Virus-neutralizing Monoclonal Antibodies

Outpatients with Covid-19

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Monoclonal Antibodies

- Predicted to reduce viral load
- Ameliorate symptoms
- Prevent hospitalization
- Given to outpatients recently diagnosed with mild to moderate COVID-19
Emergency Use Authorization

• The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) of Monoclonal Antibodies for the treatment of mild to moderate Coronavirus -19 disease in adults and pediatric patients over the age of 12 years.

• Some Physicians have recently started ordering Monoclonal Antibodies for patients exposed to COVID without a positive COVID test.
Limitations of Authorized Use

Monoclonal antibodies are not authorized for use in patients:

• Who are hospitalized due to COVID-19
• Who require oxygen therapy due to COVID-19
• Who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying Non-COVID related co-morbidity
• Benefit of treatment has not been observed in patients hospitalized due to COVID-19
• Monoclonal antibodies can be associated with worse clinical outcomes when administered to hospitalized patients requiring high flow 02 or mechanical ventilation
The Following Medical Conditions May Place Adults and Pediatric Patients (age 12-17 & weighing at least 40kg) at Higher Risk for Progression to Severe COVID-19

- Older age (greater than 65 years)
- Obesity (BMI greater than 25 kg/m² or if age 12-17, BMI greater than 85th percentile for age and gender) (CDC Growth Charts)
- Pregnancy
- Chronic Kidney Disease
- Diabetes
- Immunosuppressive disease or treatment
- Cardiovascular disease (including congenital heart disease) or hypertension
Higher Risk for Progression to Severe COVID-19 (Cont.)

• Chronic Lung Diseases (COPD, Asthma, Interstitial lung disease, Cystic fibrosis, and pulmonary hypertension).
• Sickle cell disease
• Neuro developmental disorders, cerebral palsy, genetic or metabolic syndromes, severe congenital anomalies
• Having a medical-related technological dependence (Tracheostomy, gastrostomy, positive pressure ventilation not related to COVID).
Personal Protective Equipment

• N-95 Mask
• Gown
• Face Shield
• Gloves
COVID-19 Antibody Treatment Indication Checklist

This guide is intended to help inform appropriate prescribing for healthcare in accordance with the Emergency Use Authorization (EUA) and clinical decision making and support medical necessity. This guide is not intended to supersede guidance from the Food and Drug Administration, state/local health departments, or other regulatory bodies. For complete information, refer to www.cdc.gov/mmpa.

Criteria for Authorized Use

☐ Positive results of direct SARS-CoV-2 viral testing (state of positive test result: ________________)
  Date of symptom onset: ________________
  Symptoms should be present as long as possible after a positive test and within 10 days of symptom onset

☐ Mild to moderate coronavirus disease 2019 (COVID-19)
  □ Illness consistent with SARS-CoV-2 infection (e.g., fever, cough, sore throat, headache, muscle pain, or rash)
  □ Symptoms persisting more than 10 days

☐ Moderate coronavirus disease 2019 (COVID-19)
  □ Evidence of lower respiratory disease during clinical assessment or imaging
  □ SpO2 ≤ 90% on room air at sea level

☐ Weight at least 40 kg (100 lbs)

☐ At high risk for progressing to severe COVID-19 and/or hospitalization due to the following:
  (provide additional info next to criteria, e.g., diagnosis, medications)
  □ Age 65 years or older (yes________ no ________)
  □ Body mass index (BMI) ≥ 35 kg/m²
  □ Chronic kidney disease, stage 1 or 2
  □ Type 2 diabetes
  □ Asthma
  □ Inflammatory arthritis
  □ At present or in the previous 28 days, received immunosuppressive treatment:
    □ Age 65 years or older
    □ At least one of the following:
      □ Cardiovascular disease
      □ Chronic kidney disease
      □ Liver disease
      □ Chronic obstructive pulmonary disease
      □ Asthma
      □ Chronic respiratory failure attributable to chronic respiratory disease
    □ Age 19 – 64 years
    □ At least one of the following:
      □ BMI ≥ 30 kg/m²
      □ Sickle cell disease
      □ Chronic kidney disease, stage 3 or 4
      □ Neurodevelopmental disorders (including autism)
      □ A medical-related condition (e.g., cancer)
      □ Severe respiratory failure attributable to chronic respiratory disease that requires hospitalization for COVID-19

☐ Does not receive supplemental oxygen due to COVID-19 or for increase in baseline requirement or chronic oxygen therapy unrelated to COVID-19

Updated 11/22/20
FACILITY LAYOUT

Note: Denning and Defining areas along with Hot and Cold zones are dependent on facility layout.

Entrance or Check-In Station
- Staffing: 1 RN and 2 Healthcare workers.
- Critical Functions: At this station, patients and visitors will be greeted, provided a surgical mask, referred-validated, medically evaluated (e.g., history, vitals, known medication allergies, other medical criteria). Both patients and visitors will be masked for the duration of their course of treatment or stay.
- The patient's treatment and monitoring plan and any questions will be discussed.
- Runner: Following intake, an identified runner (one of the Healthcare workers) will escort the checked-in patient to the identified infusion station and conduct a hand-off with the IV technician. During the hand-off, the patient will be introduced to the tech and their personal information and treatment course will be confirmed prior to infusion.

Infusion Area
- Staffing: 2 RNs, 1 Healthcare worker with IV insertion skills, 1 environmental staff and 1 Mid-Level provider (ideally ACLS certified).
- Critical Functions: Identified area for 15 infusion chairs/bays to be placed for infusion services and equipment. At this station, 16 patients would be undergoing infusion.
- The length of infusion service for both casirivimab and imdevimab should be at least 60 minutes followed by a post-infusion observation period of at least 60 minutes. At the time of infusion completion, the patient will be flagged as complete and escorted by the infusing RN to the post-infusion observation area.
- A handoff from infusing RN to post-infusion RN will be made where the patient will be introduced and their personal information and treatment course will again be confirmed.
  • Consider implementing a visual flag system to indicate phase in infusion process - i.e., green is initiating; blue is recovery.
- All beds, stations, and equipment should be cleaned and disinfected between patients.
- Staff should have immediate access to medications to treat a severe infusion reaction, such as epinephrine, and the ability to activate the emergency medical system (EMS), as necessary.

Post-Infusion Observation
- Staffing: 1 Physician, 2 RNs, 1 environmental staff, 1 Healthcare worker (paramedic or second RN).
- Critical Functions: Identified area for 15 infusion chairs/bays to be safely placed for post-infusion observation. At this station, 16 patients would be undergoing direct observation (eyes-on-patient open area) for at least 60 minutes.
- Emergency response equipment required.
- At the conclusion of post-infusion monitoring, patients will have their final medical evaluation for clearance to leave the facility and will receive post-procedure instructions for proper follow-up with a primary care provider.
- Runner: Escort the patient directly to the facility exit.
- All beds, stations, and equipment should be cleaned and disinfected between patients.
PATIENT CONSENT FORM FOR COVID-19 TREATMENT PURPOSE OF INFORMED CONSENT

As your physician has discussed with you, you have been diagnosed with COVID-19 (or SARS-CoV-2). At the present time, there are few Food and Drug Administration (FDA) approved, or clinically proven therapies for treatment of COVID-19. As new clinical data emerge, local treatment guidelines have been developed and will be updated as new information becomes available. CDC guidelines reflect what is known about therapies that may work against the SARS-CoV-2 virus, have been used to treat other coronaviruses, or may theoretically target the underlying cause of virus-related severe lung conditions that make breathing difficult.

The FDA has granted Emergency Use Authorization (EUA) to permit investigational therapies in patients with confirmed or suspected COVID-19. Investigational therapies are not approved for any indication. They are authorized only for the duration of the declaration that circumstances exist justifying the use of the EUA and are revoked or rescinded if the declaration is terminated or revoked. If you check below and sign, you consent to the use of any authorized therapy.

TREATMENT
In order for you to be treated with the therapy by the infusion team, you must sign this form to show that you agree to the use of investigational or label treatment; that you have been informed of the benefits and risks of taking such therapy as well as the benefits and risks of declining or refusing such use. The infusion team will annotate the monoclonal antibody therapy available below for your account and the particular therapy chosen is based upon availability. You will be provided a patient information sheet and informed regarding the specific monoclonal antibody infusions before the infusion begins. You have the right to refuse to take the medication(s) for any reason.

Attention Health Care Professional:
Either medication may be administered and have similar safety and side effect profiles and treatment outcomes.

The medication checked below is the one you will receive for your one-time infusion.

☐ Bamlanivimab
☐ Bamlanivimab + Evレンンバリバ
☐ Casirivimab/Imdevimab (Regeneron)

BACKGROUND
Bamlanivimab, Regeneron, and Bamlanivimab + Evレンンバリバ are investigational medicines which are monoclonal antibodies used for the treatment of COVID-19 in non-hospitalized adults and adolescents 12 years of age and older with mild-to-moderate symptoms who weigh 40 pounds (18 kg) or more, and who are at high risk for developing severe COVID-19 or infections or need for hospitalization. The FDA has issued an Emergency Use Authorization (EUA) to permit the use of this unapproved medication. Clinical trials are ongoing to study its safety and efficacy.

POSSIBLE BENEFITS
It is possible that the medications listed above may help to control your symptoms, slow or stop the growth of the virus, shorten the duration or lessen the severity of illness in you. Possible benefits primarily include improvement in lung function, ability to breathe without assistance, and normalization of blood pressure. However, there is the possibility that these medications may not have direct medical benefits to you. Your condition may get worse.

POSSIBLE RISKS AND KNOWN SIDE EFFECTS
It is possible that the medication prescribed may not improve your symptoms and not shorten the duration or severity of the illness. It is possible that the medication will unexpectedly interfere with your ability to improve, worsen damage to the lungs or other organs, and shorten your life.

Bamlanivimab / Regeneron or Bamlanivimab + Evレンンバリバ

There is limited clinical data available for these treatments and unexpected adverse events may occur that have not been previously reported. Side effects may include allergic reactions and injection site reactions. It is possible that these treatments could interfere with your body's own ability to fight off a future or an infection of SARS-CoV-2. These treatments may also reduce your body's immune response to a vaccine for SARS-CoV-2. If you receive this therapy, it could reduce or delay your response to any COVID-19 vaccine for up to 90 days following the infusion and should consider waiting 90 days for a COVID-19 vaccine. Alternatively, there are few approved therapies for the treatment of COVID-19 (specifically). Medical care relies on helping the patient through the many complications. Most hospitalized patients survive their disease with standard medical care.

CERTIFICATION AND SIGNATURES
I have read this informed consent form and all of my questions have been answered to my satisfaction by my physician. I understand that I have the right to refuse to take this medication(s), for any reason. If I choose not to take this medication(s), this decision will not necessarily affect my status as a patient. I voluntarily consent to take this monoclonal antibody medication by intravenous infusion, with my physician, and infusion team members as described in this consent form.

CONSENT
The FDA has granted Emergency Use Authorization (EUA) to permit investigational therapies in patients with confirmed or suspected COVID-19. Investigational therapies are not approved for any indication. They are authorized only for the duration of the declaration that circumstances exist justifying the use of the EUA and are revoked or rescinded if the declaration is terminated or revoked. If you check below and sign, you consent to the use of any authorized therapy.

Patient Name: __________________________
Patient Signature: _______________________
Patient Date: __________________________
Patient Time: __________________________

(if patient is a minor or unable to sign, indicate reason (e.g., patient in COVID isolation))

Name of Person Signing for Patient: __________________________
Signature of Person Signing for Patient: __________________________
Name of Witness: __________________________
Signature of Witness: __________________________
Name Date: __________________________
Name Time: __________________________

Witness to complete translations if applicable: __________________________
Language Used: __________________________
Transcribed by: __________________________
Date: __________________________
Time: __________________________

By typing your name in the "Signature" fields above, it will be considered the legal equivalent of your signature.
REGEN-COV Infusion Referral Orders

Date: Patient Name

DOG

Allergies

Client/Provider Address:

Client/Provider Phone Number:

NURSING ORDERS

- Insert Peripheral Infusion Lock: Routine Once
- Document IV: Routine Once

MEDICATIONS ORDERS

- Cetirizine 50 mg and Indomethacin 60 mg (REGEN-COV)
  Both administered as a single intravenous (IV) infusion over at a minimum of 30 minutes.
  Patient should be monitored during infusion and observed for at least 1 hour after infusion is complete.

Pre-Medication

- Aescin vasoconstrictor (TYCENAL 1,000 mg PO x 1 dose). For mild adverse reaction to infusion - do not give if provided as PRE-MED due to fever.
- Diphenhydramine (BENADRYL) 12.5 mg, 1/4 tsp or tablet: 1 mg x 1 dose for history of amylase/pancreatitis
-Ondansetron (ZOFAN 4 mg IV stat if infusion prior to infusion

Anaphylaxis Orders - In case of anaphylactic reaction (sudden decrease in BP, increases in pulse, increased respiration, SOB, and diaphoresis)

- General Oxygen: If condition worsens or progresses to symptoms of anaphylaxis, start O2:
  Delivery Device: Nasal Cannula Simple Face Mask Non-Rebreather Mask Other
  Titrate per Oxygen Tension Protocol: Adult: Yes No
  Sudden Cardiac 0.9% IV Continuous (10 mL/hr)
- EPINEPHrine (ADRENALINE) 1 mg/mL (1:1,000) 1 mL, inject 0.3 mL every 15 min PEN anaphylactic reaction. Give once. At bedside to give STAT. May repeat third time 1 minute after 2nd dose of needed. (1 dose total)
- Diphenhydramine (BENADRYL) 50 mg/mL, inject 25 mg IV once PEN anaphylactic reaction. For 1 dose.
  Give after Epinephrine. At bedside to give STAT. DO NOT GIVE if diphenhydramine was given as PRE-Medication.
- Atropine (ATROPINE) 0.4 mg IV once PEN anaphylactic reaction. At bedside to give STAT.
- Furosamide (FURICO) inject 20 mg IV once PEN anaphylactic reaction. At bedside to give STAT.

Hypersensitivity Reactions (skin rash, hives, itching, runny nose, fever)

- Diphenhydramine (BENADRYL) 12.5 mg, 1/4 tsp or tablet: 1 mg PEN for hypersensitivity reaction.
- Aescin vasoconstrictor (TYCENAL 1,000 mg PO x 1 dose). For mild adverse reaction to infusion - do not give if provided as PRE-MED due to fever.
- Methylprednisolone (Solu-MEDROL) inject 12 mg IV once PEN anaphylactic reaction. For 1 dose.
- Dexamethasone 4 mg IV once PEN for hypersensitivity reaction
- Furosamide (FURICO) inject 20 mg IV once PEN. At bedside to give STAT
- General Oxygen: If condition worsening or progresses to symptoms of anaphylaxis, start O2:
  Delivery Device: Nasal Cannula Simple Face Mask Non-Rebreather Mask Other
  Titrate per Oxygen Tension Protocol: Adult: Yes No

Signature:

Call Number (used for notifying of decisions and questions)

Please Print Name and Title
MONOCLONAL ANTIBODY INFUSION FORM

INFLUENZA
Pt. Name: ____________________ Date of Service: __________

DOB: ___________ Age: __________

Time: ___________ Hx of Anaphylaxis?: Y ☐ N ☐

Height: ___________ Weight: ___________ Date of Symptom Onset: ___________

Date of Positive Test Result: ___________

IV Site: ___________ Catheter Site: ___________ Number of Attempts: ___________

Pre-Infusion Time: ___________ VITALS: B/P: ___________ HR: ___________ RR: ___________

Number of Attempts: ___________ Temp: ___________ SpO2: ___________

Provider Signature: ____________________

POST-INFUSION:

Clinically monitor patient for 1 hour after infusion is complete.

Post-Infusion Arrival Time: ___________

VITALS: B/P: ___________ HR: ___________ RR: ___________ Temp: ___________ SpO2: ___________

Y ☐ N ☐ Notify Provider of any changes in vital signs/hypersensitivity

45 Minutes After Arrival Time: ___________

VITALS: B/P: ___________ HR: ___________ RR: ___________ Temp: ___________ SpO2: ___________

IV Catheter removed: ___________ Time: ___________

Site: ___________ Pressure applied: ___________

Flow controlled: ___________

Discharged Time: ___________

☐ ambulatory ☐ wheelchair ☐ walker ☐ stretcher ☐ stable condition

Post-infusion instructions given: ___________

Provider Signature: ____________________

OBSERVATION PARAMETERS

Vital Signs

☐ For ALL PATIENTS: Obtain BP, HR, Temperature, IR. Observation of IV site, SpO2 at intake, pre-infusion, 15 minutes into infusion, at completion of infusions

☐ Notify Provider based on parameters below – pre-infusion, during infusion and 1 hour observation period

☐ Temperature: ≥99F

☐ Increase or Decrease in BP by more than 10% from baseline value

☐ BP greater than Systolic 140 or Diastolic 95 or less than Systolic 100 or Diastolic 70

☐ Increase in BP > 20mm, change from baseline, visible respiratory distress

☐ HR less than 50/min or greater than 120/min

☐ SpO2 ≤ 94%

☐ Redness or Swelling at IV Site

☐ Notify Provider if any changes in symptoms

☐ STOP infusion and Notify Provider if:

☐ Initial infusion reaction including fever, chills, headache, rash including hives, pruritus, myalgia, diaphoresis during and in 1 hour observation period following Regin-COVID (HM/IV/IM) infusion

☐ Obtain and document orders if the infusion should be restarted

☐ STOP infusion – Activate Anaphylaxis Protocol, BLS and EMS and notify Provider if:

☐ Systolic BP of less than 80mmHg or greater than 10% decrease from baseline
The EUA for REGEN-COV is in effect for the duration of the COVID-19 declaration justifying emergency use of these products, unless terminated or revoked (after which the products may no longer be used).

REGENERON
Manufactured by:
Regeneron Pharmaceuticals, Inc.
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Tarrytown, NY 10591-4707
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I HAVE READ AND UNDERSTAND THE INFORMATION ON THIS FORM:

PATIENT SIGNATURE: ____________________________________________
DATE: ____________

PLEASE CALL 911 IF YOUR SYMPTOMS WORSEN OR YOU HAVE INCREASING SHORTNESS OF BREATH UPON RETURNING HOME.
REGEN-COV

• Monoclonal Antibody

• Combination of:
  * Casirivimab
  * Imdevimab
For Intravenous Infusion:

• Co-formulated casirivimab & imdevimab solution in a vial and casirivimab & imdevimab solutions in individual vials which must be diluted prior to IV administration.

• Administer 600 mg of casirivimab and 600mg of imdevimab together as a single IV infusion via pump or gravity.

• Clinically monitor patients during infusion and observe patients for at least one hour after infusion.
For Subcutaneous Injection:

• Administer 600 mg of casirivimab & 600mg imdevimab using the co-formulated solution in a vial or using the individual vials.

• Clinically monitor patients after injections and observe patients for at least an hour after injections. Subcutaneous injection is an alternative route of administration when intravenous administration is not feasible and would lead to delay in treatment.

• The dosage of 600mg of casirivimab & 600 mg imdevimab for subcutaneous administration for treatment was selected based on the totality of the scientific evidence, incorporating clinical data, viral load reduction data and pharmacokinetic data.
Warnings

There is limited clinical data available for REGEN-COV.

Serious and unexpected adverse events may occur that have not been previously reported with REGEN-COV use.
Hypersensitivity Including Anaphylaxis and Infusion-Related Reactions

• Serious hypersensitivity reactions, including anaphylaxis, have been observed with administration of REGEN-COV. If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate medications and/or supportive therapy.

• Infusion-related reactions, occurring during the infusion and up to 24 hours after the infusion, have been observed with administration of REGEN-COV.

• These reactions may be severe or life-threatening.
Signs and Symptoms of Infusion-Related Reactions

Fever, difficulty breathing, reduced oxygen saturation, chills, fatigue, arrhythmia (atrial fibrillation, tachycardia, bradycardia), chest pain or discomfort, weakness, altered mental status, nausea, headache, bronchospasm, hypotension, hypertension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, vasovagal reactions, dizziness, diaphoresis.
Consider slowing or stopping the infusion and administer appropriate medications and/or supportive care if an infusion-related reaction occurs.
Clinical Worsening After REGEN-COV Administration

Clinical worsening of COVID-19 after administration of REGEN-COV has been reported and may include signs and symptoms of fever, hypoxia, or increased respiratory difficulty, arrhythmia, fatigue, and altered mental status.

Some of these events required hospitalization.

It is not known if these events were related to REGEN-COV use or were due to progression of COVID-19.
Serious Adverse Events

• Pharmacist will report to FDA Med Watch.
• Defined as:
  * Death
  * Life-threatening adverse event
  * Inpatient hospitalization
  * Persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
  * A congenital anomaly/birth defect
  * Medical or surgical intervention to prevent death
YOUR PATIENTS

- Even with mild to moderate illness....they are sick
- Many are dehydrated
- IV access may be difficult
- Age ranges vary from young to old
- Some fully vaccinated....some not
- Many are scared
- All are grateful