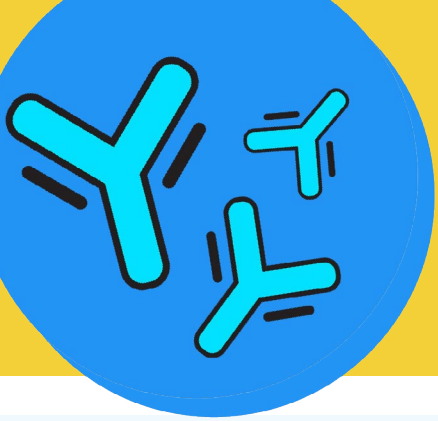


EMS Template Protocol for COVID-19 Monoclonal Antibody Administration:

Treatment and Post-Exposure Prophylaxis of REGEN-COV (casirivimab and imdevimab)

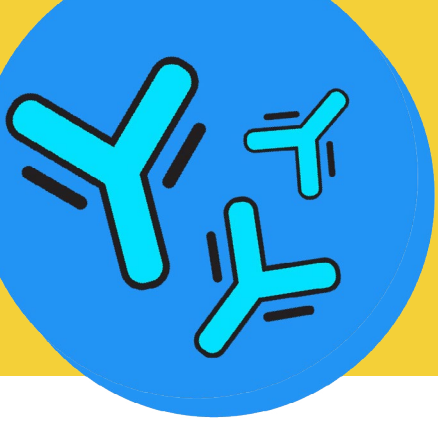
Purpose:

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of REGEN-COV (casirivimab and imdevimab) co-formulated product and REGEN-COV (casirivimab and imdevimab) supplied as individual vials to be administered together, for the treatment of mild to moderate coronavirus disease 2019 (COVID -19) in adult 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 progression to severe COVID-19, including hospitalization or death. Monoclonal antibodies are used to neutralize the COVID-19 virus and intended to prevent progression of disease. The U.S. Government is currently supplying REGEN-COV (casirivimab and imdevimab) for the treatment and post-exposure prophylaxis of COVID-19. The dosing is the same for both indications (casirivimab 600mg and imdevimab 600mg).

Who is eligible?

Adult or pediatric (>12 years of age and weighing at least 40 kg) patients at **high-risk** for progressing to severe disease or death

- **Treatment Dosing:** Patients who are COVID positive, with mild-to-moderate symptoms, not hospitalized due to COVID symptoms, and not requiring oxygen or an increase in home oxygen therapy are eligible.
- **Post-Exposure Prophylaxis (PEP)**: Individuals who are not fully vaccinated **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) **AND**
  - have been exposed to an individual infected with SARS-CoV-2 consistent with close contact criteria per CDC **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)
  - *Limitations of Authorized Use:*
    - PEP with REGEN-COV is not a substitute for vaccination against COVID-19
    - REGEN-COV is not authorized for pre-exposure prophylaxis for prevention of COVID-19
    - REGEN-COV is not authorized for use in patients:
      - who are hospitalized due to COVID-19, **OR**
      - who require oxygen therapy due to COVID-19, **OR**
      - who require an increase in baseline oxygen flow rate due to COVID -19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.
    - Monoclonal antibodies, such as REGEN-COV, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.



EMS Template Protocol for COVID-19 Monoclonal Antibody Administration:

Treatment and Post-Exposure Prophylaxis of REGEN-COV (casirivimab and imdevimab)

Risk factors for development of severe COVID include, but are not limited to: (for both treatment and PEP indications)

- 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 ibrosis, 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).

What are the routes of administration for REGEN-COV?

1. Intravenous (IV): casirivimab 600mg and imdevimab 600mg by infusion
2. Subcutaneous: four injections given in the same visit totaling casirivimab 600mg and imdevimab 600mg.
3. For treatment of symptomatic COVID-19, the intravenous route is preferred under the EUA, but if there would be a delay in providing IV administration, subcutaneous administration is acceptable.
4. For PEP, subcutaneous and intravenous administration are viewed clinically equivalent.

EMS Template Protocol for COVID-19 Monoclonal Antibody Administration:

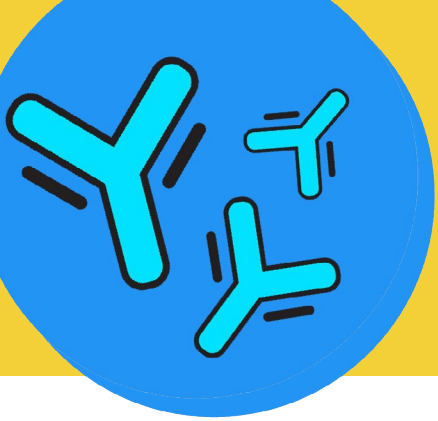
Treatment and Post-Exposure Prophylaxis of REGEN-COV (casirivimab and imdevimab)

Management of adverse reaction to intravenous infusion or subcutaneous administration:

- Implement the following actions in case of hypersensitivity or allergic reactions:
  NOTE: these actions should be based on local EMS protocol as approved by the EMS Medical Director

Shortness of Breath	Tightness in the Chest	Glossal Edema
Angioedema	Periorbital or Facial Edema	Hypotension
Rash/Urticaria	Nausea/Vomiting	Tachycardia
Lightheadedness/ Dizziness	Diarrhea	

1. Stop infusion or do not administer additional subcutaneous injections
2. Stay with patient
3. Activate transporting EMS agency
4. Maintain patent airway and administer oxygen as needed per protocol
5. Establish IV access and initiate cardiac monitoring
6. Be prepared to administer emergency medications per protocol
   - Epinephrine (1:1,000) **Intramuscular** Injection – 0.3mg IM or epi auto-injector
   - Benadryl IV Injection
   - Hydrocortisone, Methylprednisolone or Dexamethasone IV Injection
   - Albuterol 2.5mg nebulized or via MDI if wheezing/dyspnea
7. Obtain 12 Lead ECG if epinephrine administered
8. Initiate transport per local EMS protocol
9. Consult online medical control as appropriate



EMS Template Protocol for COVID-19 Monoclonal Antibody Administration:

Treatment and Post-Exposure Prophylaxis of REGEN-COV (casirivimab and imdevimab)

Basic Equipment:

Equipment requirements may vary by medical direction. Follow your local requirements when determining the equipment needed for your treatment setting. The following equipment should be considered to ensure the most optimal care environment for patients receiving REGEN-COV. This list is not intended to substitute for your independent medical judgment.

Personal Protective Equipment

- Gloves/gowns
- Eye and face protection (e.g., goggles, safety glasses, face shields)
- NIOSH-certified facepiece respirators or better

Infusion Supplies

Administration set

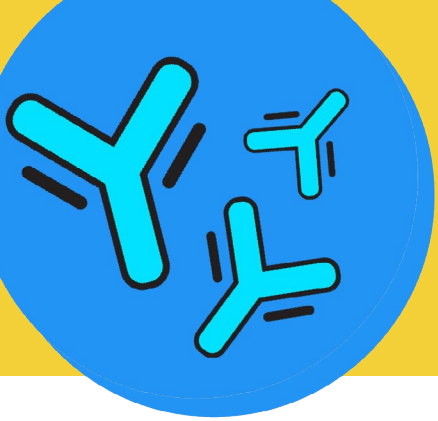
- Sterile in-line 0.2/0.22 micron filter (may be integrated into administration set or separate add-on device)
- IV 0.9% normal saline and catheters
- Infusion pumps (if available)
- 3-mL saline syringes
- Appropriately sized syringes
- Alcohol wipes
- 2x2 gauze pads
- Adhesive bandages
- Occlusive dressing
- Absorbent under pads (blue pads)
- Extension set tubing
- 18-gauge stainless steel needles
- Sharps container
- Tape

Injection Supplies

- 3-mL or 5-mL polypropylene Luer lock syringe with Luer connection
- 21 gauge 1.5-inch transfer needles
- 25-gauge or 27-gauge needle for subcutaneous injection

General Supplies

- Bag-valve-mask
- Vital signs equipment
- Adverse reaction management kit
  - IV diphenhydramine,
  - IV corticosteroid (e.g., methylprednisolone 125 mg),
  - epinephrine (auto-injector preferred),
  - oxygen and delivery devices (nasal cannula and non-rebreather mask)
- Locking refrigerator with temperature monitoring capability
- Biohazard disposal bag
- Disposable disinfection wipes
- Thermometer probe covers (if required)
- 70% alcohol wipes
- Paper towels
- Trash bins and liners



EMS Template Protocol for COVID-19 Monoclonal Antibody Administration:

Treatment and Post-Exposure Prophylaxis of REGEN-COV (casirivimab and imdevimab)

Storage and Handling:

Casirivimab and imdevimab are preservative-free. Discard any unused portion after use. Store unopened vials in a refrigerator at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light.

DO NOT FREEZE—DO NOT SHAKE—DO NOT EXPOSE TO DIRECT LIGHT OR HEAT

If given by intravenous infusion, solution in vial requires dilution prior to administration. The prepared infusion solution is intended to be used immediately. If immediate administration is not possible, store diluted casirivimab and imdevimab solution in the refrigerator at 2°C to 8°C (36°F to 46°F) for no more than 36 hours or at room temperature up to 25°C (77°F) for no more than 4 hours. If refrigerated, allow the infusion to equilibrate to room temperature for approximately 30 minutes prior to administration.

If given by subcutaneous injection, the prepared syringes should be used immediately. If immediate administration is not possible, store the prepared casirivimab and imdevimab syringes in the refrigerator at 2°C to 8°C (36°F to 46°F) for no more than 4 hours or at room temperature up to 25°C (77°F) for no more than 4 hours. If refrigerated, allow the syringes to equilibrate to room temperature for approximately 20 minutes prior to administration.

Medication Administration:

Preparation for Intravenous Infusion

- Prepared infusion solution should not be administered with any other medication.
- Casirivimab and imdevimab will be prepared by placing casirivimab 600mg and imdevimab 600mg in a 100 mL NS bag. The total volume of 110 mL is to be infused IVPB in a NS KVO primary line over **21 minutes (310 mL/hr)**.
- Prime the medication IV bag with a polyvinyl chloride (PVC), polyethylene (PE)-lined PVC or polyurethane (PU) infusion set containing a 0.20 or 0.22 micron filter (provided by pharmacy).
- Take vital signs (VS) before start of infusion. Monitor the patient for 2-3 minutes after the start of the infusion for any signs of hypersensitivity or allergic reactions such as:

Shortness of Breath	Tightness in the Chest	Glossal Edema
Angioedema	Periorbital or Facial Edema	Hypotension
Rash/Urticaria	Nausea/Vomiting	Tachycardia
Lightheadedness/Dizziness	Diarrhea	

Follow the usual documentation requirements relevant to medication administration, patient assessments, and vital signs monitoring, including any adverse reactions.

- After infusion is complete, flush the line to ensure complete medication administration per protocol.
- Take vital signs for 60 minutes after infusion or completion of all four subcutaneous injections.

COVID-19 Monoclonal Antibody Administration: Subcutaneous Injection REGEN-COV (casirivimab and imdevimab)

Preparation for Subcutaneous Injection

Remove the casirivimab and imdevimab vial(s) from refrigerated storage and allow to equilibrate to room temperature for approximately 20 minutes before preparation. Do not expose to direct heat. Do not shake the vial(s).

Inspect casirivimab and imdevimab vial(s) visually for particulate matter and discoloration prior to administration. Should either be observed, the vial must be discarded, and a new vial must be used. The solution for each vial should be clear to slightly opalescent, colorless to pale yellow.

1. 600 mg of casirivimab and 600 mg of imdevimab should be prepared using 4 syringes (see table below). Obtain four 3-mL or 5-mL polypropylene Luer lock syringes with Luer connection and four 21-gauge, 1½-inch transfer needles.

2. Withdraw 2.5 mL into each syringe (total of 4 syringes) (see table below). Prepare all 4 syringes at the same time.

    - If individual vials of casirivimab and imdevimab are being used, consider labeling syringes during preparation to ensure the two syringes of casirivimab and two syringes of imdevimab are identifiable

3. Replace the 21-gauge transfer needle with a 25-gauge or 27-gauge needle for subcutaneous injection.

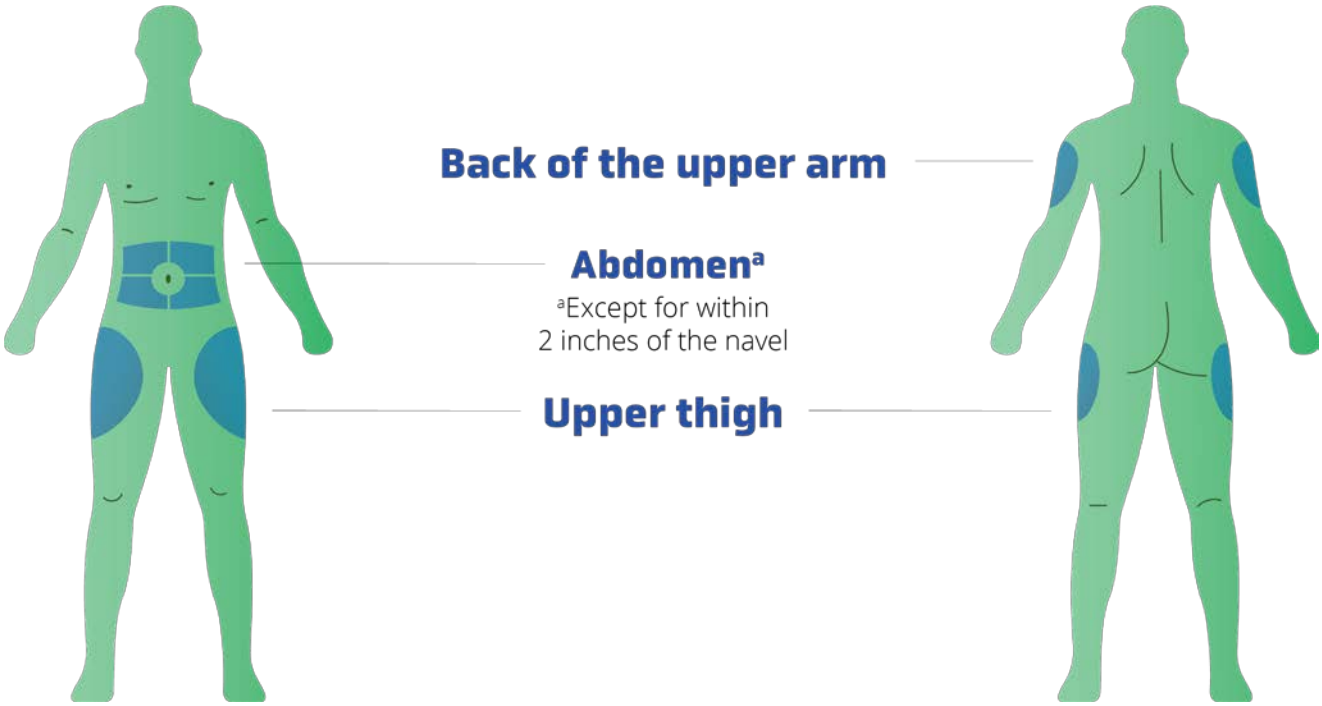
4. This product is preservative-free and therefore, the prepared syringes should be administered immediately. If immediate administration is not possible, store the prepared casirivimab and imdevimab syringes in the refrigerator between 2 ºC to 8 ºC (36 ºF to 46 ºF) for no more than four hours or at room temperature up to 25 ºC (77 ºF) for no more than four total hours. If refrigerated, allow the syringes to equilibrate to room temperature for approximately 20 minutes prior to administration.

COVID-19 Monoclonal Antibody Administration: Subcutaneous Injection REGEN-COV (casirivimab and imdevimab)

Administration for Subcutaneous Injection

- For the administration of 600 mg of casirivimab and 600 mg of imdevimab, gather four syringes (see table on prior page) and prepare for subcutaneous injections.
- Administer 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.**
- When administering the subcutaneous injections, it is recommended that providers use different quadrants of the abdomen or upper thighs or back of the upper arms to space apart each 2.5 mL subcutaneous injection of casirivimab and imdevimab. **DO NOT inject into skin that is tender, damaged, bruised, or scarred.**
- Clinically monitor patients after injections and observe patients for at least one hour.

Subcutaneous Injection Sites



Additional Resources:

COVID-19 Monoclonal Antibody Therapeutics: www.phe.gov/mAb

REGEN-COV Dosing & Administration: https://www.regencov.com/hcp/dosing/dosing-administration

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