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Health Alert:

Concerns re: the Use of Bamlanivimab Monotherapy in the Setting of SARS-CoV2 Variants

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Bamlanivimab is an investigational monoclonal antibody product that received emergency use authorization (EUA) from the U.S. Food and Drug Administration (FDA) in November 2020 for the treatment of mild-to-moderate COVID-19 in non-hospitalized adult and pediatric patients who are at high risk for progression to severe disease.

The California Department of Public Health recommends facilities and providers stop administering bamlanivimab monotherapy in California. Below is updated information regarding federal concerns of decreased clinical effectiveness for bamlanivimab monotherapy in the setting of emerging SARS-CoV2 variants. This notice also includes information on alternative monoclonal antibody products that are still authorized for use and how to acquire these products.

1. Update re: bamlanivimab monotherapy in the setting of SARS-CoV2 variants

The federal government recently shared concerns regarding the use of bamlanivimab monotherapy in regions where the SARS-CoV2 mutation L452R found in B.1.429/B.1.427 lineages (a.k.a. 20C/CAL.20C) is circulating in high numbers. Given these concerns that the clinical activity of bamlanivimab monotherapy is impacted by this variant and therefore may be less effective, the Health and Human Services Office of the Assistant Secretary for Preparedness and Response (HHS/ASPR) has stopped the distribution of this product to California.

Additionally, the FDA has released revised fact sheets for health care providers, which now include information on susceptibility of SARS-CoV2 variants to each of the monoclonal antibody therapies that are available through an EUA for the treatment of COVID-19. The revised fact sheet for bamlanivimab monotherapy can be found here:

- [Fact Sheet For Health Care Providers Emergency Use Authorization \(EUA\) Of Bamlanivimab \(fda.gov\)](https://www.fda.gov/oc/2021/03/19/fact-sheet-for-health-care-providers-emergency-use-authorization-eua-of-bamlanivimab)

Per the revised fact sheet, bamlanivimab monotherapy is unlikely to be active against the B.1.429/B.1.427 variant, which is circulating in relatively high numbers in California. Health care providers should review the Antiviral Resistance Information in Section 15 of this fact sheet for details regarding specific variants and resistance. For more information regarding variants in



California, please refer to the Centers for Disease Control and Prevention (CDC) website ([Variant Proportions in the U.S. | CDC](#)) as well as the California Department of Public Health website ([Tracking Variants \(ca.gov\)](#)).

While HHS/ASPR is working with the CDC, the National Institutes of Health, and the FDA on recommendations for bamlanivimab monotherapy moving forward, **the California Department of Public Health recommends facilities and providers stop administering bamlanivimab monotherapy in California.** We will continue to update our stakeholders with any new recommendations.

Note that this recommendation only applies to the administration of bamlanivimab monotherapy at this time. The use of the alternative authorized monoclonal antibodies – (1) bamlanivimab plus etesevimab and (2) casirivimab plus imdevimab – that are expected to retain activity against circulating viral variants may reduce the potential risk of treatment failure should a patient be infected with a SARS-CoV-2 viral variant that is resistant to bamlanivimab alone. Antiviral resistance information can be found in the fact sheets for health care providers for these other two authorized monoclonal antibody products. Health care providers should review the Antiviral Resistance Information in Section 15 of these fact sheets for details regarding specific variants and resistance.

- [Fact Sheet For Health Care Providers Emergency Use Authorization \(EUA\) Of Bamlanivimab And Etesevimab \(fda.gov\)](#)
- [Fact Sheet For Health Care Providers Emergency Use Authorization \(EUA\) Of Regen-Cov™ \(Casirivimab With Imdevimab\) \(fda.gov\)](#)

2. New EUA for monoclonal antibody combination bamlanivimab plus etesevimab

On February 9, the FDA issued an EUA for bamlanivimab and etesevimab administered together for the treatment of mild to moderate COVID-19 in adults and pediatric patients who test positive for SARS-CoV-2 and who are at high risk for progressing to severe COVID-19.

Phase 3 data of the BLAZE-1 trial showed subjects treated with bamlanivimab plus etesevimab had a 70% relative reduction in hospitalizations or death compared to placebo.

This combination product is available via direct ordering (see #3 below for more information).

Additional resources:

- [Fact Sheet For Health Care Providers Emergency Use Authorization \(EUA\) Of Bamlanivimab And Etesevimab \(fda.gov\)](#)

- [Bamlanivimab and Etesevimab EUA Letter of Authorization February 9 2021](#)
- [Bamlanivimab plus Etesevimab FDA press release](#)
- [Bamlanivimab plus Etesevimab FDA FAQs](#)
- [Effect of Bamlanivimab as Monotherapy or in Combination With Etesevimab on Viral Load in Patients With Mild to Moderate COVID-19: A Randomized Clinical Trial | Global Health | JAMA | JAMA Network](#)

3. Direct ordering of monoclonal antibodies

Bamlanivimab plus etesevimab, and casirivimab plus imdevimab, are available for direct ordering from AmeriSource Bergen Corporation (ABC).

All treatment sites can now order these products directly from ABC. The products remain free of charge to requesting sites. Treatment sites should review the [direct ordering process guide](#) and place orders directly with ABC at this [site](#).

The products available for direct ordering include bamlanivimab plus etesevimab, casirivimab plus imdevimab, and etesevimab.

- Note that etesevimab is only authorized for use in combination with bamlanivimab but can be ordered by itself to be combined with any bamlanivimab stock a facility already has on-hand.

Should you have any questions or concerns regarding the direct order process for COVID-19 monoclonal antibodies, you may contact HHS/ASPR at COVID19Therapeutics@hhs.gov or ABC at C19therapies@amerisourcebergen.com.

In addition to the above direct ordering process, both bamlanivimab and casirivimab/imdevimab are readily available from the California Department of Public Health (CDPH). Contact your county's Medical and Health Operational Area Coordinator (MHOAC) to request either of these products from CDPH.

- **Note that bamlanivimab monotherapy is not recommended by CDPH for treatment of COVID-19 (see #1 above).** However, under its EUA, bamlanivimab can be combined with etesevimab for the treatment of mild-to-moderate COVID-19 in those patients at high risk for progressing to severe disease. See the [Bamlanivimab plus Etesevimab EUA Fact Sheet for Providers](#) for more information.

For facilities and healthcare providers interested in setting up infusions for high-risk patients with COVID-19, ASPR has many [resources available](#). This includes [free digital content](#) that your

facility can use on social media platforms to help educate providers and patients. HHS has also provided [CombatCovid.HHS.gov](https://www.combatcovid.hhs.gov) as a resource for your patients.

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