

The COVID-19 Treatment Guidelines Panel's Statement on the Updated Emergency Use Authorization of the Anti-SARS-CoV-2 Monoclonal Antibody Combination Casirivimab Plus Imdevimab for the Treatment of COVID-19

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On June 3, 2021, the Food and Drug Administration (FDA) updated the Emergency Use Authorization (EUA) of the anti-SARS-CoV-2 monoclonal antibody combination casirivimab plus imdevimab for the treatment of nonhospitalized individuals with COVID-19.¹ The authorized dosage has been reduced from a single intravenous (IV) infusion of casirivimab 1,200 mg plus imdevimab 1,200 mg to casirivimab 600 mg plus imdevimab 600 mg. In addition, the same doses of casirivimab and imdevimab may now be administered by subcutaneous (SQ) injection when IV infusion is not feasible or may delay treatment. It should be noted that SQ administration requires four injections (2.5 mL per injection) at four different sites (see the [FDA EUA](#) for details).

The COVID-19 Treatment Guidelines Panel (the Panel) currently recommends that nonhospitalized patients with COVID-19 who are at high risk for disease progression receive one of three authorized anti-SARS-CoV-2 monoclonal antibody regimens (see the [Panel's Statement on the Emergency Use Authorizations of Anti-SARS-CoV-2 Monoclonal Antibodies for the Treatment of COVID-19](#)). The Panel has reviewed the data that were provided in the updated EUA for casirivimab plus imdevimab and reported publicly.^{2,3} For the casirivimab plus imdevimab combination regimen (if selected from the three authorized regimens), the Panel recommends:

- Using the dose of **casirivimab 600 mg plus imdevimab 600 mg (AIIa)**.
- Using IV infusion of **casirivimab plus imdevimab (AIIa)**.
- When IV infusion is not feasible or would lead to delay in treatment, SQ injection of **casirivimab plus imdevimab** can be used as an alternative route of administration (**BIII**).

Rationale

The recommendation for the use of the lower dose of casirivimab 600 mg plus imdevimab 600 mg IV is based on the Phase 3 results from the R10933-10987-COV-2067 study (*ClinicalTrials.gov* Identifier [NCT04425629](#)). This study is a double-blind, placebo-controlled randomized trial in outpatients with mild to moderate COVID-19. This trial included 4,057 participants; 736 received IV casirivimab 600 mg plus imdevimab 600 mg and 748 received placebo.^{2,3}

The modified full analysis set included participants aged ≥ 18 years who had a positive SARS-CoV-2 polymerase chain reaction result from a nasopharyngeal swab at randomization and had one or more risk factors for disease progression to severe COVID-19. The primary outcome was COVID-19-related hospitalizations or death from any cause, which was reported in 7 of 736 participants (1.0%) in the IV casirivimab 600 mg plus imdevimab 600 mg arm and in 24 of 748 participants (3.2%) in the placebo arm ($P = 0.0024$), a 2.2% absolute reduction and a 70% relative reduction in hospitalization or death among the casirivimab plus imdevimab recipients compared to the placebo recipients. These results are comparable to IV infusion of casirivimab 1,200 mg plus imdevimab 1,200 mg in which COVID-19-related hospitalizations or death from any cause were reported in 18 of 1,355 participants (1.3%) in the casirivimab plus imdevimab arm and in 62 of 1,341 participants (4.6%) in the placebo arm ($P < 0.0001$), a 3.3% absolute reduction and a 71% relative reduction in hospitalization or death among the

casirivimab plus imdevimab recipients compared to the placebo recipients.

The recommendation for the use of SQ injection is based on the Phase 1 R10933-10987-HV-2093 study (*ClinicalTrials.gov* Identifier [NCT04519437](https://clinicaltrials.gov/ct2/show/study/NCT04519437)), a double-blind, placebo-controlled randomized trial that compared casirivimab plus imdevimab administered SQ to placebo in healthy volunteers. Injection site reactions were observed in 12% of the 729 casirivimab plus imdevimab participants and 4% of the 240 placebo participants. According to the FDA EUA, in a separate trial among symptomatic participants, there were similar reductions in viral load between the IV and SQ arms, but neither a preprint nor a published report is currently available, and clinical outcomes data have not been reported.¹ Because the safety and efficacy data for casirivimab plus imdevimab administered SQ is limited, this route of administration should only be used when IV infusion is not feasible or would lead to a delay in treatment **(BIII)**.

References

1. Food and Drug Administration. Fact sheet for healthcare providers: emergency use authorization (EUA) of REGEN-COV (casirivimab and imdevimab). 2020. Available at: <https://www.fda.gov/media/145611/download>.
2. Weinreich DM, Sivapalasingam S, Norton T, et al. REGEN-COV antibody cocktail clinical outcomes study in COVID-19 outpatients. *medRxiv*. 2021;Preprint. Available at: <https://www.medrxiv.org/content/10.1101/2021.05.19.21257469v2>.
3. Regeneron. COV-2067 Phase 3 trial in high-risk outpatients shows that REGEN-COV (2400 mg and 1200 mg IV doses) significantly reduces risk of hospitalization or death while also shortening symptom duration. 2021. Available at: <https://newsroom.regeneron.com/index.php/static-files/a7173b5a-28f3-45d4-bede-b97370bd03f8>.