

# Inhaled Corticosteroids

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Last Updated: December 20, 2023

Inhaled corticosteroids have been identified as potential COVID-19 therapeutic agents because of their targeted anti-inflammatory effects on the lungs. In addition, certain inhaled corticosteroids have been shown to impair viral replication of SARS-CoV-2<sup>1</sup> and downregulate the expression of the receptors used for cell entry.<sup>2,3</sup> Several trials provide additional insights regarding the role of inhaled corticosteroids in treating outpatients with COVID-19. These trials are described below and in [Table 5b](#).

## Recommendations

- There is insufficient evidence for the COVID-19 Treatment Guidelines Panel (the Panel) to recommend either for or against the use of inhaled corticosteroids for the treatment of COVID-19.
- There is insufficient evidence for the Panel to recommend either for or against the use of the combination of inhaled budesonide plus fluvoxamine for the treatment of COVID-19 in nonhospitalized patients.
- Patients with COVID-19 who are receiving an inhaled corticosteroid for an underlying condition should continue this therapy as directed by their health care provider (**AIII**).

## Rationale

Compared to usual care, inhaled corticosteroid therapy decreased the time to recovery in 2 open-label randomized controlled trials in outpatients with mild symptoms of COVID-19.<sup>4,5</sup> However, subsequent placebo-controlled, double-blind trials have shown that corticosteroid therapy did not reduce the duration of COVID-19 symptoms.<sup>6-8</sup> The available evidence does not show that inhaled corticosteroid therapy reduces the risk of hospitalization or death due to COVID-19. However, the Panel acknowledges that there are areas of uncertainty. Studies conducted predominantly among unvaccinated patients have reported mixed results.

ACTIV-6 is the only randomized controlled trial of inhaled corticosteroid monotherapy that was conducted in a predominantly vaccinated population.<sup>8</sup> In this study, treatment with inhaled fluticasone did not reduce the number of hospitalizations or health care visits or the time to sustained recovery. However, this study included patients who were at modest risk for complications from COVID-19. The median age of the patients was 45 years, and patients were not required to have a comorbidity to be included in the study.

The mixed results from these studies make it difficult to draw definitive conclusions about the benefit of using inhaled corticosteroids in people who are at high risk of disease progression. See [Therapeutic Management of Nonhospitalized Adults With COVID-19](#) for recommendations regarding therapies for high-risk outpatients.

The combination of inhaled budesonide plus oral fluvoxamine was studied in a large, double-blind, placebo-controlled, adaptive randomized trial in Brazil.<sup>9</sup> Over 90% of the patients had received at least 2 doses of a COVID-19 vaccine. Treatment with this combination significantly reduced the incidence of the primary outcome, which was a composite of hospitalization or retention in an emergency setting for >6 hours. The proportion of patients who were hospitalized was the same in the treatment and placebo arms (0.9% vs. 1.1%), and the treatment did not significantly impact secondary outcomes such as health care attendance or the need for an emergency setting visit. It is unclear how the >6-hour emergency

setting outcome translates to other settings. In addition, the treatment with budesonide plus fluvoxamine was associated with significantly more adverse events.

For more information on these trials, see [Table 5b](#).

No clinical trials have assessed the role of inhaled corticosteroids for the treatment of COVID-19 in hospitalized patients.

## Monitoring, Adverse Effects, and Drug-Drug Interactions

Patients who are receiving inhaled corticosteroids may develop oral candidiasis.

Using a cytochrome P450 3A4 inhibitor, such as ritonavir-boosted nirmatrelvir (Paxlovid), with inhaled budesonide or fluticasone may lead to increased systemic absorption of the corticosteroid, which may result in systemic adverse effects from the corticosteroid.

## Considerations in Pregnant People

There is insufficient evidence for the Panel to recommend either for or against the use of inhaled corticosteroids for the treatment of COVID-19 in people who are pregnant. Pregnant patients with COVID-19 who are receiving an inhaled corticosteroid for an underlying condition should continue this therapy as directed by their health care provider (**AIII**).

## Considerations in Children

There is insufficient evidence for the Panel to recommend either for or against the use of inhaled corticosteroids for the treatment of COVID-19 in children. Children with COVID-19 who are receiving an inhaled corticosteroid for an underlying condition should continue this therapy as directed by their health care provider (**AIII**).

## References

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