

# Ivermectin

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Ivermectin is a Food and Drug Administration (FDA)-approved antiparasitic drug used to treat several neglected tropical diseases, including onchocerciasis, helminthiasis, and scabies.<sup>1</sup> For these indications, ivermectin has been widely used and is generally well tolerated.<sup>1,2</sup> Ivermectin is not approved by the FDA for the treatment of any viral infection, including COVID-19. See the FDA webpage [Why You Should Not Use Ivermectin to Treat or Prevent COVID-19](#) for more information.

Ivermectin has been shown to inhibit the replication of SARS-CoV-2 in cell cultures.<sup>3</sup> However, pharmacokinetic and pharmacodynamic studies suggest that achieving the plasma concentrations necessary for the antiviral efficacy detected in vitro would require administration of doses up to 100-fold higher than those approved for use in humans.<sup>4,5</sup>

The safety and efficacy of ivermectin for the prevention and treatment of COVID-19 have been evaluated in clinical trials and observational cohorts. Summaries of the studies that informed the COVID-19 Treatment Guidelines Panel's (the Panel) recommendation can be found in [Table 7b](#). The Panel reviewed additional studies, but these studies are not summarized in Table 7b because they have study design limitations or results that make them less definitive and informative.

## Recommendation

- The Panel **recommends against** the use of **ivermectin** for the treatment of COVID-19 (**AIIa**).

## Rationale

The Panel's recommendation is primarily informed by adequately powered, randomized trials of ivermectin that reported clinical outcomes. Studies that randomized participants to receive ivermectin or a matched placebo had the greatest impact on the Panel's recommendation.<sup>6-13</sup>

Trials have failed to find a clinical benefit of using ivermectin to treat COVID-19 in outpatients. In TOGETHER, an adaptive platform trial conducted in Brazil, there was no apparent difference between the ivermectin and placebo arms for the primary outcome of risk of emergency department visits or hospitalization (14.7% vs. 16.4%).<sup>14</sup> In addition, there was no statistically significant difference between the ivermectin and placebo arms in mortality (3.1% vs. 3.5%). In COVID-OUT, a randomized factorial trial, the use of ivermectin did not reduce the occurrence of a composite outcome of emergency department visits, hospitalization, or death when compared with a matched control (5.7% vs. 4.1%).<sup>6</sup>

The ACTIV-6 trial was an adaptive platform trial conducted in outpatients with mild to moderate COVID-19 in the United States.<sup>15,16</sup> Participants were randomized to receive an ivermectin regimen (either 400 µg/kg for 3 days or 600 µg/kg for 6 days) or a matching placebo. In the 400 µg/kg phase of the study, the median time to sustained recovery was 12 days for the ivermectin arm and 13 days for the placebo arm. In the 600 µg/kg phase of the study, the median time to sustained recovery was 11 days for both arms.

I-TECH, an open-label trial conducted in Malaysia, found no difference between the ivermectin and standard of care arms in the occurrence of the primary outcome of risk of progression to severe COVID-19 (21.6% vs. 17.3%).<sup>17</sup> Patients in the ivermectin arm had a lower risk of mortality than those in the standard of care arm (relative risk 0.31; 95% CI, 0.09–1.11; *P* = 0.09), but this difference was not statistically significant.

The study populations in most of the reviewed trials were patients with mild to moderate COVID-19 who had a relatively low risk of disease progression, and the number of deaths was low (as expected). In these randomized trials, completely excluding an effect of ivermectin on COVID-19 disease progression is difficult because the trials were not powered to detect differences in secondary outcomes, such as death. However, data from these trials do not provide evidence that the use of ivermectin is effective for the treatment of COVID-19. For this reason, and because other medications now have demonstrated clear clinical benefits for the treatment of COVID-19, the Panel **recommends against** the use of **ivermectin** for the treatment of COVID-19 (**AIIa**).

See [Table 7b](#) for summaries of key studies that informed the Panel’s recommendation.

## References

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