

# Planning Considerations for Monoclonal Antibody Administration

Updated September 1, 2021

**NOTE:** Please refer to the Office of the Assistant Secretary for Preparedness and Response (ASPR) [COVID-19 Monoclonal Antibody Therapeutics](#) webpage and [NIH COVID-19 Treatment Guidelines Treatment Page](#) for the most up-to-date information on this topic.

Healthcare systems in the U.S. and abroad have been increasingly administering monoclonal antibodies to treat COVID-19 positive patients. This ASPR TRACIE tip sheet—which focuses on outpatient treatment of patients with mild to moderate COVID-19—provides a background of the therapy and indications, and considerations for providers and planners to ensure the equitable and efficient provision of this treatment.

## Background

- Monoclonal antibodies are a proven therapy for a variety of diseases.
  - By binding to a virus, the antibody—introduced through this therapy—prevents the virus from entering the host cell and thus can prevent viral replication and human disease progression. Therefore, the earlier the treatment is given, the more beneficial it will be for the patient.
- Monoclonal antibody therapy appears to help in preventing progression to severe COVID-19 disease and hospitalization when given early in the course of infection. Early data from states and some health systems appears to confirm benefits identified in controlled studies, with lower rates of hospitalization among those receiving the treatment.<sup>1</sup>
- Adverse effects have been limited. The potential exists for severe allergic reactions; cases have been extremely rare.
- REGEN-COV (a product combining the antibodies casirivimab and imdevimab) is available under Emergency Use Authorization (EUA) for the treatment of mild-to-moderate COVID-19 and post-exposure prophylaxis of COVID-19.<sup>2</sup> Sotrovimab is also available under an EUA for the treatment of mild-to-moderate COVID-19.<sup>3</sup> A third monoclonal antibody treatment for mild-to-moderate COVID-19, bamlanivimab and etesevimab administered together, also has an EUA,<sup>4</sup> but its distribution is dependent on low prevalence of resistant SARS-CoV-2 variants and this treatment may not be available in all geographic areas.
- Indications:
  - Patient must be COVID-19 positive as indicated by currently available testing methods.
  - Therapy must be given within 10 days from onset of symptoms, but ideally as soon as diagnosed.
  - This treatment is for patients with mild to moderate illness and [high risk](#) patients with comorbidities and risk of severe disease progression.
  - It is not indicated for hospitalized or severely ill patients.
  - Patients must be 12 years of age or older and weigh at least 40 kg.

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<sup>1</sup> [Actemra](#) (tocilizumab) is authorized as a monoclonal antibody treatment for hospitalized COVID-19 patients receiving corticosteroids and requiring supplemental oxygen, mechanical ventilation, or extracorporeal membrane oxygenation. The considerations in this document do not apply to the treatment of hospitalized patients with Actemra.

<sup>2</sup> [REGEN-COV EUA](#)

<sup>3</sup> [Sotrovimab EUA](#)

<sup>4</sup> [Bamlanivimab and etesevimab EUA](#)

- If patient is a minor, representative must be able to provide informed consent.
- REGEN-COV may also be used as post-exposure prophylaxis in those who have not tested positive or shown symptoms if they meet the other indications AND are not fully vaccinated or not expected to mount an adequate immune response to complete vaccination AND have been a close contact or at high risk of exposure to an infected individual.
- Administration:
  - The drug must be administered by intravenous (IV) infusion and may require up to one hour infusion time, with at least an hour of observation after infusion for adverse or allergic reactions (some delayed reactions are also possible but should not require emergent treatment). Subcutaneous injection is an [authorized administration route](#) in certain circumstances.
- For specific inclusion criteria, preparation instructions, and other information, refer to the references at the end of this document.

### Provider Considerations

- Be informed of inclusion criteria for monoclonal antibodies.
- Develop and follow a policy of evaluating every COVID-19 positive patient for monoclonal antibody therapy.
- Develop and follow a policy of considering not fully vaccinated patients with exposure to SARS-CoV-2 for post-exposure prophylaxis.
- Encourage qualifying patients to seek treatment and be informed on where to refer them.
- Explain that these drugs are available under an [EUA](#) and that the apparent benefit of them justifies their use as the drugs go through the full approval process.
- Reinforce that in order to prevent disease progression, the drugs must be given before the illness becomes severe; therefore, a patient is still a good candidate for the therapy even if they “feel ok” or are not “that sick.” Explain the therapy is to prevent them from getting sicker and that they are at a higher risk for severe illness.
- Understand the process for ordering the medication, referrals, and any necessary follow up actions for the provider.

### Planning Considerations

Considerations must be taken to ensure the equitable and efficient delivery of monoclonal antibody treatment. Figure 1 illustrates the access and equity issues to be considered during planning.

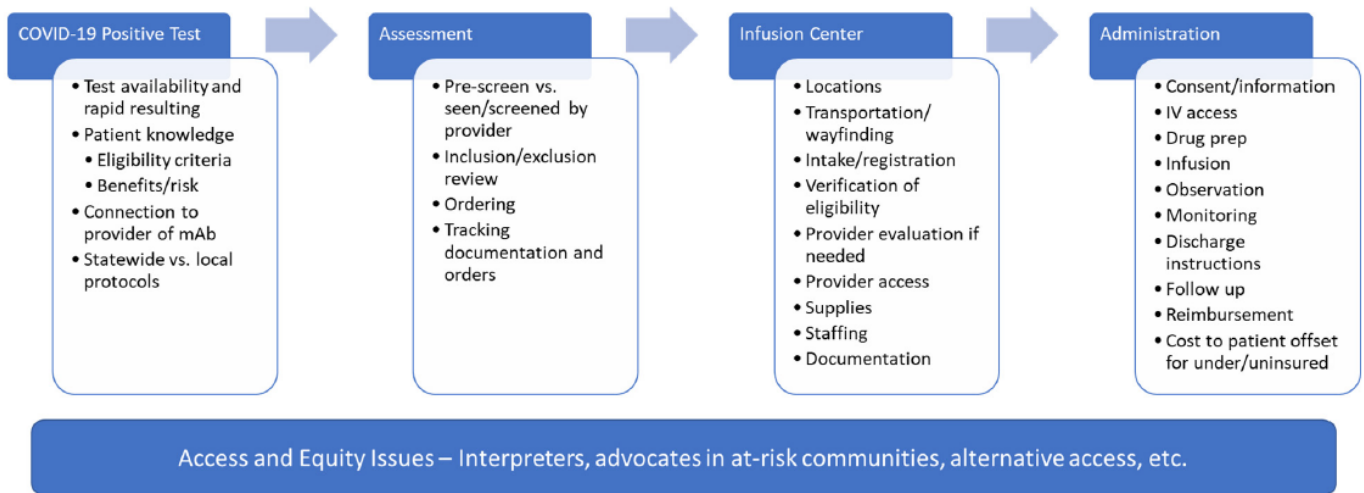


Figure 1. Courtesy of [Rapid Expert Consultation on Allocating COVID-19 Monoclonal Antibody Therapies and Other Novel Therapeutics](#) (published in 2021 by the National Academies of Sciences, Engineering, and Medicine)

Additional planning considerations include:

- Healthcare providers should emphasize early treatment of at-risk individuals to prevent hospitalizations – benefiting both the patient and the healthcare system as a whole.
- Healthcare systems, healthcare coalitions, and local public health departments should anticipate language, communication, transportation, and other barriers to receiving care.<sup>5</sup> Alternative means of information or access provision should be considered (for example, patients may not want to take public transport and may require assistance with transportation).
- Utilize reputable public messaging resources, such as those from the U.S. Department of Health and Human Services (HHS) Assistant Secretary for Preparedness and Response (ASPR) [COVID-19 Monoclonal Antibody Therapeutics Digital Toolkit](#).
- Positive COVID-19 tests:
  - Patients who test positive for COVID-19 [should receive information](#) at the time results are provided (through their healthcare provider, as well as at public or private testing sites) about indications for monoclonal antibody treatment and how to obtain more information, such as where to go and how to obtain a referral for treatment.
  - Patients should understand or be provided with information on how to contact their primary care provider or other clinician to seek treatment if they have symptoms and underlying, qualifying conditions.
- Assessment for treatment:
  - Ideally, patients are screened via a web-based form or a triage (call center) method to determine eligibility.
  - If availability of monoclonal antibody therapy is limited, a screening mechanism can help healthcare providers make allocation decisions (refer to the following section in this document).
  - Patients can be referred to an established infusion center for treatment. A referral [order](#) and appointment can also be issued at the time of the assessment for inclusion.
  - If a prioritization system is being used that favors patients with increased hospitalization risk or essential worker status, this should be incorporated into the assessment.

<sup>5</sup> [CMIST Framework](#)

- Infusion center:
  - Many options exist for monoclonal antibody therapy infusion locations, including viral clinics, emergency department space (may be more appropriate in low-volume situations and not during surge situations), existing infusion centers (used for other medication administration), outpatient health centers, and ambulatory surgical facilities. Another option may be publicly run infusion centers.
  - The footprint and administrative burden of establishing an infusion program is minimal compared to the benefit of reducing hospitalizations. A hub/spoke model (i.e., a few providers serving many patients at a time) should be considered by communities to allow economies of scale.
  - For COVID-19 outbreaks in custodial care facilities, such as long-term care facilities or jails/prisons, consider an infusion mobile or strike team that brings the therapy to the patients.
  - Consider patient entry/exit pattern, patient flow, ventilation, and potential to expose other patients in the area when selecting the infusion location.
  - On-site providers must be able to:
    - Initiate IV access.
    - Administer (and potentially prepare) IV drips.
    - Monitor patients for adverse effects.
    - Manage allergic response including anaphylaxis (e.g., administer epinephrine, antihistamines, and provide airway intervention and resuscitation), in extremely rare cases.
- Administration:
  - The IV infusion is easy to prepare and can be done at bedside.
  - Standard order set (including orders for treatment of adverse reactions) should be created.
  - A nurse/paramedic team can efficiently manage five to six patients at a time with a set of standing orders for monoclonal antibody therapy.<sup>6,7</sup>
  - Monoclonal antibodies can be given by gravity drip – a pump is not required.
  - The patient does not require advanced monitoring during infusion, although airway and patient monitoring supplies, as well as medications for allergic/anaphylactic reactions and a provider trained to provide treatment for reactions, should be readily available.
  - The monitoring time after infusion does *not* need to be performed in a patient care area. A monitored waiting area/discharge area is sufficient.
  - Centers for Medicare & Medicaid Services provides [guidance on billing for monoclonal antibody infusions](#).
  - There is a real risk of uninsured/underinsured patients paying significant out-of-pocket expenses and a plan for risk screening and financial counseling is important. Equity requires that financial considerations not dissuade patients from receiving treatment, therefore regional/state solutions should be agreed upon.
  - ASPR has developed a [training module on monoclonal antibody administration](#) that is publicly available.

## Allocation Considerations

- Because of the broad inclusion criteria and lack of current evidence for differential benefit between the eligible groups, supply may be less than predicted demand.

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<sup>6</sup> [Monoclonal Antibodies for COVID Patients: One System’s Experience](#)

<sup>7</sup> [Monoclonal Antibody Infusion Center Model \(15 Bed\)](#)

- One major challenge many areas are facing is lack of clinician information. Many simply do not know where monoclonal antibody therapy is available, what the inclusion criteria are for patients, and how to refer patients. Patients may also be unaware of their treatment options and are not able to advocate for themselves. As information delivery improves, demand should exceed supply.
- When demand exceeds supply, a number of approaches have been taken:<sup>8</sup>
  - Lottery (e.g., State of Colorado)
  - Priority based on risk of hospitalization (e.g., using the Cleveland Clinic<sup>9</sup> predictor for hospitalization risk or the two highest risk predictors from the studies – age and body mass index variables). Note: this strategy has not been validated though when reducing hospitalization is the ultimate goal of offering therapy.
  - Priority based on essential worker or long-term care resident status.
  - Priority based on clinical features (e.g., multiple risks). Note: no current evidence allows prioritization based on combination of risk factors.
  - First-come, first-served (not ethically optimal as this tends to favor those individuals with more resources).
- Approaches should be adjusted as better evidence becomes available that helps identify sub-groups with higher or lower benefit.
- Rationing should only occur when the drug supply is inadequate to meet demand. Shortages of administration locations or appointments should be corrected by expanding capacity.

## Resources

[ACEP: COVID-19 Monoclonal Antibody Toolkit](#)

[ASPR: COVID-19 Monoclonal Antibody Therapeutics](#)

[ASPR COVID-19 Monoclonal Antibody Therapeutics Digital Toolkit](#)

[Federal Response to COVID-19: Monoclonal Antibody Playbook](#)

[Monoclonal Antibodies for High-Risk COVID-19 Positive Patients \(customizable\)](#)

[Casirivimab + Imdevimab Baseball Cards](#)

[Bamlanivimab](#)

[Bamlanivimab/etesevimab](#)

[REGEN-COV](#)

[ASPR: NDMS Monoclonal Antibody Infusion Information Material Training Course](#)

[ASPR TRACIE: Hospital Operations During COVID-19 Speaker Series – Michigan Monoclonal Antibody Experience](#)

[ASPR TRACIE: Monoclonal Antibody Physician Orders](#)

[Centers for Medicare and Medicaid Services: Monoclonal Antibody COVID-19 Infusion](#)

[Combat COVID: Information for Healthcare Professionals](#)

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<sup>8</sup> [Rapid Expert Consultation on Allocating COVID-19 Monoclonal Antibody Therapies and Other Novel Therapeutics \(January 29, 2021\)](#)

<sup>9</sup> [Individualizing Risk Prediction for Positive Coronavirus Disease 2019 Testing: Results from 11,672 Patients](#)

[Eli Lilly: Lilly Bamlanivimab and Etesevimab Together Antibody Playbook](#)

[National Infusion Center Association: COVID-19 Antibody Therapy Resource Center](#)

[National Infusion Center Association: Locating Sites for COVID-19 Antibody Treatments](#)

[National Institutes of Health: COVID-19 Treatment Guidelines](#)

[Regeneron: REGEN-COV \(casirivimab and imdevimab\) EUA Guidebook](#)

[U.S. Food and Drug Administration: Drug and Biological Therapeutic Products Emergency Use Authorization](#)

[REGN-COV2, a Neutralizing Antibody Cocktail, in Outpatients with COVID-19](#)

[SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with COVID-19](#)