

Planning Considerations for Monoclonal Antibody Administration

Updated February 10, 2021

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 (no benefit has yet been demonstrated in hospitalized patients). 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.
- There currently are no studies that identify a lack of benefit from monoclonal antibody therapy. In addition, adverse effects have been limited (the potential exists for severe allergic reactions; however these have been extremely rare).
- Regeneron (product combining the antibodies casirivimab and imdevimab) and Eli Lilly (single antibody, bamlanivimab) are both available under Emergency Use Authorization (EUA)^{1,2}. The FDA issued an EUA for a new combination therapy on **February 10, 2020** - bamlanivimab and etesevimab³.
- Indications:
 - Patient must be COVID-19 positive as indicated by currently available testing methods.
 - Must be given within 10 days from onset of symptoms, but ideally as soon as diagnosed.
 - For mild to moderate illness and [high risk](#) patients with comorbidities and risk of severe disease progression.
 - Not for hospitalized or severely ill patients.
 - Patients 12 years of age or older
 - Patient representative must be able to provide informed consent.
- 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).
- 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.

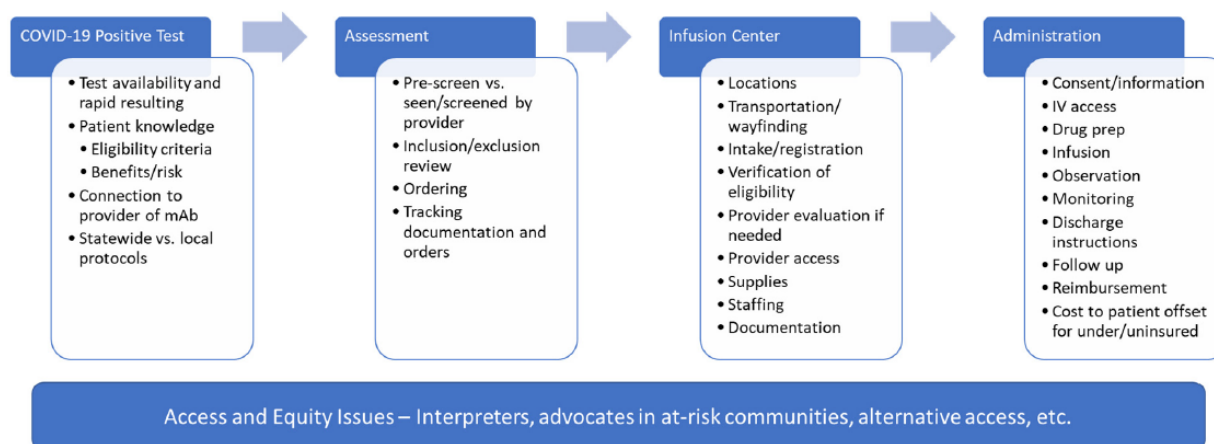
¹ [Bamlanivimab EUA](#)

² [Regeneron \(casirivimab and imdevimab combination\) EUA](#)

³ [Bamlanivimab and etesevimab EUA](#)

- Encourage qualifying patients to seek treatment and be informed on where to refer them.
- Have a discussion with the patient to 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



This figure was captured from an article published by the National Academies of Sciences, Engineering, and Medicine titled, [“Rapid Expert Consultation on Allocating COVID-19 Monoclonal Antibody Therapies and Other Novel Therapies.”](#)

- Hospitals should emphasize early treatment of at-risk individuals to prevent hospitalizations – benefiting both the patient and the healthcare system as a whole.
- Several access issues were identified. Healthcare systems, healthcare coalitions, and local public health departments should anticipate language, communications, transportation, and other barriers to receiving care⁴. 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 systems, 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.

⁴ [CMIST Framework](#)

- 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:
 - 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 included at the time of assessment as well.
- 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; however, if the medications become commercially available and cease to be provided by the federal government, this model will likely need to change.
 - A hub/spoke model should be considered by communities to allow economies of scale (i.e., a few providers serving many patients at a time). The footprint and administrative burden of establishing an infusion program is minimal compared to the benefit of reducing hospitalizations.
 - 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.
 - Consideration must be given to the following: patient entry/exit pattern, patient flow, ventilation, and potential to expose other patients in the area.
 - Providers must be available that can:
 - Initiate IV access.
 - Administer (and potentially prepare) IV drips.
 - Monitor patients for adverse effects.
 - Be prepared to manage allergic response including anaphylaxis. In hospital settings, this can involve rapid response teams or other personnel. In other settings, there should be a provider that can administer epinephrine, antihistamines, and provide airway intervention and resuscitation, in the event that would be needed (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 easily manage five to six patients at a time with a set of standing orders for monoclonal antibody therapy.^{5,6,7}
 - Monoclonal antibodies can be given by gravity drip – a pump is not required.

⁵ [Monoclonal Antibodies for COVID Patients: One System’s Experience](#)

⁶ [Monoclonal Antibody Infusion Center Model \(15 Bed\)](#)

⁷ [Michigan Emergency COVID-19 Pandemic Monoclonal Antibody Administration Protocol](#)

- 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 far less than predicted demand, although current use in many areas is low.
- Currently, a major limitation in many areas is clinician information – knowing where monoclonal antibody therapy is available, what the inclusion criteria are for patients, and how to refer patients. Patients are 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:⁸
 - Lottery (e.g., State of Colorado)
 - Priority based on risk of hospitalization (e.g., using the [Cleveland Clinic predictor](#) for hospitalization risk or the two highest risk predictors from the studies – age and body mass index variables) – note that this strategy has not been validated though if reducing hospitalization is the key benefit.
 - Priority based on essential worker or long-term care resident status.
 - Priority based on clinical features (e.g., multiple risks – note that 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.

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

Resources

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

[ACEP Prescribers Poster - Bamlanivimab](#)

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

[ASPR Information for Providers](#)

[For Providers: Monoclonal Antibody Treatment Guide for Providers \(fact sheet\)](#)

[For Patients: Understanding Your COVID-19 Treatment Options \(fact sheet\)](#)

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

[Casirivimab + Imdevimab Baseball Cards](#)

[Bamlanivimab Baseball Card](#)

[Bamlanivimab](#)

[Casirivimab/Imdevimab](#)

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

[ASPR Special Projects for Equitable and Efficient Distribution \(SPEED\) of COVID-19 Outpatient Therapeutics](#)

[ASPR Therapeutics: Monoclonal Antibody Playbook: Outpatient administration playbook version 2.2](#)

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

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

[Eli Lilly: Lilly Bamlanivimab Antibody Playbook](#)

[Locating Sites for COVID-19 Antibody Treatments](#)

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

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