IMPLEMENTATION BLUEPRINT

COVID-19 Monoclonal Antibody (mAb) Implementation Blueprint

How to Use This Document

This implementation blueprint includes common resources and specific modules. Modules can be reviewed individually.

Modules:

- Referral to mAb Treatment Sites
- Intravenous Treatment
- Subcutaneous Treatment (only REGEN-CoV)
- Local Public Health Processes

Appendix:

Educational Resources

Sample Discharge Instructions

Sample Standing Orders

OVERALL PURPOSE
Increasing Access to COVID-19 mAbs

This guide aims to provide practical guidance to help clinicians and other key stakeholders increase awareness and access to COVID-19 mAbs for outpatients with mild to moderate SARS-CoV-2 infection. In different Modules, we provide resources and examples of clinical workflows to increase:

- Referral to health care settings offering mAbs
- Intravenous treatment with mAb cocktails
- Subcutaneous treatment (e.g. REGEN-CoV)
- Local public health agency processes for increasing referrals to mAbs

This guide also includes patient and clinician handouts.

This implementation blueprint, including its component patient and clinician handouts, were developed between June 2021-December 2021. Information provided reflects information gathered prior to the rapid spread of the Omicron variant of the SARS-CoV-2 virus.

Acknowledgements

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This document is informed by experiences and includes specific resources in State of Colorado.

Introduction

From late 2020 through 2021, multiple mAb cocktails were authorized for emergency use by the FDA to treat mild to moderate COVID-19 in adults, and children. There have occurred multiple changes in eligibility criteria, methods of administration, guidance for use, and estimated or demonstrated efficacy against emerging SARS-CoV-2 variants. This implementation blueprint, including its component patient and clinician handouts, were developed and updated between June 2021-December 2021. Information provided reflects information gathered prior to the rapid spread of the Omicron variant of the SARS-CoV-2 virus. As of December 2021, the primary recommendation for outpatient COVID-19 mAbs, under an Emergency Use Authorization (EUA), is intravenous treatment with sotrovimab.

Use of mAbs is Indicated for COVID-19 for the Following:

1. **Treatment** – people who have tested positive for COVID-19 with mild/moderate symptoms and who are at high risk for progressing to severe COVID-19 and/or hospitalization. Risk can be related to age, medical conditions, and other factors, including race or ethnicity. Treatment must be given within 10 days of symptom onset, and new or worsened (from baseline) hypoxia are exclusion criteria.
2. **Prophylaxis after COVID-19 exposure** – people who have been exposed to COVID-19 (living in a household/facility where there is someone who has COVID-19) and are either unvaccinated or vaccinated and truly immunocompromised (approximately 3% of population).
3. **Pre-exposure prophylaxis** – people who are not able to get vaccinated, or are immunocompromised such that the vaccine is not able to mount a response.

People at risk of getting very sick from COVID-19 include:

- Older age ≥ 65 years old
- Obesity or overweight (Adults with BMI >25 kg/m2)
- Pregnancy
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease or treatment
- Age < 1 year old (newborn)
- Cardiovascular disease or hypertension
- Chronic lung diseases
- Sickle cell disease
- Neurodevelopmental disorders
- Having a medical-related technological dependence
- Other factors, including race or ethnicity (i.e., Native American)

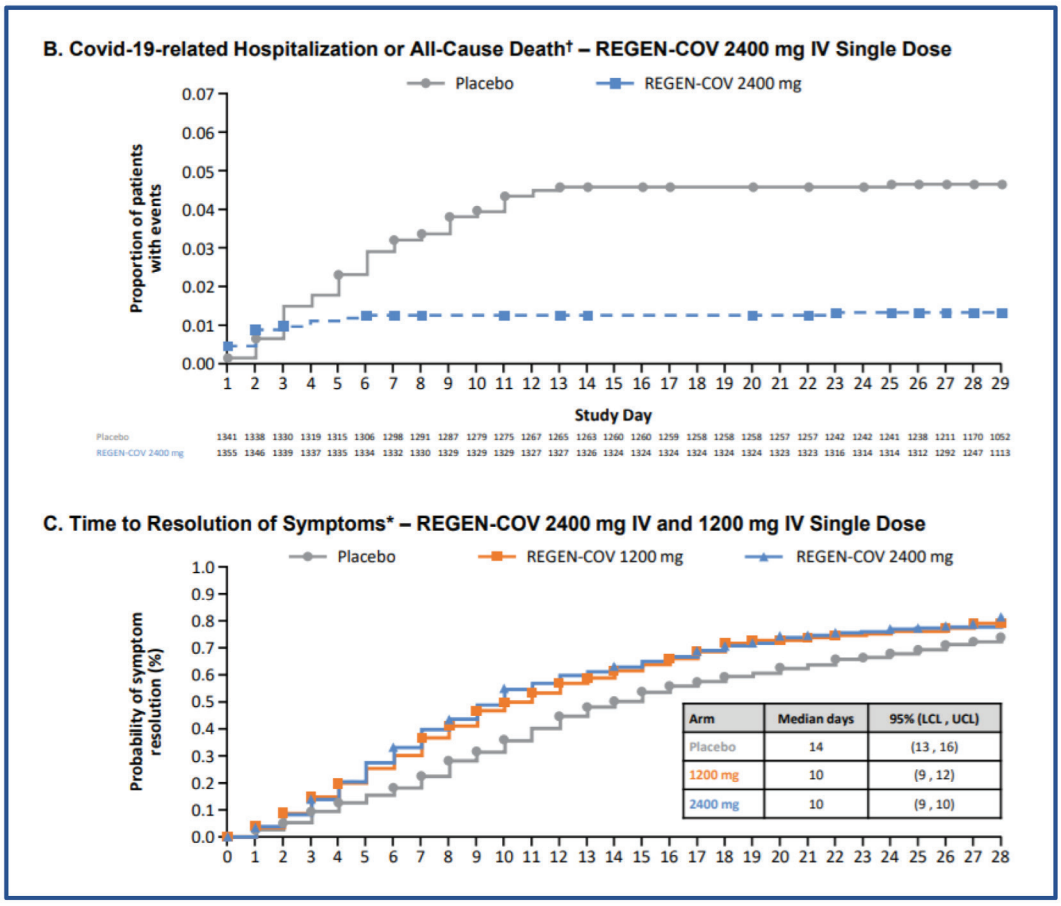
Example of Clinical Effectiveness
REGEN-COV mAb Cocktail Clinical Outcomes
COVID-19 Outpatients

Study Design

- 4,057 outpatients with mild-moderate COVID-19 with one or more risk factors for severe disease
- Randomized to placebo or various doses of casirivimab/imdevimab mAb (REGEN-COV)

Study Results

- Reduced hospitalization or all-cause death compared to placebo by 71.3%
- Symptoms resolved 4 days faster vs placebo (10 vs 14 days; p<0.0001)
- Serious adverse events more frequent in placebo group (4%) than in either dose group (1.1% and 1.3%)
- Infusion-related reactions rare (<0.3%)



Reference: Weinreich DM et al. REGEN-COV Antibody Combination and Outcomes in Outpatients with Covid-19.
N Engl J Med 2021; 385:e81. DOI: 10.1056/NEJMoa2108163

FDA Emergency Use Authorization for COVID-19 mAbs (as of December 1, 2021)

Available mAb Products					
Product	Indication		Formulation		Pediatric use
	Treatment	Post-exposure Prophylaxis	IV	SQ	
bamlanivimab/etesevimab (Lilly)	✓	✓	✓		All ages
casirivimab/imdevimab (REGEN-COV)	✓	✓	✓	✓	≥12 years and ≥40 kg
sotrovimab (GlaxoSmithKline)	✓		✓		≥12 years and ≥40 kg

NOTE – Not all products are effective for all variants

Summary

- Studies show mAbs reduce risk of hospitalization and death by 70%
- mAbs decrease symptoms by four days
- Adverse events are rare, and often occur within 30 minutes of treatment
- Casirivimab/imdevimab (REGEN-COV) can be given as a subcutaneous injection if IV is not feasible
- mAb therapy can be given regardless of vaccination status
- Vaccination can occur 90 days after mAbs
- In addition to treatment, mAbs can be given as post-exposure prophylaxis and pre-exposure prophylaxis

COLORADO-SPECIFIC INFORMATION

Guidance for Signing Up with CDPHE & Ordering mAbs (as of December 2021)

1. **To sign up as a mAb clinical site**, email cdphe.commentsoepr@state.co.us.
2. **To order mAbs**, fill out the CDPHE REDCap "Status of Supply" order form. The form is available at: https://cdphe.redcap.state.co.us/surveys/?s=LJWJ8E8JXLE4DHXN.
   Orders are due by 11:59 p.m. MT on Wednesday of each week. Orders are delivered the following week. Order form only needs to be submitted on weeks when the site needs to order more products.
3. **To be listed (or unlisted) in the CDPHE mAb Connector Tool**,
   email cdphe_Bamlanivimabworkgroup@state.co.us with your request.

For other questions about mAb products/procedures, email cdphe.commentsoepr@state.co.us

Health care sites that administer mAbs need to comply with the Health and Human Services (HHS) utilization reporting by every Wednesday, even if no doses were used.

Utilization reporting is important to demonstrate on-going need in Colorado. Good compliance results in higher allocation of mAbs for Colorado.

Reporting Requirements

1. **Reporting adverse events**
   Report adverse events to FDA MedWatch
   https://www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program
2. **Reporting mAb use** to the U.S. Department of Health and Human Services
   Sites are required to report utilization of product on a weekly basis.
   a. Instructions and links for the HHS TeleTracking COVID-19 Portal can be found here: https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Pages/COVID19-therapeutics-teletracking.aspx
   b. Complete reporting every week by 11:59 p.m. MT on Wednesday
      Note — Reporting must be completed even if not ordering more product and even if no doses have been administered in the past week

Information About mAb Costs

The medication has been purchased by the federal government. Patients will not be charged for the medication.

Depending on the patient's insurance coverage, patients may have other healthcare facility fees.

- Patients on Medicare or Medicaid should have no cost sharing, by federal policy
- Patients who are uninsured should have their claims paid by the Uninsured Relief Fund (see below for more information)
- Patients with commercial insurance cannot be balance billed or charged extra for out of network treatment, by federal policy
- Patients may be responsible for cost sharing depending on insurance

Medicare Reimbursement Information

https://www.cms.gov/medicare/medicare-part-b-drug-average-sales-price/covid-19-vaccines-and-monoclonal-antibodies

Note – Medicaid coverage is required based on section 6008(b)(4) of the Families First Coronavirus Response. Please refer to state-specific information.

Providing mAbs to People Who Are Uninsured

COVID-19 Claims Reimbursement to Health Care Providers and Facilities for Testing, Treatment, and Vaccine Administration for the Uninsured: https://www.hrsa.gov/CovidUninsuredClaim

Providers can submit claims to the U.S. Department of Health and Human Services for mAbs provided to individuals without health insurance. Reimbursement is generally at Medicare rates. The basics steps are:

1. Enroll as a provider
2. Submit patient information and claims
3. Receive payment via direct deposit

Informational resources are available for providers and patients interested in learning more about the HRSA COVID-19 Uninsured Program:

- Patient Fact Sheet: Uninsured Patient COVID Services Poster (hrsa.gov)
- Spanish version: Uninsured Patient COVID Services Poster Spanish (hrsa.gov)

General Resources Related to COVID-19 mAb Treatment

EUA Fact Sheet for Healthcare Providers

Casirivimab and Imdevimab (Regeneron) download (fda.gov)

Bamlanivimab and Etesevimab (Eli Lilly) (lilly.com)

Sotrovimab (GSK) SOTROVIMAB-EUA.PDF (gskpro.com)

EUA Fact Sheet for Patients

Casirivimab and Imdevimab (Regeneron) https://www.fda.gov/media/143893/download

Bamlanivimab and Etesevimab (Eli Lilly) https://www.fda.gov/media/145803/download

Sotrovimab (GSK) https://www.fda.gov/media/149533/download

HHS Playbook
Federal Response to COVID-19: Monoclonal Antibody Clinical Implementation Guide. Outpatient Administration Guide for Healthcare Providers (phe.gov)

Medicare Reimbursement Information
COVID-19 Vaccines and Monoclonal Antibodies | CMS

Reimbursement for people who are uninsured
https://www.hrsa.gov/CovidUninsuredClaim

Patient Fact Sheet: HRSA COVID-19 Uninsured Program Fact Sheet (English)
Uninsured Patient COVID Services Poster (hrsa.gov)

Patient Fact Sheet: HRSA COVID-19 Uninsured Program Fact Sheet (Spanish): Uninsured Patient
COVID Services Poster Spanish (hrsa.gov)

Infection Prevention and Control
Infection Control: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) | CDC

MODULE:

Referral Process for Monoclonal Antibody (mAb) Treatment for COVID-19

Purpose

This module describes a process that an outpatient setting can use to assess, counsel, and refer patients for mAbs for COVID-19. Specific information is provided about the Colorado Department of Public Health and Environment (CDPHE) resources to identify a health care setting providing mAbs.

Will This Work in My Setting?

1. **Do you have staff that can be trained** to determine eligibility, counsel patients on mAbs, and assist with providing practical and accurate information to patients interested in mAbs?

Planning for Clinical Workflows

1. **Determine eligibility** (see Appendix 1: Educational Resources for an eligibility checklist)
   Health care staff need to be able to determine patient eligibility. mAbs are for outpatients with mild to moderate COVID-19 symptoms and who meet the eligibility
   criteria, including:
   - People who are 65 years old or older
   - Babies who are less than 1 year old
   - People who are obese or overweight. This includes adults with a BMI of 25 or more. It also includes children under age 18 years old whose providers determine they meet the criteria
   - Pregnant people
   - People with certain underlying medical conditions

Examples of underlying medical conditions:

- Chronic kidney disease
- Diabetes
- Immunosuppressive disease or treatment
- Cardiovascular disease or hypertension
- Chronic lung diseases
- Sickle cell disease
- Neurodevelopmental disorders
- Having a medical-related technological dependence

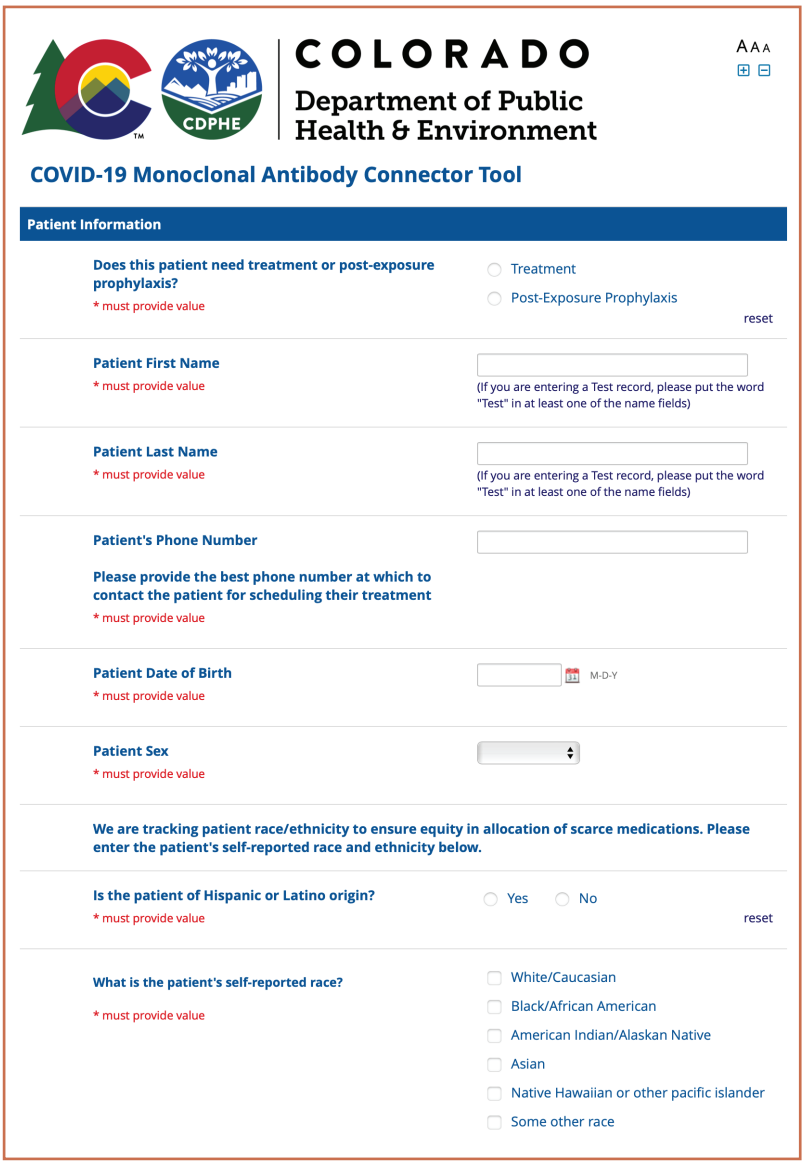
2. **Counsel patient on mAbs**
   (see Appendix 1: Educational Resources — III. Sample Shared Decision Making Language). Health care staff need to be able to facilitate shared decision-making about mAbs including brief discussion of benefits, risks of side effects, and overview of the mAb treatment process.

   Patient must be provided with the 3-page EUA Fact Sheet.

   - EUA Fact Sheet for Casirivimab and Imdevimab (Regeneron) https://www.fda.gov/media/143893/download
   - EUA Fact Sheet for Bamlanivimab and Etesevimab (Eli Lilly) https://www.fda.gov/media/145803/download
   - EUA Fact Sheet for Sotrovimab (GSK) https://www.fda.gov/media/149533/download

3. **Referral options**
   a. **mAb Connector Tool**
   https://cdphe.redcap.state.co.us/surveys/index.php?s=PX9LW9CEET

- Send a referral to the selected infusion center and give the patient the infusion center phone number to call and schedule a same- or next-day appointment.



COLORADO
Department of Public Health & Environment

AAA

COVID-19 Monoclonal Antibody Connector Tool

Patient Information

Does this patient need treatment or post-exposure prophylaxis?
* must provide value
- Treatment
- Post-Exposure Prophylaxis

reset

Patient First Name
* must provide value
(If you are entering a Test record, please put the word "Test" in at least one of the name fields)

Patient Last Name
* must provide value
(If you are entering a Test record, please put the word "Test" in at least one of the name fields)

Patient's Phone Number

Please provide the best phone number at which to contact the patient for scheduling their treatment
* must provide value

Patient Date of Birth
* must provide value
M-D-Y

Patient Sex
* must provide value

We are tracking patient race/ethnicity to ensure equity in allocation of scarce medications. Please enter the patient's self-reported race and ethnicity below.

Is the patient of Hispanic or Latino origin?
* must provide value
- Yes
- No

reset

What is the patient's self-reported race?
* must provide value
- White/Caucasian
- Black/African American
- American Indian/Alaskan Native
- Asian
- Native Hawaiian or other pacific islander
- Some other race

b. Self-referral to Colorado Department of Public Health and Environment (CDPHE) sites
Patients can make an appointment to receive treatment at a state-led clinic. In November 2021, mobile buses and static sites were introduced to increase access. Availability of sites varies based on overall mAb availability and clinical effectiveness.

- Information about COVID-19 treatment location schedule is available at: https://covid19.colorado.gov/getting-covid-19-treatment#Bus
- Call the COVID-19 hotline at 1-877-CO VAX CO (1-877-268-2926) for help making an appointment.
- Patients will be asked screening questions during the scheduling process; final eligibility is determined at the appointment.

MODULE:

Intravenous Monoclonal Antibody (mAb) Treatment for COVID-19

Purpose

This module serves as an example process that an outpatient setting can use to implement intravenous administration of mAbs for COVID-19.

Will This Work in My Setting?

Here are questions to consider for implementing mAbs via intravenous administration in your setting:

1. **Are you able to ensure that COVID-19 positive patients can remain separate from healthy patients to prevent a site of exposure?** Appropriate PPE for staff is always required.

   Options to consider:

   a. A negative pressure room

   b. An outdoor setting (i.e., mobile tent)

   c. An exam room with one patient at a time

   d. A designated space/room can be used for multiple patients receiving mAbs. When the designated space/room is needed for non-COVID positive patients, it should remain vacant for a sufficient amount of time to allow enough air changes to remove potentially infectious particles and be cleaned/disinfected per current recommendations.

2. **Do you have a registered nurse who can reconstitute the medication** (if pharmacy staff is unavailable) **and give the intravenous infusion?**
3. **Do you have a staff member who is able to identify possible side effects and allergic/anaphylaxis reactions during the administration of mAbs?** Staff member needs to be able to identify potential medical issues and activate appropriate care, including contacting EMS.
4. **Do you have ability to store the mAb medication as directed in the EUA** (refrigeration required)?

If your clinic is not able to answer, "Yes" to the above questions, a process for referring patients to an existing infusion site is recommended.

Additional Considerations: Each treatment takes approximately 90-120 minutes which includes a check-in process, mAb and patient preparation, IV infusion and post-administration observation (60 minutes). COVID-19 mAb needs to be stored refrigerated, and then brought to room temperature for 20 minutes prior to administration. Once at room temperature, mAb needs to be administered within 4 hours.

Planning for Clinical Workflows

Develop a Process for Managing Referrals and Scheduling

Patients will access mAbs in one of four ways:

1. Patient is referred from a provider **within your healthcare system** who made a direct referral/ mAb order in the electronic health record. Eligibility has been determined and the patient will need to be contacted and scheduled (same day when possible).
2. Patient is referred from an external provider **outside your healthcare system** who completed a State Connector Tool form and selected your location. In this situation, eligibility has already been determined and the patient will need to be contacted and scheduled using information provided on the form.
3. **Patient calls and requests mAbs** after a positive test at an outside site. The patient will need to be screened and, if eligible, (see Appendix 1: Educational Resources — II. Eligibility Criteria) scheduled.
4. **If your facility provides rapid COVID testing, mAbs can be administered to eligible patients at the time of diagnosis.**

Supplies Needed for Intravenous Administration

- 20 G IVs
- 30 CC syringes
- Normal saline bags (50 ml, 100 ml, 150 ml or 250 ml can be used)
- IV pump (can also hang to gravity if pump is not available)
- IV filter (0.2-micron polyethersulfone (PES) filter)
- Polyvinyl chloride (PVC), polyethylene (PE)-lined PVC, or polyurethane (PU) infusion set or IV tubing
- mAb product
- mAb product patient education paperwork
- Labels for reconstituted medication (name of mAb product, time reconstituted, and initialed by the RN)
- Vital signs (including pulse ox) prior to infusion, post-infusion, and at end of observation period
- Anaphylaxis emergency supplies/medications (e.g. epinephrine, Benadryl, solumedrol, ambu mask and bag, saline)
- Optional medications: anti-emetics, anti-pyretics

Develop a Care Process for Administering mAb Infusion

NOTE — Below is a sample process. Please also review EUA in detail for more information.

Identify which team member(s) (such as an RN) will be primarily interacting with the patient with COVID-19, including patient assessment, counseling, medication preparation, intravenous administration, monitoring process. The staff member needs to be trained and able to conduct the process.

1. **Patient check-in:** Patient does a telephone check in when they arrive and enters when room is ready. This avoids the patient waiting in a space where others could be exposed to COVID-19.
    a. Staff dressed in PPE meets the patient at the door and places the pulse oximeter on the patient while ambulating the patient to treating space. If pulse oximetry is sufficient (>90%), proceed with plans for treatment.
2. **Medication preparation:** Staff pulls the mAbs from the refigerator and writes the time pulled on the box. mAbs need to sit out at room temperature for 20 min.
3. **Vitals assessment and counseling:** RN obtains/confirms patient identifying information, checks initial vital signs, places the IV and provides the mAb education sheet (EUA, see Resources) to the patient.
4. **Medication preparation:** RN reconstitutes mAb product.
5. **Treatment:** RN begins mAb infusion. RN may stay with the patient during initial part of infusion. Rate of infusion is based on the volume used in the reconstitution per the mAb EUA instructions. RN ensures patient has access to a call light or ability to call for help if needed prior to leaving the patient during the infusion. At the completion of the infusion, RN obtains another set of vital signs, and disconnects patient from tubing while leaving the IV in.
6. **Observation:** The post-administration observation period is 60 minutes.
    a. At the completion of the observation period, the staff rechecks final vital signs, discontinues the IV, and provides patient with discharge/follow-up instructions.

MODULE:

Subcutaneous Monoclonal Antibody (mAb) Treatment for COVID-19

Purpose

This module serves as an example process that an outpatient setting can use to implement subcutaneous administration of Casirivimab and Imdevimab mAbs (REGEN-COV) for treatment of COVID-19.

Will This Work in My Setting?

Here are questions to consider for implementing mAbs via subcutaneous administration in your setting:

1. **Are you able to ensure that COVID-19 positive patients can remain separate from healthy patients to prevent a site of exposure?** Appropriate PPE for staff is always required.
    a. A negative pressure room
    b. An outdoor setting (i.e., mobile tent)
    c. An exam room with one patient at a time
    d. A designated space/room can be used for multiple patients receiving mAbs. When the designated space/room is needed for non-COVID positive patients, it should remain vacant for a sufficient amount of time to allow enough air changes to remove potentially infectious particles and be cleaned/disinfected per current recommendations.
2. **Do you have a staff member who can administer medication subcutaneously?** A trained RN, LPN, MA, or other team member can administer the subcutaneous injections.
3. **Do you have a staff member who is able to identify possible side effects and allergic/anaphylaxis reactions during the administration of mAbs?** Staff member needs to be able to identify potential medical issues and activate appropriate care, including contacting EMS.
4. **Do you have ability to store the mAb medication as directed in the EUA** (refrigeration required)?

If your clinic is not able to answer, "Yes" to the above questions, a process for referring patients to an existing infusion site is recommended.

Additional Considerations: Each treatment takes approximately 90-120 minutes which includes a check-in process, mAbs and patient preparation, subcutaneous administration and post-administration observation (60 minutes). COVID-19 mAbs needs to be stored refrigerated, and then brought to room temperature for 20 minutes prior to administration. Once at room temperature, mAbs need to be administered within 4 hours.

Planning for Clinical Workflows

Develop a Process for Managing Referrals and Scheduling

Patients will access mAbs in one of four ways:

1. Patient is referred from a provider **within your healthcare system** who made a direct referral/ mAb order in the electronic health record. Eligibility has already been determined and the patient will need to be contacted and scheduled (same day when possible).
2. Patient is referred from an external provider **outside your healthcare system** who completed a State Connector Tool form and selected your location. In this situation, eligibility has been determined and the patient will need to be contacted and scheduled using information provided on the form.
3. **Patient calls and requests mAbs** after a positive test at an outside site. The patient will need to be screened and if eligible (see Appendix 1: Educational Resources — II. Eligibility Criteria), scheduled.
4. **If your facility provides rapid COVID testing, mAbs can be administered to eligible patients at the time of diagnosis.**

Supplies Needed for Subcutaneous Administration

- REGEN-COV Fact Sheet for Patients, Parents and Caregivers. This is provided to every patient prior to treatment. REGEN-COV EUA: https://www.fda.gov/media/151863/download
- Alcohol wipes
- 3-mL or 5-mL Luer lock syringes (4 per patient receiving subcutaneous administration)
- Appropriate needles for product preparation and subcutaneous administration
  - 21 gauge 1.5-inch needles for product transfer from vials
  - 25- or 27-gauge needles for subcutaneous injection (4 per patient)
- Anaphylaxis emergency supplies/medications (e.g. epinephrine, Benadryl, solumedrol, ambu mask and bag, saline)
- Optional medications: anti-emetics, antipyretics

Develop a Care Process for Administering mAb Infusion

NOTE — Below is a sample process. Details are outlined in REGEN-COV EUA. Please review EUA in detail for more information.

Identify which team member(s) (such as an RN, LPN, MA or other) will be primarily interacting with the patient with COVID-19, including patient assessment, counseling, medication preparation, subcutaneous injection, monitoring process. The staff member needs to be trained and able to conduct the process.

1. **Patient check-in:** Patient does a telephone check in when they arrive and enters when room is ready. This avoids the patient waiting in a space where others could be exposed to COVID-19.
   a. Staff dressed in PPE meets the patient at the door and places the pulse oximeter on the patient while ambulating the patient to treating space. If pulse oximetry is sufficient (>90%), proceed with plans for treatment.
2. **Medication preparation:** Staff pulls the mAbs from the refrigerator and writes the time pulled on the box. mAbs need to sit out at room temperature for 20 minutes, and must be used within 4 hours.
3. **Vitals assessment and counseling:** Staff obtains/confirms patient identifying information, checks initial vital signs, and provides the mAb education sheet (see Appendix 1: Educational Resources — IV. Patient Handout) to the patient.
   a. Staff explains and documents that subcutaneous administration of mAbs is accepted but not the preferred method of delivery, compared to intravenous (see Appendix 1: Educational Resources — III. Sample Shared Decision Making Language).
4. **Medication preparation: Staff prepares 600 mg of casirivimab and 600 mg of imdevimab using 4 syringes (3-mL or 5-mL Luer lock syringes with Luer connection and four 21- gauge, 1½-inch transfer needles)**
   a. Staff withdraws 2.5 mL into each syringe (total of 4 syringes prepared at the same time)
   b. Staff replaces the 21-gauge transfer needle with a 25-gauge or 27- gauge needle for subcutaneous injection.
5. **Treatment:** Staff administers the subcutaneous injections consecutively, each at a different injection site, into the thigh, back of upper arm, or abdomen, except for two inches (5 cm) around the navel. The waistline should be avoided.
6. **Observation:** The post-administration observation period is 60 minutes.
   a. At the completion of the observation period, the staff rechecks final vital signs and provides patient with discharge/follow-up instructions (see Appendix for sample).

MODULE:
Monoclonal Antibody (mAb) Treatment for COVID-19

A Model for Local Public Health Agencies (LPHA)

Purpose

This document serves as an example process that Local Public Health Agencies (LPHAs) can use in partnership with a health system to refer people for mAb treatment of COVID-19.

Will This Work in My Setting?

Here are questions to consider for implementing a referral process for mAbs in your setting:

1. **Is there a health system to partner with?**
2. **Can case investigators be trained to ask basic questions to see if an individual meets the referral criteria?** Those who meet the criteria and are interested would be referred to the partner health system via a REDCap form.

   NOTE — Case investigators are not providing medical advice, determining risk factors, or acting as a health provider in any way.

Overview of Process

LPHA Case Investigators

- Confirm patient is symptomatic, and that less than 7 days have elapsed since symptom onset
- Convey treatment exists
- Ask if person wants to learn more
- Put contact info in REDCap

Partner Health System Clinicians

- Provider calls person
- Assesses eligibility
- Sends Rx for mAbs
- Informs patient of follow up call from infusion center

Infusion Centers

- Receives prescription and contacts patient to schedule

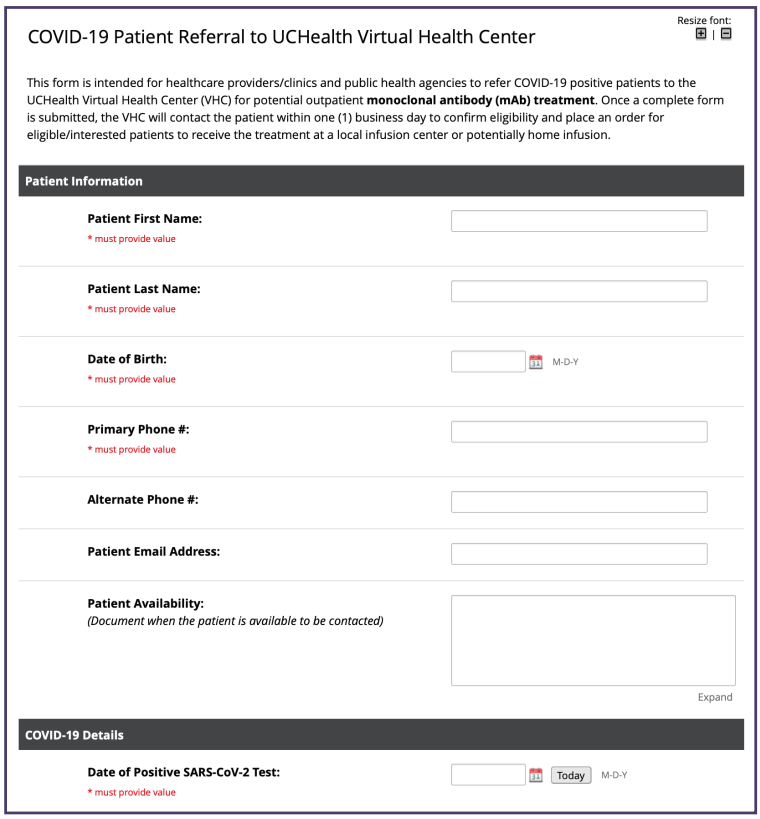
Planning for Clinical Workflows

Roles and responsibilities of Case Investigator (Local Public Health Agency)

1. **Case Investigator informs person of COVID-19 positive result**
2. Case investigator determines whether **the person has symptoms**, and the date symptoms started (must be <7 days since their symptom onset)
3. Case Investigator determines if an **individual meets referral criteria based on health system or public infusion site guidance** —
   ONE of the following:
   a. ≥50 years old, OR
   b. Unvaccinated or partially vaccinated and ≥12 years, OR
   c. Reports being immunocompromised and ≥12 years
4. Case investigator uses a script to share that COVID-19 is treatable with mAbs

> **Script:** *"There is a treatment for early COVID that can prevent it from getting worse. It also helps you to feel better faster (average of 4 days). You might be eligible to receive this treatment, but it must be given soon.*
>
> *I'd like to have one of the clinicians from the COVID treatment team give you a call. Would that be OK?"*

5. Case investigator send information to the Team Lead for eligible and interested individuals
6. Case investigator Team Lead completes and submits REDCap referral form



COVID-19 Patient Referral to UCHealth Virtual Health Center

Resize font:

This form is intended for healthcare providers/clinics and public health agencies to refer COVID-19 positive patients to the UCHealth Virtual Health Center (VHC) for potential outpatient **monoclonal antibody (mAb) treatment**. Once a complete form is submitted, the VHC will contact the patient within one (1) business day to confirm eligibility and place an order for eligible/interested patients to receive the treatment at a local infusion center or potentially home infusion.

Patient Information

Patient First Name:
* must provide value

Patient Last Name:
* must provide value

Date of Birth:
* must provide value
M-D-Y

Primary Phone #:
* must provide value

Alternate Phone #:

Patient Email Address:

Patient Availability:
(Document when the patient is available to be contacted)

Expand

COVID-19 Details

Date of Positive SARS-CoV-2 Test:
* must provide value
Today M-D-Y

Roles and responsibilities of Partner Health System

1. An automated email with a summary of the referral is sent from the REDCap form to the partner health system
2. The health system nurse or staff member will contact the person to ask them about when they tested positive for COVID, when they started to have symptoms, and about their medical history to see if they are eligible for mAbs
3. If eligible, a clinician will talk with the person by phone to describe mAbs and find out whether the person is interested in receiving mAbs
4. If the person is eligible, the partner health system will help find a treatment center where the person can receive mAbs. The health system doctor or team will send the referral and orders

LPHAs can also provide information regarding self-referral to the Colorado Department of Public Health and Environment (CDPHE) sites.

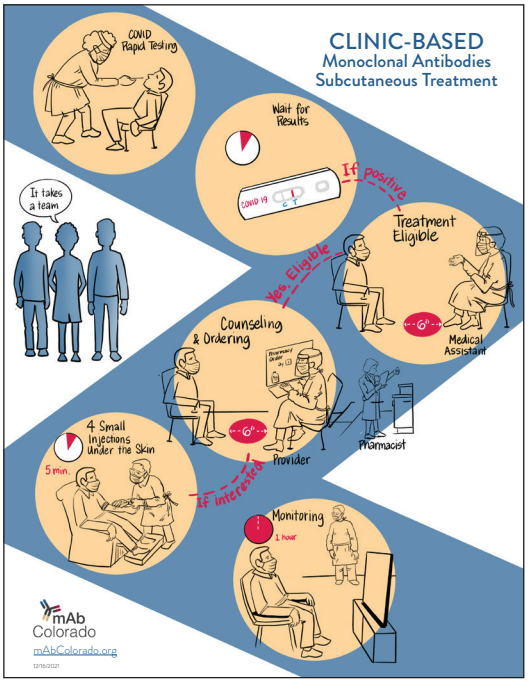
Self-referral to Colorado Department of Public Health and Environment (CDPHE) sites

Patients can make an appointment to receive treatment at a state-led clinic. In November 2021, mobile buses and static sites were introduced to increase access. Availability of sites varies based on overall mAb availability and clinical effectiveness.

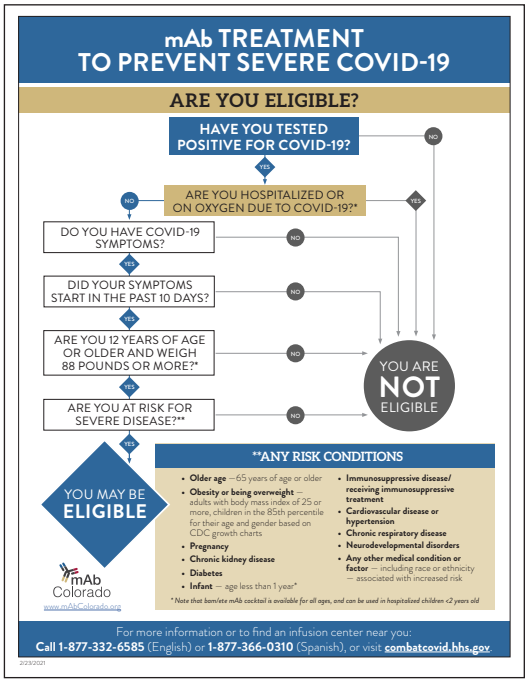
- Information about COVID-19 treatment location schedule is available at: https://covid19.colorado.gov/getting-covid-19-treatment#Bus
- Call the COVID-19 hotline at 1-877-CO VAX CO (1-877-268-2926) for help making an appointment.
- Patients will be asked screening questions during the scheduling process; final eligibility is determined at the appointment.

Appendix 1 – Educational Resources

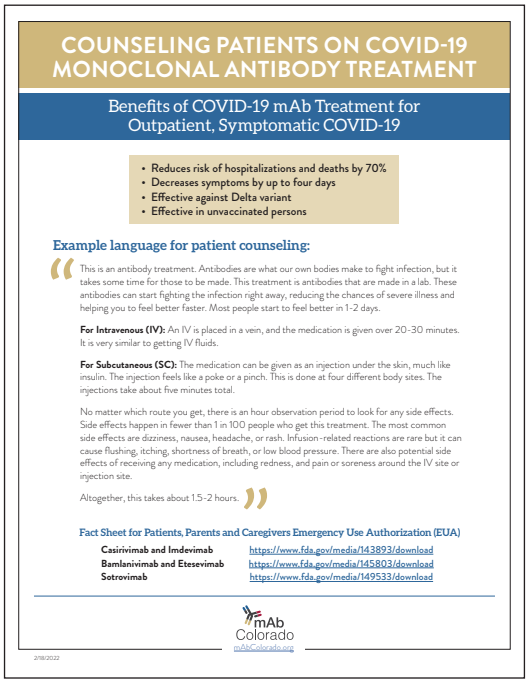
I. Overview of Subcutaneous Treatment



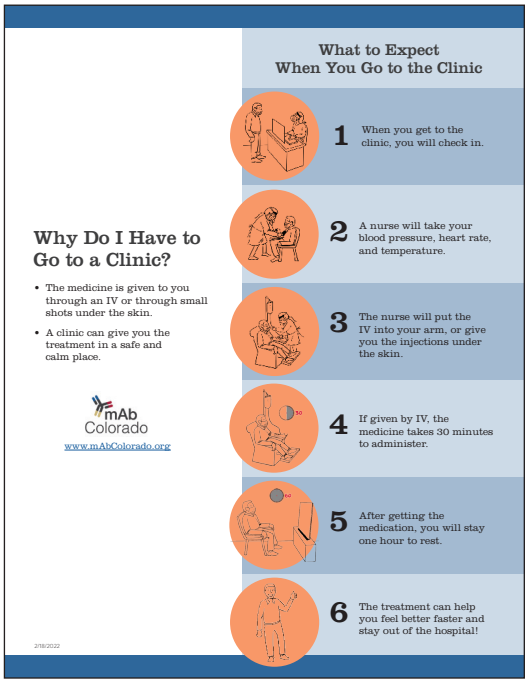
II. Eligibility Criteria



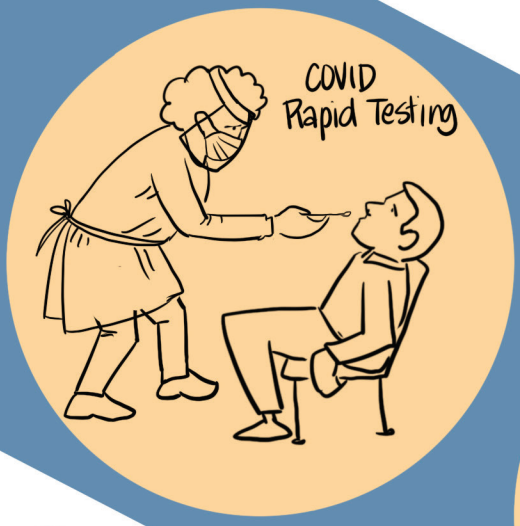
III. Sample Shared Decision Making Language

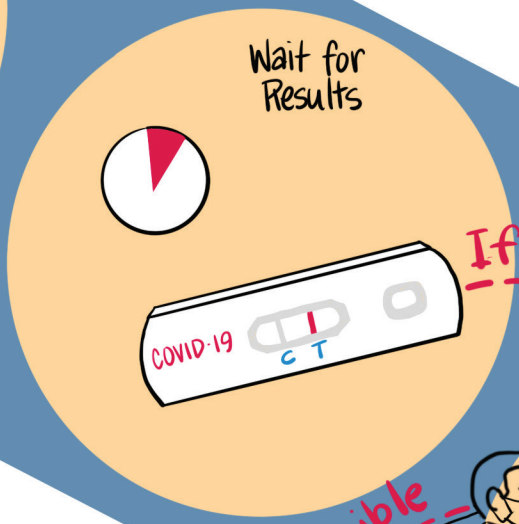


IV. Patient Handout of "What to Expect for Treatment in Clinic"

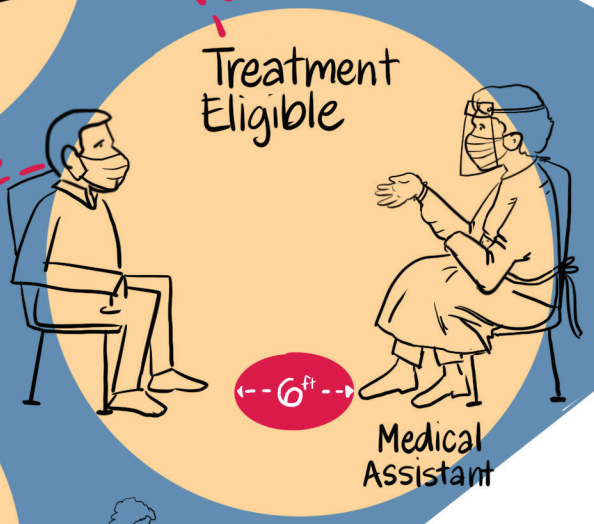


CLINIC-BASED
Monoclonal Antibodies Subcutaneous Treatment

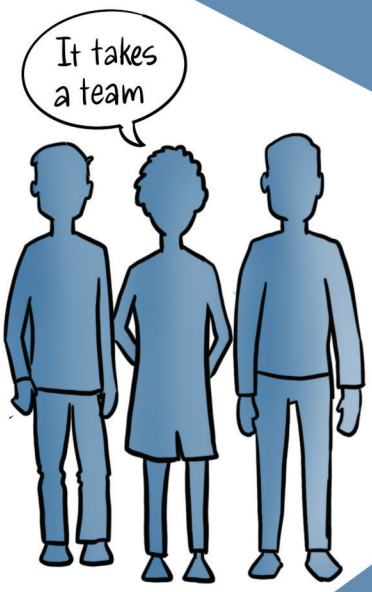


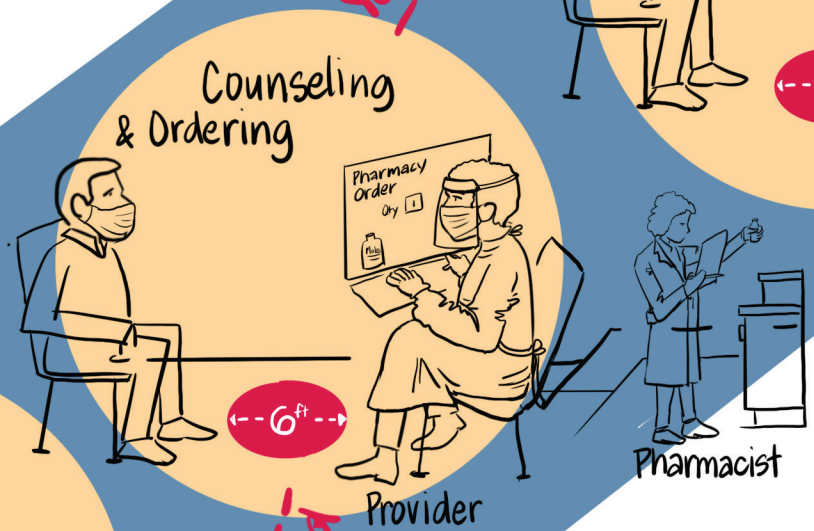


If positive

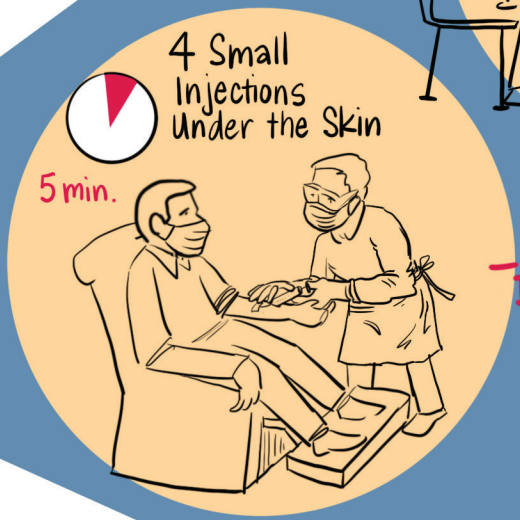


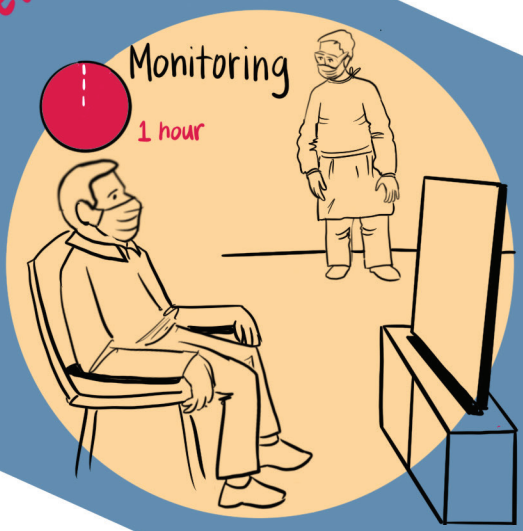
Yes, Eligible





If interested





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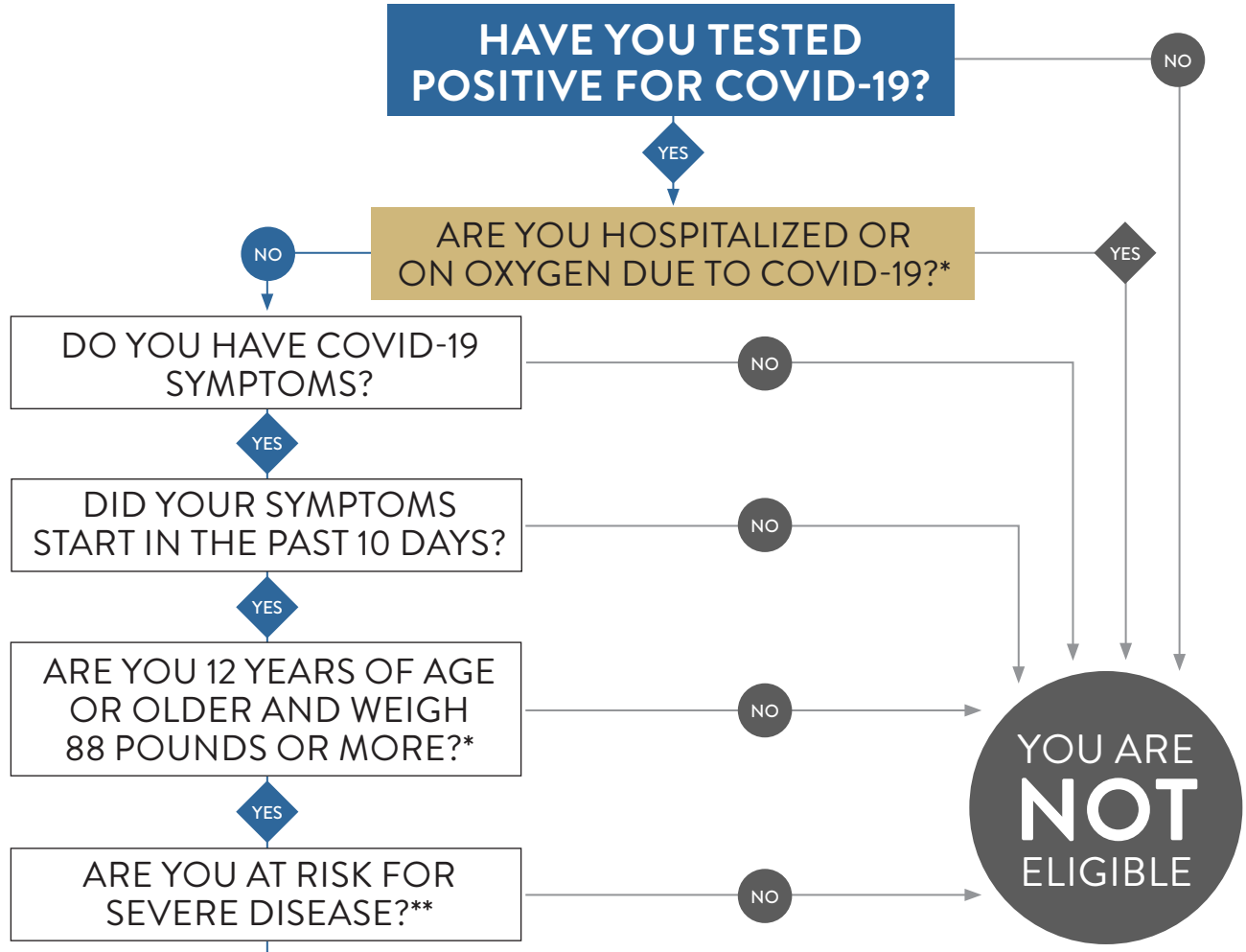
12/16/2021

mAb TREATMENT TO PREVENT SEVERE COVID-19

ARE YOU ELIGIBLE?



**ANY RISK CONDITIONS

- **Older age** —65 years of age or older
- **Obesity or being overweight** — adults with body mass index of 25 or more, children in the 85th percentile for their age and gender based on CDC growth charts
- **Pregnancy**
- **Chronic kidney disease**
- **Diabetes**
- **Infant** — age less than 1 year*
- **Immunosuppressive disease/ receiving immunosuppressive treatment**
- **Cardiovascular disease or hypertension**
- **Chronic respiratory disease**
- **Neurodevelopmental disorders**
- **Any other medical condition or factor** — including race or ethnicity — associated with increased risk

** Note that bam/ete mAb cocktail is available for all ages, and can be used in hospitalized children <2 years old*

mAb Colorado
www.mAbColorado.org

For more information or to find an infusion center near you:
Call 1-877-332-6585 (English) or **1-877-366-0310** (Spanish), or visit **combatcovid.hhs.gov**.

2/23/2021

COUNSELING PATIENTS ON COVID-19 MONOCLONAL ANTIBODY TREATMENT

Benefits of COVID-19 mAb Treatment for Outpatient, Symptomatic COVID-19

- Reduces risk of hospitalizations and deaths by 70%
- Decreases symptoms by up to four days
- Effective against Delta variant
- Effective in unvaccinated persons

Example language for patient counseling:

"This is an antibody treatment. Antibodies are what our own bodies make to fight infection, but it takes some time for those to be made. This treatment is antibodies that are made in a lab. These antibodies can start fighting the infection right away, reducing the chances of severe illness and helping you to feel better faster. Most people start to feel better in 1-2 days.

For Intravenous (IV): An IV is placed in a vein, and the medication is given over 20-30 minutes. It is very similar to getting IV fluids.

For Subcutaneous (SC): The medication can be given as an injection under the skin, much like insulin. The injection feels like a poke or a pinch. This is done at four different body sites. The injections take about five minutes total.

No matter which route you get, there is an hour observation period to look for any side effects. Side effects happen in fewer than 1 in 100 people who get this treatment. The most common side effects are dizziness, nausea, headache, or rash. Infusion-related reactions are rare but it can cause flushing, itching, shortness of breath, or low blood pressure. There are also potential side effects of receiving any medication, including redness, and pain or soreness around the IV site or injection site.

Altogether, this takes about 1.5-2 hours."

Fact Sheet for Patients, Parents and Caregivers Emergency Use Authorization (EUA)

Casirivimab and Imdevimab	https://www.fda.gov/media/143893/download
Bamlanivimab and Etesevimab	https://www.fda.gov/media/145803/download
Sotrovimab	https://www.fda.gov/media/149533/download

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2/18/2022

Why Do I Have to Go to a Clinic?

- The medicine is given to you through an IV or through small shots under the skin.
- A clinic can give you the treatment in a safe and calm place.

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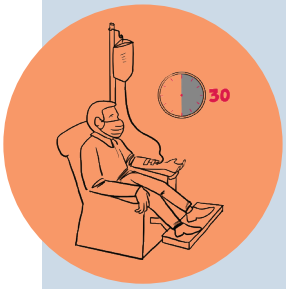
What to Expect When You Go to the Clinic

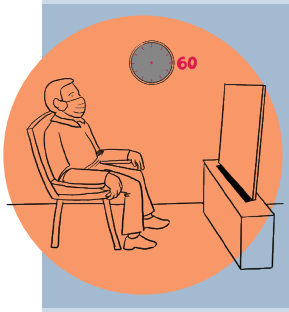
1 When you get to the clinic, you will check in.

2 A nurse will take your blood pressure, heart rate, and temperature.

3 The nurse will put the IV into your arm, or give you the injections under the skin.



4 If given by IV, the medicine takes 30 minutes to administer.



5 After getting the medication, you will stay one hour to rest.

6 The treatment can help you feel better faster and stay out of the hospital!

2/18/2022

Appendix 2

Sample Discharge Instructions

Today you received: REGEN-COV (casirivimab + imdevimab) monoclonal antibodies subcutaneous injections

After your treatment, you should go home and rest.
To help stop the spread of COVID-19, stay home and away from others until your healthcare provider or contact tracer tells you it is safe to resume normal activities.

Bruising and slight discomfort at the injection sites is common and should go away in a few days.
You may use a cold compress for comfort today if needed. After that, warmth (like a heating pad) can help heal bruising at the site. If you notice changes such as pain, redness, drainage, numbness or tingling, or other concerning symptoms near the injection sites, contact your healthcare provider.

Tell your healthcare provider if you have side effects*, including:

- Upset stomach (nausea, vomiting, or diarrhea)
- Itching, swelling, rash, or hives
- Dizziness or low blood pressure
- Changes in your heartbeat
- Any new or worsening symptoms

Clinic phone number: XXX-XXX-XXXX
You can also report side effects to FDA MedWatch at www.fda.gov/medwatch or by calling 1-800-FDA-1088

Wait at least 90 days before you get a COVID-19 vaccine.
Vaccines teach your body how to identify and fight the virus. Since you already have COVID-19, your body is learning that lesson right now! By waiting 90 days, you will allow your body to make the best use of the vaccine when you receive it. It is uncommon to be reinfected with COVID-19 during this time, as your body's immune system will still remember how to fight the virus from your current infection.

If you have any of these emergency warning signs*, get medical attention right away:

- Pain or pressure in the chest
- New confusion
- Trouble breathing
- Inability to wake or stay awake
- Bluish lips or face
- Swollen lips, face, or throat
- Wheezing (noisy breathing that may sound musical or like whistling)

This is not a complete list of possible symptoms. Please call your medical provider for any other symptoms that are severe or concerning to you.

Appendix 3

Sample Standing Orders

This is a sample standing order that can be adapted by a practice setting. Note that this is provided for REGEN-COV. Additional standing orders can be created that are specific to other monoclonal antibodies, including the associated details for administration, dosing, monitoring, etc.

PRACTICE NAME
Standing Order for REGEN-COV Monoclonal Antibodies
Approved **DATE**

This Standing Order is issued by Dr. **NAME**, Medical Director of **PRACTICE NAME**. The purpose is to reduce morbidity and mortality from SARS-CoV-2, the virus that causes COVID-19, by efficiently and quickly administering monoclonal antibodies to qualifying individuals.

This Standing Order authorizes **PRACTICE NAME** staff to administer REGEN-COV mAb therapy under this order and in accordance with established protocols. Treatment criteria have been established by the U.S. Food and Drug Administration (FDA), and are outlined in the Emergency Use Authorization (EUA) for REGEN-COV (this document may change frequently; the most current version can be found at https://www.regencov.com/).

PATIENT ELIGIBILITY

Under these standing orders, **PRACTICE NAME** staff are authorized to administer REGEN-COV to individuals age 12 years and older (adults age 18 years and older, and children ages 12-17 years who weigh at least 40kg) with positive results of direct SARS-CoV-2 testing and within 10 days of symptom onset who have been determined to be eligible. Patient eligibility is determined by a screening process to ensure they meet the criteria defined by the EUA for REGEN-COV (https://www.regencov.com/).

Monoclonal antibodies are not authorized for use in patients:

- Who are hospitalized due to COVID-19, OR
- Who require new 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, OR
- Who have had a previous severe hypersensitivity reaction, including anaphylaxis, to REGEN-COV.

Benefit of treatment with monoclonal antibodies has not been observed in patients hospitalized due to COVID-19. SARS-CoV-2 monoclonal antibodies may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

Appendix 3 Con't.

HYPOXIC PATIENT

Should a patient present to **PRACTICE NAME** for a REGEN-COV treatment and be found to be hypoxic (oxygen saturation < 88%) on no oxygen or their baseline oxygen requirement, they should be transferred to **PRACTICE NAME** itself for medical evaluation and treatment. REGEN-COV should not be administered.

PLAN OF CARE

1. Order to Dispense

a. The **PRACTICE NAME** staff is authorized to dispense the below formulations of monoclonal antibodies:

- REGEN-COV (casirivimab and imdevimab) formulations
  - Single product vials:
    a. Casirivimab 120 mg/mL - 5mL total (from 2.5 or 11.1 mL vials) for 600 mg casirivimab
    b. Imdevimab 120 mg/mL - 5mL total (from 2.5 or 11.1 mL vials) for 600 mg imdevimab
  - Co-formulated vials:
    a. Casirivimab and imdevimab (60 mg-60mg)/mL - 10mL total for 600 mg casirivimab and 600mg imdevimab

2. Dosing, Preparation & Administration

a. Dosing, preparation and administration procedures may frequently change with this new product. The **PRACTICE NAME** staff shall keep up to date and follow the latest published protocols to ensure safety and efficacy, found online: **https://www.regencov.com/hcp/dosing/dosing-administration**.

b. REGEN-COV may be administered either as an intravenous infusion or as a subcutaneous injection, per the EUA. Intravenous infusion is the preferred route.

c. Prior to being treated, the patient shall be provided with approved educational information about the product, such as a copy of the Patient Fact Sheet (the latest version may be found on **https://www.regencov.com/**).

3. Monitoring

a. Patients must be clinically monitored during administration of the medication AND observed for at least one-hour post-treatment to assess for potential adverse reactions.

b. Please see the "Adverse Events" section below.

c. Vital signs shall be obtained prior to treatment, immediately following treatment, and at the end of the one-hour observation period. They can additionally be obtained at any point should the patient

Appendix 3 Con't.

have symptoms or complaints.

ADVERSE EVENTS: AS NEEDED ORDERS

1. **Nausea**
   a. If a patient develops nausea, administer Zofran 4 mg IV x 1 or 4 mg ODT. May repeat in 1 hour if not improved.
2. **Headache or Fever**
   a. If a patient develops a headache or fever, administer 1000 mg of acetaminophen if not allergic.
3. **Hives or Itching**
   a. Discontinue infusion or injection. Leave IV in place.
   b. Transfer patient to **PRACTICE NAME** itself for medical provider evaluation and treatment.
4. **Facial or Airway Angioedema, Bronchospasm, Anaphylaxis, Hypotension (SBP<90)**
   a. Discontinue infusion or injection. Leave IV in place.
   b. Transfer patient to **PRACTICE NAME** itself for medical provider evaluation and treatment.
5. **For other complaints, contact PRACTICE NAME Attending Physician.**

REPORTING

1. **Nursing staff shall complete a medical screening exam (MSE) note for documentation of the treatment within the EPIC medical record.**
2. **Adverse events and additional medication treatments should be additionally documented in the EPIC medical record.**
3. **Any unusual adverse events or findings should additionally be messaged to Dr. NAME via secure EPIC messaging or PHI protected email.**

STATEMENT OF APPROVAL

This standing order for REGEN-COV monoclonal antibodies has been approved for use by **PRACTICE NAME** Clinic staff from **DATE** through **DATE**.

NAME M.D.
Medical Director, **PRACTICE NAME**