The Science Behind Monoclonal Antibodies for COVID-19: Frequently Asked Questions

Q: What monoclonal antibody treatments are authorized for use?

A: The U.S. Food and Drug Administration (FDA) has granted emergency use authorizations (EUAs) for the following monoclonal antibodies to treat *outpatients* with mild to moderate COVID-19 and who are at high risk of developing severe symptoms. These treatments include:

- **REGEN-COV™ (Casirivimab and Imdevimab):** Fact Sheet[1] and EUA[2]
- **Bamlanivimab and Etesevimab:** Fact Sheet[3] and EUA[4]
- **Sotrovimab:** Fact Sheet[5] and EUA[6]

Q: What methods of administration are available?

A: The FDA has authorized intravenous (IV) infusion of monoclonal antibody treatments for emergency use. IV infusion is strongly recommended. The FDA also authorized subcutaneous injection for certain monoclonal antibody treatments that are currently available.[2] Subcutaneous injection is an alternative route of administration when intravenous infusion is not feasible and would lead to delay in treatment.

Note: On June 25, the Assistant Secretary for Preparedness and Response (ASPR) paused all distribution of bamlanivimab and etesevimab together on a national basis until further notice.[7] The distribution was paused due to combined frequency of the SARS-CoV-2 Gamma variant (P.1; first identified in Brazil) and the Beta variant (B.1.351; first identified in South Africa) that now exceed 11% and are trending upward throughout the United States.[8] Results from in vitro assays that are used to assess the susceptibility of viral variants to particular monoclonal antibodies suggest that bamlanivimab and etesevimab administered together are not active against either the P.1 or B.1.351 variants. In addition, the FDA recommends that healthcare providers nationwide use alternative authorized monoclonal antibody therapies.

The FDA also granted an EUA for the following monoclonal antibody for the treatment of COVID-19 in *hospitalized* adults and pediatric patients (2 years of age and older) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO):

- **Actemra® (tocilizumab):** Fact Sheet[9] and EUA[10]

The NIH COVID-19 Treatment Guidelines Panel recommends (AIIa) using either REGEN-COV (casirivimab and imdevimab) or sotrovimab to treat *outpatients* with mild to moderate COVID-19 who are at high risk of clinical progression, as defined by the Emergency Use Authorization (EUA).[11] Furthermore, the Panel recommends against the use of bamlanivimab plus etesevimab (AIII) at this time, due to the increasing prevalence of circulating variants in the U.S. These include the P.1 (Gamma) and B.1.351 (Beta) variants of concern, which have reduced susceptibility to both bamlanivimab and etesevimab. The Panel also recommends (BIIa) the use of tocilizumab in the *inpatient* setting for certain patients, as defined by the EUA.[12]

Rating of Recommendations:
A = Strong; **B** = Moderate; **C** = Optional

Rating of Evidence:
I = One or more randomized trials without major limitations
IIa = Other randomized trials or subgroup analyses of randomized trials
IIb = Nonrandomized trials or observational cohort studies
III = Expert opinion

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Q: Which outpatients can be treated with the authorized monoclonal antibodies?

A: Monoclonal antibodies are authorized for the treatment of mild to moderate COVID-19 in adult or pediatric (age 12 years and older and ≥ 40 kg) patients with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.[1,3,5] Treatment must be given within 10 days of symptom onset, so it is critical to identify eligible patients at the point of diagnosis and inform them about the availability of monoclonal antibody treatment.[13,14]

Q: Which inpatients can be treated with the authorized monoclonal antibody?

A: The monoclonal antibody tocilizumab is authorized for the treatment of COVID-19 in hospitalized adults and pediatric patients (2 years of age and older) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).[9,15]

Q: What data supported the Emergency Use Authorization of the monoclonal antibodies?

A: For outpatient use, data from controlled clinical trials that showed that high-risk patients who received monoclonal antibodies had a decrease in the risk of progression to severe disease, hospitalization, or death compared to patients who received placebo was used in support of the EUA.[1,3,5]

For inpatient use, data from clinical trials of hospitalized patients with COVID-19 showed that patients who received the monoclonal antibody in addition to the routine care patients receive for treatment of COVID-19, which included corticosteroid therapy, had a reduced risk of death through 28 days of follow-up and saw a decrease in the amount of time they remained hospitalized. The risk of patients being placed on ventilators or death through 28 days of follow-up was also decreased.[9,15]

The safety and efficacy of these therapies for use in the treatment of COVID-19 continue to be evaluated.

During certain types of emergencies,[16] the FDA may permit authorization based on the best available evidence to provide timely access to critical care when there are no adequate, approved, and available alternatives. This may include authorization of investigational products based on significantly less data than would be required for approval by the FDA.

Q: Are monoclonal antibodies effective against new SARS-CoV-2 variants?

A: Certain outpatient monoclonal antibody treatments under emergency use remain effective against the major variants of concern circulating in the U.S., based on laboratory results. However, the science and the clinical data on this question is evolving. The FDA recently authorized updates to the fact sheets for healthcare providers, including Antiviral Resistance information in Section 15 of the fact sheets for each of the currently available outpatient treatments under emergency use. For further information, please reference the information on CDC variant classifications and definitions.[17]

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Q: How do SARS-CoV-2 variants impact treatment decisions?

A: To guide treatment decisions, healthcare providers should:

- Review the Antiviral Resistance information in Section 15 of the authorized fact sheets for each outpatient monoclonal antibody therapy available under EUA[16] for details on specific variants and resistance.
- Refer to the CDC website,[8] as well as information from state and local health authorities, for reports of viral variants in their region.

For more information, visit
CombatCOVID.hhs.gov
English: 1-877-332-6585 • Spanish: 1-877-366-0310

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