

# The COVID-19 Treatment Guidelines Panel's Statement on the Emergency Use Authorization of Baricitinib for the Treatment of COVID-19

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*Last Updated: December 14, 2020*

Baricitinib is an oral Janus kinase (JAK) inhibitor that is selective for JAK1 and JAK2. It is being evaluated for the treatment of COVID-19 because it may prevent cellular immune activation and inflammation. Baricitinib is approved by the Food and Drug Administration (FDA) to treat moderate to severe rheumatoid arthritis. On November 19, 2020, the FDA issued an Emergency Use Authorization (EUA) for the use of baricitinib in combination with remdesivir in hospitalized adults and children aged  $\geq 2$  years with COVID-19 who require supplemental oxygen, invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).<sup>1,2</sup>

The issuance of an EUA does not constitute FDA approval. An EUA indicates that a product may be effective in preventing, diagnosing, or treating a serious or life-threatening disease or condition. FDA approval occurs when a product has been determined to provide benefits that outweigh the known and potential risks for the intended population.

The COVID-19 Treatment Guidelines Panel (the Panel) has reviewed the evidence that was used to support the EUA. The Panel's recommendations for baricitinib are primarily based on findings from the Adaptive COVID-19 Treatment Trial 2 (ACTT-2). However, the Panel also considered the results of the Randomised Evaluation of COVID-19 Therapy (RECOVERY) trial. Like ACTT-2, the RECOVERY trial included patients with COVID-19 who required supplemental oxygen at enrollment. The RECOVERY trial reported that dexamethasone conferred a survival benefit among these patients (see [Therapeutic Management of Patients With COVID-19](#)).<sup>3</sup>

Each of the Panel's recommendations is assigned two ratings according to the scheme presented at the end of this statement.

## **After reviewing the available evidence for baricitinib, the Panel has determined the following:**

- There are insufficient data for the Panel to recommend either for or against the use of baricitinib in combination with remdesivir for the treatment of COVID-19 in hospitalized patients in cases where corticosteroids can be used instead.
- In the rare circumstances where corticosteroids cannot be used, the Panel recommends using baricitinib in combination with remdesivir for the treatment of COVID-19 in hospitalized, nonintubated patients who require oxygen supplementation (**BIIa**).
- The Panel **recommends against** the use of baricitinib in the absence of remdesivir, except in a clinical trial (**AIII**).
- There are insufficient data for the Panel to recommend either for or against the use of baricitinib in combination with corticosteroids for the treatment of COVID-19. Since both agents are potent immunosuppressants, there is potential for an additive risk of infection.
- More data are needed to clarify the role of baricitinib in the management of COVID-19, especially data from randomized trials that compare the use of baricitinib with the current standard of care and evaluate which subpopulations benefit the most from baricitinib. Health care providers are encouraged to discuss participation in baricitinib clinical trials with their patients.

## Clinical Trial Data

The Panel’s recommendations for baricitinib are largely based on data from ACTT-2, a multinational, randomized, placebo-controlled trial.<sup>4</sup> This trial included 1,033 hospitalized patients with COVID-19 and evidence of pneumonia. Participants were randomized 1:1 to receive baricitinib 4 mg orally or placebo for up to 14 days (or until hospital discharge); both groups of participants also received intravenous remdesivir for 10 days (or until hospital discharge).

The primary endpoint was time to recovery, which was defined as reaching category 1, 2, or 3 on an 8-point ordinal scale during the first 28 days. Patients were excluded from the trial if they were receiving any medications that were used off-label for the treatment of COVID-19, including corticosteroids. During the study, 10.9% of patients in the baricitinib plus remdesivir group and 12.9% of those in the placebo plus remdesivir group received corticosteroids. The median time to recovery was shorter in the baricitinib plus remdesivir group (7 days) than in the placebo plus remdesivir group (8 days) in the overall cohort (rate ratio 1.16; 95% CI, 1.01–1.32;  $P = 0.03$ ). In a subgroup analysis of participants who required high-flow oxygen or noninvasive ventilation, the largest difference in time to recovery occurred between the baricitinib group (10 days) and the placebo group (18 days; rate ratio 1.51; 95% CI, 1.10–2.08). However, the treatment effect within this subgroup should be interpreted with caution. It was not possible to estimate the median time to recovery within the first 28 days for patients who were on invasive mechanical ventilation or ECMO at study entry. There was no statistically significant difference in mortality by Day 28 between the baricitinib and placebo arms (OR 0.65; 95% CI, 0.39–1.09). Serious adverse events were less frequent in the baricitinib arm than in the placebo arm (16.0% vs. 21.0%; between-group difference of -5.0 percentage points, 95% CI, -9.8 to -0.3;  $P = 0.03$ ). New infections also occurred less frequently in the baricitinib arm (5.9% vs. 11.2%; between-group difference of -5.3 percentage points, 95% CI, -8.7 to -1.9;  $P = 0.003$ ).

### Recommendation Rating Scheme

**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

## References

1. Food and Drug Administration. Letter of authorization: EUA for baricitinib (Olumiant), in combination with remdesivir (Veklury), for the treatment of suspected or laboratory confirmed coronavirus disease 2019 (COVID-19). 2020. Available at: <https://www.fda.gov/media/143822/download>. Accessed December 11, 2020.
2. Food and Drug Administration. Fact sheet for healthcare providers: emergency use authorization (EUA) of baricitinib. 2020. Available at: <https://www.fda.gov/media/143823/download>. Accessed December 11, 2020.
3. RECOVERY Collaborative Group, Horby P, Lim WS, et al. Dexamethasone in hospitalized patients with COVID-19—preliminary report. *N Engl J Med*. 2020. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/32678530>.
4. Kalil AC, Patterson TF, Mehta AK, et al. Baricitinib plus remdesivir for hospitalized adults with COVID-19. *N Engl J Med*. 2020. Available at: <https://www.nejm.org/doi/full/10.1056/NEJMoa2031994>.