

The Medical Letter[®]

on Drugs and Therapeutics

Volume 62

December 28, 2020

ISSUE No.
1614

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Volume 62 (Issue 1614)

December 28, 2020

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An EUA for Casirivimab and Imdevimab for COVID-19

Revised 3/22/21, 6/17/21, 1/6/2022: See page 202 and [COVID-19 Updates](#)

The FDA has issued an Emergency Use Authorization (EUA) for Regeneron's investigational monoclonal antibodies casirivimab and imdevimab (*REGEN-COV*) to be administered together by IV infusion or SC injection for treatment of mild to moderate COVID-19 in adults and pediatric patients (≥ 12 years old and weigh ≥ 40 kg) who are at high risk of progressing to severe COVID-19 and/or hospitalization.¹

Pronunciation Key

Casirivimab: cas i riv' i mab Imdevimab: im dev' i mab

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 outpatients ≥ 12 years old who are overweight or pregnant or have cardiovascular disease, hypertension, or chronic respiratory disease are now eligible to receive monoclonal antibody treatment (see Table 1).^{2,3}

Monoclonal antibodies may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 who require high-flow oxygen or mechanical ventilation. Casirivimab and imdevimab are not authorized for use in patients who are hospitalized for COVID-19 or require oxygen therapy because of COVID-19.

MECHANISM OF ACTION – Casirivimab and imdevimab bind to different sites on the receptor binding domain of the spike protein of SARS-CoV-2, blocking its attachment to the human ACE2 receptor.

CLINICAL STUDY – Authorization of casirivimab and imdevimab was based on the interim phase 1/2 results of a double-blind trial (COV-2067) after 799 outpatients with mild to moderate COVID-19 had completed at least 28 days of study duration.³ The patients had been randomized to receive a single IV infusion of 2400 mg of casirivimab and imdevimab (1200 mg each), 8000 mg of casirivimab and imdevimab (4000 mg each), or placebo within

Table 1. High-Risk Conditions for COVID-19 Outpatients¹

- ▶ Age ≥ 65 years
- ▶ BMI ≥ 25 kg/m² (or, in patients 12-17 years old, BMI ≥ 85 th percentile for age and gender²)
- ▶ 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 casirivimab and imdevimab. Available at: <https://bit.ly/36NmbDm>. Accessed June 10, 2021).
2. Based on CDC growth charts (<https://bit.ly/36U0twf>). Accessed December 10, 2020.

3 days of a positive SARS-CoV-2 test result. The time-weighted average reduction from baseline in viral load at day 7, the primary endpoint, was significantly larger with the pooled doses of the antibodies than with placebo. The predefined secondary endpoint of medically attended visits related to COVID-19 (defined as hospitalization, emergency department visit, urgent care visit, or physician office/telemedicine visit) within 28 days occurred in 2.8% of patients who received casirivimab and imdevimab and in 6.5% of those who received placebo, a statistically significant difference. Results with the two doses of casirivimab and imdevimab were similar for all endpoints.

A post-hoc analysis found that 2% of casirivimab- and imdevimab-treated patients and 4% of placebo-treated patients were hospitalized or visited the emergency department for COVID-19 within 28 days after treatment; among patients at high risk for disease progression, the rates were 3% with casirivimab and imdevimab and 9% with placebo. The median time to symptom improvement was 5 days with casirivimab and imdevimab and 6 days with placebo.

In a subsequent phase 3 component of COV-2067, 3867 patients with mild to moderate COVID-19 and at least one risk factor for progression to severe disease were randomized to receive a single IV infusion containing 1200 mg of casirivimab and imdevimab (600 mg each), 2400 mg of casirivimab and imdevimab (1200 mg each), or placebo. The primary endpoint, COVID-19-related hospitalization or death from any cause by day 29, occurred in 1.0% of patients who received the 1200-mg dose compared to 3.2% of those concurrently randomized to placebo (HR 0.30; NNT 44.3), and in 1.3% of patients who received the 2400-mg dose compared to 4.6% of those concurrently randomized to placebo (HR 0.29; NNT 30.3). Based on these data, the FDA changed the authorized dose of casirivimab and imdevimab from 1200 mg to 600 mg of each antibody.^{3,4}

Viral load reductions with IV and SC casirivimab and imdevimab appear to be similar, but clinical outcomes data with SC administration of the antibodies are limited.³ No studies directly comparing casirivimab and imdevimab with other monoclonal antibodies for COVID-19 are available.

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.³

ADVERSE EFFECTS — Infusion- and injection-related reactions and anaphylaxis have been reported with use of casirivimab and imdevimab.³

DOSAGE AND ADMINISTRATION — Casirivimab and imdevimab are packaged both separately in 120 mg/mL vials and as a co-formulated solution in 60 mg/60 mg/mL vials. The vials must be refrigerated during storage and should be allowed to sit at room temperature for 20 minutes before dose preparation. The two antibodies are only authorized for administration together; they should be given as soon as possible after a positive SARS-CoV-2 test result and within 10 days of COVID-19 symptom onset.

The preferred authorized dosage of *REGEN-COV* is 600 mg of casirivimab and 600 mg of imdevimab administered as a single IV infusion after dilution in 50, 100, 150, or 250 mL of normal saline at a maximum rate of 310 mL/hr (180 mL/hr if diluted in 50 mL). If the solution cannot be used immediately after dilution, it can be refrigerated for up to 36 hours or left at room temperature for up to 4 hours, including infusion time. If the solution is refrigerated after dilution,

it should sit at room temperature for 30 minutes before administration.

If IV infusion is not feasible and would lead to a delay in treatment, casirivimab and imdevimab can be administered subcutaneously. The authorized dosage is 600 mg of casirivimab and 600 mg of imdevimab administered as four consecutive 2.5-mL injections (2 injections of each antibody packaged separately, or 4 injections of the co-formulated formulation) into different sites on the thigh, the back of the upper arm, or the abdomen (except 2 inches around the navel). If a prepared syringe cannot be used immediately after dilution, it can be refrigerated or left at room temperature for up to 4 hours. If refrigerated, the syringe should sit at room temperature for 20 minutes before administration.

Casirivimab and imdevimab should be administered in a facility staffed and equipped to manage anaphylaxis. Patients should be monitored for hypersensitivity reactions during and for at least 1 hour after administration of the antibodies.

AVAILABILITY — Casirivimab and imdevimab will be allocated to state health departments by the US Department of Health and Human Services (HHS) based on case counts and severity of outbreaks. These state health departments will be responsible for allocating the antibodies to local health facilities.

CONCLUSION — The FDA has issued an Emergency Use Authorization (EUA) for the monoclonal antibodies casirivimab and imdevimab (*REGEN-COV*) to be administered together for treatment of COVID-19. Administration of the antibodies to high-risk outpatients recently diagnosed with mild to moderate COVID-19 reduced viral load and decreased the risk of hospitalization and emergency department visits. How casirivimab and imdevimab compare with other monoclonal antibodies for COVID-19 remains to be determined. ■

1. FDA News Release. Coronavirus (COVID-19) update: FDA authorizes monoclonal antibodies for treatment of COVID-19. November 21, 2020. Available at: <https://bit.ly/2lhDxP5>. Accessed June 10, 2021.
2. FDA News Release. Coronavirus (COVID-19) update: May 21, 2021. Available at: <https://bit.ly/3fFoEUB>. Accessed June 10, 2021.
3. 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.
4. FDA News Release. Coronavirus (COVID-19) update: June 4, 2021. Available at: <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-june-4-2021>. Accessed June 10, 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 disease 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.

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