



Remdesivir

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Remdesivir is a nucleotide prodrug of an adenosine analog. It binds to the viral RNA-dependent RNA polymerase and inhibits viral replication by terminating RNA transcription prematurely. Remdesivir has demonstrated in vitro and in vivo activity against SARS-CoV-2.¹ Remdesivir retains in vitro neutralization activity against the Omicron variant and its subvariants.²⁻⁵

Intravenous remdesivir is approved by the Food and Drug Administration (FDA) for the treatment of COVID-19 in adults and pediatric patients aged ≥ 28 days and weighing ≥ 3 kg. In nonhospitalized patients with mild to moderate COVID-19 who are at high risk of progressing to severe disease, remdesivir should be started within 7 days of symptom onset and administered for 3 days. Hospitalized patients should receive remdesivir for 5 days or until hospital discharge, whichever comes first.⁶ See [Table 4e](#) for more information.

Remdesivir has been studied in several clinical trials for the treatment of COVID-19. The recommendations from the COVID-19 Treatment Guidelines Panel (the Panel) are based on the results of these studies. See [Table 4a](#) for more information.

Recommendations

- For the Panel's recommendations and information on the clinical efficacy of using remdesivir to treat high-risk, nonhospitalized patients with mild to moderate COVID-19, see [Therapeutic Management of Nonhospitalized Adults With COVID-19](#).
- For the Panel's recommendations and information on the clinical efficacy of using remdesivir with or without immunomodulators to treat certain hospitalized patients, see [Therapeutic Management of Hospitalized Adults With COVID-19](#).
- The data on using combinations of antiviral therapies for the treatment of COVID-19 are limited.⁷ Clinical trials are needed to determine the role of combination therapy in treating certain patients.

Monitoring, Adverse Effects, and Drug-Drug Interactions

Remdesivir can cause gastrointestinal symptoms (e.g., nausea), elevated transaminase levels, an increase in prothrombin time without a change in the international normalized ratio, and hypersensitivity reactions.

Before starting patients on remdesivir, the FDA recommends performing estimated glomerular filtration rate (eGFR), liver function, and prothrombin time tests as clinically appropriate and repeating these tests during treatment as clinically indicated. However, it should be noted that in the PINETREE study, in which outpatients with mild to moderate COVID-19 received remdesivir for 3 days, baseline serum creatinine was not required by the protocol for patients weighing >48 kg.⁸ Remdesivir may need to be discontinued if a patient's alanine transaminase (ALT) level increases to >10 times the upper limit of normal, and it should be discontinued if increases in ALT levels and signs or symptoms of liver inflammation are observed.⁶

Remdesivir should be administered in a setting where severe hypersensitivity reactions, such as anaphylaxis, can be managed. Patients should be monitored during the infusion and observed for at least 1 hour after the infusion as clinically appropriate.

Patients who are severely immunocompromised may have a prolonged duration of SARS-CoV-2 replication, which may lead to rapid viral evolution. There is concern that using a single antiviral agent in these patients may result in the emergence of resistant virus.⁹ Additional studies are needed to assess this risk. The role of combination antiviral therapy in the treatment of COVID-19 is not yet known.

Currently, no clinical drug-drug interaction studies of remdesivir have been conducted. In vitro, remdesivir is a minor substrate of cytochrome P450 (CYP) 3A4 and a substrate of the drug transporters organic anion transporting polypeptide (OATP) 1B1 and P-glycoprotein. It is also an inhibitor of CYP3A4, OATP1B1, OATP1B3, and multidrug and toxin extrusion protein (MATE) 1.⁶ See [Table 4e](#) for more information.

Considerations in Patients With Renal Insufficiency

Each 100-mg vial of remdesivir lyophilized powder contains 3 g of sulfobutylether beta-cyclodextrin sodium (SBECD), and each 100-mg/20-mL vial of remdesivir solution contains 6 g of SBECD.⁶ SBECD is a vehicle that is primarily eliminated through the kidneys. A patient with COVID-19 who receives a loading dose of remdesivir 200 mg would receive 6 g to 12 g of SBECD, depending on the formulation. This amount of SBECD is within the safety threshold for patients with normal renal function.¹⁰ Accumulation of SBECD in patients with renal impairment may result in liver and renal toxicities. Clinicians may consider preferentially using the lyophilized powder formulation (which contains less SBECD) in patients with renal impairment.

Because both remdesivir formulations contain SBECD, patients with an eGFR of <50 mL/min were excluded from some clinical trials of remdesivir; other trials had an eGFR cutoff of <30 mL/min. The FDA product label does not recommend using remdesivir in patients with an eGFR of <30 mL/min due to a lack of data.¹¹

The CATCO study was a multicenter, open-label randomized controlled trial that compared the use of remdesivir to standard of care in hospitalized adults with COVID-19.¹² The study did not exclude patients with renal impairment. A post hoc analysis was done for 59 patients with a baseline eGFR of <30 mL/min; 15 of these patients were on dialysis. The median age of the cohort was 74 years. Thirty-four patients received the lyophilized powder formulation of remdesivir for a median duration of 10 days, while 25 patients received standard of care. More men were enrolled in the standard of care arm, and patients in this arm also had a lower median eGFR at baseline (12.4 mL/min) than those in the remdesivir arm (22.7 mL/min).

Clinical laboratory evaluations were performed only on Day 5. There was no increased risk of renal toxicity at Day 5 among the individuals who received remdesivir when compared with those who received standard of care. There were also no statistically significant differences between the arms in the need for new dialysis, the need for new mechanical ventilation, or mortality.

This study has limitations, including a small sample size. However, it provides reassurance regarding the safety of using remdesivir in patients with renal impairment. The results are consistent with a systematic review of observational studies¹³ and other retrospective studies that have reported that the use of remdesivir was not associated with an increased incidence of adverse effects in patients with COVID-19 who had baseline eGFRs of <30 mL/min.¹⁴ These data suggest that remdesivir can be used in patients with an eGFR of <30 mL/min if the potential benefits outweigh the risks.

Considerations in Pregnancy

Remdesivir should be offered to pregnant individuals if it is indicated.

While pregnant patients were excluded from the clinical trials that evaluated the safety and efficacy of remdesivir for the treatment of COVID-19, subsequent reports on the use of remdesivir in pregnant patients have been reassuring. Among 86 pregnant and postpartum patients who were hospitalized with severe COVID-19 and who received remdesivir through a compassionate use program, the therapy was well tolerated, with a low rate of serious adverse effects.¹⁵

Among 95 pregnant patients with moderate, severe, or critical COVID who were included in a secondary analysis of data from a COVID-19 pregnancy registry in Texas, the composite maternal and neonatal outcomes were similar between those who received remdesivir (n = 39) and those who did not.¹⁶ Remdesivir was discontinued in 16.7% of patients due to elevated levels of transaminases. It was not possible to determine whether these elevated levels were secondary to the drug, COVID-19, or pregnancy-related conditions.

The results of the secondary analysis should be interpreted with caution, given that clinicians were more likely to choose to administer remdesivir to pregnant patients with more severe illness. Those who were treated with remdesivir were more likely to have had COVID-19 for a longer duration by the time they were admitted to the hospital. They were also more likely to require oxygen support at admission and to have a longer hospital stay.

A systematic review of 13 observational studies that included 113 pregnant people also reported few adverse effects of remdesivir in pregnant patients with COVID-19. The most common adverse effect was a mild elevation in transaminase levels.¹⁷

Considerations in Children

Please see [Special Considerations in Children](#), [Therapeutic Management of Nonhospitalized Children With COVID-19](#), and [Therapeutic Management of Hospitalized Children With COVID-19](#).

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