

This document is intended to provide guidance to PMH facilities when **Emergency Use Authorization** has been granted by the Federal and State government.

Use of Remdesivir under Emergency Use Authorization status:

1. Background:

On May 1, 2020, U.S. Food and Drug Administration (FDA) issued an emergency use authorization (EUA) for the investigational antiviral drug remdesivir for the treatment of suspected or laboratory-confirmed COVID-19 in adults and children hospitalized with severe disease. While there is limited information known about the safety and effectiveness of using remdesivir to treat people in the hospital with COVID-19, the investigational drug was shown in a clinical trial to shorten the time to recovery in some patients.

Remdesivir is an adenosine nucleotide prodrug that is metabolized to remdesivir triphosphate. Remdesivir triphosphate acts as an analog of adenosine triphosphate (ATP) and competes with the natural ATP substrate for incorporation into nascent RNA chains by the SARS-CoV-2 RNA-dependent RNA polymerase, which results in delayed chain termination during replication of the viral RNA. Remdesivir triphosphate is a weak inhibitor of mammalian DNA and RNA polymerases with low potential for mitochondrial toxicity.

The issuance of an EUA is different than FDA approval. In determining whether to issue an EUA, the FDA evaluates the available evidence and carefully balances any known or potential risks of any unproven products with any known or potential benefits of making them available during the emergency. Based on evaluation of the EUA criteria and the scientific evidence available, it was determined that it is reasonable to believe that remdesivir may be effective in treating COVID-19, and that, given there are no adequate, approved, or available alternative treatments, the known and potential benefits to treat this serious or life-threatening virus currently outweigh the known and potential risks of the drug's use.

Distribution of remdesivir will be determined by the Federal and State governments with priority given to highly impacted areas.

2. Minimum Use Criteria:

- a. A multi-disciplinary team (ICU, ID, Pulmonology, Pharmacy etc.) must be involved in appropriate patient selection, past treatment evaluation and patient consent.
- b. Suspected or laboratory confirmed coronavirus disease 2019 (COVID-19) in adults and children hospitalized with severe disease
- c. **Severe disease: Patients with oxygen saturation (SpO2) \leq 93% on room air or requiring mechanical ventilation or requiring extracorporeal membrane oxygenation (ECMO)**
- d. Remdesivir is not recommended in patients with eGFR $<$ 30 mL/min
- e. Remdesivir is not recommended in patients with ALT \geq 5 times the upper normal limit at baseline
- f. Pediatric & Pregnant Patients: Apply for Gilead Compassionate Use Program for separate supply. Reserve EUA supply for non-pediatric and non-pregnant patients.

- g. Providers must order via the Electronic Medical Record; local restrictions may apply and this agent is often restricted to Infectious Diseases Specialists only.

3. Dosing:

- a. Body weight \geq 40 kg: Remdesivir 200mg IV on Day 1, followed by remdesivir 100mg IV daily on Days 2 to 5.
- b. Body Weight < 40 kg: Remdesivir 5 mg/kg IV on Day 1, followed by remdesivir 2.5 mg/kg IV daily on Days 2 to 5. Use actual body weight (ABW).

4. Preparation and Administration Instructions:

- a. **Remdesivir for Injection, 100 mg, Lyophilized Powder:** Pharmacy will reconstitute remdesivir for injection lyophilized powder with 19 mL of Sterile Water for Injection for a total concentration of 100 mg/20 mL (5 mg/mL) of remdesivir solution. Dilute remdesivir concentrated solution in 0.9% saline prior to administration. OR
- b. **Remdesivir Injection, 5 mg/mL, Solution:** Dilute remdesivir injection concentrated solution in 0.9% saline prior to administration. **Remdesivir under the EUA is available in a diluted form.**

Remdesivir Dose	Volume of 0.9% NaCl infusion bag	Volume of 0.9% NaCl to be withdrawn and discarded	Required volume of remdesivir solution	Infusion time	Rate of infusion
200 mg (2 vials) Loading Dose	250 mL	40 mL	2 x 20 mL	60 min	4.17 mL/min
100 mg (1 vial)	250 mL	20 mL	20 mL	60 min	4.17 ml/min

For weight-based dosing, see remdesivir fact sheet

- c. Prepare solution for infusion on same day as administration.
- d. After infusion is complete, flush with at least 30 mL of 0.9% saline.
- e. Store under refrigeration.

5. Common Known Side Effects

- a. **Infusion-Related Reactions:** Signs and symptoms may include hypotension, nausea, vomiting, diaphoresis, and shivering. If signs and symptoms of a clinically significant infusion reaction occur, immediately discontinue administration of remdesivir and initiate appropriate treatment.
- b. **Increased Risk of Transaminase Elevation:** Hepatic laboratory testing should be performed in all patients prior to starting remdesivir and daily while receiving remdesivir. Remdesivir should not be initiated in patients with ALT \geq 5 times the upper limit of normal at baseline. Remdesivir should be discontinued in patients who develop ALT \geq 5 times the upper limit of normal during treatment with remdesivir, or experience ALT elevation accompanied by signs

or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or INR. Remdesivir may be restarted when ALT is < 5 times the upper limit of normal.

6. Mandatory Documentation:

- a. **Fact Sheet for Patients and Parents/Caregivers:** As the health care provider, communicate to your patient or parent/caregiver information consistent with the “Fact Sheet for Patients and Parents/Caregivers” prior to the patient receiving remdesivir. Health care providers (to the extent practicable given the circumstances of the emergency) **must** document in the patient’s medical record that the patient/caregiver has been:
 - i. Given the Fact Sheet for Patients and Parents/Caregivers,
 - ii. Informed of alternatives to receiving remdesivir, and,
 - iii. Informed that remdesivir is an unapproved drug that is authorized for use under EUA.
- b. **Patient consent form:** Must receive patient consent prior to therapy initiation.
- c. **Renal and Hepatic Monitoring:** Adult and pediatric patients (>28 days old) must have an eGFR determined and full-term neonates (≥ 7 days to ≤ 28 days old) must have serum creatinine determined prior to remdesivir first administration. Hepatic laboratory testing should be performed in all patients prior to starting remdesivir and daily while receiving remdesivir.
- d. **FDA MedWatch: The prescribing health care provider and/or the provider’s designee are/is responsible for mandatory reporting of all medication errors and adverse events (death, serious adverse events*) considered to be potentially related to remdesivir occurring during remdesivir treatment within 7 calendar days from the onset of the event.** The reports should include unique identifiers and the words “Remdesivir under Emergency Use Authorization (EUA)” in the description section of the report. Submit adverse event reports to FDA MedWatch using one of the following methods:
 - i. Complete and submit the report online: www.fda.gov/medwatch/report.htm, or
 - ii. By using a postage-paid Form FDA 3500 (available at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf>) and returning by mail (MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787), or by fax (1800-FDA-0178), or
 - iii. Call 1-800-FDA-1088 to request a reporting form

Please access COVID-19 SharePoint site for the complete list of PMH guidance documents as referenced above. <https://pmhcorp.sharepoint.com/sites/COVID19/>