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 activity against SARS-CoV-2. In a rhesus macaque model of SARS-CoV-2 infection, remdesivir treatment was initiated soon after inoculation; the remdesivir-treated animals had lower virus levels in the lungs and less lung damage than the control animals. Remdesivir is expected to be active against the Omicron (B.1.1.529) variant of concern and its BA.2 subvariant.

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 high-risk, nonhospitalized patients with mild to moderate COVID-19, 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. See Table 4d 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 remdesivir in 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 remdesivir with or without immunomodulators in certain hospitalized patients, see Therapeutic Management of Hospitalized Adults With COVID-19.

There are no data on using combinations of antiviral therapies or combinations of antiviral therapies and anti-SARS-CoV-2 monoclonal antibodies for the treatment of COVID-19. Clinical trials are needed to determine the role of combination therapy in certain patients.

Monitoring and Adverse Effects

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 in patients weighing >48 kg. 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.

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 prolonged 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. Additional studies are needed to assess this risk. The role of combination antiviral therapy in the treatment of COVID-19 is not yet known.

**Considerations in Patients With Renal Insufficiency**

Each 100-mg vial of remdesivir lyophilized powder contains 3 g of sulfobutylether beta-cyclodextrin sodium (SBEDCD), and each 100 mg/20-mL vial of remdesivir solution contains 6 g of SBEDCD. SBEDCD 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 SBEDCD, depending on the formulation. This amount of SBEDCD is within the safety threshold for patients with normal renal function. Accumulation of SBEDCD in patients with renal impairment may result in liver and renal toxicities. Clinicians may consider preferentially using the lyophilized powder formulation (which contains less SBEDCD) in patients with renal impairment.

Because both remdesivir formulations contain SBEDCD, 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.

In 2 observational studies that evaluated the use of the solution formulation of remdesivir (not the reconstituted lyophilized powder formulation) in hospitalized patients with COVID-19, no significant differences were reported in the incidences of adverse effects or acute kidney injury between patients with an estimated creatinine clearance (CrCl) of <30 mL/min and those with an estimated CrCl of ≥30 mL/min. In 1 study, 20 patients had an estimated CrCl of <30 mL/min and 115 had an estimated CrCl of ≥30 mL/min; the other study included 40 patients who had an estimated CrCl of <30 mL/min and 307 patients who had an estimated CrCl of ≥30 mL/min. These observational data suggest that remdesivir can be used in patients with an eGFR of <30 mL/min if the potential benefits outweigh the risks.

**Drug-Drug Interactions**

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.

Minimal to no reduction in remdesivir exposure is expected when remdesivir is coadministered with dexamethasone, according to information provided by Gilead Sciences (written communication, July 2020).

See Table 4d for more information.

**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.\textsuperscript{13}

Among 95 pregnant patients with moderate, severe, or critical COVID-19 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.\textsuperscript{14} 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, although in each case the elevated levels occurred before the patient received remdesivir.

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 advent was a mild elevation in transaminase levels.\textsuperscript{15}

**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.

**References**

6. Remdesivir (Veklury) [package insert]. Food and Drug Administration. 2020. Available at: [https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/214787Orig1s000lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/214787Orig1s000lbl.pdf).


