FACT SHEET FOR HEALTH CARE PROVIDERS
EMERGENCY USE AUTHORIZATION (EUA) OF REMDESIVIR (GS-5734™)

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved product remdesivir for treatment of suspected or laboratory confirmed coronavirus disease 2019 (COVID-19) in adults and children hospitalized with severe disease. Severe disease is defined as patients with an oxygen saturation (SpO2) ≤ 94% on room air or requiring supplemental oxygen or requiring mechanical ventilation or requiring extracorporeal membrane oxygenation (ECMO).

This EUA is for the use of remdesivir to treat COVID-19
Remdesivir must be administered by intravenous (IV) infusion

Health care providers must submit a report on all medication errors and **ALL SERIOUS ADVERSE EVENTS** related to remdesivir.
See specific reporting instructions below.

The optimal duration of treatment for COVID-19 is unknown. Under this EUA for remdesivir to treat COVID-19:

- The suggested dose for adults and pediatric patients weighing ≥40 kg requiring invasive mechanical ventilation and/or ECMO is a single loading dose of 200 mg infused intravenously over 30 to 120 minutes on Day 1 followed by once-daily maintenance doses of 100 mg infused intravenously over 30 to 120 minutes for 9 days (days 2 through 10).
- The suggested dose for adults and pediatric patients weighing ≥40 kg not requiring invasive mechanical ventilation and/or ECMO is a single dose of 200 mg infused intravenously over 30 to 120 minutes on Day 1 followed by once-daily maintenance doses of 100 mg infused intravenously over 30 to 120 minutes for 4 days (days 2 through 5). If a patient does not demonstrate clinical improvement, treatment may be extended for up to 5 additional days (i.e., up to a total of 10 days).
- The suggested dose for pediatric patients with body weight between 3.5 kg and <40 kg requiring invasive mechanical ventilation and/or ECMO is a single loading dose of remdesivir 5 mg/kg IV (infused over 30 to 120 min) on Day 1 followed by remdesivir 2.5 mg/kg IV (infused over 30 to 120 min) once daily for 9 days (days 2 through 10).
- The suggested dose for pediatric patients with body weight between 3.5 kg and <40 kg not requiring invasive mechanical ventilation and/or ECMO is a single loading dose of remdesivir 5 mg/kg IV (infused over 30 to 120 min) on Day 1 followed by remdesivir 2.5 mg/kg IV (infused over 30 to 120 min) once daily for 4 days (days 2 through 5). If a patient does not demonstrate clinical improvement, treatment may be extended for up to 5 additional days (i.e., up to a total of 10 days).

For information on clinical trials that are testing the use of remdesivir in COVID-19, please see www.clinicaltrials.gov.

INSTRUCTIONS FOR ADMINISTRATION

This section provides essential information on the unapproved use of remdesivir, an unapproved drug, to treat suspected or laboratory confirmed COVID-19 in adults and children hospitalized with severe disease under this EUA. For more information, see the long version of the "Fact Sheet for Health Care Providers," available at https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization.

Contraindications

Remdesivir is contraindicated in patients with known hypersensitivity to any ingredient of remdesivir.

Dosing

Treatment Initiation and Dosing Regimens

- Empiric treatment of hospitalized patients with suspected COVID-19 can be considered pending laboratory confirmation of SARS-CoV-2 infection.
- A treatment course of 10 days is recommended for adults and pediatric patients requiring invasive mechanical ventilation and/or extracorporeal membrane oxygenation.
- A treatment course of 5 days is recommended for adults and pediatric patients not requiring invasive mechanical ventilation and/or ECMO. If a patient does not demonstrate clinical improvement, treatment may be extended for up to 5 additional days (i.e., up to a total of 10 days).
- Remdesivir can be used at any time after onset of symptoms in hospitalized patients.
- All patients must have an estimated glomerular filtration rate (eGFR) determined before dosing.
- Hepatic laboratory testing should be performed in all patients prior to starting remdesivir and daily while receiving remdesivir.

Adult Patients

- For adults requiring invasive mechanical ventilation and/or ECMO, the dosage of remdesivir is a single loading dose of 200 mg infused intravenously over 30 to 120 minutes on Day 1 followed by once-daily maintenance doses of 100 mg infused intravenously over 30 to 120 minutes for 9 days (days 2 through 10).
- For adults not requiring invasive mechanical ventilation and/or ECMO, the dosage of remdesivir is a single loading dose of 200 mg infused intravenously over 30 to 120 minutes on Day 1 followed by once-daily maintenance doses of 100 mg infused intravenously over 30 to 120

minutes for 4 days (days 2 through 5). If a patient does not demonstrate clinical improvement, treatment may be extended for up to 5 additional days (i.e., up to a total of 10 days).

Pediatric Patients

- For pediatric patients with body weight ≥40 kg requiring invasive mechanical ventilation and/or ECMO, the adult dosage regimen of one loading dose of remdesivir 200 mg IV (infused over 30 to 120 minutes) on Day 1 followed by remdesivir 100 mg IV (infused over 30 to 120 minutes) once daily for 9 days (days 2 through 10) will be administered.
- For pediatric patients with body weight ≥40 kg not requiring invasive mechanical ventilation and/or ECMO, the adult dosage regimen of one loading dose of remdesivir 200 mg IV (infused over 30 to 120 minutes) on Day 1 followed by remdesivir 100 mg IV (infused over 30 to 120 minutes) once daily for 4 days (days 2 through 5) will be administered. If a patient does not demonstrate clinical improvement, treatment may be extended for up to 5 additional days (i.e., up to a total of 10 days).
- Use of the adult dose in these pediatric patients is expected to maintain exposures of both remdesivir and the nucleoside analog GS-441524 generally within the expected adult steady-state exposure range following administration of the adult therapeutic dosage regimen in healthy volunteers.
- For pediatric patients with body weight between 3.5 kg and <40 kg, use remdesivir for injection, 100 mg, lyophilized powder only. Administer a body weight-based dosing regimen of one loading dose of remdesivir 5 mg/kg IV (infused over 30 to 120 min) on Day 1 followed by remdesivir 2.5 mg/kg IV (infused over 30 to 120 min) once daily for 9 days (for pediatric patients requiring invasive mechanical ventilation and/or ECMO, days 2 through 10) or for 4 days (for pediatric patients not requiring invasive mechanical ventilation and/or ECMO, days 2 through 5). If a patient does not demonstrate clinical improvement, treatment may be extended for up to 5 additional days (i.e., up to a total of 10 days). Use of this weight-based dosing regimen is expected to maintain remdesivir exposure that is comparable to that observed in adults while limiting the exposure of the nucleoside analog GS-441524 in very young children.

Pregnancy

Remdesivir should be used during pregnancy only if the potential benefit justifies the potential risk for the mother and the fetus.

Renal Impairment

The pharmacokinetics of remdesivir have not been evaluated in patients with renal impairment. Use in patients with renal impairment are based on potential risk and potential benefit considerations. Patients with eGFR greater than or equal to 30 mL/min have received remdesivir for treatment of COVID-19 with no dose adjustment of remdesivir.

All patients must have an eGFR determined before dosing. Remdesivir is not recommended in adult and pediatric patients (>28 days old) with eGFR less than 30 mL/min or in full-term neonates (≥7 days to ≤28 days old) with serum creatinine greater than or equal to 1 mg/dL unless the potential benefit outweighs the potential risk.

Hepatic Impairment

The pharmacokinetics of remdesivir have not been evaluated in patients with hepatic impairment. It is not known if dosage adjustment is needed in patients with hepatic impairment and remdesivir should only be used in patients with hepatic impairment if the potential benefit outweighs the potential risk.

Hepatic laboratory testing should be performed in all patients prior to starting remdesivir and daily while receiving remdesivir.

Dose Preparation

Care should be taken during admixture to prevent inadvertent microbial contamination. As there is no preservative or bacteriostatic agent present in this product, aseptic technique must be used in preparation of the final parenteral solution. It is always recommended to administer IV medication immediately after preparation when possible.

Store diluted remdesivir solution for infusion up to 4 hours at room temperature (20°C to 25°C [68°F to 77°F]) or 24 hours at refrigerated temperature (2°C to 8°C [36°F to 46°F]).

Important Preparation and Administration Instructions

- **Remdesivir for Injection, 100 mg:** Reconstitute remdesivir for injection lyophilized powder with 19 mL of Sterile Water for Injection and dilute in 0.9% saline prior to administration.
- **Remdesivir Injection, 5 mg/mL:** Dilute remdesivir injection concentrated solution in 0.9% saline prior to administration.
- Prepare solution for infusion on same day as administration.
- Administer remdesivir as an intravenous infusion over 30 to 120 minutes.
- After infusion is complete, flush with at least 30 mL of 0.9% saline.
- Discard any remaining reconstituted remdesivir lyophilized powder, reconcentrated solution, and diluted solution.

Storage and Handling of Prepared Dosages

IMPORTANT:

This product contains no preservative. Any unused portion of a single-dose remdesivir vial should be discarded after a diluted solution is prepared.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Should either be observed, the solution should be discarded and fresh solution prepared.

The prepared diluted solution should not be administered simultaneously with any other medication. The compatibility of remdesivir injection with IV solutions and medications other than 0.9% saline is not known.

Warnings

There are limited clinical data available for remdesivir. Serious and unexpected adverse events may occur that have not been previously reported with remdesivir use.

Infusion-Related Reactions

Infusion-related reactions have been observed during, and/or have been temporally associated with, administration of remdesivir. 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. The use of remdesivir is contraindicated in patients with known hypersensitivity to remdesivir.

Increased Risk of Transaminase Elevations

Transaminase elevations have been observed in the remdesivir clinical development program, including in healthy volunteers and patients with COVID-19. In healthy volunteers who received up to 150 mg daily for 14 days, alanine aminotransferase (ALT) elevations were observed in the majority of patients, including elevations up to 10 times baseline values in one subject without evidence of clinical hepatitis; no ≥ Grade 3 adverse events were observed. Transaminase elevations have also been reported in patients with COVID-19 who received remdesivir, including one patient with ALT elevation up to 20 times the upper limit of normal. As transaminase elevations have been reported as a component of COVID-19 in some patients, discerning the contribution of remdesivir to transaminase elevations in this patient population is challenging.

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 ≥ 5 times the upper limit of normal at baseline
- Remdesivir should be discontinued in patients who develop:
    - ALT ≥ 5 times the upper limit of normal during treatment with remdesivir. Remdesivir may be restarted when ALT is < 5 times the upper limit of normal.
      OR
    - ALT elevation accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or INR

Serious Side Effects
An adverse reaction associated with remdesivir in clinical trials in healthy adult subjects was increased liver transaminases. Additional adverse reactions associated with the drug, some of which may be serious, may become apparent with more widespread use.

INSTRUCTIONS FOR HEALTH CARE PROVIDERS

As the health care provider, you must communicate to your patient or parent/caregiver information consistent with the "Fact Sheet for Patients and Parents/Caregivers" (and provide a copy of the Fact Sheet) prior to the patient receiving remdesivir, including:

- FDA has authorized the emergency use of remdesivir, which is not an FDA approved drug.
- The patient or parent/caregiver has the option to accept or refuse remdesivir.
- The significant known and potential risks and benefits of remdesivir, and the extent to which such risks and benefits are unknown.
- Information on available alternative treatments and the risks and benefits of those alternatives.

If providing this information will delay the administration of remdesivir to a degree that would endanger the lives of patients, the information must be provided to the patients as soon as practicable after remdesivir is administered.

For information on clinical trials that are testing the use of remdesivir for COVID-19, please see www.clinicaltrials.gov.

MANDATORY REQUIREMENTS FOR REMDESIVIR ADMINISTRATION UNDER EMERGENCY USE AUTHORIZATION:

In order to mitigate the risks of using this unapproved product under EUA and to optimize the potential benefit of remdesivir, the following items are required. Use of unapproved remdesivir under this EUA is limited to the following (all requirements **must** be met):

1. Treatment of suspected or laboratory confirmed coronavirus disease 2019 (COVID-19) in adults and children hospitalized with severe disease. Severe disease is defined as patients with an oxygen saturation (SpO2) ≤ 94% on room air or requiring supplemental oxygen or requiring invasive mechanical ventilation or requiring ECMO. Specifically, remdesivir is authorized only for the following patients who are admitted to a hospital and under the care or consultation of a licensed clinician (skilled in the diagnosis and management of patients with potentially life-threatening illness and the ability to recognize and manage medication-related adverse events):
    a. Adult patients for whom use of an IV agent is clinically appropriate.
    b. Pediatric patients for whom use of an IV agent is clinically appropriate.
2. 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:
    a. Given the Fact Sheet for Patients and Parents/Caregivers,
    b. Informed of alternatives to receiving remdesivir, and
    c. Informed that remdesivir is an unapproved drug that is authorized for use under EUA.
3. 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.
4. Hepatic laboratory testing should be performed in all patients prior to starting remdesivir and daily while receiving remdesivir.
5. Patients with known hypersensitivity to any ingredient of remdesivir must not receive remdesivir.
   The prescribing health care provider and/or the provider's designee are/is responsible for mandatory responses to requests from FDA for information about adverse events and medication errors following receipt of remdesivir.
6. 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:
  - Complete and submit the report online: www.fda.gov/medwatch/report.htm, or
  - 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 (1-800-FDA-0178), or
  - Call 1-800-FDA-1088 to request a reporting form
  - Submitted reports should include in the field name, “Describe Event, Problem, or Product Use/Medication Error” a statement “**Remdesivir under Emergency Use Authorization (EUA).”**

*Serious Adverse Events are defined as:

- death;
- a life-threatening adverse event;
- inpatient hospitalization or prolongation of existing hospitalization;
- a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- a congenital anomaly/birth defect;
- a medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly.

[see Adverse Reactions and Medication Errors Reporting Requirements and Instructions (8)]

OTHER REPORTING REQUIREMENTS
In addition please provide a copy of all FDA MedWatch forms to:
Gilead Pharmacovigilance and Epidemiology
Fax: 1-650-522-5477
E-mail: Safety_fc@gilead.com

APPROVED AVAILABLE ALTERNATIVES

There is no approved available alternative product. There are EUAs for other COVID-19 treatments. Additional information on COVID-19 treatments can be found at https://www.cdc.gov/coronavirus/2019-ncov/index.html. The health care provider should visit https://clinicaltrials.gov/ to determine whether the patient may be eligible for enrollment in a clinical trial.

AUTHORITY FOR ISSUANCE OF THE EUA

The Secretary of HHS has declared a public health emergency that justifies the emergency use of remdesivir to treat COVID-19 caused by SARs-CoV-2. In response, the FDA has issued an EUA for the unapproved product, remdesivir, for the treatment of COVID-19.[1] As a health care provider, you must comply with the mandatory requirements of the EUA (see below).

FDA issued this EUA, requested by Gilead Sciences, Inc. and based on their submitted data.

Although limited scientific information is available, based on the totality of the scientific evidence available to date, it is reasonable to believe that remdesivir may be effective for the treatment of COVID-19 in patients as specified in this Fact Sheet. You may be contacted and asked to provide information to help with the assessment of the use of the product during this emergency.

This EUA for remdesivir will end when the Secretary determines that the circumstances justifying the EUA no longer exist or when there is a change in the approval status of the product such that an EUA is no longer needed.

[1] The health care provider should visit clinicaltrials.gov to determine whether there is an active clinical trial for the product in this disease/condition and whether enrollment of the patient(s) in a clinical trial is more appropriate than product use under this EUA.

FULL EUA PRESCRIBING INFORMATION

FULL EUA PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

1. AUTHORIZED USE

Remdesivir is authorized for use under an EUA for treatment of patients hospitalized with suspected or laboratory confirmed SARS-CoV-2 infection and severe disease. Severe disease is defined as patients with an oxygen saturation (SpO2) ≤94% on room air or requiring supplemental oxygen or requiring mechanical ventilation or requiring extracorporeal membrane oxygenation (ECMO). Specifically, remdesivir is only authorized for hospitalized adult and pediatric patients for whom use of an intravenous agent is clinically appropriate.

2. DOSAGE AND ADMINISTRATION

2.1 General Information

- The optimal dosing and duration of treatment is unknown. The suggested dose and duration may be updated as data from clinical trials becomes available.
- 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 before dosing of remdesivir.
- Hepatic laboratory testing should be performed in all patients prior to starting remdesivir and daily while receiving remdesivir.
- Remdesivir should be administered via intravenous (IV) infusion only. Do not administer as an intramuscular (IM) injection.