Interim Guidance for the use of Monoclonal Antibodies for Treatment of COVID-19  
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Monoclonal antibodies are laboratory-produced molecules that act as substitute antibodies that can restore, enhance, or mimic your immune system’s response. These antibodies work by directly neutralizing the SARS-CoV-2 virus in the body, reducing the risk of progression to severe disease and hospitalization for high-risk COVID-19 patients.

Key Facts

- As of June 25th, 2021, the FDA has paused the distribution of bamlanivimab and etesevimab nationwide due to the rise of SARS-CoV-2 variants that may be resistant to bamlanivimab and etesevimab. It is recommended that providers switch to one of the alternative monoclonal antibody therapies that remain available and effective against commonly circulating variants.
- Currently, there are three monoclonal antibody products on emergency use authorization (EUA) from the FDA for the treatment of mild to moderate COVID-19:
  - Bamlanivimab and etesevimab
  - REGEN-COV™ (casirivimab and imdevimab)
  - Sotrovimab
  - Note: the EUA for bamlanivimab administered alone was revoked in April 2021 due to its ineffectiveness against certain circulating variants of SARS-CoV-2
- These monoclonal antibody products are currently authorized for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive test results of direct SARS-CoV-2 viral testing and who are considered at high risk for progressing to severe COVID-19 and/or hospitalization.
- Since May 2021, the FDA has expanded the definition of who is considered high-risk for progression to severe COVID-19, giving providers more latitude in using clinical judgement to determine who is eligible for monoclonal antibody treatment.
- The National Institutes of Health (NIH) COVID-19 Treatment Guidelines Panel now strongly recommends the use of monoclonal antibody therapy to treat outpatients with mild to moderate COVID-19 who are at high risk of clinical progression.
- Monoclonal antibodies for the treatment of COVID-19 should be given to eligible patients within 10 days of symptom onset.
- Monoclonal antibody therapies have a rare risk of serious hypersensitivity reaction, including anaphylaxis.
- Large quantities of Bamlanivimab/etesevimab and casirivimab/imdevimab have been purchased by the federal government and are available to NC providers at no cost.
- Providers can bill Medicare for the administration fee associated with monoclonal antibody infusions.
FDA Emergency Use Authorization (EUA)

The FDA has issued EUAs for monoclonal antibody therapies for use in high-risk outpatients with COVID-19. An EUA is not an approval but a determination that potential benefits outweigh potential risks. All three currently authorized monoclonal antibody therapies work directly to neutralize the SARS-CoV-2 virus in the body and may decrease the incidence of emergency department visits and hospitalizations in patients at greatest risk for progression to severe disease. Under the EUAs, adults and pediatric patients (age 12-17 years and weighing at least 40 kg) with mild and moderate COVID-19 who are at high-risk of progressing to severe disease and/or hospitalization are eligible for treatment. These therapies must be administered within 10 days of symptom onset and are ideally administered as soon as possible following a positive viral test for COVID-19. The following medical conditions or factors may place patients at higher risk of progression to severe COVID-19:

- Older age (for example age > 65 years of age)
- Obesity or being overweight (for example, adults with BMI >25 kg/m², or if age 12-17, have BMI ≥85th percentile for their age and gender based on CDC growth charts, [https://www.cdc.gov/growthcharts/clinical_charts.htm](https://www.cdc.gov/growthcharts/clinical_charts.htm))
- Pregnancy
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease or immunosuppressive treatment
- Cardiovascular disease (including congenital heart disease) or hypertension
- Chronic lung diseases (for example, chronic obstructive pulmonary disease, asthma [moderate-to-severe], interstitial lung disease, cystic fibrosis, and pulmonary hypertension)
- Sickle cell disease
- Neurodevelopmental disorders (for example, cerebral palsy) or other conditions that confer medical complexity (for example, genetic or metabolic syndromes and severe congenital anomalies)
- Having a medical-related technological dependence (for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19))

The EUA also acknowledges that authorization of these products is not limited to the medical conditions or factors listed above. Other factors (such as race or ethnicity) may also place patients at high risk for progression to severe disease. Healthcare providers should consider the benefit-risk for an individual patient when making treatment decisions. Please see CDC’s website: [https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html](https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html) for more information on medical conditions or factors associated with increased risk for progression to severe COVID-19.

These monoclonal antibody therapies are NOT authorized for use in patients who:

- Are hospitalized due to COVID-19
- Require oxygen therapy due to COVID-19
- Require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to an underlying non-COVID-19 related condition.
The Therapies

1. **REGEN-COVTM (casirivimab and imdevimab)**

   On November 21st, 2020 the FDA issued an EUA for REGEN-COVTM manufactured by Regeneron. Casirivimab and imdevimab are two recombinant human monoclonal antibodies that bind to non-overlapping epitopes of the spike protein receptor binding domain of SARS-CoV-2. In clinical trials REGEN-COVTM demonstrated a 70% reduction in COVID-19 related hospitalization or death compared to placebo. Detailed clinical trial results and data supporting the EUA can be found in the [FDA-authorized REGEN-COVTM Fact Sheet for Healthcare Providers](#).

   In June of 2021, the FDA updated the REGEN-COVTM EUA to include the authorization for a subcutaneous route of administration as an alternative for those who cannot receive intravenous infusion. Currently, REGEN-COVTM is the only monoclonal antibody for COVID-19 authorized to be administered subcutaneously.

2. **Bamlanivimab and Etesevimab**

   On February 9th, 2021, the FDA issued an EUA for the combination of bamlanivimab and etesevimab which is manufactured by Lilly and is given as a single infusion. Bamlanivimab and Etesevimab are monoclonal antibodies that are specifically directed against the spike protein of SARS-CoV-2, designed to block the virus’ attachment and entry into human cells. This EUA is based on analysis of the BLAZE-1 phase 2/3, randomized, double-blind, placebo-controlled trial in non-hospitalized adults with mild to moderate COVID-19 symptoms who were at high risk for progressing to severe COVID-19. Data from the clinical trial shows an 87% relative reduction of hospitalization in the treatment group when compared to placebo. Detailed clinical trial results and data supporting the EUA can be found in the [FDA-authorized Bamlanivimab and Etesevimab Fact Sheet for Healthcare Providers](#).

3. **Sotrovimab**

   On May 26th, 2021, the FDA issued an EUA for sotrovimab, a monoclonal antibody manufactured by GlaxoSmithKline (GSK). A recombinant human monoclonal antibody that binds to a conserved epitope on the SARS-CoV-2 spike protein, Sotrovimab inhibits an undefined step in the fusion process between viral and cellular membranes. Results from the Phase 1/2/3 COMET-ICE trial show that progression of COVID-19 at day 29 was reduced by 85% (adjusted relative risk reduction) in recipients of sotrovimab compared to placebo. Detailed clinical trial results and data supporting the EUA can be found in the [FDA-authorized Sotrovimab Fact Sheet for Healthcare Providers](#).

Monoclonal Antibodies and SARS-CoV-2 Variants

As SARS-CoV-2 viral variants continue to be identified and quantified across the country, the FDA, CDC and the National Institutes of Health (NIH) are working together to monitor the impacts they may have
on the use of monoclonal antibody therapies authorized for emergency use. Recently the FDA updated the authorized “Fact Sheet for Healthcare Providers” for all monoclonal antibody products currently authorized for use to contain a section with information related to antiviral resistance for each product. Providers are encouraged to reference the variant information found in section 15 of these fact sheets, as well as CDC’s information showing proportions of SARS-CoV2 variants of concern by state and the number of COVID-19 cases caused by variants when making treatment decisions.

Monitoring the prevalence of SARS-CoV-2 variants circulating in the United States has led to two actions from the federal government related to monoclonal antibodies.

1. On April 16th, 2021, the FDA revoked the EUA for bamlanivimab administered alone citing the increased risk of treatment failure due to the sustain increase in SARS-CoV-2 viral variants that are resistant to bamlanivimab when administered alone. The full FDA announcement can be found here.

2. On June 25th, 2021, the Assistant Secretary for Preparedness and Response (ASPR) and the FDA paused, until further notice, the nationwide distribution of bamlanivimab and etesevimab citing an increase of SARS-CoV-2 variants resistant to the combination therapy. The FDA recommends that providers nationwide currently use one of the alternative authorized monoclonal antibody treatments when treating COVID-19 patients. The EUA for bamlanivimab and etesevimab has not been revoked and it is possible that distribution of the product could resume as changes in the nationwide variant profile occur. The full statement from ASPR regarding the distribution pause can be found here.

Obtaining Monoclonal Antibody Products in North Carolina

Allocation and distribution of REGEN-COVTM and bamlanivimab and etesevimab are currently controlled by the United States Department of Health and Human Services (US HHS). Since February 2021, US HHS has determined that supply of these products is no longer scarce and has implemented a direct ordering process for acquiring these monoclonal antibodies. Any interested provider, who can meet the requirements of the EUA, can order product as needed directly from AmerisourceBergen using this special-order form: https://app.smartsheet.com/b/form/255d164d67834793b4ab549e160941e8. There is currently no cost for either REGEN-COVTM or bamlanivimab and etesevimab.

Providers receiving and administering REGEN-COVTM or bamlanivimab and etesevimab are required to report inventory and administration data to the federal government on a weekly basis. Upon placing their first order, new providers will receive an email from protect-noreply@hhs.gov with instructions for how to create a TeleTracking account which is the system US HHS uses to collect inventory reports.

Sotrovimab distribution is NOT controlled by the federal government. Information on how providers can purchase sotrovimab can be found at https://www.sotrovimab.com/hcp/access/. The wholesale acquisition cost for sotrovimab is $2,100 per dose. There is no requirement to report inventory of sotrovimab to the Federal Government.
Providers looking to refer patients to an existing COVID-19 monoclonal antibody infusion site can use the National Infusion Center Association (NICA) COVID-19 Infusion Center Locator Tool to find North Carolina providers currently administering monoclonal antibodies.

**Federal Monoclonal Antibody Call Center**

The federal government has established a call center where patients and/or providers can get more information about monoclonal antibody treatments or help identifying an infusion center in their area.

For English: 1-877-332-6585  
For Spanish: 1-877-366-0310

**Provider Resources:**

ASPR Statement Regarding the Pause in the Distribution of Bamlanivimab and Etesevimab  
NIH COVID-19 Treatment Guidelines Panel statement regarding the use of monoclonal antibodies  
Federal Response to COVID-19: Monoclonal Antibody Playbook  
REGEN-COV™ EUA Fact Sheets for:  
- Healthcare Providers  
- Patients, Parents and Caregivers (English)  
- Patients, Parents and Caregivers (Spanish)  
Frequently Asked Questions on the Emergency Use Authorization for REGEN-COV™  
Regeneron’s REGEN-COV™ EUA Guidebook  
Bamlanivimab and Etesevimab Fact Sheets for:  
- Healthcare Providers  
- Patients, Parents and Caregivers (English)  
- Patients, Parents and Caregivers (Spanish)  
Frequently Asked Questions on the Emergency Use Authorization for bamlanivimab/etesevimab  
Lilly Bamlanivimab and Etesevimab Together Antibody Playbook  
Sotrovimab EUA Fact Sheets for:  
- Healthcare Providers  
- Patients, Parents and Caregivers (English)  
- Patients, Parents and Caregivers (Spanish)  
Frequently Asked Questions on the Emergency Use Authorization for sotrovimab  
GSK’s Detailed Guide for the Use of Sotrovimab Under Emergency Use Authorization  
FDA Letter revoking the EUA for Bamlanivimab Administered Alone  
Centers for Medicare & Medicaid Services (CMS) Monoclonal Antibody COVID-19 Infusion Guidance  
National Infusion Center Association (NICA) COVID-19 Antibody Therapies Resource Center  
HHS COMBAT COVID Website

For more information, please contact Tim Davis (tim.davis@dhhs.nc.gov).