



INDIAN HEALTH SERVICE

National Pharmacy and Therapeutics Committee

Formulary Brief: COVID-19 Treatment Update

-February 2022-



Background:

The Indian Health Service (IHS) [National Pharmacy and Therapeutics Committee \(NPTC\)](#) reviewed COVID-19 medical countermeasures, including an update of COVID-19 treatments. The COVID-19 pandemic caused by the SARS-CoV-2 virus continues to have a significant impact, especially in American Indian and Alaska Native communities, where rates of morbidity and mortality have exceeded those among other racial and ethnic groups.¹ In addition to public health measures, emerging treatments and vaccines play a critical role in the prevention and treatment of SARS-CoV-2 infection, helping to mitigate the clinical and public health impacts among American Indian and Alaska Native people. The IHS National Pharmacy and Therapeutics Committee remains committed to providing comprehensive, timely, and relevant clinical guidance and safety monitoring of COVID medical countermeasures, including medications and vaccines to support Agency clinical and public health decision making, including distribution of [NPTC Emerging Treatments Updates](#).²

Discussion:

The IHS adheres to the National Institutes of Health (NIH) COVID-19 Treatment Guidelines.³ Available COVID-19 medications include monoclonal antibodies, antiviral agents, and immunomodulators. Currently authorized monoclonal antibodies include [sotrovimab](#) and [bebtelovimab](#), which are for the treatment of COVID-19 in the outpatient setting, and [Evusheld™](#), which is for pre-exposure prevention. Sotrovimab is administered as a single intravenous (IV) infusion, as soon as possible and within 10 days of symptom onset, to treat non-hospitalized patients (aged ≥12 years and weighing ≥40 kg) with mild to moderate COVID-19 who are at high risk of clinical progression. Treatment with [sotrovimab](#) should also be considered for patients with mild to moderate COVID-19 who are hospitalized for a reason other than COVID-19 if they otherwise meet the Emergency Use Authorization (EUA) criteria for outpatient treatment.³ It is administered as a single IV infusion as soon as possible and within 10 days of symptom onset, for the treatment of non-hospitalized patients ages 12 years or older and weighing at least 40 kg who have mild-to-moderate COVID-19 and are at increased risk of clinical progression. [Bebtelovimab](#) is considered an alternative COVID-19 treatment option when other options are not accessible or clinically appropriate.³ The efficacy data for this agent comes from the Phase II component of the BLAZE-4 trial which was conducted prior to the emergence of the Omicron variant, although the Food and Drug Administration's (FDA) authorization announcement indicates that bebtelovimab has in vitro activity against both Omicron and the BA.2 subvariant (using so-called pseudovirus testing).⁴ The BLAZE-4 trial demonstrated reductions in viral load among subjects who received bebtelovimab as well as a slightly lower proportion of subjects who required hospitalization or died by day 29 compared with those treated with bamlanivimab or etesevimab monotherapy.

[Evusheld™](#) is a long-acting monoclonal antibody combination administered as intramuscular injections given as SARS-CoV-2 pre-exposure prophylaxis for adults and adolescents (aged ≥12 years and weighing ≥40 kg) who do not have SARS-CoV-2 infection, who have not been recently exposed to an individual with SARS-CoV-2 infection, AND who are moderately to severely immunocompromised and may have an inadequate immune response to COVID-19 vaccination; or are not able to be fully vaccinated with any available COVID-19 vaccines due to a documented history of severe adverse reaction to a COVID-19 vaccine or any of its components.³ Evusheld™ is not a substitute for COVID-19 vaccination and should not be used in unvaccinated individuals for whom COVID-19 vaccination is recommended and who are anticipated to have an adequate response. **On Feb. 24, the FDA revised the EUA for [Evusheld \(tixagevimab co-packaged with cilgavimab\)](#) to change the [dosing for the authorized use](#) as pre-exposure prophylaxis (prevention) of COVID-19 in certain adults and pediatric patients. Based on the most recent information and data available, Evusheld may be less active against certain Omicron subvariants. The dosing regimen was revised because available data indicate that a higher dose of Evusheld may be more likely to prevent infection by the COVID-19 Omicron subvariants BA.1 and BA.1.1 than the originally authorized Evusheld dose.**⁵

[Remdesivir](#) (Veklury®) is a nucleotide prodrug of an adenosine analog.² It binds to the viral RNA-dependent RNA polymerase and inhibits viral replication by terminating RNA transcription prematurely. Remdesivir has demonstrated in vitro activity against SARS-CoV-2. Intravenous remdesivir is approved by the FDA for the treatment of COVID-19 in hospitalized adult and pediatric patients (aged ≥12 years and weighing ≥40 kg). In January 2022, the FDA [expanded the approved indication](#) for Veklury® to include its use in adults and pediatric patients (12 years of age and older who weigh at least 40 kilograms, which is about 88 pounds) with positive results of direct SARS-CoV-2 viral testing, and who are not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death. The FDA also [revised the EUA](#) for remdesivir to additionally authorize the drug for treatment of pediatric patients weighing 3.5 kilograms to less than 40 kilograms or pediatric patients less than 12 years of age weighing at least 3.5 kilograms, with

positive results of direct SARS-CoV-2 viral testing, and who are not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death.

[Paxlovid®](#) is an orally bioavailable combination of nirmatrelvir and ritonavir.² Nirmatrelvir is a SARS-CoV-2 main protease inhibitor which stops the virus from replicating. Ritonavir is an HIV-1 protease and CYP3A4 inhibitor, which has no activity against SARS-CoV-2 on its own but which slows the CYP3A-mediated metabolism of nirmatrelvir to help it remain in the body for a longer period at higher concentrations. It is currently authorized as a 5-day course for the treatment of mild-to-moderate COVID-19 in adults who are at high risk for progression to severe COVID-19, including hospitalization and death. Because Paxlovid® contains a CYP3A inhibitor, there is a risk of serious adverse drug interactions resulting from co-administration with drugs metabolized by CYP3A.

[Molnupiravir](#) is an orally-administered nucleoside analogue that inhibits SARS-CoV-2 replication by introducing errors into the virus' genetic code (viral mutagenesis).² It is currently authorized as a 5-day course for the treatment of mild-to-moderate COVID-19 in adults who are at high risk for progression to severe COVID-19, including hospitalization and death. Based on findings from animal reproduction studies, molnupiravir may cause fetal harm when administered to pregnant individuals. Therefore, molnupiravir is not recommended for use during pregnancy. Females of childbearing potential are advised to use a reliable method of birth control correctly and consistently during treatment with molnupiravir and for four days after the final dose. Males of reproductive potential who are sexually active with females of childbearing potential are advised to use a reliable method of birth control correctly and consistently during treatment with molnupiravir and for at least three months after the final dose. Currently, molnupiravir should only be used in adults for whom alternative COVID-19 treatment options are not accessible or clinically appropriate.³

[Dexamethasone](#), a systemic corticosteroid, was the first medication to demonstrate reduction in mortality due to COVID-19 in July 2020.² The RECOVERY trial was a multicenter, open-label trial in the United Kingdom that randomly assigned 6,425 hospitalized patients to receive up to 10 days of dexamethasone plus standard care or standard care alone.⁶ Mortality at 28 days was lower among the patients who received dexamethasone than among those who received standard care alone. This benefit of dexamethasone was observed in patients who were mechanically ventilated or who required supplemental oxygen at enrollment; in contrast, no benefit was seen in patients who did not require supplemental oxygen at enrollment. If dexamethasone is not available, alternative glucocorticoids (such as prednisone, methylprednisolone, hydrocortisone) can be used. Note, however, that studies of these other agents had insufficient sample size to assess efficacy. Lastly, there are no data to support the use of systemic corticosteroids in non-hospitalized patients with COVID-19.

[Tocilizumab](#) is an interleukin-6 receptor (IL-6) antagonist, currently FDA-approved for the treatment of adult patients with various inflammatory arthritides and vasculitides.² Higher levels of IL-6 have been positively correlated with cases of critical and severe COVID-19 and have also been found to be predictive of the likelihood of need for mechanical ventilation, whereas lower levels of IL-6 have been correlated with mild disease. Tocilizumab may be prescribed under EUA for treatment of COVID-19 in hospitalized adults and pediatric patients (2 years of age and older) who are receiving systemic corticosteroids and are requiring supplemental oxygen, invasive mechanical ventilation, or extracorporeal membrane oxygenation. It is administered as a 60-minute IV infusion with weight-based dosing. When tocilizumab is indicated but unavailable, sarilumab is an alternative option according to the current NIH guidelines.³

[Baricitinib](#) is a janus kinase inhibitor approved for treatment of TNF-refractory rheumatoid arthritis.² It appears to have antiviral effects through its affinity for certain AP2- associated proteins, thereby reducing SARS-CoV-2 endocytosis. Baricitinib may be prescribed under EUA, in combination with remdesivir and dexamethasone for the treatment of suspected or laboratory-confirmed COVID-19 in hospitalized adults and pediatric patients 2 years of age or older requiring supplemental oxygen, invasive mechanical ventilation, or extracorporeal membrane oxygenation. It is administered orally for 14 days or until discharge with age-based dosing. When baricitinib is indicated but unavailable, tofacitinib is an alternative option according to the current NIH guidelines.³

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the [NPTC website](#).

References:

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4. Food and Drug Administration. Bebtelovimab: [FACT SHEET FOR HEALTHCARE PROVIDERS](#). Released February 11, 2022.
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