The Medical Letter®

on Drugs and Therapeutics

Volume 63 October 18, 2021

ISSUE No. 1635

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The Medical Letter®
on Drugs and Therapeutics

Volume 63 (Issue 1635) October 18, 2021

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Bamlanivimab and Etesevimab for Post-Exposure Prophylaxis of COVID-19

Revised 1/6/2022: The Variants paragraph has been updated. See also COVID-19 Updates.

In February 2021, the FDA issued an Emergency Use Authorization (EUA) for the investigational monoclonal antibodies bamlanivimab and etesevimab (Lilly) for use together to treat mild to moderate COVID-19 in persons ≥12 years old who weigh ≥40 kg and are at high risk of progression to severe disease or hospitalization.[1] The FDA has now expanded this EUA to allow use of the antibodies together for post-exposure prophylaxis of COVID-19 in such persons if they are not fully vaccinated against COVID-19 or are unlikely to have an adequate immune response to full vaccination and have been in close contact with a SARS-CoV-2-infected individual or are likely to be exposed to SARS-CoV-2 in the setting of an institutional outbreak (see Table 1).[2] Bamlanivimab plus etesevimab is the second monoclonal antibody combination to receive an EUA for post-exposure prophylaxis of COVID-19; casirivimab plus imdevimab *(REGEN-COV)* was authorized earlier.[3]

ELIGIBILITY — In May 2021, the FDA expanded the criteria by which a patient with COVID-19 can be considered at high risk for disease progression. All persons ≥12 years old who are overweight, pregnant, or have cardiovascular disease, hypertension, or chronic respiratory disease are now considered high-risk (see Table 2).[4]

Table 1. Indications for Post-Exposure Prophylaxis of COVID-19 with Bamlanivimab plus Etesevimab[1]

- Age ≥12 years and weight ≥40 kg

AND

- Considered at high risk for progression to severe COVID-19, including hospitalization or death (see Table 2)

AND

- Not fully vaccinated against COVID-19 (has not received 2 doses of the Pfizer/BioNTech or Moderna vaccines or one dose of the Johnson & Johnson vaccine ≥2 weeks previously) **OR** unlikely to mount an adequate immune response to vaccination (immunocompromised)

AND

- Exposed to a SARS-CoV-2-infected individual consistent with CDC close contact criteria[2] **OR** at high risk of exposure because of occurrence of SARS-CoV-2 infection among other individuals in the same institutional setting (e.g., nursing home, prison)

1. FDA. Fact sheet for health care providers. Emergency Use Authorization (EUA) of bamlanivimab and etesevimab. September 16, 2021. Available at: https://bit.ly/3qfS6DN. Accessed September 30, 2021.
2. CDC. COVID-19. Contact tracing. Case investigation and contact tracing guidance. Appendices. September 21, 2021. Available at: https://bit.ly/3CfNDaA. Accessed September 30, 2021.

Table 2. High-Risk Conditions for COVID-19 Progression[1]

- Age ≥65 years
- BMI ≥25 kg/m² (or, in patients 12-17 years old, BMI ≥85th percentile for age and gender[2])
- Pregnancy
- Chronic kidney disease
- Diabetes
- Cardiovascular disease
- Hypertension
- COPD, moderate to severe asthma, or other chronic respiratory disease
- Immunosuppressive disease or currently receiving immunosuppressive treatment
- Sickle cell disease
- Congenital or acquired heart disease
- Neurodevelopmental disorders (e.g., cerebral palsy) or other conditions that confer medical complexity
- A medical-related technological dependence (e.g., tracheostomy, gastrostomy, or positive pressure ventilation [not related to COVID-19])

BMI = body mass index; COPD = chronic obstructive pulmonary disease

1. Adult and pediatric patients (≥12 years old and weighing ≥40 kg) with ≥1 of the criteria listed are considered at high risk for progressing to severe COVID-19 or hospitalization. (FDA. Fact sheet for health care providers. Emergency Use Authorization [EUA] of bamlanivimab and etesevimab. September 16, 2021. Available at: https://bit.ly/3qfS6DN. Accessed September 30, 2021).
2. Based on CDC growth charts. Available at: https://bit.ly/36U0twf. Accessed September 30, 2021.

CLINICAL STUDIES — In an unpublished double-blind trial (BLAZE-2 Part 1; summarized in the FDA Fact Sheet), 966 SARS-CoV-2-negative residents or staff of skilled nursing facilities where a confirmed SARS-CoV-2 infection occurred were randomized to receive a single dose of bamlanivimab 2800 mg (without etesevimab) or placebo.

The risk of symptomatic COVID-19 within 8 weeks of randomization, the primary endpoint, was significantly lower in patients who received bamlanivimab than in those who received placebo in both the overall population (8.5% vs 15.2%; number needed to treat [NNT] 15.1; adjusted OR 0.43 [95% CI 0.28-0.68]) and the prespecified subgroup of nursing facility resi-

dents (8.9% vs 22.5%; NNT 7.4; adjusted OR 0.20 [95% CI 0.08-0.49]). There were no deaths due to COVID-19 in the bamlanivimab group versus 4 in the placebo group.[2,5]

No data on the use of bamlanivimab plus etesevimab for post-exposure prophylaxis of COVID-19 are available. Because the combination has greater antiviral activity than bamlanivimab alone, the FDA presumed it to be effective based on the results of BLAZE-2 Part 1. No clinical trials have compared bamlanivimab plus etesevimab with casirivimab plus imdevimab.

ADVERSE EFFECTS — Infusion-related reactions and anaphylaxis have been reported with use of bamlanivimab plus etesevimab.

VARIANTS — Bamlanivimab plus etesevimab is not active against the Omicron variant of SARS-CoV-2. The combination retains activity against the Delta variant of the virus.[2]

DOSAGE AND ADMINISTRATION — The authorized dosage of bamlanivimab plus etesevimab for post-exposure prophylaxis is 700 mg of bamlanivimab and 1400 mg of etesevimab given as a single IV infusion as soon as possible after exposure to SARS-CoV-2. Patients should be monitored during the infusion and for at least 1 hour after its completion. Unlike *REGEN-COV*, bamlanivimab and etesevimab cannot be given by subcutaneous injection. Detailed instructions on preparation and administration of the antibodies are available in the FDA Fact Sheet.[2]

CONCLUSION — The FDA has authorized administration of the monoclonal antibodies bamlanivimab and etesevimab together for IV post-exposure prophylaxis of COVID-19 in certain high-risk persons. In a double-blind trial in SARS-CoV-2-negative residents and staff of nursing facilities in which a confirmed infection occurred, IV infusion of bamlanivimab alone significantly decreased the risk of symptomatic COVID-19 compared to placebo. The overall effectiveness of the two antibodies together for post-exposure prophylaxis remains to be determined. Bamlanivimab plus etesevimab retains efficacy against the Delta variant of SARS-CoV-2. ■

1. An EUA for bamlanivimab and etesevimab for COVID-19. Med Lett Drugs Ther 2021; 63:49.
2. FDA. Fact sheet for health care providers. Emergency Use Authorization (EUA) of bamlanivimab and etesevimab. December 22, 2021. Available at: https://bit.ly/3qfS6DN. Accessed January 6, 2022.
3. Casirivimab and imdevimab (REGEN-COV) for post-exposure prophylaxis of COVID-19. Med Lett Drugs Ther 2021; 63:130.
4. FDA News Release. Coronavirus (COVID-19) update: May 21, 2021. Available at: https://bit.ly/3fFoEUB. Accessed September 30, 2021.
5. Lilly. What is the effect of bamlanivimab and etesevimab prevention treatment on COVID-19 symptoms? Medical information request response, September 23, 2021.

The Medical Letter®
on Drugs and Therapeutics

Volume 64 (Issue 1642) January 24, 2022

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COVID-19 UPDATES

Pfizer-BioNTech COVID-19 Vaccine

On January 3, the FDA amended its Emergency Use Authorization (EUA) for the Pfizer-BioNTech COVID-19 vaccine *(Comirnaty)* to incorporate the following changes:

1. A third primary dose of the vaccine can now be given ≥28 days after the second to children 5-11 years old who have undergone solid organ transplantation or have an equivalent level of immune compromise.[1,2]
2. Booster doses of the vaccine are now authorized for use in children 12-15 years old.[1,3]
3. The length of time after completion of a primary series with the vaccine at which patients become eligible for booster immunization has been reduced from 6 months to 5 months.[1,3]

On January 7, the FDA amended the EUA of the Moderna COVID-19 vaccine to shorten the interval between completion of a primary series and receipt of a booster dose from 6 months to 5 months.[4]

Booster Schedules – Patients can now receive a booster dose of a COVID-19 vaccine 5 months after completion of a primary series with the Pfizer-BioNTech or Moderna vaccine or 2 months after receiving a primary dose of the Johnson & Johnson/Janssen vaccine. ■

1. FDA News Release. Coronavirus (COVID-19) update: FDA takes multiple actions to expand use of Pfizer-BioNTech COVID-19 vaccine. January 3, 2022. Available at: https://bit.ly/3qVaN18. Accessed January 6, 2022.
2. FDA. Fact sheet for health care providers administering vaccine (vaccination providers). Emergency Use Authorization (EUA) of the Pfizer-BioNTech COVID-19 vaccine to prevent coronavirus disease 2019 (COVID-19). For 5-11 years of age. January 3, 2022. Available at: https://bit.ly/3jX9xri. Accessed January 6, 2022.
3. FDA. Fact sheet for health care providers administering vaccine (vaccination providers). Emergency Use Authorization (EUA) of the Pfizer-BioNTech COVID-19 vaccine to prevent coronavirus disease 2019 (COVID-19). For 12 years of age and older. January 3, 2022. Available at: https://bit.ly/3bBH5GV. Accessed January 6, 2022.
4. FDA. Fact sheet for healthcare providers administering vaccine (vaccination providers). Emergency Use Authorization (EUA) of the Moderna COVID-19 vaccine to prevent coronavirus disaese 2019 (COVID-19). January 7, 2022. Available at: https://bit.ly/3nosylA. Accessed January 7, 2022.

Monoclonal Antibodies for COVID-19

The anti-SARS-CoV-2 antibody combinations casirivimab plus imdevimab *(REGEN-COV)* and bamlanivimab plus etesevimab are not active against the Omicron variant of SARS-CoV-2. These antibodies remain available, however, through federal distribution. NIH guidelines state that their use can be considered in regions where the Delta variant still causes a significant proportion of COVID-19 cases if alternative drugs are unavailable or contraindicated.[1,2]

Sotrovimab, which is authorized by the FDA for treatment of mild to moderate COVID-19 in patients ≥12 years old who weigh ≥40 kg and are at high risk of progressing to severe disease, is the only monoclonal antibody available in the US that has activity against the Omicron variant of SARS-CoV-2.[2,3] ■

1. HHS Public Health Emergency. Updated guidelines regarding allocation of bamlanivimab/etesevimab and REGEN-COV therapeutics: states and territories can continue to order both products. December 31, 2021. Available at: https://bit.ly/3sZHD3o. Accessed January 6, 2022.
2. NIH. The COVID-19 Treatment Guidelines Panel's statement on therapies for high-risk, nonhospitalized patients with mild to moderate COVID-19. December 30, 2021. Available at: https://bit.ly/3EUXjHz. Accessed January 6, 2022.
3. An EUA for sotrovimab for treatment of COVID-19. Med Lett Drugs Ther 2021; 63:97.

Additional Content Available Online: COVID-19 Charts

More information on vaccines and drugs for COVID-19 can be found in the COVID-19 Resources section of our website: www.medicalletter.org/drugs-for-covid-19.