



October 23, 2020

FDA APPROVAL: Remdesivir (Veklury®)

Current Status^{1,2}:

On October 22, 2020, the FDA officially approved [remdesivir](#) for use in adult and pediatric patients (12 years of age and older and weighing at least 40 kilograms) for the treatment of COVID-19 requiring hospitalization. Remdesivir is the first treatment to be approved by the FDA for COVID-19 and does not include the entire population (e.g., pediatrics) originally authorized for use by the May 1, 2020 Emergency Use Authorization (EUA). Clinical trials evaluating safety and efficacy within the pediatric population are currently underway. Additionally, remdesivir should only be administered in a hospital or comparable healthcare setting.

On May 1, 2020, the FDA first issued an EUA for remdesivir use in hospitalized adult and pediatric patients with severe COVID-19, defined as oxygen saturation $\leq 94\%$ on room air, or requiring supplemental oxygen or mechanical ventilation or extracorporeal membrane oxygenation (ECMO). On August 28, 2020, the FDA updated the remdesivir EUA and expanded its use to include treatment of all hospitalized adult and pediatric patients with suspected or laboratory-confirmed COVID-19, regardless of disease severity.

Availability:

The FDA's approval of remdesivir has not altered its current distribution process within IHS. Supply of remdesivir remains available through request to the IHS National Supply Service Center (via submission of IHS Issue Request for Stores Stock Supplies Form 413). Additionally, remdesivir is also available for purchase through the pharmaceutical vendor, AmerisourceBergen.

Recommended Dosing³:

Remdesivir is supplied in 100 mg vials for reconstitution and does not contain preservatives or a bacteriostatic agent. Any unused portion of a single-dose vial should be discarded after a diluted solution is prepared. Administer IV medication immediately after preparation when possible.

Dosing guidance provided in the FDA approval document ([Prescribing Information](#)) recommends the following:

- Adults and pediatric patients 12 years and older (>40 kg):
 - Single loading dose of 200 mg IV on day 1, then 100 mg IV daily from day 2 infused over 30-120 minutes

Duration of therapy is determined by the need for mechanical ventilation and/or extracorporeal membrane oxygenation (ECMO). In patients requiring mechanical ventilation and/or ECMO, 10 days of remdesivir are recommended. Patients not mechanically ventilated and/or requiring ECMO should receive 5 days of remdesivir. Therapy may be extended up to 10 days if the patient does not demonstrate clinical improvement.

Testing Before Initiating and During Treatment³:

- Determine eGFR in all patients before starting remdesivir and monitor while receiving remdesivir as clinically appropriate. *NOTE: Remdesivir is not recommended in patients with eGFR ≤ 30 ml/min.*
- Perform hepatic laboratory testing in all patients before starting remdesivir and while receiving remdesivir as clinically appropriate. *NOTE: Consider discontinuing if ALT levels increase to greater than 10 times the upper limit of normal. Discontinue if ALT elevation is accompanied by signs or symptoms of liver inflammation.*
- Determine prothrombin time in all patients before starting remdesivir and monitor while receiving remdesivir as clinically appropriate

Efficacy³⁻⁶:

NIAID ACTT-1 Study in Subjects with Mild/Moderate and Severe COVID-19⁴ – [published October 8, 2020](#)

Design: Phase 3 adaptive, randomized, double-blinded, placebo-controlled trial launched in the U.S.
Patients: 1063 adults hospitalized with mild, moderate, and severe COVID-19 and lung involvement
1° Outcome: Faster time to recovery was reported for patients receiving remdesivir (10 vs. 15 days, $p < 0.001$)

Study GS-US-540-5774 in Subjects with Moderate COVID-19⁵ – [published August 21, 2020](#)

Design: Phase 3 multi-site, international, randomized, open-label trial in 15 countries including the U.S.
Patients: 584 adults hospitalized for COVID-19 with pneumonia received placebo, 5- or 10-day durations
1° Outcome: On day 11, 5-day course had better clinical status vs. placebo (OR 1.65, $p = .02$); no differences in clinical status noted on day 11 between 10-day course and placebo ($p = .18$)

Study GS-US-540-5773 in Subjects with Severe COVID-19⁶ – [published May 27, 2020](#)

Design: Phase 3 multi-site, international, randomized, open-label trial in 15 countries including the U.S.
Patients: 397 adults hospitalized for COVID-19 with pneumonia received either 5- or 10-day durations
1° Outcome: No difference in improvement on Day 14 between remdesivir durations (65% vs. 54%, $p = 0.014$)

Warnings and Precautions³:

- *Hypersensitivity including infusion-related and anaphylactic reactions:* Hypersensitivity reactions have been observed during and following administration of remdesivir. Slower infusion rates, with a maximum infusion time of up to 120 minutes, can be considered to potentially prevent signs and symptoms of hypersensitivity. If signs and symptoms of a clinically significant hypersensitivity reaction occur, immediately discontinue administration of remdesivir and initiate appropriate treatment.
- *Increased risk of transaminase elevations:* Transaminase elevations have been observed in healthy volunteers and have also been reported in patients with COVID-19 who received remdesivir. Perform hepatic laboratory testing in all patients before starting remdesivir and while receiving remdesivir as clinically appropriate. Consider discontinuing remdesivir if ALT levels increase to greater than 10 times the upper limit of normal. Discontinue remdesivir if ALT elevation is accompanied by signs or symptoms of liver inflammation.
- *Risk of reduced antiviral activity when co-administered with chloroquine phosphate or hydroxychloroquine sulfate:* Co-administration of remdesivir and chloroquine phosphate or hydroxychloroquine sulfate is not recommended based on cell culture data demonstrating an antagonistic effect of chloroquine on the intracellular metabolic activation and antiviral activity of remdesivir.

Adverse Reactions³:

The most common adverse reactions (incidence greater than or equal to 5%, all grades) observed with treatment with remdesivir are nausea, ALT increased, and AST increased. Less common adverse reactions reported include hypersensitivity reactions, generalized seizure and rash.

Information on IHS adverse reaction reporting to the FDA MedWatch program can be found on the [IHS Pharmacovigilance website](#).

References:

1. FDA News Release. October 22, 2020. [FDA Approves First Treatment for COVID-19](#). Accessed October 23, 2020.
2. U.S. Food and Drug Administration. Fact Sheet for Health Care Providers. [Emergency Use Authorization of Remdesivir. \(Veklury\)](#).
3. VEKLURY (remdesivir). October 2020. [Prescribing Information](#). Gilead Sciences, Inc. Foster City, CA. 94404.
4. Beigel JH, Tomashek KM, et al. [Remdesivir for the treatment of COVID-19 – Final Report](#). NEJM. Oct 8, 2020. DOI: 10.1056/NEJMoa2007764
5. Spinner CD, Gottlieb RL, et al. [Effect of Remdesivir vs Standard Care on Clinical Status at 11 Days in Patients With Moderate COVID-19](#). JAMA. 2020; 324(199): 1048-1057.
6. Goldman JD, Lye DC, et al. [Remdesivir for 5 or 10 days in patients with severe COVID-19](#). NEJM. May 27, 2020. DOI: 10.1056/NEJMoa2015301