

# Monoclonals and More – Allocation and Distribution of Outpatient COVID-19 Treatments (Supplemental Resource)

Current as of January 7, 2021

In November 2021, ASPR TRACIE hosted [a webinar](#) where speakers discussed current recommendations for the use of monoclonal antibodies (mAbs) and upcoming therapies for COVID-19 and the allocation challenges and opportunities they may pose when multiple treatment options are available. This resource (based on webinar content and speaker review) serves as a supplement to the information provided in that webinar and provides an overview of some common issues and challenges with distribution of outpatient treatments for COVID-19. The target audience is healthcare and public health planners and leadership, though clinicians may find significant value in the information as well.

This supplemental resource highlights information on the currently available mAbs and introduces additional COVID-19 prophylactics and treatments anticipated to be authorized in the future. It also outlines six key issues for those making resource allocation decisions. Links to additional resources are also offered throughout the document.

## Current and Future Therapies

- Monoclonal Antibodies – [Bamlanivimab/etesevimab](#) and [casirivimab/imdevimab](#) (REGEN-COV) offer about 70% and [sotrovimab](#) 85% reduction<sup>1</sup> in hospitalization and death in high-risk individuals ages 12 and older (bamlanivimab/etesevimab is authorized for all ages, including newborns) with mild to moderate illness; treatment should be initiated as soon as possible and within 10 days of symptom onset. Ideally, they are administered for treatment by the intravenous route though casirivimab/imdevimab can be given subcutaneously. Bamlanivimab/etesevimab and casirivimab/imdevimab may be used for post-

The pandemic is an ever-changing emergency and treatments are being developed and authorized on a continual basis. Stakeholders can access these resources for the most current information on COVID-19 treatment:

- [COVID-19 Treatment Guidelines](#)
- [Side-by-Side Overview of Outpatient Therapies Authorized for Treatment of Mild-Moderate COVID-19](#)

<sup>1</sup> These figures are based on studies conducted prior to the emergence of the Omicron variant.

exposure prophylaxis as well as treatment.

[Distribution](#) of these medications is managed by the U.S. Department of Health and Human Services (HHS) in cooperation with states, territories, and other legal jurisdictions.

- Antiviral Treatments – [Molnupiravir](#) is an antiviral that interferes with viral mRNA synthesis, rendering viral copies non-functional. The U.S. Food and Drug Administration (FDA) issued an emergency use authorization (EUA) on December 23, 2021. It is estimated to provide about a 30% reduction in hospitalization and death when given to high risk adults within 5 days of symptoms onset. Other antiviral agents either alone or in combination with antiretroviral and other therapies offer considerable promise for early treatment. Recent data shows an 89% reduction in hospitalization and deaths with the oral antiviral [PAXLOVID](#), for which FDA issued an EUA on December 22, 2021. Distribution of these agents is also managed by HHS and the jurisdictions.
- Prophylactic Therapies – Some agents such as [EVUSHELD](#) (AZD7442, a combination of two long-acting antibodies), which received an FDA EUA on December 8, 2021, and casirivimab/imdevimab, which is being reviewed by the FDA, have been studied for pre-exposure prophylaxis in persons with compromised immunity who are unable to respond to vaccination. **Note:** This document does not address the specific considerations of prophylaxis though many of the issues and tenets apply to these medications as well.
- Other Available Treatments – Clinical trials suggest there may be benefit of [fluvoxamine](#) (an anti-depressant) and [inhaled steroids](#) at reducing progression and symptom duration, although the data are not definitive. Information changes rapidly and providers should monitor [National Institutes of Health](#) (NIH) and other guidelines for updates and advice. These medications are available through usual pharmacy sources at the discretion of the provider and based on availability.

#### Related ASPR TRACIE Resources

- [COVID-19 Outpatient Resources Collection](#)
- [Healthcare Operations during the COVID-19 Pandemic Speaker Series – Monoclonal Antibody Infusion Clinics](#)
- [Monoclonals and More: Issues and Opportunities with Early COVID-19 Treatment Options](#)
- [Planning Considerations for Monoclonal Antibody Administration](#)

## Issues for Allocation

1. Ethical Framework
  - a. The [Crisis Standards of Care](#) (CSC) framework should be applied to distribution and allocation guidelines
  - b. In general, a utilitarian model (greatest good for the greatest number of persons) should be adopted to maximize beneficial outcomes
  - c. However, key underlying tenets of the CSC framework are consistency, proportionality, and accountability.

- i. Dynamic supply and demand will require jurisdictions and healthcare systems to ramp up and ramp down administration as well as restrictions on who may receive the therapies
    - ii. Equity – Equal access to therapies is critical. This may involve disproportionate efforts to reach at-risk populations with information, testing, and early treatment.
    - iii. Consistent decisions require guidance from expert bodies to establish a framework for the state or region to adapt national recommendations to local distribution availability.
  2. Distribution – Currently, HHS manages [distribution](#) of the mAbs and oral antivirals in cooperation with states, territories and other legal jurisdictions. Distribution strategies to the states are based on current cases and hospitalizations, current utilization rates, and the activity of each product against currently circulating SARS-CoV-2 variants. HHS takes steps to ensure a consistent baseline amount that the states can expect to receive, though week to week total amounts can vary. HHS does not place any requirements on how states use or distribute the medications.
  3. Available Guidance
    - a. NIH [Coronavirus Disease 2019 \(COVID-19\) Treatment Guidelines](#)
    - b. Infectious Diseases Society of America (IDSA) [Guidelines on the Treatment and Management of Patients with COVID-19](#)
  4. Treatment vs. Prophylaxis – Based on medication availability jurisdictions may consider steps that align with the standards of care continuum:
    - a. Conventional – Offer both treatment and prophylaxis to all who meet inclusion criteria.
    - b. Contingency – When there is an adequate supply for treatment and limited prophylaxis, offer prophylaxis to high-risk exposures in the highest risk patients (i.e., those who due to immunosuppression would not be expected to mount an effective response to vaccination).
    - c. Contingency – When there is an adequate supply for treatment only, offer treatment, not prophylaxis. Monitor and offer interval testing to those with high-risk exposures and offer treatment as soon as diagnosis is made.
    - d. Crisis – When there is an inadequate supply to treat all patients that meet inclusion criteria:
      - i. Consider directing treatment to patients with specific medical conditions shown to most benefit from [treatment](#).
      - ii. Most of the studies used inclusion criteria or showed real-world benefit when given in the first several days of [illness](#). However, many disadvantaged populations may delay seeking care and restricting access within the approved timeframe (10 days for mAbs) may pose equity issues.
      - iii. Some healthcare systems and states have used scoring systems to determine which patients are most likely to benefit from available treatments. For example, the Monoclonal Antibody Screening Score (MASS) developed by

Mayo Clinic has been validated and could be incorporated into decision [tools](#). Some [states](#) have adopted risk calculators that are available but the evidence behind them is not published. Alternatively, a more general [model](#) of COVID-19 predicted mortality may be used to determine risk of a poor outcome.

- iv. Some states have included pregnancy status as a priority feature though data on pregnancy outcomes related to COVID-19 and treatment effects are scant. Pregnancy is an at-risk condition in the expanded 2021 inclusion criteria.
  - v. Racial groups that were disproportionately affected by COVID-19 were included in the expanded 2021 criteria. Ensuring that these groups have access to treatments is critical. Data continues to be gathered on whether race is an independent predictor of outcome once ill that may allow more effective prioritization in specific groups. At this time, race should be regarded as a social, not medical, factor in prioritization frameworks.
  - vi. Though vaccinated individuals are less likely to require hospitalization or die, they still benefit from early treatment, particularly those with high-risk conditions. Therefore, vaccination status is not recommended as a prioritization mechanism for early treatment unless products are in limited supply.
5. Reciprocity – Some states have incorporated consideration of healthcare workers and social vulnerability status into allocation frameworks. There is not ethical consensus on whether this is appropriate within a decision tool versus making sure that eligible patients among at-risk groups have equal access to the treatments available. Notably, some states include/included prioritization of healthcare workers prior to vaccination being available and/or during staffing shortages to ideally return providers to work as soon as possible. States should ensure that reciprocity is approached uniformly as ad hoc decisions are to be avoided. Building reciprocity into allocation decision frameworks has major ethical implications and should be carefully considered by a diverse cross section of experts and with adequate community feedback prior to adoption.
6. Monoclonal Antibody Administration Issues
- a. Route – Monoclonal antibodies for treatment optimally should be given intravenously (IV) but casirivimab/imdevimab can be given subcutaneously (SQ) when IV administration is not feasible and would lead to delay in treatment. SQ injections can be given by a much wider range of providers and with much less resource and time commitment compared to IV use. SQ route should be considered during contingency and crisis operations, particularly in situations where the therapy would not otherwise be offered if restricted to IV administration. Thus, expansion plans during high demand should consider SQ administration options to increase throughput and broaden administration options.
  - b. Training – At least one provider in the location where mAb therapies are provided must have training to treat potential allergic reactions including anaphylaxis. This does not mean that all providers need this expertise, though all should be able to recognize

- allergic reactions and take appropriate action to cease administration and obtain assistance.
- c. Observation – One hour of observation time has been stipulated following administration, though anecdotally most of the reactions occur early in the infusion. Note that many sites move the patient to observation/holding areas after administration to complete this requirement with a medical provider monitoring them for new symptoms.
  - d. Location – Multiple locations have been used, including:
    - i. Congregate sites – May be in conjunction with rapid testing so that patients can rapidly be offered therapy. Often provided in public-private partnerships to leverage public spaces, logistics, and personnel for screening/queuing with medical providers on contract or through a local healthcare system to administer the treatment.
    - ii. Home/Long-Term Care (LTC) Administration – Community paramedics and homecare agencies as well as home infusion providers have gone into LTC facilities or homes of those with mobility/access issues. This may reduce the potential exposures created by moving a known positive COVID-19 patient but also is difficult to scale effectively. As previously mentioned, consider SQ administration to help increase efficiency and the range of providers that can administer.
    - iii. Clinic – Designated clinic space can be used for administration; however, the patients will need a separate or controlled entrance to ensure they are isolated from non-COVID patients. Evening and weekend dedicated use of space may be helpful.
    - iv. Emergency Department (ED) – The observation period required after treatment administration does not lend itself to routine administration in the ED. However, SQ administration should be considered to ensure close coupling of diagnosis to treatment when possible. Current ED crowding may require referral to an alternate location for administration and/or observation (note that the patient must continue to be isolated).
  - e. Incorporation of Oral Agents/Balancing with Injectables
    - i. Efficacy – Patients must receive information and understand the potential outcomes differences between treatments and be allowed to make a choice. Ideally this should be provided at the time of testing when a symptomatic person is identified as at-risk and within the treatment window.
    - ii. Preference – It is likely that many patients will prefer oral agents. However, the state may wish to limit patient preference in favor of strategies that maximize the use of all medications.
    - iii. Potential Strategies
      - 1. Allocate some antivirals to ED and hospital pharmacy use to ensure efficient linkage of a positive test to immediate treatment for at-risk individuals.

2. Establish contracts/contacts with regional delivery services/couriers that can deliver oral therapy to at-risk individuals, particularly those in rural areas or those in urban areas that do not have an option for safe transportation or have other barriers to seeking treatment with injectables.
3. Preferentially make oral agents available in pharmacies located in areas with high Area Deprivation Index or Social Vulnerability Index scores.
4. Identify areas of the state that have few/no providers who can safely administer injectable treatments and identify a vetting/prescribing strategy for those populations, particularly in remote areas.
5. Consider focusing administration of injectables in the highest risk population including LTC and the immunocompromised, particularly in areas where there are larger numbers of these individuals.
6. As a surge occurs, increasing healthcare responsibilities may make it difficult to devote resources to injectable medications. Consider national and state strategies to prioritize oral agents to those regions/communities with the highest case numbers to increase availability and likelihood of treatment (providing individual as well as potential community benefit while reducing workload/expertise required from the healthcare sector).

iv. Caveats

1. All states are different, and different geography, services, and populations will require tailored solutions.
2. Evidence for efficacy of early treatment is good, but somewhat limited, and will be more limited for new agents coming into the system. Adoption and acceptance of the new oral agents may be very contingent on messaging and evolving data.
3. Some populations may much more readily accept and some reject novel treatments. Monitoring and tailoring of strategies, outreach, and distribution will need to be tailored to evolving demand.

## Resources

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