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The Medical Letter®
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Casirivimab and Imdevimab (*REGEN-COV*) for Post-Exposure Prophylaxis of COVID-19

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

The investigational monoclonal antibodies casirivimab and imdevimab (*REGEN-COV* – Regeneron) have been available in the US under an Emergency Use Authorization (EUA) since late 2020 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] Casirivimab and imdevimab are the first drugs to receive an EUA for post-exposure prophylaxis of COVID-19.

Table 1. Indications for Post-Exposure Prophylaxis of COVID-19 with *REGEN-COV*[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 (i.e., 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 (e.g., 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 REGEN-COV™ (casirivimab and imdevimab). July 2021. Available at: https://bit.ly/3A4N0i7. Accessed August 5, 2021.
2. CDC. COVID-19: case investigation and contact tracing guidance. Appendices. August 3, 2021. Available at: https://bit.ly/3CfNDaA. Accessed August 5, 2021.

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 or pregnant or have cardiovascular disease, hypertension, or chronic respiratory disease are now considered high-risk (see Table 2).[3]

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

- Age ≥65 years
- BMI ≥25 kg/m^2 (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
- 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 and/or hospitalization. (FDA. Fact sheet for health care providers. Emergency Use Authorization (EUA) of REGEN-COV™ (casirivimab and imdevimab). July 2021. Available at: https://bit.ly/3A4N0i7. Accessed August 5, 2021).
2. Based on CDC growth charts. Available at: https://bit.ly/36U0twf. Accessed August 5, 2021.

CLINICAL STUDIES — Expansion of the EUA was based on the results of a randomized, double-blind, placebo-controlled trial in 1505 healthy, unvaccinated patients ≥12 years old without evidence of prior immunity who were household contacts of persons with SARS-CoV-2 infection (positive test within the prior 96 hours). Patients received a single subcutaneous dose of casirivimab and imdevimab (600 mg each) or placebo.

Symptomatic SARS-CoV-2 infection within 4 weeks of randomization, the primary endpoint, occurred significantly less often in patients who received the antibodies than in those who received placebo (1.5% vs 7.8%; adjusted OR 0.17 [95% CI 0.09-0.33]; NNT 15.4). Among patients who developed symptomatic infection, the duration of symptoms was significantly shorter in the antibody group (mean 1.2 vs 3.2 weeks

with placebo). There were no hospitalizations or emergency department visits due to COVID-19 in the antibody group, compared to 4 in the placebo group.[4]

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

ADVERSE EFFECTS — Infusion- and injection-related reactions and anaphylaxis have been reported with use of casirivimab and imdevimab.

DOSAGE AND ADMINISTRATION — The authorized dosage of *REGEN-COV* for post-exposure prophylaxis is 600 mg of casirivimab and 600 mg of imdevimab given as either 4 consecutive SC injections at one time or a single IV infusion. There is no preference for IV over SC administration of *REGEN-COV* when it is used for post-exposure prophylaxis. In patients with ongoing exposure to SARS-CoV-2, additional 300-mg doses of casirivimab and imdevimab can be administered every 4 weeks. Detailed instructions on preparation and administration of the antibodies are available in the FDA Fact Sheet.[2]

CONCLUSION — The FDA has authorized the monoclonal antibodies casirivimab and imdevimab *(REGEN-COV)* to be administered together for post-exposure prophylaxis of COVID-19 in certain high-risk individuals. In a double-blind trial in household con-tacts of SARS-CoV-2-infected persons, subcutaneous administration of *REGEN-COV* reduced the risk of symptomatic infection significantly more than placebo. Casirivimab plus imdevimab has retained activity against all SARS-CoV-2 Variants of Concern to date. ■

1. An EUA for casirivimab and imdevimab for COVID-19. Med Lett Drugs Ther 2020; 62:201.
2. FDA. Fact sheet for health care providers. Emergency Use Authorization (EUA) of REGEN-COV™ (casirivimab and imdevimab). December 2021. Available at: https://bit.ly/3A4N0i7. Accessed January 6, 2022.
3. FDA News Release. Coronavirus (COVID-19) update: May 21, 2021. Available at: https://bit.ly/3fFoEUB. Accessed August 5, 2021.
4. MP O'Brien et al. Subcutaneous REGEN-COV antibody combination to prevent Covid-19. N Engl J Med 2021 August 4 (epub).

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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.