



Updates on COVID-19 Monoclonal Antibody (mAb) Treatment in the Outpatient Setting

Overview

- All providers should know how and when to refer patients for monoclonal antibody (mAb) treatment.
- mAb treatment, when given early after symptom onset, can decrease the risk of hospitalization and death due to COVID-19 by as much as 70% to 85%.
- Eligibility criteria for mAb treatment have been expanded to include additional medical conditions and factors that may place patients at high risk for progression to severe COVID-19.
- Continue to refer eligible symptomatic patients for mAb treatment, regardless of vaccination status.
- Sotrovimab is a new mAb product that has been granted emergency use authorization (EUA) by the Food and Drug Administration (FDA).
- The EUA for REGEN-COV (casirivimab + imdevimab) has been updated to reduce the dose and allow for subcutaneous administration.
- The EUA for REGEN-COV has also been expanded to include use as post-exposure prophylaxis for people exposed to someone with COVID-19 and at high risk for severe illness.
- Health care providers should use only REGEN-COV or sotrovimab for the treatment of COVID-19 until further notice due to increasing prevalence of SARS-CoV-2 variants resistant to bamlanivimab and etesevimab.

August 20, 2021

Dear Colleague,

This letter summarizes important updates on monoclonal antibody (mAb) emergency use authorizations (EUAs) and treatment guidance. mAbs are the only authorized treatment option for patients with mild to moderate COVID-19 who are at high risk of developing severe illness. It is also the only option for post-exposure prophylaxis (PEP). As cases of COVID-19 continue to rise in New York City (NYC) due to more contagious and dangerous variants, it is critical that providers assist eligible patients to access this life-saving treatment by increasing patient awareness, encouraging prompt diagnostic testing following a COVID-19 exposure or symptom onset, and offering or referring patients for treatment.

Although NYC has made great strides in [COVID-19 vaccination](#), more than 40% of New Yorkers remain unvaccinated, with the lowest rates among Black and Latino individuals and in certain neighborhoods with higher rates of [chronic medical conditions and social factors](#) that can increase the potential for severe outcomes. Even among people who are fully vaccinated, some

people with [immunocompromising conditions](#)—including those taking immunosuppressive medications or on hemodialysis—are unable to generate a robust antibody-driven immune response to COVID-19 vaccines and may benefit from mAbs as treatment or PEP.

With early administration, mAb treatment may reduce the risk of hospitalization and death by as much as 70% to 85% ([Dougan 2021](#); [Gupta 2021](#); [Weinreich 2021](#)). Further, studies demonstrate the real-world benefits of mAb treatments in reducing emergency department visits, hospitalizations, hospital lengths of stay, and death ([Rainwater-Lovett 2021](#); [Bariola 2021](#); [Verderese 2021](#)).

Expansion of mAb eligibility criteria

On May 14, 2021, the FDA expanded the definition of “high-risk” patients eligible for treatment and gave health care providers greater latitude to exercise clinical judgment. Providers may now refer any symptomatic patient age 12 years and older, weighing at least 40 kg/88 lbs, with confirmed COVID-19 for mAb treatment if they have a medical condition or other factors that increase their risk for severe illness. For example, individual risk can be impacted by longstanding systemic health and social inequities that put people of color, people with disabilities and others at increased risk of getting sick and dying from COVID-19.

For additional information on medical conditions and factors associated with increased risk for progression to severe COVID-19, see Appendix A below and the Centers for Disease Control and Prevention's (CDC's) [website](#). For more details, see the EUA fact sheets for health care providers:

- [Casirivimab and imdevimab](#) (REGEN-COV)
- [Bamlanivimab and etesevimab](#)
- [Sotrovimab](#)

FDA authorizes sotrovimab mAb treatment

On May 26, 2021, the FDA authorized use of a new mAb product, sotrovimab (GlaxoSmithKline/Vir Biotechnology), for the treatment of mild to moderate COVID-19 given intravenously as a single dose. Sotrovimab is a single agent recombinant human IgG1k mAb that binds to a conserved epitope on the spike protein receptor binding domain of SARS-CoV-2. An interim analysis showed treatment of 291 patients with sotrovimab 500 mg IV reduced hospitalization or death by 85% when compared to 292 patients in the placebo group (1% vs 7%; $p=0.002$) ([Gupta 2021](#)).

Sotrovimab is commercially available and will **not** be distributed by the federal government. Further information on this new therapy can be found at the following links:

- [FDA healthcare provider fact sheet](#)
- [EUA letter of authorization](#)
- [FDA press release](#)
- [National Institutes of Health \(NIH\) COVID-19 treatment guidelines](#)

Updated EUA for REGEN-COV

Effective June 3, 2021, the FDA has [authorized](#) a lower dose of REGEN-COV (600 mg casirivimab and 600 mg imdevimab), half the dose that was originally authorized. Additionally, a single vial of co-formulated product containing one full treatment is now available to [order via AmerisourceBergen](#). The revised EUA also allows REGEN-COV to be administered as a subcutaneous injection when IV infusion is not feasible. This change will improve access to outpatient mAb treatment. Ambulatory providers not already offering mAb treatment should consider this option based on the needs of their patient population. Refer to the FDA's [Dear Healthcare Provider document](#) for more details on updated dosing and administration.

Also, effective July 30, 2021, the [EUA](#) allows for use of REGEN-COV as PEP in patients who meet the following criteria:

- 12 years of age and older weighing at least 40 kg/88 lbs;
- At high risk for progressing to severe COVID-19;
- Not fully vaccinated or are not expected to mount an adequate immune response (such as immunocompromised patients); **and**
- Have either been exposed to an individual with COVID-19 **or** are at high risk of exposure because of occurrence of COVID-19 in other individuals in the same institutional setting (such as nursing homes or correctional facilities).

The authorization for PEP was based on a phase 3, randomized, double-blind, placebo-controlled trial in which treatment of asymptomatic contacts within 96 hours after a household member tested positive reduced the risk of symptomatic COVID-19 by 81.4% compared to the placebo group. The duration of symptoms was reduced and risk of developing asymptomatic or symptomatic infection was reduced by 66.4% in the treated group ([O'Brien 2021](#)).

Several studies have shown a reduced immune response to COVID-19 vaccines in some people who are moderately to severely immunocompromised ([Haidar 2021](#); [Mahil 2021](#)). Health care providers should consider whether an immunocompromised patient's clinical condition makes protection from vaccination unlikely enough to warrant PEP. This expanded use of mAb therapy is not a substitute for vaccination against COVID-19 and providers should assess whether [a third dose](#) of COVID-19 vaccine is appropriate for their immunocompromised patients.

Changes to recommendations due to variants

Guidance on the selection of mAb treatment has been revised because certain circulating COVID-19 variants have shown resistance to some therapeutics. Most recently, the distribution of bamlanivimab and etesivimab (as well as etesivimab alone to complement existing bamlanivimab supplies) have been [paused nationally](#) until further notice. This pause was implemented because in vitro studies suggest that the bamlanivimab and etesivimab combination is not active against the gamma (P.1) and beta (B.1.351) variants, and the combined frequency of these two variants was more than 10% at the time of the decision to pause ([CDC's variant data tracker](#)). The delta variant (B.1.617.2), which currently accounts for more than 90% of [sequenced cases in NYC](#) and nationally, is resistant to bamlanivimab, though there may be only a modest reduction in activity when combined with etesivimab (unpublished data).

REGEN-COV and sotrovimab are likely to retain activity against the known circulating variants of concern, including the delta variant (B.1.617.2). The FDA recommends that health care providers use only these products until further notice. All mAb treatment sites can continue ordering REGEN-COV free of charge from the authorized federal distributor, AmerisourceBergen, by following the [existing ordering and reporting procedures](#). Sotrovimab is commercially available, and information on availability and ordering can be found at sotrovimab.com.

Information on specific mAb products' antiviral activity against SARS-CoV-2 variants can be found in section 15 of the respective EUA Fact Sheets for health care providers (see links above).

How to refer and offer mAb treatment

A list of treatment sites in the Downstate New York region and information on how to refer patients can be found on the Health Information Tool for Empowerment (HITE) Site (hitesite.org/monoclonalantibody). Additional treatment sites may be found on the Department of Health and Human Services' (HHS') [treatment locator](#). NYC Health + Hospitals offers mAb treatment throughout NYC and accepts patient referrals regardless of immigration status or ability to pay. Patients or providers can contact Health + Hospitals by visiting expresscare.nyc or calling 212-COVID19 (212-268-4319) to talk to a provider who can determine eligibility and schedule treatment.

If you are interested in offering mAbs at your facility, go to combatcovid.hhs.gov for information on [ordering, administering, coding and billing](#) and the updated [Monoclonal Antibody Playbook for Outpatient Administration](#) for details on becoming a mAb treatment provider. For uninsured patients, facilities may request reimbursement for the treatment costs through the [COVID-19 Uninsured Program](#).

Providers should ensure that patients at higher risk for severe COVID-19 are aware of the option for mAb treatment in the event that they become infected or exposed. **It is essential that patients understand the importance of getting tested for COVID-19 right away if they develop COVID-19 symptoms, since there is a safe and effective treatment option that works best when given as soon as possible after they become sick.** Consider sharing the NYC Department of Health and Mental Hygiene (Health Department)'s [Monoclonal Antibody Treatment for COVID-19](#) patient handout when testing patients for COVID-19 and during visits with patients known to be at increased risk of severe disease (soon available in multiple languages on the Health Department's [COVID-19 Symptoms and Care webpage](#)). Given the low risk and high potential benefit, providers should recommend and offer or refer eligible patients for mAb treatment, regardless of vaccination status. Providers should also [use every opportunity to encourage vaccination](#) as the best protection against COVID-19.

Thank you for your ongoing efforts to keep New Yorkers safe.

Sincerely,

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Additional Resources

- NYC Health Department’s [COVID-19: Information for Providers](#), section on Monoclonal Antibody Treatment:
 - [Comprehensive overview](#) of mAb therapeutics (March 30)
 - [Additional treatment information](#) for clinicians (June 17)
 - [Patient handout with FAQs](#), available soon in multiple languages (updated August 6)
- [HHS Monoclonal Antibody Treatment Resources for Clinicians](#)
- [NIH COVID-19 Treatment Guidelines](#)
- [Infectious Diseases Society of America \(IDSA\) COVID-19 Treatment Guidelines](#)
- [COVID-19 Monoclonal Antibody Therapeutics Digital Toolkit](#)
- [Monoclonal Antibody Playbook for Outpatient Administration](#)

Appendix A

The following medical conditions or other factors may place adults and pediatric patients at higher risk for progression to severe COVID-19:

- Older age (e.g., ≥65 years of age)
- Obesity or overweight (e.g., adults with body mass index [BMI] >25 kg/m², or if 12 to 17 years of age, have BMI ≥85th percentile for their age and gender based on [CDC growth charts](#))
- Pregnancy
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease or immunosuppressive treatment
- Cardiovascular disease (including congenital heart disease) or hypertension
- Chronic lung disease (e.g., chronic obstructive pulmonary disease, asthma [moderate to severe], interstitial lung disease, cystic fibrosis or pulmonary hypertension)
- Sickle cell disease
- Neurodevelopmental disorder (e.g., cerebral palsy) or other condition that confers medical complexity (e.g., genetic or metabolic syndromes or severe congenital anomalies)
- Having a medical-related technological dependence (e.g., tracheostomy, gastrostomy, or positive pressure ventilation [not related to COVID-19])

Eligibility is not limited to the medical conditions or factors listed above. Health care providers should consider the benefits and risks for an individual patient when making mAb treatment recommendations.