2021

Scope of this playbook

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

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

Overview of therapeutic

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

mAbs are most effective when **given early in infection**

Product delivered via **IV infusion or subcutaneous injection**

Evolving evidence demonstrates promise of mAb products in outpatient settings

- Evidence from Eli Lilly mAb cocktail **showed potential to reduce hospitalization and death** in infected people if given early in infection (Phase 3 data of BLAZE-1 clinical trial)
- Phase 1 and 2 data from Regeneron mAb cocktail trial showed potential to decrease **viral load** and **reduced medical visits** in infected people if given early (Outpatient 2067 clinical trial)
- Phase 1/2/3 data from Regeneron mAb cocktail supported a revised dosage in the June 2021 EUA (revised dosing: 600 mg casirivimab/ 600mg imdevimab)

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

Indications for Monoclonal Therapy & Appropriate mAbs for Treatment

- Post-Exposure Prophylaxis in vulnerable persons (i.e. not fully vaccinated or immunocompromised) who are at high risk for progression to severe COVID-19
  - REGEN-COV (casirivimab and imdevimab)

- Active COVID-19 Infection in high risk individuals with mild to moderate symptoms
  - REGEN-COV (casirivimab and imdevimab)
  - Bamlanivimab/Etesevimab (currently paused)
  - Sotrovimab (commercially available)

Post-Exposure Prophylaxis Indications

Eligibility for Post-Exposure Prophylaxis**

REGEN-COV (casirivimab and imdevimab) is authorized for post-exposure prophylaxis of COVID-19 in individuals who are:

- Adult or pediatric (≥ 12 years of age and weighing at least 40kg) patient **at high risk for progressing to severe disease or death**
- Not fully vaccinated[1] **or** who are not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination (for example, individuals with immunocompromising conditions including those taking immunosuppressive medications[2]) **AND**
  - have been exposed to an individual infected with SARS-CoV-2 consistent with close contact criteria per CDC[3] **OR**
  - **who are at high risk of exposure to an individual infected with SARS-CoV-2** because of occurrence of COVID-19 in other individuals in the same institutional setting (for example, nursing homes, prisons) [*see limitations of authorized use]*

***Limitations of Authorized Use:**

- *Post-exposure prophylaxis with REGEN-COV (casirivimab and imdevimab) is not a substitute for vaccination against COVID-19*
- *REGEN-COV (casirivimab and imdevimab) is not authorized for pre-exposure prophylaxis for prevention of COVID-19*

[1] CDC's Have You Been Fully Vaccinated?
[2] CDC's Science Brief: COVID-19 Vaccines and Vaccination
[3] CDC's Quarantine and Isolation

Eligibility for Post-Exposure Prophylaxis

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

[2] *CDC's Science Brief: COVID-19 Vaccines and Vaccination* at https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html

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

Eligibility for Treatment of Mild-Moderate Covid-19 Infection in High Risk Individuals

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:

- Adult or pediatric (≥ 12 years of age and weighing at least 40kg) patient
- 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 (or increase from baseline chronic oxygen therapy)**

HIGH RISK FACTORS INCLUDE, BUT ARE NOT LIMITED TO:

- Older age (for example ≥ 65 years of age)
- Obesity or being overweight (for example, adults with BMI ≥ 25, or if age 12-17, have BMI ≥ 85th percentile for their age and gender based on CDC growth charts)
- Pregnancy
- Chronic Kidney Disease
- Diabetes
- Immunosuppressive disease or immunosuppressive treatment
- Cardiovascular disease (including congenital heart disease) or hypertension
- Chronic lung diseases (for example, chronic obstructive pulmonary disease, asthma [moderate-to-severe], interstitial lung disease, cystic fibrosis, and pulmonary hypertension)
- Sickle cell disease
- Neurodevelopmental disorders (for example, cerebral palsy) or other conditions that confer medical complexity (for example, genetic or metabolic syndromes and severe congenital abnormalities)
- Having a medical-related technological dependence (for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19)

Other medical conditions or factors (for example, race or ethnicity) may also place individual patients at high risk for progression to severe COVID-19 and **authorization of mAb therapy is not limited to the medical conditions or factors listed above**. For additional information on medical conditions and factors associated with increased risk for progression to severe COVID-19, visit the CDC website:

Underlying Medical Conditions: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html

CDC's Clinical Growth Charts: https://www.cdc.gov/growthcharts/clinical_charts.htm

Indications for Patients with Confirmed COVID-19 Infection

EUA summary: bamlanivimab/ etesevimab (Eli Lilly)

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

EUA summary: REGEN-COV (casirivimab/ imdevimab) (Regeneron)

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, **including hospitalization or death**

Post-exposure prophylaxis indication added July 2021.

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

Intravenous infusion of casirivimab/imdevimab is strongly recommended. Subcutaneous injection is an alternative route of administration when intravenous infusion is not feasible and would lead to delay in treatment.

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

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

HIGH RISK FACTORS INCLUDE, BUT ARE NOT LIMITED TO:

- Older age (for example ≥ 65 years of age)
- Obesity or being overweight (for example, adults with BMI ≥ 25, or if age 12-17, have BMI ≥ 85th percentile for their age and gender based on CDC growth charts)
- Pregnancy
- Chronic Kidney Disease
- Diabetes
- Immunosuppressive disease or immunosuppressive treatment
- Cardiovascular disease (including congenital heart disease) or hypertension
- Chronic lung diseases (for example, chronic obstructive pulmonary disease, asthma [moderate-to-severe], interstitial lung disease, cystic fibrosis, and pulmonary hypertension)
- Sickle cell disease
- Neurodevelopmental disorders (for example, cerebral palsy) or other conditions that confer medical complexity (for example, genetic or metabolic syndromes and severe congenital abnormalities)
- Having a medical-related technological dependence (for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19)

Other medical conditions or factors (for example, race or ethnicity) may also place individual patients at high risk for progression to severe COVID-19 and **authorization of mAb therapy is not limited to the medical conditions or factors listed above**. For additional information on medical conditions and factors associated with increased risk for progression to severe COVID-19, visit the CDC website:

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CDC's Clinical Growth Charts: https://www.cdc.gov/growthcharts/clinical_charts.htm

Reminder | CDC variants of concern and other lineages by state
Providers should assess variant prevalence in their geographic area when choosing mAb therapeutic

- **Estimated biweekly proportions** of the most common SARS-CoV-2 lineages circulating in the U.S available from the CDC variant proportions data tracker *(note the image below is an example and the most updated data is available on the tracker[2])*

Unweighted Proportions of Variants of Concern and Other Lineages by State or Jurisdiction

State	B.1.1.7	B.1.351	B.1.617.2	P.1	Other lineages	Total Available Sequences
Arizona	32.4%		37.2%	18.7%	11.7%	487
California	22.8%	0.1%	56.8%	9.0%	11.3%	4,332
Colorado	25.8%		66.9%	3.8%	3.5%	1,282
Florida	33.8%	0.0%	36.8%	13.4%	16.0%	2,688
Georgia	42.7%		39.9%	6.7%	10.7%	522
Illinois	31.1%		49.0%	11.9%	8.0%	498
Massachusetts	21.5%		27.1%	12.6%	38.8%	446
Missouri	6.9%		90.3%	1.1%	1.7%	1,000
Nevada	16.0%	0.1%	71.4%	4.8%	7.8%	2,044
New Jersey	22.9%		56.6%	6.4%	14.1%	846
New York	22.9%		41.0%	9.0%	27.1%	402
North Carolina	35.6%	0.2%	38.8%	5.0%	20.4%	963
Oregon	57.1%		11.5%	16.7%	14.7%	312
Texas	31.9%	0.0%	45.9%	6.2%	16.0%	2,737
Washington	35.9%	0.2%	40.7%	13.3%	9.8%	1,261

Variant proportions are based on representative CDC sequence data (NS3 + CDC-funded contract sequencing) collected over a 4-week period ending July 3, 2021 for states with at least 300 sequences.

Updated July 27, 2021

- **Information on variants** of concern updated in **Section 15 of FDA fact sheets**[1]

Table 6: Pseudotyped Virus-Like Particle Neutralization Data for SARS-CoV-2 Variant Substitutions with Casirivimab and Imdevimab Together

Lineage with Spike Protein Substitution	Key Substitutions Tested	Fold Reduction in Susceptibility
B.1.1.7 (UK origin)	N501Y[a]	no change[d]
B.1.351 (South Africa origin)	K417N, E484K, N501Y[b]	no change[d]
P.1 (Brazil origin)	K417T + E484K[c]	no change[d]
B.1.427/B.1.429 (California origin)	L452R	no change[d]
B.1.526 (New York origin)[e]	E484K	no change[d]
B.1.617.1/B.1.617.3 (India origin)	L452R+E484Q	no change[d]
B.1.617.2 (India origin)	L452R+K478T	no change[d]

[a] Pseudotyped VLP expressing the entire variant spike protein was tested. The following changes from wild-type spike protein are found in the variant: del69-70, del145, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H.
[b] Pseudotyped VLP expressing the entire variant spike protein was tested. The following changes from wild-type spike protein are found in the variant: D80Y, D215Y, del241-243, K417N, E484K, N501Y, D614G, A701V.
[c] Pseudotyped VLP expressing the entire variant spike protein was tested. The following changes from wild-type spike protein are found in the variant: L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y, D614G, H655Y, T1027I, V1176F
[d] No change: ≤2-fold reduction in susceptibility.
[e] Not all isolates of the New York lineage harbor the E484K substitution (as of February 2021).

Table 3: Pseudotyped Virus-Like Particle Neutralization Data for SARS-CoV-2 Variant Substitutions with Bamlanivimab and Etesevimab Together (1:2 Molar Ratio)

Lineage with Spike Protein Substitution	Key Substitutions Tested[a]	Fold Reduction in Susceptibility
B.1.1.7 (UK origin)	N501Y	no change[b]
B.1.351 (South Africa origin)	K417N + E484K + N501Y	215[c]
P.1 (Brazil origin)	K417T + E484K + N501Y	>46[c]
B.1.427/B.1.429 (California origin)	L452R	9[d]
B.1.526 (New York origin)[e]	E484K	31

[a] For variants with more than one substitution of concern, only the substitution(s) with the greatest impact on activity is(are) listed. For B.1.351, P.1 and B.1.427/B.1.429, spike variants reflective of the consensus sequence for the lineage were tested.
[b] No change: <5-fold reduction in susceptibility.
[c] Bamlanivimab and etesevimab together are unlikely to be active against variants from this lineage. No activity observed at the highest concentration tested for the P.1 variant.
[d] Etesevimab retains activity against this variant.
[e] Isolates of the B.1.526 lineage harbor several spike protein amino acid substitutions, and not all isolates contain the E484K substitution (as of February 2021). This assay was conducted using pseudotyped VLPs with the E484K substitution only.

1. FDA factsheets: REGEN-COV™; bamlanivimab/etesevimab
2. CDC Variant tracker

WHO announces simple, easy-to-say labels for SARS-CoV-2 Variants of interest and concern

Variants of Concern

A SARS-CoV-2 variant that meets the definition of a VOI (see below) and, through a comparative assessment, has been demonstrated to be associated with one or more of the following changes at a degree of global public health significance:

- Increase in transmissibility or detrimental change in COVID-19 epidemiology; or
- Increase in virulence or change in clinical disease presentation; or
- Decrease in effectiveness of public health and social measures or available diagnostics, vaccines, therapeutics.

WHO label	Pango lineage	GISAID clade/lineage	Nextstrain clade	Earliest documented samples	Date of designation
Alpha	B.1.1.7	GRY (formerly GR/501Y.V1)	20I/S:501Y.V1	United Kingdom, Sep-2020	18-Dec-2020
Beta	B.1.351	GH/501Y.V2	20H/S:501Y.V2	South Africa, May-2020	18-Dec-2020
Gamma	P.1	GR/501Y.V3	20J/S:501Y.V3	Brazil, Nov-2020	11-Jan-2021
Delta	B.1.617.2	G/452R.V3	21A/S:478K	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021

WHO announces simple, easy-to-say labels for SARS-CoV-2 Variants of interest and concern... cont'd

Variants of Interest

A SARS-CoV-2 isolate is a Variant of Interest (VOI) if, compared to a reference isolate, its genome has mutations with established or suspected phenotypic implications, and either:

- has been identified to cause community transmission/multiple COVID-19 cases/clusters, or has been detected in multiple countries; OR
- is otherwise assessed to be a VOI by WHO in consultation with the WHO SARS-CoV-2 Virus Evolution Working Group.

WHO label	Pango lineage	GISAID clade/lineage	Nextstrain clade	Earliest documented samples	Date of designation
Epsilon	B.1.427/B.1.429	GH/452R.V1	20C/S.452R	United States of America, Mar-2020	5-Mar-2021
Zeta	P.2	GR	20B/S.484K	Brazil, Apr-2020	17-Mar-2021
Eta	B.1.525	G/484K.V3	20A/S484K	Multiple countries, Dec-2020	17-Mar-2021
Theta	P.3	GR	20B/S:265C	Philippines, Jan-2021	24-Mar-2021
Iota	B.1.526	GH	20C/S:484K	United States of America, Nov-2020	24-Mar-2021
Kappa	B.1.617.1	G/452R.V3	21A/S:154K	India, Oct-2020	4-Apr-2021

Monoclonal antibodies are **under evaluation** for additional indications

Participation encouraged in clinical trials to assess additional drugs and indications

Clinical trial information available at *https://www.combatcovid.hhs.gov*

Lilly clinical trials:
https://trials.lillytrialguide.com/en-US/

Regeneron clinical trials:
https://www.regeneron.com/covid19

For Patients Not Eligible for Treatment Under EUA:

Consider Clinical Trials

Based on what we have learned to date - early administration of treatment needs fast testing turn-around 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

Onset of symptoms	Clinical visit and diagnostic test	Confirmed positive test	Treatment
	≤ 3 days *post symptom onset*	***≤ 2 days*** *post diagnostic test*	***≤3 days*** *post positive test result*

Treatment needed within 10 days of symptom onset

Testing sites should recommend COVID+ patients that are high risk confer with their HCP on potential suitability for Tx

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

Drug ordering and storage | Pre-treatment | Treatment | Post- treatment

Out of scope of this playbook

For Additional Information on Ordering Monoclonal Antibodies:

https://www.phe.gov/emergency/events/COVID19/healthcare-facilities/Pages/default.aspx#step3

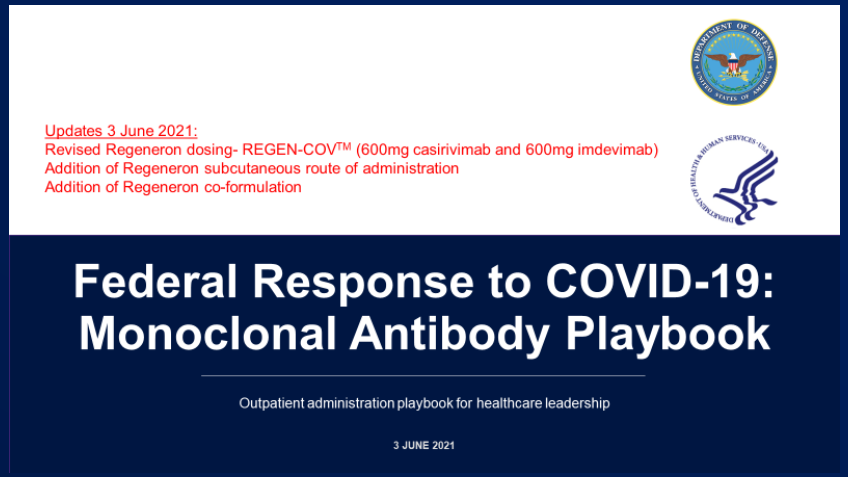
Key challenges for administration and strategies for success

- Existing infusion centers currently **treat immune-compromised patients** and may not be the logical site for COVID-19 treatment
- Many sites are not traditionally outfitted to do infusions in outpatient setting (besides hospitals and ERs), however successful models have been demonstrated in a variety of outpatient settings (stand-alone mAb infusion sites, skilled nursing facilities, and home infusion)
- Subcutaneous administration of Regeneron is an alternate route **when intravenous infusion is not feasible and would lead to delay in treatment** (1-hour post administration monitoring is required after subcutaneous administration)
- **Length of infusion process** (infusion time may be up to ~1 hour infusion[1] followed by 1 hour post-infusion monitoring) needing dedicated space and personnel. EUA revisions have allowed shorter infusion times. Patients must still be monitored for 1 hour post infusion
- **Quick turn-around time for testing** needed to diagnose patients within window for treatment (on site testing expedites infusion capabilities)

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

Please reference Lilly and Regeneron EUA factsheets for specific treatment guidelines

Federal Monoclonal Antibody Playbook

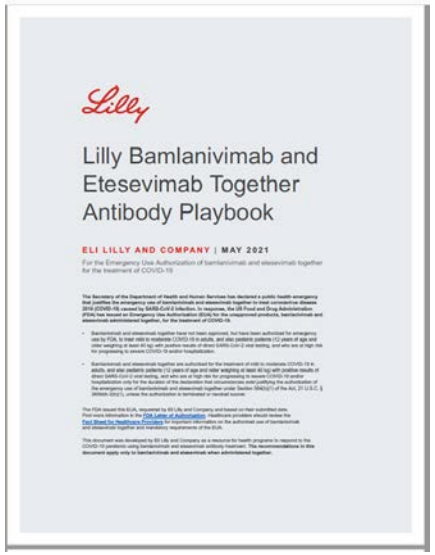


Objective to summarize requirements to administer monoclonal antibodies for healthcare facilities interested in administering the product

This document

Additional Resources Can be Found at https://combatcovid.hhs.gov/ https://phe.gov

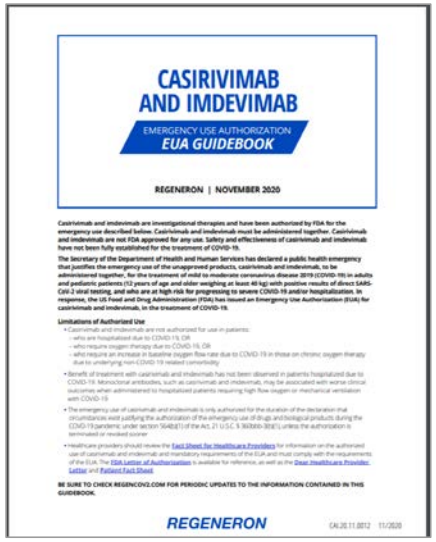
Product-specific playbooks for monoclonal antibody administration



Eli Lilly Bamlanivimab/ Etesevimab Antibody Playbook

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

https://www.covid19.lilly.com/assets/pdf/bam-ete/lilly-antibodies-playbook.pdf



Regeneron EUA guidebook

Provides additional detail on administration requirements for Regeneron mAbs product

https://www.regencov.com/content/pdf/guidebook.pdf

July 2021 EUA Update Pending

Please note… EUA guidelines continue to evolve

Please reference EUA fact-sheets for latest treatment guidelines and information, including:

- mAb dosing
- Administration routes
- Dilution requirements and infusion time for intravenous administration

https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs

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
- ❑ **Establish direct ordering account** for monoclonal antibody product

Prepare your site and staff for outpatient mAbs administration

- ❑ Ensure **sufficient supply** of needed materials for storage and treatment
  - ❑ Administration 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
- ❑ Review and establish **reimbursement process** for administration fees
- ❑ 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 sites to treatment
- ❑ Ensure administration site staff and providers 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 administration site

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;**

- ❑ Vital sign monitoring equipment, emergency medications
- ❑ IV Administration: IV kits, infusion chair, IV pole
- ❑ Subcutaneous administration: Needles and syringes required for dose preparation and administration

Assign **sufficient personnel** to meet expected demand

- ❑ Sufficient staffing plans in place for Nurse/IV tech, Provider, 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 administration
- ❑ Treatment: Up to ~1-hour treatment for intravenous administration[1] and 1-hour post-treatment observation for IV and subcutaneous routes
  - ❑ 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

1. 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 administration 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

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 18 and 20 of this document)
- Supplies needed on site (e.g., rescue medication, administration supplies, etc – page 27 of this document)

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

Important to manage patient flow in a healthcare setting

Ensure appropriate infection control practices in place based on latest CDC guidelines, e.g.:

- Have patient **wait to enter the site** until 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**
- As all patients treated are confirmed positive for COVID-19, **multiple patients may be treated simultaneously in one area**.
- 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

Pharmacy needs

Note pharmacy does not need to be onsite, product can be prepared for infusion and subcutaneous administration bedside by any qualified medical professional

Administration 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 control mechanism including temperature monitoring process

Please see EUA manufacturer fact sheet for drug-specific requirements

Testing needs: Symptomatic Patients

Outpatient monoclonal antibody treatments are to 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

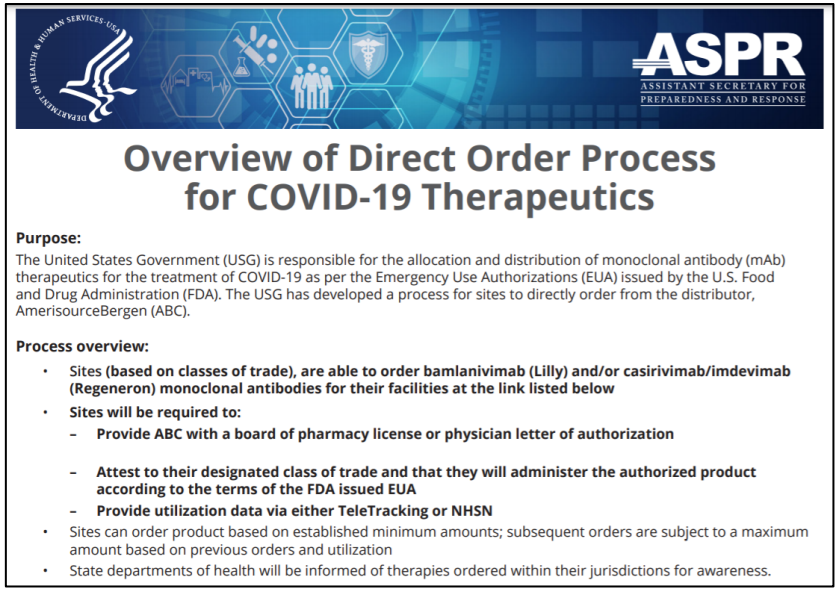
- On-site point-of-care rapid testing or PCR tests ideal to provide quick diagnosis and treat patients on the same day
- Alternatives include partnership with off-site testing facility nearby with reliable and quick turnaround and robust patient tracking and reporting mechanism
  - Accelerated testing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

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

https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs

Distribution – Direct ordering for mAb products under EUA

- 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,** casirivimab / imdevimab and bamlanivimab / etesevimab can be requested **via direct ordering for all sites** (no further allocations to states are currently planned)
- **Questions** regarding the direct order process: HHS: COVID19Therapeutics@hhs.gov



ASPR
ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE

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 4 hours**

Prepared subcutaneous doses of Regeneron should be administered immediately. If not used immediately:

- Syringes may be held at refrigerated conditions for no more than 4 hours and room temperature for no more than 4 **total** hours

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

Activity 2: Ensure sufficient supplies

Site supplies needed

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

1. **Confirm sufficient supplies of administration 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

Please reference EUA factsheet for final requirements

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

Administration supplies

- Infusion chairs – *recommended only*
- Intravenous administration
  - 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
- Subcutaneous administration
  - Appropriately sized needles for preparation and administration
- 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

Activity 3: Develop plan for staffing and personnel

Treating patients needs support of…

Healthcare provider

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

- Licensed healthcare provider (MD/PA/NP)
- HCP will need to be on site or available via telehealth or phone for treatment
- At least 1 team member (nurse or healthcare provider) 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 licensed professional

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

- Pharmacy does not need to be physically located at the site of administration
- Note that intravenous or subcutaneous administration can be prepared by any qualified medical professional

Nurses

Administer mAb therapy

- 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)
- Subcutaneous: 1 hour monitoring post administration

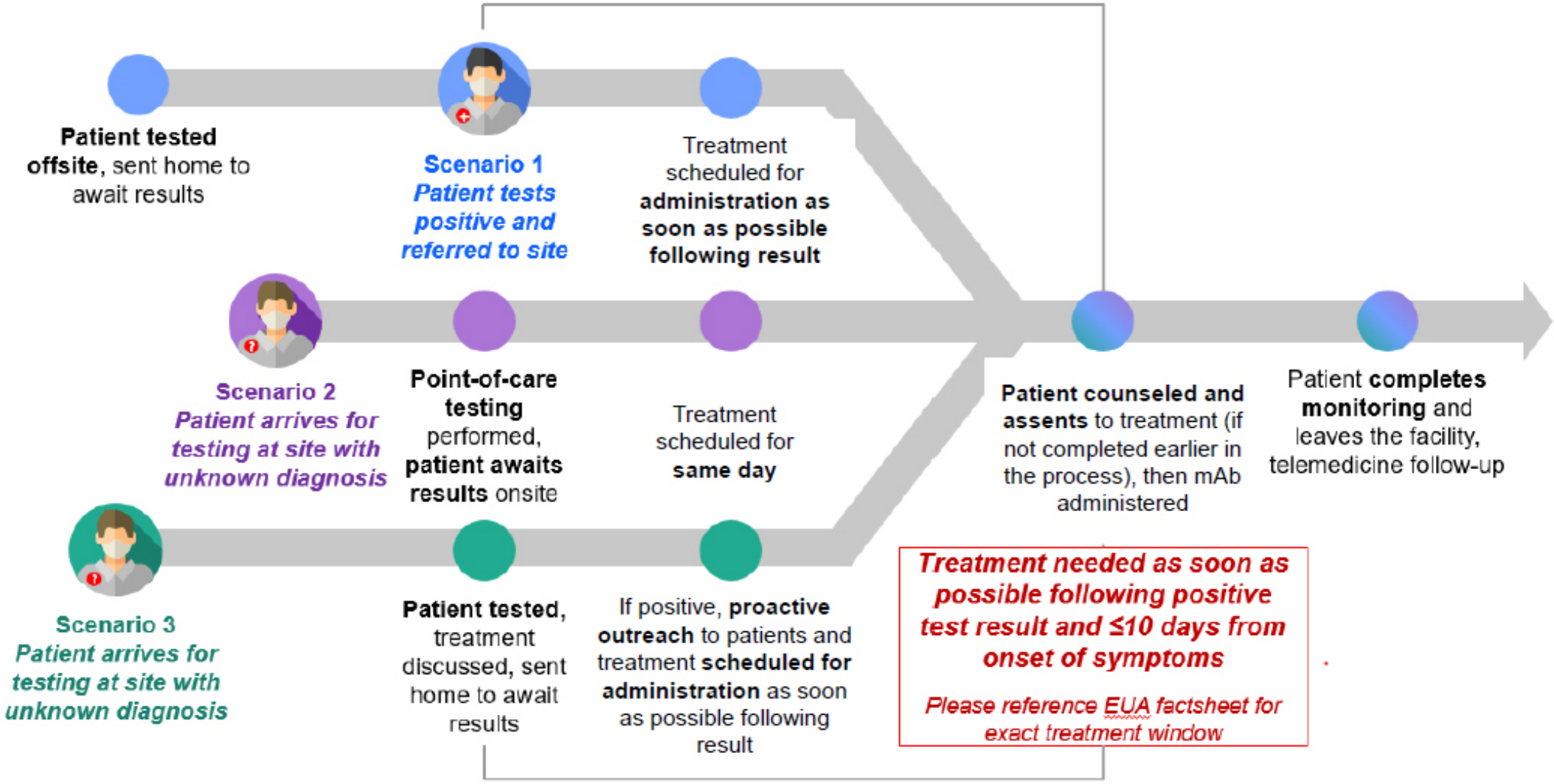
Please reference EUA factsheet for specific administration guidelines

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 **Subcutaneous: Administer injections**	Nurse or other alternate healthcare team member trained in administering an IV or subcutaneous injection (determined by route of administration)
Infusion monitoring	Nurse or other alternate healthcare team member trained in monitoring for adverse reaction
Post administration observation	Nurse or other alternate healthcare team member trained in monitoring for adverse reaction
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

Pre-treatment

Confirm documentation of COVID-19 infection via either

- Participant-provided lab report
- Medical record lab report
- Direct communication from a provider or laboratory

Discuss treatment with patient

- Ensure patient meets treatment requirements and understands risks

Schedule the patient to come in for treatment ASAP

- Provide guidance on site visit protocols to patients
- Provide patient education on what to expect with administration

Pre-treatment steps should be completed via telemedicine as possible (~30 mins)

Treatment

Pre-book time for administration space and follow clear protocol for coming onsite

- Ensure operationally ready to receive and treat the patient
- Use CDC recommended practices to minimize exposure to others

Provide treatment to patient

- Infusion duration up to ~1 hr[1] with an additional 1 hr of observation post infusion (checks during infusion and observation)
- Infusion pumps or gravity-based infusion acceptable
- Subcutaneous administration if appropriate per EUA[2]

Ensure preparation for administration reactions as unlikely but possible side effect

- Infusion rate may be reduced based on patient circumstances
- Ensure emergency action plan in place; ability to activate EMS if necessary, a requirement for administration under EUA

Post-treatment

Discharge patient immediately following monitoring completion

- Follow clear protocol to minimize risk of exposure to others

Post-treatment care encouraged to be via telemedicine as possible

- Normal follow-up care, no special data tracking requirements

1. Contingent on product dilution, reference EUA fact sheet for dilution and infusion timing
2. Reference EUA for route of administration

Patient flow for outpatient mAbs product

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

Same process as Scenario 1

Pre-treatment

Direct patient to typical testing process for site (onsite or offsite)

- Quick response testing needed for early diagnosis to enable early treatment

Assuming patient discharged to await test results, once patient confirmed positive outreach on treatment *(~30 mins)* :

- Discuss treatment with patient
  - Ensure patient meets treatment requirements and understands risks
  - Provide guidance on administration and site visit protocols to patients
- Schedule the patient to come in for treatment ASAP
- Pre-treatment discussion and scheduling should be via telemedicine as possible

In case of point-of-care rapid testing, consider same-day administration. Needs

- Isolated location for patient to wait
- Availability of treatment space and staff

Treatment

Pre-book time for administration space and follow clear protocol for coming onsite

- Ensure operationally ready to receive and treat the patient
- Use CDC recommended practices to minimize exposure to others

Provide treatment to patient

- Infusion duration up to ~1 hr[1] with an additional 1 hr of observation post infusion (checks during infusion and observation)
- Infusion pumps or gravity-based infusion acceptable
- Subcutaneous administration if appropriate per EUA[2]

Ensure preparation for administration reactions as unlikely but possible side effect

- Infusion rate may be reduced based on patient circumstances
- Ensure emergency action plan in place; ability to activate EMS if necessary, a requirement for administration under EUA

Post-treatment

Discharge patient immediately following monitoring completion

- Follow clear protocol to minimize risk of exposure to others

Post-treatment care encouraged to be via telemedicine as possible

- Normal follow-up care, no special data tracking requirements

1. Contingent on product dilution, reference EUA fact sheet for dilution and infusion timing
2. Reference EUA for route of administration

General Guidelines for bamlanivimab/etesevimab Dosing, Dilution, and Administration

Table 1: Recommended Dilution and Administration Instructions for Bamlanivimab and Etesevimab for IV Infusion[a] in Patients Weighing 50 kg or More

Drug[a]: Add 20 mL of bamlanivimab (1 vial) and 40 mL of etesevimab (2 vials) for a total of 60 mL to a prefilled infusion bag and administer as instructed below		
Size of Prefilled 0.9% Sodium Chloride Infusion Bag	**Maximum Infusion Rate**	**Minimum Infusion Time**
50 mL	310 mL/hr	21 minutes
100 mL	310 mL/hr	31 minutes
150 mL	310 mL/hr	41 minutes
250 mL	310 mL/hr	60 minutes

[a] 700 mg of bamlanivimab and 1,400 mg of etesevimab are added to the same infusion bag and administered together as a single intravenous infusion.

Table 2: Recommended Dilution and Administration Instructions for Bamlanivimab and Etesevimab for IV Infusion in Patients Weighing Less Than 50 kg

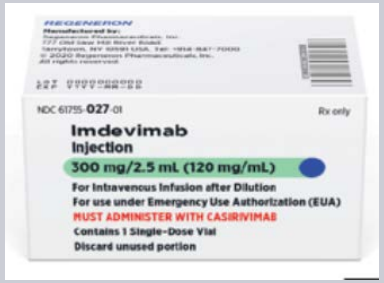
Drug[a]: Add 20 mL of bamlanivimab (1 vial) and 40 mL of etesevimab (2 vials) for a total 60 mL to an infusion bag and administer as instructed below		
Size of Prefilled 0.9% Sodium Chloride Infusion Bag	**Maximum Infusion Rate**	**Minimum Infusion Time**
50 mL	310 mL/hr	21 minutes
100 mL	310 mL/hr	31 minutes
150 mL	310 mL/hr	41 minutes

1 Patient Course of bamlanivimab/etesevimab

Notes for Eli Lilly: **BAMLANIVIMAB MUST BE ADMINISTERED TOGETHER WITH ETESEVIMAB AFTER DILUTION BY INTRAVENOUS (IV) INFUSION ONLY.** ***Note: not all 50mL & 100mL saline bags will allow addition of 60mL of bam / ete – ensure bag allows for mixing***

http://pi.lilly.com/eua/bam-and-ete-eua-factsheet-hcp.pdf

casirivimab/imdevimab formulations and dose preparation
Dose: REGEN-COV (casirivimab 600mg and imdevimab 600mg)*

Administration Route	Single Product Vials	REGEN-COV
Intravenous **(Mixed and administered per EUA instructions)** Intravenous infusion is strongly recommended for treatment of active infection. Subcutaneous injection is an alternative route of administration when intravenous infusion is not feasible and would lead to delay in treatment. *For Post-Exposure prophylaxis either subcutaneous injection or intravenous route can be used.* https://www.regeneron.com/downloads/treatment-covid19-eua-fact-sheet-for-hcp.pdf	casirivimab (REGN10933) **5ml total** (from 2.5 or 11.1 mL vials)   imdevimab (REGN10987) **5ml total** (from 2.5 or 11.1 mL vials)  	**10 mL total** 
Subcutaneous	Two syringes with 2.5 mL each of casirivimab (REGN10933) (**total of 5 ml casirivimab**) Two syringes with 2.5 mL each of imdevimab (REGN10987) (**total of 5 ml imdevimab**)	Four syringes each containing 2.5mL REGEN-COV for a **total of 10mL**

REGEN-COV (casirivimab 1200mg and imdevimab 1200mg) dosing no longer authorized under EUA

General Guidelines for REGEN-COV Intravenous Dosing, Dilution, and Administration

Dilution Instructions for REGEN-COV (600 mg Casirivimab and 600mg Imdevimab) for intravenous infusion

Size of Prefilled 0.9% Sodium Chloride Infusion Bag	Preparing Using Co-Formulated Casirivimab and Imdevimab Vial	Preparing Casirivimab and Imdevimab Using Individual Vials[a]
50 mL	Add 10 mL of co-formulated casirivimab and imdevimab (1 vial) into a prefilled 0.9% sodium chloride infusion bag and administer as instructed below	Add: • 5 mL of casirivimab (may use 2 vials of 2.5 ml OR 5 mL from 1 vial of 11.1 mL) • 5 mL of imdevimab (may use 2 vials of 2.5 ml OR 5 mL from 1 vial of 11.1 mL) and inject into a prefilled 0.9% sodium chloride infusion bag and administer as instructed below
100 mL		
150 mL		
250 mL		

[a] 600 mg of casirivimab and 600 mg of imdevimab are added to the same infusion bag and administered together as a single intravenous infusion.

Table 2: Recommended Administration Rate for Casirivimab and Imdevimab for Intravenous Infusion.

Size of Prefilled 0.9% Sodium Chloride Infusion Bag used	Maximum Infusion Rate	Minimum Infusion Time
50 mL[a]	180 mL/hr	20 minutes
100 mL	310 mL/hr	21 minutes
150 mL	310 mL/hr	31 minutes
250 mL	310 mL/hr	50 minutes

[a] The minimum infusion time for patients administered casirivimab and imdevimab together using the 50 mL prefilled 0.9% Sodium Chloride infusion bag must be at least 20 minutes to ensure safe use.

EUA Fact Sheet for HCP: https://www.regeneron.com/downloads/treatment-covid19-eua-fact-sheet-for-hcp.pdf

General Guidelines for REGEN-COV Subcutaneous Dosing and Administration

Administration Instructions for REGEN-COV (600 mg Casirivimab and 600mg Imdevimab) for subcutaneous injection[1]

Prepare 600 mg of Casirivimab and 600 mg of Imdevimab	Preparation of 4 Syringes
Using Casirivimab and Imdevimab Co-formulated Vial	Withdraw 2.5 mL solution per syringe into FOUR separate syringes.
Using Casirivimab and Imdevimab Individual Vials	• **Casirivimab:** Withdraw 2.5 mL solution per syringe into TWO separate syringes. • **Imdevimab:** Withdraw 2.5 mL solution per syringe into TWO separate syringes. For total of 4 syringes.

Intravenous infusion is strongly recommended for treatment of active infection. Subcutaneous injection is an alternative route of administration when intravenous infusion is not feasible and would lead to delay in treatment.

For Post-Exposure Prophylaxis either subcutaneous or intravenous route can be used.

Preparation and Administration:

- Obtain four 3mL or 5mL luer lock syringes and four 21 gauge 1½ inch transfer needles
- Withdraw 2.5 mL into each syringe per preparation instructions. **Prepare all four syringes at the same time.**
- Replace the 21 gauge transfer needle on each syringe with a 25-gauge or 27-gauge needle for subcutaneous injection
- Administer the subcutaneous injections consecutively, **each at a different injection site**, into the thigh, back of the upper arm, or abdomen, except for 2 inches (5 cm) around the navel. The waistline should be avoided.
- **It is recommended that providers use different quadrants of the abdomen, upper thighs, or back of the upper arms to space apart each injection**
- DO NOT inject into skin that is tender, damaged, bruised, or scarred

EUA Fact Sheet for HCP: https://www.regeneron.com/downloads/treatment-covid19-eua-fact-sheet-for-hcp.pdf

Guidelines for REGEN-COV Repeat Dosing for Post-Exposure Prophylaxis ★

- For individuals whom repeat dosing is determined to be appropriate for ongoing exposure to SARS-CoV-2 for longer than 4 weeks and who are not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination

- The initial dose is 600 mg of casirivimab and 600 mg of imdevimab by subcutaneous injection or intravenous infusion

- Followed by subsequent repeat dosing of 300 mg of casirivimab and 300 mg of imdevimab by subcutaneous injection or intravenous infusion once every 4 weeks for the duration of ongoing exposure.

Utilizing previously shipped REGEN-COV (casirivimab and imdevimab) Dose Pack

NDC 61755-**035**-02
Combination of 2 vials

1 vial of casirivimab 11.1 mL

AND

1 vial of imdevimab 11.1 mL

NDC 61755-**036**-08
Combination of 8 vials

4 vials of casirivimab 2.5 mL

AND

4 vials of imdevimab 2.5 mL

Previously created REGEN-COV Dose Pack contains **2 patient courses** as of the June 2021 EUA[1] (enclosed information sheet has dosing from prior EUA).
1 patient course is 5ml casirivimab/ 5ml imdevimab

The dose pack may be utilized for two doses. **Once punctured, the vials should be discarded after 4 hours.**

Refer to the "Regeneron Important Prescribing Letter" for more information

https://www.regeneron.com/downloads/treatment-covid19-eua-preventing-medication-errors.pdf

Please contact Regeneron Medical Affairs with any questions about using **existing** inventory to treat patients at 1-844-734-6643

June 3, 2021 updated EUA authorized dose change
FROM casirivimab 1200 mg and imdevimab 1200mg TO casirivimab 600mg and imdevimab 600mg
https://www.regeneron.com/downloads/treatment-covid19-eua-fact-sheet-for-hcp.pdf

Activity 5: Prepare for reimbursement and ordering

Reimbursement process for mAbs therapeutic under EUA

Follow process for direct ordering procedures to receive mAb product

Under initial phase of treatment, **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

CMS Monoclonal Reimbursement

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

[1]Services must be furnished within the scope of the product's FDA authorization or approval and within the provider's scope of practice.
[2]Under 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.
[3]Cost-sharing may apply to Medicare beneficiaries when they receive care from a provider that doesn't participate in Medicare.
[4]Certain 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 $450 for the administration of certain monoclonal antibody products4 . Home infusion is reimbursed at a higher rate.
- 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 can be found at https://www.cms.gov/files/document/covid-infographic-coverage-monoclonal-antibody-products-treat-covid-19.pdf

CMS billing codes

Please reference https://www.cms.gov/medicare/covid-19/monoclonal-antibody-covid-19-infusion for additional information

Eli Lilly product codes

Q0245:

- Long descriptor: Injection, bamlanivimab and etesevimab, 2100 mg
- Short descriptor: bamlanivimab and etesevima

M0245:

- Long Descriptor: intravenous infusion, bamlanivimab and etesevimab, includes infusion and post administration monitoring
- Short Descriptor: Bamlan and etesev infusion

M0246:

- Long Descriptor: intravenous infusion, bamlanivimab and etesevimab, includes infusion and post administration monitoring in the home or residence
- Short Descriptor: Bamlan and etesev infus home

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

M0244:

- Long Descriptor: intravenous infusion, casirivimab and imdevimab includes infusion and post administration monitoring in the home or residence
- Short Descriptor: casirivi and imdevi infus home

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

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

HHS Protect Reporting Requirement

Sites are required to report utilization of product to HHS through their state or TeleTracking system.

First-time users will receive enrollment and reporting instructions in an e-mail from protect-noreply@hhs.gov with the subject line of “Invitation: HHS TeleTracking COVID-19 Portal.”

This email provides step-by-step instructions to access the Portal for the first time.

If you do not receive an email in the next 48 hours, please contact TeleTracking Technical Support at hhs-protect@teletracking.com.

Questions?

https://combatcovid.hhs.gov

Email: covid19therapeutics@hhs.gov

Thank you!