



NC DEPARTMENT OF
**HEALTH AND
HUMAN SERVICES**

Interim Guidance for the Use of Monoclonal Antibodies for Treatment of COVID-19

Posted January 15, 2021, Updated September 21, 2021

Monoclonal antibodies (mAbs) 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.

If you are interested in receiving mAbs updates from NCDHHS, please provide the requested information in [this form](#).

Becoming a Monoclonal Antibody Provider

If you would like to become a new monoclonal antibody provider, or are a current provider and have yet to register with AmerisourceBergen (ABC), please first fill out the following survey: [New mAb Provider Registration Information \(state.nc.us\)](#). In addition to filling out the survey, you will have to complete an LOA form, which will be requested from ABC directly. Once we have received your information from the survey, and ABC has received the LOA form, we will work with ABC to have your location registered and able to receive shipment.

Key Facts

- **As of August 27, 2021, the FDA has opened the use and distribution of Bamlanivimab and Etesevimab. Please see the [EUA](#) for more guidance.**
- 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
- 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.
- Quantities of Bamlanivimab/Etesevimab and Casirivimab/Imdevimab have been purchased by the federal government and are available to NC providers at no product cost.
- Providers can bill third party payors including Medicare and Medicaid for the administration fee associated with monoclonal antibody treatment.

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)
- 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> 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

REGEN-COV™ (Casirivimab and Imdevimab)

On November 21, 2020 the FDA [issued an EUA](#) for REGEN-COV™ 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-COV™ 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-COV™ Fact Sheet for Healthcare Providers](#). In June of 2021, the FDA updated the REGEN-COV™ EUA to include the authorization for a subcutaneous route of administration as an alternative for those who cannot receive intravenous infusion. Currently, REGEN-COV™ is the only monoclonal antibody for COVID-19 authorized to be administered subcutaneously.

Bamlanivimab and Etesevimab

On February 9, 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 [FDA-authorized Bamlanivimab and Etesevimab Fact Sheet for Healthcare Providers](#).

Sotrovimab

On May 26, 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.

Requesting Monoclonal Antibody Products in North Carolina

Allocation and distribution of REGEN-COV™ and Bamlanivimab and Etesevimab were previously controlled by the United States Department of Health and Human Services (US HHS). On September 13, the federal government shifted this to a state allocation process. The State receives a top-line allocation based on cases, hospitalizations and then adjusted based on reported utilization/inventory to suballocate to providers. This change was made not due to a supply shortage, but to ensure distribution across the nation. Since February 2021, US HHS has determined that supply of these products is no longer scarce. **Any interested provider, who can meet the requirements of the EUA, can order product as needed from the State of North Carolina using [this form](#).**

Please review the ordering timeline below to ensure that you submit your mAbs request using the State’s allocation request form in a timely manner to receive shipments for your location’s administration needs the following week. For the latest mAbs ordering process and guidelines, please review the [mAbs requesting guidance](#).

Order Request Deadline	Ordering Date	Doses Delivered*
Wednesdays at 12 PM	Fridays	The following Tuesday, dependent upon AmerisourceBergen

**This is an estimate based on information from AmerisourceBergen. The State does not have any control over order shipping.*

Once NCDHHS has reviewed all requests and placed orders, providers will be informed of the status of their request by email. The State will indicate if orders have been confirmed or denied and how much product was ordered, if any. Exact delivery dates will be determined by AmerisourceBergen and are not within the control of the State. Sites will receive an email from the shipper when the product is picked up from AmerisourceBergen. This email will have a tracking number, which will serve as the best source of information to estimate arrival.

Reporting Monoclonal Antibody Utilization

Providers receiving and administering REGEN-COV™ 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.

All mAb administrations must be reported via HHS tele-tracking (or the State for some hospitals) **every week by noon on Wednesdays**. In the future, utilization as reported to HHS tele-tracking or through the state for some hospitals will be required to receive an allocation. In addition, reported use will need to exceed 70% of your previous allocation to receive allocation the next week. 70% is the required

utilization rate the federal government has set for states to meet in order to avoid allocation decreases due to lack of utilization. We are seeking clarity on the necessary reporting steps when mAbs is transferred between providers. At this time, the provider that transfers mAbs OUT should indicate that transfer amount as used when reporting.

Sotrovimab distribution is NOT controlled by the federal or state governments. 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.

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:

[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 Angel Callicutt (Angel.Callicutt@dhhs.nc.gov)