



Inhaled Corticosteroids

Last Updated: July 21, 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-2¹ and downregulate the expression of the receptors used for cell entry.^{2,3} Several trials provide additional insights regarding the role of inhaled corticosteroids in outpatients with COVID-19, as 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.^{4,5} However, subsequent placebo-controlled, double-blind trials have shown that corticosteroid therapy did not reduce the duration of COVID-19 symptoms.⁶⁻⁸ The totality of evidence did not show an effect of inhaled corticosteroid therapy on 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 conducted among a predominantly vaccinated population.⁸ In this study, treatment with inhaled fluticasone did not reduce hospitalizations, health care visits, or the time to sustained recovery. However, this study included patients at modest risk for complications from COVID-19. The median age of the patients was 45 years, and participants were not required to have a comorbidity to be included in the study.

Because of the mixed results reported, it is not possible to draw definitive conclusions about the benefit of inhaled corticosteroids in people at high risk for disease progression. See [Therapeutic Management of Nonhospitalized Adults With COVID-19](#) for recommended therapies for high-risk outpatients.

The combination of inhaled budesonide and oral fluvoxamine was studied in a large, double-blind, placebo-controlled, adaptive randomized trial in Brazil.⁹ More than 90% of the patients had received at least 2 doses of COVID-19 vaccine. The treatment resulted in a significant reduction in the incidence of the primary outcome, which was defined as a composite of hospitalization or retention in a COVID-19 emergency setting for >6 hours (1.8% in the combination arm vs. 3.7% in the placebo arm). Hospitalization was not different between arms (0.9% in combination arm vs. 1.1% in placebo arm). The treatment also did not significantly affect secondary outcomes such as health care attendance (i.e., a hospitalization for any cause or an emergency department visit of >6 hours). It is unclear how the outcome of >6 hours in a COVID-19 emergency setting would translate to other settings. In addition,

the treatment was associated with significantly more adverse events. For additional information on these trials, see [Table 5b](#).

No clinical trial data assess the role of inhaled corticosteroids for the treatment of COVID-19 in hospitalized patients.

Monitoring, Adverse Effects, and Drug-Drug Interactions

- Patients 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 Pregnancy

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

Considerations in Children

There is insufficient evidence 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.

References

1. Matsuyama S, Kawase M, Nao N, et al. The inhaled steroid ciclesonide blocks SARS-CoV-2 RNA replication by targeting the viral replication-transcription complex in cultured cells. *J Virol*. 2020;95(1):e01648-20. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/33055254>.
2. Finney LJ, Glanville N, Farne H, et al. Inhaled corticosteroids downregulate the SARS-CoV-2 receptor ACE2 in COPD through suppression of type I interferon. *J Allergy Clin Immunol*. 2021;147(2):510-519.e5. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/33068560>.
3. Peters MC, Sajuthi S, Deford P, et al. COVID-19-related genes in sputum cells in asthma. relationship to demographic features and corticosteroids. *Am J Respir Crit Care Med*. 2020;202(1):83-90. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/32348692>.
4. Ramakrishnan S, Nicolau DV Jr, Langford B, et al. Inhaled budesonide in the treatment of early COVID-19 (STOIC): a Phase 2, open-label, randomised controlled trial. *Lancet Respir Med*. 2021;9(7):763-772. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/33844996>.
5. Yu LM, Bafadhel M, Dorward J, et al. Inhaled budesonide for COVID-19 in people at high risk of complications in the community in the UK (PRINCIPLE): a randomised, controlled, open-label, adaptive platform trial. *Lancet*. 2021;398(10303):843-855. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/34388395>.
6. Clemency BM, Varughese R, Gonzalez-Rojas Y, et al. Efficacy of inhaled ciclesonide for outpatient treatment of adolescents and adults with symptomatic COVID-19: a randomized clinical trial. *JAMA Intern Med*. 2022;182(1):42-49. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/34807241>.
7. Ezer N, Belga S, Daneman N, et al. Inhaled and intranasal ciclesonide for the treatment of covid-19 in adult outpatients: CONTAIN Phase II randomised controlled trial. *BMJ*. 2021;375:e068060. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/34728476>.

8. Boulware DR, Lindsell CJ, Stewart TG, et al. Inhaled fluticasone furoate for outpatient treatment of COVID-19. *N Engl J Med*. 2023;389(12):1085-1095. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/37733308>.
9. Reis G, Dos Santos Moreira Silva EA, Medeiros Silva DC, et al. Oral fluvoxamine with inhaled budesonide for treatment of early-onset COVID-19: a randomized platform trial. *Ann Intern Med*. 2023;176(5):667-675. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/37068273>.