Remdesivir Quick Point-of-Care Reference

Last reviewed: 5/23/22

Remdesivir (brand name Veklury) has been FDA-approved for the treatment of COVID-19 in hospitalized adults and children 12 years and older since October 2020 and FDA-authorized for emergency use in certain outpatient and pediatric populations since January 2022. **Full FDA approval for its use in hospitalized and non-hospitalized high-risk children under 12 years and under 40 kg was granted in April 2022.**

CLINICAL INFORMATION

Eligibility: FDA's remdesivir approval covers adult and pediatric patients at least 28 days of age and weighing at least 3 kg (6.6 lb) with positive SARS-CoV-2 test results who are hospitalized OR have mild-to-moderate COVID-19 and are at high risk for progression to severe disease. Treatment for nonhospitalized patients should begin as soon as possible after diagnosis and must be within 7 days of symptom onset.

Outpatient Dosing (3 days, within 7 days of symptom onset): For nonhospitalized adults and pediatric patients ≥12 years old and weighing ≥40 kg, a course of remdesivir consists of 200 mg IV on day one followed by 100 mg IV on days two and three. For nonhospitalized patients younger than 12 years, the dose is 5 mg/kg IV on day one and 2.5 mg/kg IV on days two and three.

Inpatient Dosing (5 days): For hospitalized adults and pediatric patients ≥12 years old and weighing ≥40 kg who have an oxygen requirement, a course of remdesivir consists of 200 mg IV on day one followed by 100 mg IV on days 2 through 5. For hospitalized patients younger than 12 years, the dose is 5 mg/kg IV on day one and 2.5 mg/kg IV on days 2 through 5.

Clinical Decision-Making (also see Table 1 below):

Outpatient: In nonhospitalized patients with mild-to-moderate COVID-19 at high risk for progression to severe disease, IDSA guidelines suggest 3 days of remdesivir, initiated within 7 days of symptom onset (conditional recommendation, low certainty of evidence).

NIH guidelines suggest remdesivir for nonhospitalized patients with mild-to-moderate COVID-19 aged ≥12 years and weighing ≥40 kg who are at high risk of disease progression (moderate recommendation).

Inpatient: In hospitalized patients with severe COVID-19, IDSA guidelines suggest remdesivir over no antiviral treatment (conditional recommendation, low certainty of evidence).

NIH guidelines suggest dexamethasone plus remdesivir for hospitalized patients who require oxygen (due to sustained room air SaO_2 ≤94%) through a high-flow device or noninvasive ventilator but are not requiring mechanical ventilation or ECMO (moderate recommendation). For hospitalized patients who do not require supplemental oxygen, NIH guidelines find insufficient evidence to recommend either for or against remdesivir but state that use may be appropriate in patients at high risk of disease progression.

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Table 1. Comparison of NIH and IDSA Guidelines for Remdesivir Use in COVID-19[1]

Patient Category	NIH Guidelines	IDSA Guidelines
Non-hospitalized, at high risk of disease progression	Remdesivir[2] (3-day course) is a reasonable option to consider (Class BIIa) Options in order of preference and strength of recommendation: • Ritonavir-boosted nirmatrelvir (Paxlovid) (AIIa) • Sotrovimab (AIIa) • Remdesivir (BIIa) • Molnupiravir (CIIa)	Recommend initiation of 3-day course of remdesivir[2] within 7 days of symptom onset (conditional recommendation, low certainty of evidence)
Hospitalized, not requiring supplemental O_2, at high risk of disease progression	Insufficient evidence to recommend either for or against the routine use of remdesivir. For patients who are at high risk for disease progression, remdesivir may be appropriate.	Recommend initiation of 3-day course of remdesivir[2] within 7 days of symptom onset (conditional recommendation, low certainty of evidence)
Hospitalized, requires non-high-flow supplemental oxygen (or has SpO_2 < 94% on room air)	Recommend remdesivir[1] (BIIa) OR dexamethasone plus remdesivir (BIIb) OR dexamethasone alone (BI)	Recommend remdesivir over no antiviral treatment (conditional recommendation, moderate certainty of evidence) Recommend treatment with 5 days of remdesivir rather than 10 days of remdesivir (conditional recommendation, low certainty of evidence)
Hospitalized, requires supplemental oxygen through high-flow device or non-invasive ventilation	Recommend remdesivir plus dexamethasone (BII) OR dexamethasone alone (AI)	Recommend remdesivir over no antiviral treatment (conditional recommendation, moderate certainty of evidence)
Hospitalized, requires mechanical ventilation or ECMO	Recommend AGAINST remdesivir monotherapy (AIIa), but the combination of dexamethasone and remdesivir may be considered in patients who have recently been intubated (CIII)	Recommend AGAINST initiation of remdesivir (conditional recommendation, very low certainty of evidence)

[1] For an explanation of strength of NIH recommendation rankings (e.g., AII, BIIb, etc.), see https://www.covid19treatmentguidelines.nih.gov/about-the-guidelines/introduction/

[2] Benefit greatest when remdesivir used early on in disease course, within 10 days of the onset of symptoms. NIH guidance recommends against continuing remdesivir after hospital discharge (AIIa)

The Real-Time Learning Network's COVID-19 Outpatient Treatment Guidelines Roadmap and HHS's COVID-19 Therapeutics Clinical Decision Aid offer paths to evaluate current U.S. treatment options.

NIH's COVID-19 Treatment Guidelines Panel offers a prioritization scheme based on four key elements: age, vaccination status, immune status and clinical risk factors, with highest priority assigned to the higher risk groups (Risk Group 1>2>3>4):

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SAFETY ISSUES

Although a full understanding of remdesivir's safety profile remains incomplete, notable considerations include:

Liver Test Abnormalities: According to NIH guidelines: "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.

"Liver function tests and prothrombin time tests should be performed for all patients before they receive remdesivir, and these tests should be repeated during treatment as clinically indicated. 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 an increase in ALT level and signs or symptoms of liver inflammation are observed." This is concordant with FDA label guidance (see package insert sections 5.2 and 2.1).

Bradycardia: There have been reports of bradycardia in patients receiving remdesivir, and an analysis of WHO safety reports found an increased likelihood of bradycardia among remdesivir recipients, compared to other agents, with a reporting OR of 1.65 (95% CI, 1.23-2.22) (Touafchia, February 2021; Barkas, February 2021; Gubitosa, November 2020).

Considerations in Patients with Renal Insufficiency (eGFR <30 mL/min): In the FDA prescribing information, remdesivir is not recommended in people with eGFR <30 mL/min due to a concern about accumulation of its renally-cleared excipient, sulfobutylether beta-cyclodextrin sodium (SBECD) (see package insert). NIH guidelines state the amount of SBECD in a course of remdesivir "is within the safety threshold (250 mg/kg/day of SBECD) for patients with normal renal function, but 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 — 3 g per 100 mg dose, as compared to 6 g per 100 mg dose in the liquid formulation) in patients with renal impairment." IDSA guidelines state "additional research into safety of remdesivir in patients with reduced renal function is needed to ascertain whether this concern is substantiated." Concerns can be partially allayed by accumulating safety data on the use of remdesivir in patients with eGFR <30 mL/min and the favorable safety record of IV voriconazole, which contains the same SBECD excipient, and is used routinely in people with eGFR < 30 mL/min. (See these articles for more information: article 1, article 2, article 3.) Clinicians should monitor kidney function in all patients on remdesivir, particularly those with preexisting renal impairment and those receiving other nephrotoxins.

Interactions With Other Therapeutics: Remdesivir has not been studied in clinical drug-drug interaction studies. In vitro, it is a substrate for CYP3A4 and OATP1B1 as well as P-glycoprotein transporters and an inhibitor of CYP3A4 and OATP1B1; the clinical relevance of this has not been established (see package insert).

SUPPLY & ACCESS

Distribution: Remdesivir is currently available on the commercial marketplace and can be ordered via the AmerisourceBergen ABC online ordering portal; nonhospitals may apply to register for access online.

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CODING, BILLING & REPORTING

Coding:

Drug Name	Dosage	Package Size	NDC
Remdesivir	100 mg/1	1 Vial, Single-Dose in 1 Carton > 1 Injection, Powder, Lyophilized, for Solution in 1 Vial, Single-Dose	61958-2901-1
Remdesivir	5 mg/mL	1 Vial, Single-Dose in 1 Carton > 20 Ml in 1 Vial, Single-Dose	61958-2902-1

Billing:

Outpatient: Use HCPCS code J0248 for remdesivir when administered in the outpatient setting (long descriptor: "Injection, remdesivir, 1 mg"; short descriptor: "Inj, remdesivir, 1 mg").

Inpatient:

ICD-10-PCS Code	Description
XW033E5	Introduction of remdesivir anti-infective into peripheral vein, percutaneous approach, new technology group 5
XW043E5	Introduction of remdesivir anti-infective into central vein, percutaneous approach, new technology group 5

Reporting: All serious adverse events and medication errors potentially related to remdesivir should be submitted to FDA's MedWatch adverse event report online or by calling 1-800-FDA-1088.

FURTHER INFORMATION

Real-Time Learning Network Remdesivir Literature Reviews
FDA Remdesivir Approval Label/Prescribing Information
NIH Treatment Guidelines Panel Statement on High-Risk, Nonhospitalized Patients
University of Liverpool COVID-19 Drug Interactions

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