

The COVID-19 Treatment Guidelines Panel's Statement on the Emergency Use Authorization of Bamlanivimab Plus Etesevimab as Post-Exposure Prophylaxis for SARS-CoV-2 Infection

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Vaccination remains the most effective way to prevent SARS-CoV-2 infection. However, despite widespread availability of SARS-CoV-2 vaccines, a number of individuals are either not fully vaccinated or cannot mount adequate responses to the vaccine. Some of these people, if infected, are at high risk of progression to serious COVID-19. On September 16, 2021, the Food and Drug Administration (FDA) expanded the Emergency Use Authorization (EUA) indication for the anti-SARS-CoV-2 monoclonal antibodies (mAbs) bamlanivimab plus etesevimab to allow this combination to be used as post-exposure prophylaxis (PEP) for selected individuals, as described below.¹ Casirivimab plus imdevimab can also be used for this indication (see the [Panel's statement on using casirivimab plus imdevimab as PEP](#)).

The authorized dosage is bamlanivimab 700 mg plus etesevimab 1,400 mg administered as a single intravenous (IV) infusion (for a list of individuals who are considered to be at high risk of progressing to severe COVID-19, see the [FDA EUA](#)). Bamlanivimab plus etesevimab should be administered as soon as possible after exposure.

Summary Recommendations and Considerations

Recommendation for Individuals With Symptoms That Are Consistent With COVID-19

- The COVID-19 Treatment Guidelines Panel (the Panel) recommends that individuals who have recently been exposed to SARS-CoV-2 and have symptoms that are consistent with COVID-19 be evaluated for SARS-CoV-2 infection by either a nucleic acid amplification test (NAAT) or an antigen test **(AIII)**.
- Individuals with positive SARS-CoV-2 NAAT or antigen test results who meet the Food and Drug Administration (FDA) Emergency Use Authorization (EUA) criteria for therapeutic use of anti-SARS-CoV-2 monoclonal antibodies should be referred for treatment (see [Anti-SARS-CoV-2 Monoclonal Antibodies](#)).
- Those with negative test results should be considered for post-exposure prophylaxis (PEP) as discussed below.

Recommendations for Post-Exposure Prophylaxis

- Based on the EUA, the Panel recommends using **bamlanivimab 700 mg plus etesevimab 1,400 mg** administered as an intravenous (IV) infusion **(BIII)** as PEP for people who are at high risk for progression to severe COVID-19 if infected with SARS-CoV-2^a **AND** who have the following vaccination status **AND** exposure history.

Vaccination Status:

- Not fully vaccinated (defined as people who were never vaccinated or those who received the second vaccine dose in a two-dose series or a single-dose vaccine <2 weeks ago); *or*
- Fully vaccinated, but not expected to mount an adequate immune response (e.g., those with immunocompromising conditions, including those who are taking immunosuppressive medications)

AND

Exposure History to SARS-CoV-2:

- Recent exposure to an individual with SARS-CoV-2 infection that is consistent with the Centers for Disease Control and Prevention (CDC) close contact criteria;^b *or*
 - At high risk of exposure to an individual with SARS-CoV-2 infection because of recent occurrence of SARS-CoV-2 infection in other individuals in the same institutional setting (e.g., nursing homes, prisons)
- The doses should be administered as soon as possible and preferably within 7 days of high-risk exposure **(BIII)**.
 - Bamlanivimab 700 mg plus etesevimab 1,400 mg is administered as a single IV infusion. Patients should be monitored for at least 1 hour after the infusion is complete.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

^a For a list of individuals who are considered to be at high risk of progressing to severe COVID-19, see the [FDA EUA](#). It should be noted that the relative risk **is not identical** for all risk factors listed in the EUA. The presence of multiple risk factors in an individual is associated with a higher risk of progression. Providers should use clinical judgement when determining a patient's risk of progression.

^b For the CDC definition of close contact, visit the [CDC Glossary of Key Terms](#).

Rationale

The COVID-19 Treatment Guidelines Panel's (the Panel) recommendations for the use of bamlanivimab plus etesevimab for PEP are based on the EUA indication.¹ BLAZE-2, a Phase 3, randomized, placebo-controlled trial, is currently the only clinical trial that has used one of these drugs for PEP.² It enrolled residents and staff of skilled nursing or assisted living facilities where there was at least one confirmed index case of SARS-CoV-2 infection. The study included a regimen and a study population that were distinct from those authorized through the EUA, which accounts for the Panel's rating for the recommendation for using this therapy for PEP.

The differences between the clinical trial and the EUA include the following:

- The clinical trial studied bamlanivimab monotherapy at a single dose of 4,200 mg. The EUA calls for administering the combination of bamlanivimab 700 mg plus etesevimab 1,400 mg as a single IV infusion; this dose for the combination received an EUA for the treatment of nonhospitalized patients with mild to moderate COVID-19.
- The clinical trial enrolled residents and staff of skilled nursing and assisted living facilities with at least one confirmed SARS-CoV-2 index case. It is worth noting that a statistically significant benefit for bamlanivimab monotherapy was only seen amongst the residents and not the staff.
- The clinical trial did not consider the type of exposure, which is a key criterion in the EUA.
- The clinical trial enrolled participants at a time when the predominant SARS-CoV-2 variants circulating in the United States were susceptible to bamlanivimab. Currently, most of the predominant circulating variants are not susceptible to bamlanivimab, but they do retain in vitro susceptibility to etesevimab (see [Anti-SARS-CoV-2 Monoclonal Antibodies](#)).

Clinical Trial Data on Bamlanivimab as Post-Exposure Prophylaxis

The updated EUA expanded the indication to allow bamlanivimab 700 mg plus etesevimab 1,400 mg to be administered as an IV infusion for PEP in individuals who are at high risk for progressing to severe disease if infected with SARS-CoV-2 **AND** who have a specific exposure history **AND** vaccine status.¹ The only clinical trial that supports the use of either of these mAbs for PEP is BLAZE-2.

BLAZE-2 enrolled residents and staff of 74 skilled nursing and assisted living facilities who were at least 18 years of age and who had no known history of COVID-19. Participants were enrolled within 7 days of at least one confirmed SARS-CoV-2 case at their facility. All participants provided both nasal and nasopharyngeal (NP) swabs for reverse transcriptase polymerase chain reaction (RT-PCR)-based diagnostic tests and blood for SARS-CoV-2 antibody testing. Nasal and NP swabs were obtained weekly for 57 days.

Participants who were ultimately found to be RT-PCR and antibody negative were considered the

prevention population. The safety population included those who received bamlanivimab or placebo regardless of their RT-PCR or antibody status. There were 1,175 participants who were randomized 1:1 to receive either the study drug or placebo between August and November 2020. The prevention population included 484 participants who received bamlanivimab (323 staff and 161 residents) and 482 participants who received placebo (343 staff and 139 residents). The baseline characteristics of the staff and resident populations were very different; for example, the residents had a median age that was >30 years higher than the staff (76 years vs. 43 years), and the residents had greater risks for disease progression.

In the overall prevention population, 114 participants (11.9%) experienced mild or worse COVID-19 by Day 57. There was a significantly lower incidence of mild or worse COVID-19 in the bamlanivimab arm than in the placebo arm (8.5% vs. 15.2%; OR 0.43; 95% CI, 0.28–0.68; $P < 0.001$), with an absolute risk difference of -6.6 percentage points (95% CI, -10.7 to -2.6). The difference was most significant in the resident population, where the incidence of mild or worse COVID-19 was 8.8% in the bamlanivimab arm compared to 22.5% in the placebo arm (OR 0.20; 95% CI, 0.08–0.49; $P < 0.001$), with an absolute difference of -13.7 percentage points (95% CI, -21.9 to -5.4). In contrast, the difference between the bamlanivimab and placebo arms did not achieve statistical significance in the staff prevention population, with 8.4% of participants experiencing mild or worse COVID-19 in the bamlanivimab arm compared to 12.2% in the placebo arm (OR 0.58; 95% CI, 0.33–1.02; $P = 0.06$). The absolute difference between the arms was -3.8 percentage points (95% CI, -8.4 to 0.8). Similar findings were observed for the secondary endpoint of the incidence of moderate or worse COVID-19.

In the prevention population, 198 participants (20.6%) had positive RT-PCR results within 4 weeks of randomization. The frequency of positive results was significantly lower in the bamlanivimab arm than in the placebo arm (17.9% vs. 23.3%; OR 0.66; 95% CI, 0.46–0.94; $P = 0.02$), with an absolute risk difference of -5.4 percentage points (95% CI, -10.5 to -0.3). The difference was significant for the resident prevention population but not the staff prevention population. An additional secondary endpoint in this study was mortality due to COVID-19; a total of four participants died, all of whom were residents who were randomized to receive placebo.

The overall safety population included 1,175 participants. Serious adverse events were reported in 3.7% of bamlanivimab recipients and 3.2% of placebo recipients. Any adverse events were reported in 20.1% of participants in the bamlanivimab arm and 18.9% of those in the placebo arm. The types of events were balanced across the study arms. Hypersensitivity reactions that occurred within 24 hours of study product infusion were reported in three participants (0.5%) in the bamlanivimab arm and none in the placebo arm.

Considerations in Pregnant and Lactating People

Anti-SARS-CoV-2 mAbs as PEP should not be withheld from pregnant or lactating individuals who have been exposed to SARS-CoV-2, especially those with additional conditions that increase their risk of progressing to severe disease. Pregnant or lactating patients and their providers should determine whether the potential benefits of the drugs outweigh the potential risks.

Considerations in Children

The BLAZE-2 trial did not include those aged <18 years. The rate of severe COVID-19 in the general adolescent population is lower than the rate of severe disease in adults. Therefore, there is insufficient evidence to recommend the routine use of mAbs as PEP in pediatric patients. Certain high-risk populations, such as those who are highly immunocompromised or those who are unvaccinated and have multiple comorbidities and medical-related technological dependence, may benefit from PEP in the setting of high-risk SARS-CoV-2 exposure (e.g., exposure from a household contact, prolonged indoor

exposure without masks), and the use of bamlanivimab plus etesevimab could be considered for these patients on a case-by-case basis.

References

1. Food and Drug Administration. Fact sheet for healthcare providers: emergency use authorization (EUA) of bamlanivimab and etesevimab. 2021. Available at: <https://www.fda.gov/media/145802/download>. Accessed February 17, 2021.
2. Cohen MS, Nirula A, Mulligan MJ, et al. Effect of bamlanivimab vs placebo on incidence of COVID-19 among residents and staff of skilled nursing and assisted living facilities: a randomized clinical trial. *JAMA*. 2021;326(1):46-55. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/34081073>.