Anti-SARS-CoV-2 Monoclonal Antibodies Guideline

This guidance does not address the use of immune-modulating monoclonal antibodies for the treatment of severe COVID-19 infection

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Intended Use:

Prophylaxis or treatment of mild to moderate COVID-19 in patients who are at high risk for progressing to severe COVID-19.

Inclusion Criteria:

Patient Eligibility:
A. Eligibility is based on the current FDA EUA for each product.
B. A review team consisting of Immunodeficiency and Infectious Disease providers will review and will determine approval for Anti-SARS-CoV-2 Monoclonal Antibodies administration based on EUA criteria, circulating variant type, and resource availability (product/facilities).
C. Treatment: Monoclonal Antibodies are authorized for treatment in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing (i.e. a PCR or antigen test, not an antibody test) who are at high risk for progressing to severe COVID-19 and/or hospitalization.
1. Adults and pediatric patients 12-17 years of age, weighing at least 40 kg may receive sotrovimab, bebtelovimab, bamlanivimab/etesevimab, or casirivimab/imdevimab. Bamlanivimab/etesevimab, or casirivimab/imdevimab temporarily not authorized as of 1/24/22.

2. Pediatric patients <12 years of age or < 40 kg may receive bamlanivimab/etesevimab. Temporarily not authorized as of 1/24/22.

3. Anti-SARS-CoV-2 Monoclonal Antibodies should be used for patients who have mild to moderate, symptomatic COVID-19 disease, plus one or more high risk criteria, as soon as possible after diagnosis and within 7 days of symptom onset.

4. Clinical data do not support the use of Anti-SARS-CoV-2 Monoclonal Antibodies in patients with severe symptoms (including new or increasing oxygen requirement).

D. Post-Exposure Prophylaxis: Temporarily not authorized as of 1/24/22. Sotrovimab and bebtelovimab are not approved for post-exposure prophylaxis. Bamlanivimab/etesevimab and casirivimab/imdevimab (previously approved for post-exposure prophylaxis) are not authorized for use as of 1/24/2022.

E. Pre-Exposure Prophylaxis: Anti-SARS-CoV-2 Monoclonal Antibodies are authorized for use for pre-exposure prophylaxis of COVID-19 in adult and pediatric individuals who do not have SARS-CoV-2 infection, who have not been recently exposed to an individual with SARS-CoV-2 infection, and who are moderately to severely immunocompromised and may have inadequate immune response to COVID-19 vaccination or are not able to be fully vaccinated with any available COVID-19 vaccines due to a documented history of severe adverse reactions to a COVID-19 vaccine or any of its components.

1. Adults and pediatric patients 12-17 years of age, weighing at least 40 kg may receive tixagevimab plus cilgavimab (Evusheld).

2. Additional information on relative contraindications to use and administration instructions is available in the Evusheld Fact Sheet and education forms on the CW website.

Exclusion Criteria:
Specifically, Anti-SARS-CoV-2 Monoclonal Antibodies is not authorized for use with:
A. Hospitalization due to COVID-19 (2 years and older only; use with hospitalization permitted for <2 years of age), OR
B. Oxygen therapy requirement due to COVID-19, OR
C. Increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.

Summary
- Anti-SARS-CoV-2 Monoclonal Antibodies for COVID-19 have been granted emergency use authorization by the U.S. Food and Drug Administration for high-risk pediatric patients and adults as pre-exposure prophylaxis or treatment of mild or moderate COVID-19 not requiring hospitalization due to COVID-19 (≥ 2 years of age) or irrespective of hospitalization status (< 2 years of age).
• Criteria for authorized use, instructions related to storage and administration, and data reporting requirements are now available through the published EUAs and the manufacturers’ websites.

Risk Definitions

A. Data collection during the pandemic resulted in a refined list of risk criteria from the FDA in December 2021:

• Older age (for example age ≥ 65 years of age)
• <1 year old
• Obesity or being overweight
• 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 anomalies)
• 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 severe COVID-19
• For additional information on medical conditions and factors associated with increased risk for progression to severe COVID-19, see the CDC website: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html. Healthcare providers should consider the benefit-risk for an individual patient.

B. When resources are limited (mAb supply, special isolation unit availability, staffing constraints), mAb approvals may be limited to a subset of patients at highest risk for progression to severe COVID-19 infection. Per NIH guidance and available literature, mAb prioritization is based on relative risk of severe disease in pediatric patients. All attempts will be made to maintain mAb availability for patients meeting High Priority criteria. Patients meeting criteria for the Medium and Low Priority lists may receive mAb when resources allow.

Pediatric Tier 1, High Priority. Immunocompromised individuals not expected to mount an adequate immune response to vaccine
1. Any patients with absent or near absent T cells (<300 cells in infants or <100 cells in older children)
   a. Organ transplant recipients receiving anti-thymocyte globulin (ATG) or high dose immunosuppression within 3 months
   b. Patients with recent conditioning for bone marrow transplant (BMT), hemophagocytic lymphohistiocytosis (HLH) treatment, or high-dose immunosuppression for aplastic anemia
   c. Patients receiving induction therapy which depletes T cells for malignancy
2. Patients with common variable immunodeficiency, congenital agammaglobulinemias, or other primary immunodeficiencies characterized by an absent or poor specific Ab response to vaccination.
3. Patients with autoimmune diseases with high dose immunosuppression (i.e. systemic lupus erythematosus, steroids greater than 40mg daily and cytoxan therapy, multiple T cell inhibitors, or rituximab)

Pediatric Tier 2, Medium Priority, Unvaccinated individuals with clinical risk factors for severe disease

1. Patients with at least two risk factors for severe COVID-19 including obesity (≥95th percentile for age), moderate-severe asthma, hypertension, poorly-controlled diabetes, DKA, chronic lung disease, congenital heart disease, developmental disability, chronic liver disease, and chronic kidney disease
2. Patients on less intensive immunosuppression or mild-moderate immunodeficiency AND with chronic organ damage
3. Patients with end-stage lung or cardiac disease (including dependence on chronic respiratory support, pulmonary hypertension, single ventricle disease with significant cyanosis, ventricular-assist devices, surfactant deficiency, or CF with FEV1<40% predicted or after lung transplant)
4. Sickle cell disease
5. Severe obesity (≥99th percentile for age)

Pediatric Tier 4- Low priority, Vaccinated individuals with clinical risk factors for severe disease

1. Same risk factors of Tier 2
2. Priority within this group to individuals who have not received a booster dose

Approval Process for Anti-SARS-CoV-2 Monoclonal Antibodies

A. Approval from the mAb review committee is required before ordering of any anti-SARS-CoV-2 monoclonal antibody at CW.
1. Approval requests should involve a CW subspecialist or other provider with CW admitting privileges whenever possible to allow ordering and responsibility during the infusion to remain with the patient’s care team.

B. Providers seeking approval for a patient to receive mAb can use one of the following methods:
   1. Complete online intake form (preferred). The online intake form is found on Connect COVID page and chw.org (COVID-19 resources for medical professionals).
   2. Voalte or page Outpatient COVID-19 Treatment Liaison Monday through Friday, 8 am to 4 pm (refer to ID call schedule)
   3. Email Outpatient COVID-19 Treatment Liaison Sunday through Thursday evenings (refer to ID call schedule)
   4. Page ID on-call for urgent questions on evening/weekends (refer to ID call schedule)

C. The Outpatient COVID-19 Treatment Liaison or ID on-call will communicate with the requesting provider with the decision on mAb approval and next steps. If mAb is not approved but the patient is a candidate for outpatient remdesivir IV x 3 days, the Outpatient COVID-19 Treatment Liaison can also assist the requesting provider with coordinating that process.

Ordering, Scheduling, and Administration of Anti-SARS-CoV-2 Monoclonal Antibodies

Preparation and administration should not proceed until the review team has approved the use of Anti-SARS-CoV-2 Monoclonal Antibodies and patient/parent has provided verbal consent. Inpatient administration of treatment mAb will not be approved for patients ≥2 years hospitalized for COVID-19 infection symptoms.

Outpatient Ordering and Scheduling
A. Patient meets criteria for Anti-SARS-CoV-2 Monoclonal Antibodies and has been approved by review team.
   1. Outpatient COVID-19 Treatment Liaison or review team communicates with the pharmacy team to notify them of the need for Anti-SARS-CoV-2 Monoclonal Antibody and which product.
   2. Referring healthcare provider communicates to patient or parent/caregiver, as age appropriate, information consistent with the “Fact Sheet for Patients, Parents and Caregivers” prior to the patient receiving Anti-SARS-CoV-2 Monoclonal Antibodies. Healthcare providers (to the extent practical given the circumstances of the emergency) must document in the patient’s medical record that the patient/caregiver has been:
      a. Given the “Fact Sheet for Patients, Parents and Caregivers”,
      Fact Sheet for Evusheld
      Fact Sheet for sotrovimab
      Fact Sheet for babtelovimab
      Fact Sheet for bamlanivimab/etesevimab
      Fact Sheet for casirivimab/imdevimab
b. Informed of alternatives to receiving authorized Anti-SARS-CoV-2 Monoclonal Antibodies, and  
c. Informed that Anti-SARS-CoV-2 Monoclonal Antibodies is an unapproved drug that is authorized for use under this Emergency Use Authorization.

B. Outpatient COVID-19 Treatment Liaison or review team notifies infusion clinic and MACC Fund SIU of need for Anti-SARS-CoV-2 Monoclonal Antibodies:

C. For outpatients, an infusion scheduling or a MACC scheduling order must be placed in EPIC by ordering provider.

1. Place orders-only encounter via the quick navigator (found by clicking down arrow by wrench and sidebar summary) and choose admissions. Via the Smart set/Order set, search for Covid or Anti-SARS-CoV-2 Monoclonal Antibody Therapy. Prescribing Provider will provide in the orderset the name/contact information as to who will be immediately available to the Infusion Clinic staff in the event of infusion reaction or other need. Consulting services need to notify hospital medicine of patient should the need to admit arise.

D. Once complete, the order is signed and held.

E. SARS-CoV-2 positive patients must be seen in negative pressure room on as an outpatient.

1. Preferably, as soon as possible after positive viral test and within 10 days of symptom onset.

   a. Monday-Friday 0730-1800
   b. Will need a 2-3 day window to accommodate Anti-SARS-CoV-2 Monoclonal Antibodies infusion request if possible.
   c. Patients may need to be seen later in the day, due to limited negative pressure room availability.
   d. Patients with no recent exposure to SARS-CoV-2 and no current infection (i.e. candidates for Evusheld) do NOT require negative pressure rooms.
   e. Patient will be staffed by either an Infusion RN or MACC Fund Day Hospital RN and will follow infusion guidelines.

Administration

A. Anti-SARS-CoV-2 Monoclonal Antibodies for treatment in SARS-CoV-2 positive patients may only be administered in ambulatory settings with negative pressure rooms. Infusion clinic does not have a negative pressure room, therefore the special isolation or the heightened isolation precautions unit will be used for this infusion.

B. If the patient arrives for treatment with new oxygen requirement or oxygen requirement above baseline, the ordering provider will be contacted as the patient no longer meets EUA eligibility criteria for mAb treatment.

C. The ordering provider or designee must be immediately available (i.e. onsite/responsible and able to assess patient) during the infusion in the event of a reaction.

D. The authorized route of administration for Anti-SARS-CoV-2 Monoclonal Antibodies for treatment is a single intravenous (IV) infusion (preferred route), or subcutaneous injections (casirivimab/imdevimab only) administered as soon as possible after positive viral test for SARS-CoV-2 and within 10 days of symptom onset. The dosage of Anti-SARS-CoV-2
Monoclonal Antibodies for pre-exposure prophylaxis (Evusheld) is two intramuscular (IM) injections (3 ml) in a large muscle (gluteal) or four intramuscular (IM) injections (1.5 ml).

1. Anti-SARS-CoV-2 Monoclonal Antibodies will be diluted by pharmacy (if applicable) and dispensed ready to administer
2. For sotrovimab, casiribimab/imdevimab, or bamlanivimab/etesevimab: Administer Anti-SARS-CoV-2 Monoclonal Antibodies via IV infusion via infusion pump or by subcutaneous injections.
3. For bebtelovimab: Administer via IV push over over at least 30 seconds.
4. Clinically monitor patients during infusion and observe patients for at least 1 hour after infusion or injections are complete.
5. Patients treated with Anti-SARS-CoV-2 Monoclonal Antibodies after a positive COVID-19 test should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect “high touch” surfaces, and frequent hand washing) according to CDC guidelines. Patients receiving post-exposure prophylaxis should quarantine per local and CDC guidelines.

**Adverse Event and Error Reporting**

A. The pharmacy, in collaboration with the prescribing health care provider and/or the provider’s designee, are/is responsible for mandatory reporting of all medication errors and serious adverse events* potentially related to Anti-SARS-CoV-2 Monoclonal Antibodies treatment within 7 calendar days from the onset of the event. The reports should include unique identifiers and the words “Anti-SARS-CoV-2 Monoclonal Antibodies treatment under Emergency Use Authorization (EUA)” in the description section of the report.

1. *Serious Adverse Events are defined as:
   a. death;
   b. a life-threatening adverse event;
   c. inpatient hospitalization or prolongation of existing hospitalization;
   d. a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
   e. a congenital anomaly/birth defect;
   f. a medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly.

2. Staff needs to submit a MIDAS event report.
3. Submit adverse event reports to the drug manufacturer and to FDA MedWatch completing and submitting the report online: [www.fda.gov/medwatch/report.htm](http://www.fda.gov/medwatch/report.htm)
4. Pharmacy in collaboration with the prescribing health care provider and/or the provider’s designee are/is to provide mandatory responses to requests from FDA for information about adverse events and medication errors following receipt of Anti-SARS-CoV-2 Monoclonal Antibodies.
**Education, discharge, and follow-up**
A. Education of caregivers on expectations for post-[Anti-SARS-CoV-2 Monoclonal Antibodies](#) therapy
B. Plan for when caregiver should call for assistance post-infusion or post-injection.
C. Follow-up appointment made with primary care team upon discharge.

**Supporting Documents**
Addendum A: Nursing Education Sheet

**References**
For additional information visit:
https://www.regeneron.com/medicines/casirivimab-imdevimab

Additional information on COVID-19 therapies can be found at https://www.cdc.gov/coronavirus/2019-ncov/index.htmlhttps://clinicaltrials.gov/
The health care provider should visit to determine whether the patient may be eligible for enrollment in a clinical trial.
FDA will make this determination considering current variant frequency data (available at: https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variant-proportions.html), trends in variant frequency over time, the precision of the estimates and information regarding emerging variants of concern.

NIH COVID-19 Treatment Guidelines for Prioritization for Outpatient Anti-SARS-CoV-2 Therapies or Preventive Strategies (available at: https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-patient-prioritization-for-outpatient-therapies/)


**Addendum A: Nursing Education Sheet**

Anti-SARS-CoV-2 Monoclonal Antibodies are a medication(s) given for post-exposure prophylaxis or treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adults and pediatric patients, including neonates, 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.

**Administration Instructions:**
- Anti-SARS-CoV-2 Monoclonal Antibodies may be given intravenously (sotrovimab, bebtelovimab, bamlanivimab/etesevimab, or casirivimab/imdevimab), subcutaneously (casirivimab/imdevimab only), or intramuscularly (Evusheld).
- Premedications may be given (provider discretion)
• Intravenous administration of sotrovimab, bamlanivimab/etesevimab and casirivimab/imdevimab must be administered with a (PVC) infusion set containing a 0.2 micron in-line filter.
  o Prime tubing with Anti-SARS-CoV-2 Monoclonal Antibody
• Intravenous administration of bebtelovimab is via slow IV push and does NOT require a filter.
• Upon completion of IV infusion or injection, flush tubing with NS
• Vital signs should be obtained at baseline, 15 min, and hourly until completion.
  o Patient should be monitored for a minimum of 1 hour post infusion

Side Effects:
• Risk for infusion-related reaction and anaphylaxis
  o Be sure to have orders for Epinephrine and Benadryl, and obtain from Omnicell to be at bedside.
  o Ensure anaphylaxis sign is at the bedside, which includes patient name, weight, Epinephrine dose in mg and mL, and Benadryl dose in mg and mL.
  o Symptoms include: fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, dizziness.
  o If s/s of anaphylaxis or infusion-related reaction occur:
    ▪ STOP the infusion
    ▪ Notify provider
    ▪ Administer appropriate medications and provide supportive care

Note the Following:
• The patient or parent/caregiver has the option to accept or refuse Anti-SARS-CoV-2 Monoclonal Antibodies.
• Notify patients or parent/caregiver of the significant known and potential risks and benefits of Anti-SARS-CoV-2 Monoclonal Antibodies, and the extent to which such potential risks and benefits are unknown.
• Patients treated with Anti-SARS-CoV-2 Monoclonal Antibodies should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect “high touch” surfaces, and frequent hand washing)
• Post-exposure prophylaxis patients who are deemed high risk:
  o High risk of progression to severe COVID-19, including hospitalization or death, and 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 Centers for Disease Control and Prevention (CDC) or o who are at high risk of exposure to an individual infected with SARS-CoV-2 because of occurrence of SARS-CoV-2 infection in other individuals in the same institutional setting (for example, nursing homes, prisons)
• The following medical conditions or other factors may place adults and pediatric patients, including neonates, at higher risk for progression to severe COVID-19:
  o Older age (for example age ≥65 years of age)
  o <1 year old
  o Obesity or being overweight
  o Pregnancy
  o Chronic kidney disease
  o Diabetes
  o Immunosuppressive disease or immunosuppressive treatment
  o Cardiovascular disease (including congenital heart disease) or hypertension
  o Chronic lung diseases (for example, chronic obstructive pulmonary disease, asthma [moderate-to-severe], interstitial lung disease, cystic fibrosis and pulmonary hypertension)
  o Sickle cell disease
  o Neurodevelopmental disorders (for example, cerebral palsy) or other conditions that confer medical complexity (for example, genetic or metabolic syndromes and severe congenital anomalies)
  o 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 mAbs under the EUA 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, see the CDC website: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html. Healthcare providers should consider the benefit-risk for an individual patient.
Medical Disclaimer

Medicine is a dynamic science; as research and clinical experience enhance and inform the practice of medicine, changes in treatment protocols and drug therapies are required. The authors have checked with sources believed to be reliable in their effort to provide information that is complete and generally in accord with standards accepted at the time of publication. However, because of the possibility of human error and changes in medical science, neither the authors nor Children’s Hospital and Health System, Inc. nor any other party involved in the preparation of this work warrant that the information contained in this work is in every respect accurate or complete, and they are not responsible for any errors in, omissions from, or results obtained from the use of this information. Readers are encouraged to confirm the information contained in this work with other sources.