

Interferons

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Interferons are a family of cytokines with in vitro and in vivo antiviral properties. Interferon beta-1a has been approved by the Food and Drug Administration (FDA) to treat relapsing forms of multiple sclerosis, and pegylated formulations of interferon alfa-2a and interferon alfa-2b have been approved by the FDA to treat hepatitis B and hepatitis C virus infections. Several interferons, including interferon alfa, beta, and lambda, have been evaluated for the treatment of COVID-19. Interferon lambda is not currently approved or authorized by the FDA for any use.

Recommendations

- For nonhospitalized patients with mild to moderate COVID-19, the COVID-19 Treatment Guidelines Panel (the Panel) **recommends against** the use of **interferon alfa** or **beta**, except in a clinical trial (**AIIa**).
- For hospitalized patients with COVID-19, the Panel **recommends against** the use of **systemic interferon alfa**, except in a clinical trial (**AIIa**).
- For hospitalized patients with COVID-19, the Panel **recommends against** the use of **systemic interferon beta** (**AI**).
- The Panel is unable to recommend either for or against the use of interferon lambda because this product is not currently available for clinical use.

Rationale

Interferon Alfa and Beta

Many of the studies that evaluated the use of systemic interferons for the treatment of hospitalized adults with COVID-19 were conducted in early 2020, before the widespread use of remdesivir or corticosteroids and other immunomodulators. In addition, these studies administered interferons with other drugs that have since been shown to have no clinical benefit in people with COVID-19, such as lopinavir/ritonavir and hydroxychloroquine.¹⁻³

More recent studies have shown no benefit of using interferon beta-1a to treat patients with COVID-19, and some of the trials have suggested that interferon beta-1a can cause harm in patients with severe disease, such as those who require high-flow oxygen, noninvasive ventilation, or mechanical ventilation.^{4,5} In a large randomized controlled trial of hospitalized patients with COVID-19, the combination of interferon beta-1a plus remdesivir showed no clinical benefit when compared to remdesivir alone.⁴ Similarly, the World Health Organization Solidarity trial did not show a benefit of administering interferon beta-1a to hospitalized patients, approximately 50% of whom were on corticosteroids.⁵

Systemic interferon alfa and inhaled interferons have also been evaluated in patients with COVID-19. The trials that have evaluated the use of interferon alfa have generally been small or moderate in size and have not been adequately powered to assess whether this agent provides a clinical benefit for patients with COVID-19.⁶⁻⁸

Interferon Lambda

Pegylated interferon lambda was studied in a randomized, double-blind, adaptive clinical trial that

enrolled nonhospitalized patients with COVID-19 in Brazil and Canada.⁹ A total of 1,941 patients with risk factors for severe COVID-19 were randomized to receive either a single subcutaneous injection of pegylated interferon lambda 180 µg or placebo. Eighty-three percent of these patients had received at least 1 dose of a COVID-19 vaccine. The primary outcome was a composite of observation in an emergency department for >6 hours or hospitalization, and 1 of the secondary outcomes was a composite of hospitalization or death. By Day 28 after randomization, the use of interferon lambda was associated with a 51% decrease in the occurrence of the primary outcome and a 39% decrease in the occurrence of this secondary outcome. Patients with a high baseline SARS-CoV-2 viral load who received interferon lambda were more likely to have cleared the virus by Day 7 than those who received placebo.

The drug was generally well tolerated. However, since pegylated interferon lambda is an investigational agent that is not currently available for clinical use, the Panel cannot make a recommendation for its use at this time.

Summaries of the studies that informed the Panel's recommendations can be found in [Table 4d](#).

Considerations in Pregnant People

According to analyses of data from several large pregnancy registries, exposure to interferon beta-1b prior to conception or during pregnancy does not lead to an increased risk of adverse birth outcomes (e.g., spontaneous abortion, congenital anomaly).^{10,11} In a study that used data from pregnancy registries in Sweden and Finland, women who were exposed to interferon beta during pregnancy did not report significant changes in the birth weight, height, or head circumference of their infants.¹²

Considerations in Children

There are insufficient data on the use of interferons to treat respiratory viral infections in children to make any recommendations for treating children with COVID-19.

References

1. Alavi Darazam I, Hatami F, Mahdi Rabiei M, et al. An investigation into the beneficial effects of high-dose interferon beta 1-a, compared to low-dose interferon beta 1-a in severe COVID-19: The COVIFERON II randomized controlled trial. *Int Immunopharmacol*. 2021;99:107916. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/34224994>.
2. Hung IF, Lung KC, Tso EY, et al. Triple combination of interferon beta-1b, lopinavir-ritonavir, and ribavirin in the treatment of patients admitted to hospital with COVID-19: an open-label, randomised, Phase 2 trial. *Lancet*. 2020;395(10238):1695-1704. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/32401715>.
3. Rahmani H, Davoudi-Monfared E, Nourian A, et al. Interferon beta-1b in treatment of severe COVID-19: a randomized clinical trial. *Int Immunopharmacol*. 2020;88:106903. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/32862111>.
4. Kalil AC, Mehta AK, Patterson TF, et al. Efficacy of interferon beta-1a plus remdesivir compared with remdesivir alone in hospitalised adults with COVID-19: a double-blind, randomised, placebo-controlled, Phase 3 trial. *Lancet Respir Med*. 2021;9(12):1365-1376. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/34672949>.
5. WHO Solidarity Trial Consortium. Repurposed antiviral drugs for COVID-19—interim WHO Solidarity trial results. *N Engl J Med*. 2021;384(6):497-511. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/33264556>.
6. Yu J, Lu X, Tong L, et al. Interferon-alpha-2b aerosol inhalation is associated with improved clinical outcomes in patients with coronavirus disease-2019. *Br J Clin Pharmacol*. 2021;87(12):4737-4746. Available at: <https://pubmed.ncbi.nlm.nih.gov/33982806>.
7. Wang B, Li D, Liu T, Wang H, Luo F, Liu Y. Subcutaneous injection of IFN alpha-2b for COVID-19:

an observational study. *BMC Infect Dis*. 2020;20(1):723. Available at: <https://pubmed.ncbi.nlm.nih.gov/33008327>.

8. Pandit A, Bhalani N, Shashi Bhushan BL, et al. Efficacy and safety of pegylated interferon alpha-2b in moderate COVID-19: a phase II, randomized, controlled, open-label study. *Int J Infect Dis*. 2021;105:516-521. Available at: <https://pubmed.ncbi.nlm.nih.gov/33713817>.
9. Reis G, Moreira Silva EAS, Medeiros Silva DC, et al. Early treatment with pegylated interferon lambda for COVID-19. *N Engl J Med*. 2023;388(6):518-528. Available at: <https://pubmed.ncbi.nlm.nih.gov/36780676>.
10. Sandberg-Wollheim M, Alteri E, Moraga MS, Kornmann G. Pregnancy outcomes in multiple sclerosis following subcutaneous interferon beta-1a therapy. *Mult Scler*. 2011;17(4):423-430. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21220368>.
11. Hellwig K, Duarte Caron F, Wicklein EM, Bhatti A, Adamo A. Pregnancy outcomes from the global pharmacovigilance database on interferon beta-1b exposure. *Ther Adv Neurol Disord*. 2020;13:1756286420910310. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/32201504>.
12. Burkill S, Vattulainen P, Geissbuehler Y, et al. The association between exposure to interferon-beta during pregnancy and birth measurements in offspring of women with multiple sclerosis. *PLoS One*. 2019;14(12):e0227120. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/31887199>.