



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

(Posted January 15, 2021; Updated March 31, 2021)

Monoclonal antibodies are proteins made by immune cells in response to pathogens. They work by binding to viral targets that are used to enter cells and inhibit infection. Patients who are hospitalized with COVID-19 have been found to have high viral loads and thus, monoclonal antibodies were developed to reduce viral burden based on the hypothesis that reducing the amount of virus would lead to clinical improvement.

Key Facts

- There are three products that have currently received emergency use authorization (EUA) from the FDA for the treatment of mild to moderate COVID-19.
 - Eli Lilly's Bamlanivimab - a single antibody therapy
 - Eli Lilly's Bamlanivimab/Etesevimab combination therapy
 - Regeneron's REGN-COV2 (Casirivimab/Imdevimab) combination therapy
- Current available data shows that bamlanivimab administered alone may not be effective against several SARS-CoV-2 variants consistently increasing in prevalence in the United States. Given this information, it is currently recommended that providers consider the use of alternative authorized monoclonal antibody therapies that are expected to retain activity against these circulating variants.
- All three products are administered via intravenous infusion followed by continued observation for one hour afterwards, with an estimated real-world treatment time of two to three hours.
- All three products are 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 at high risk for progressing to severe COVID-19 and/or hospitalization.
- Anyone 65 years or older with mild to moderate COVID-19 (i.e. not hospitalized and not requiring oxygen due to COVID-19) is considered high risk for progression to severe COVID-19 per the EUA. Thus, monoclonal antibody therapies may be especially useful for skilled nursing and assisted living facilities.
- 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.
- Monoclonal antibody therapies for COVID-19 have been purchased by the federal government and are available to NC providers at no cost through the contracted distributor AmerisourceBergen.

- Providers can bill Medicare for the administration fee associated with monoclonal antibody infusions.

FDA Emergency Use Authorization (EUA)

The FDA has issued EUA for monoclonal antibody therapies for use in high-risk outpatients with COVID-19. Bamlanivimab, bamlanivimab/etesevimab, and casirivimab/imdevimab are monoclonal antibody therapies that work directly to neutralize the SARS-CoV-2 virus in the body and may decrease the incidence of ED visits and hospitalizations in patients at greatest risk for progression to severe disease. Under the EUA, **eligible patients are outpatients with mild and moderate COVID-19 with no more than 10 days of symptoms, and the therapies should be administered as soon as possible after positive viral test for COVID-19. These patients must be at high-risk for progressing to severe COVID-19 and/or hospitalization due to age, elevated BMI, or specified chronic conditions (definitions [here](#), [here](#) and [here](#), respectively)**. Notably, the EUA is not an approval but a determination that potential benefits outweigh potential risks. Also, given low numbers of clinical events in Phase 2 trials done thus far, both the degree of benefit and who would benefit the most is not certain.

The Therapies

1. Bamlanivimab

Note: Bamlanivimab is not currently recommended based on concerns about effectiveness against currently circulating variants. See “Monoclonal Antibodies and SARS-CoV-2 Variants” section below.

On November 9th, 2020 the FDA [issued an EUA](#) for bamlanivimab, which is manufactured by Lilly. Bamlanivimab is a neutralizing monoclonal antibody that binds to the receptor binding domain of the spike protein of SARS-CoV-2. The EUA was based on an interim analysis from the BLAZE-1 phase 2 randomized, double-blind, placebo-controlled clinical trial in 465 non-hospitalized adults with mild to moderate COVID-19 symptoms. For patients at high risk for disease progression, hospitalizations and emergency room visits occurred in 3% of bamlanivimab-treated patients on average compared to 10% in placebo-treated patients.” The safety in the antibody group was similar to the placebo group. The published NEJM research paper is found [here](#).

2. Casirivimab and Imdevimab (REGEN-COV™)

On November 21st, 2020 the FDA [issued an EUA](#) for casirivimab and imdevimab, which is manufactured by Regeneron and is given as a single infusion. 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. The EUA was based on an interim analysis of Phase 1/2 randomized, double-blinded, placebo-controlled trial in 799 non-hospitalized adults with mild to moderate COVID-19 symptoms. Per the EUA: “For patients at high risk for disease progression, hospitalizations and emergency room visits occurred in 3% of casirivimab and imdevimab-treated patients on average compared to 9% in placebo-treated patients.” The

safety in the antibody group was similar to the placebo group. The published NEJM research paper is found [here](#).

3. 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 3, randomized, double-blind, placebo-controlled trial in 1,035 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 a 70% reduction of hospitalization or death in the bamlanivimab/etesevimab group when compared to placebo. The safety in the antibody group was similar to the placebo group. Clinical trial data can be found in the EUA documentation [here](#).

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 three monoclonal antibody products currently authorized for use ([bamlanivimab](#), [bamlanivimab with etesevimab](#), and [casirivimab with imdevimab](#)). The updated fact sheets now 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.

Current available data shows that bamlanivimab administered alone may not be effective against several SARS-CoV-2 variants consistently increasing in prevalence in the United States. Given this information, it is currently recommended that providers consider the use of alternative authorized monoclonal antibody therapies that are expected to retain activity against these circulating variants. Alternatives currently authorized include the combination therapies bamlanivimab/etesevimab and casirivimab/imdevimab. Using an alternative authorized monoclonal antibody therapy may reduce the risk of treatment failure should a patient be infected with a SARS-CoV-2 viral variant that is resistant to bamlanivimab alone.

Obtaining Monoclonal Antibody Products in North Carolina

Allocation and distribution of COVID-19 monoclonal antibody products are controlled by the United States Department of Health and Human Services (US HHS). As of February 19th, US HHS has moved to a direct ordering process for acquiring monoclonal antibodies. **Any interested provider, who can meet**

the requirements of the EUA, can order product as needed directly from AmerisourceBergen using this special form: <https://app.smartsheet.com/b/form/255d164d67834793b4ab549e160941e8>.

As of March 24th, 2021, US HHS has ceased distribution of bamlanivimab alone. This is due to the sustained increase of SARS-CoV-2 viral variants in the United States that are resistant to bamlanivimab administered alone. The combination products casirivimab/imdevimab and bamlanivimab/etesevimab are expected to retain activity against these variants and will remain available for distribution to providers. Providers can also order etesevimab alone to be paired with their existing bamlanivimab inventory to be administered as the authorized combination therapy. Etesevimab is not authorized to be administered alone for the treatment of COVID-19.

Providers receiving and administering COVID-19 monoclonal antibody therapeutics are required to report inventory and administration data 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 is using to collect inventory reports.

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 Initiative

US HHS has also implemented a program at the federal level called Special Projects for Equitable and Efficient Distribution (SPEED). The goal of the SPEED initiative is to assist states in identifying non-hospital facilities that serve priority populations such as nursing homes, dialysis centers and Federally Qualified Health Centers (FQHCs). Through SPEED, providers who serve these priority populations were eligible for their own direct allocation of monoclonal antibodies from the federal government. SPEED providers are now being transitioned to the direct ordering process described above. Providers seeking more information about the SPEED program should visit:

<https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Pages/SPEED.aspx>.

Additional Resources:

[Bamlanivimab EUA Fact Sheet for Health Care Providers](#)

[Bamlanivimab EUA Fact Sheet for Patients, Parents and Caregivers](#)

[Frequently Asked Questions on the Emergency Use Authorization for Bamlanivimab](#)

[HHS ASPR's Bamlanivimab website](#)

[Casirivimab/Imdevimab EUA Fact Sheet for Health Care Providers](#)

[Casirivimab/Imdevimab EUA Fact Sheet for Patients, Parents and Caregivers](#)

[Frequently Asked Questions on the Emergency Use Authorization for Casirivimab/Imdevimab](#)

[HHS ASPR's Casirivimab/Imdevimab website](#)

[Bamlanivimab/Etesevimab EUA Fact Sheet for Health Care Providers](#)

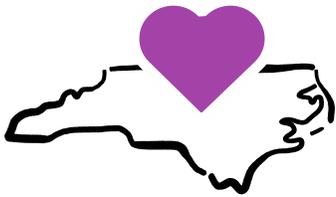
[Bamlanivimab/Etesevimab EUA Fact Sheet for Patients, Parents and Caregivers](#)

[Frequently Asked Questions on the Emergency Use Authorization for bamlanivimab/etesevimab](#)

[Centers for Medicare & Medicaid Services \(CMS\) Monoclonal Antibody COVID-19 Infusion Guidance](#)

[National Infusion Center Association COVID-19 Antibody Therapies Resource Center](#)

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



#StayStrongNC

**Staying apart brings us together.
Protect your family and neighbors.**

Learn more at nc.gov/covid19.



NC DEPARTMENT OF
**HEALTH AND
HUMAN SERVICES**