Currently there is no FDA approved antiviral therapy for SARS-COV-2 infection. The mainstay of therapy is supportive care. The treatment algorithm presented here is based on a review of currently available literature, particularly the NIH and IDSA published treatment guidelines. On May 1, 2020 the FDA issued an Emergency Use Authorization (EUA) for use of Remdesivir for the treatment of hospitalized COVID-19 patients. The EUA was revised August 2020. The treatment algorithm will be updated to reflect new data as it becomes available.

**COVID-19 patient**

1. Clinical symptoms + positive pcr test
2. If remdesivir was initiated at another VT hospital, the remaining doses should be transported with the patient for continuation of therapy. Confirm ongoing eligibility (table 2).
3. Remdesivir criteria of use: Positive COVID-19 pcr test, O2 sat < 94%, CrCl ≥ 30 ml/min, AST & ALT < 5x ULN, use of IV medication is clinically appropriate, weight ≥ 3.5kg.
4. See table 1 for information about remdesivir
5. See table 2 for information about remdesivir consent and monitoring.

**Multisystem Inflammatory Syndrome (MIS-C)**

- Patient <21 years old with fever, laboratory evidence of inflammation, and clinically severe illness requiring hospitalization with multisystem involvement
- No alternative plausible diagnosis
- Recent or current +COVID-19 pcr or +SARS-CoV-2 Ab or Confirmed exposure to COVID-19 within 4 weeks prior to the onset of symptoms
- Consult pediatric ID and rheumatology

**Outpatient**
- Supportive care

**Inpatient admission for acute COVID-19**
- SpO2 > 94%
- SpO2 ≤ 94%
- Supportive care
- Discussion with patient/caregiver about remdesivir
- Patient/caregiver prefer supportive care or patient not eligible for remdesivir
- Remdesivir eligible
- Consult Pediatric Infectious Diseases
- Supportive care
# Table 1. Remdesivir

Remdesivir is an investigational nucleotide analog with antiviral activity. It is infused as an adenosine nucleotide prodrug, then metabolized to its pharmacologically active form of nucleoside triphosphate metabolite. It acts as an analog of adenosine triphosphate (ATP) to compete with the natural ATP substrate for incorporation into nascent RNA chains by the SARS-CoV-2 RNA-dependent RNA polymerase, resulting in delayed chain termination during replication of viral RNA\(^1\). Remdesivir is not FDA approved.

<table>
<thead>
<tr>
<th>Supply Source &amp; Formulation</th>
<th>Dosing</th>
<th>Notes</th>
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| **Donated supply from US Government**
  Solution: children weighing > 40kg | children weighing > 40kg: 200 mg IV on day 1, then 100 mg IV daily for up to 4 days, or hospital discharge, whichever comes first. | Infectious Diseases consult required. |
| Lyophilized powder: children weighing 3.5 kg – ≤40 kg | Children 3.5kg - ≤ 40kg: 5mg/kg IV on day 1, then 2.5mg/kg IV daily for up to 4 days, or hospital discharge, whichever comes first. | Remdesivir is currently available in limited supply through an [FDA Emergency Use Authorization (EUA) letter](https://www.gilead.com/-/media/files/pdfs/remdesivir/eua-fact-sheet-for-hcps_01may2020.pdf). The EUA was revised on August 28, 2020. The major revision is to include expand eligibility of remdesivir to hospitalized patients not needing supplemental oxygen. This decision was based on this study published in JAMA. The study concludes that patients who received 5 days of remdesivir had a statistically significant difference in clinical status (favorable) compared to standard of care or 10 days of remdesivir at 11 days of care. The authors state that they are uncertain of the clinical importance of these findings. Due to the limited supply of remdesivir, UVMMC will continue to follow the previously agreed upon clinical criteria by the VT CMO group of initiation of remesdivir for patients who have \(O_2\) sat ≤ 94% on ambient air. |
| 5 days of therapy is recommended for patients not requiring invasive mechanical ventilation or ECMO, but can be extended up to 10 days of no substantial clinical improvement is seen at day 5. | Current criteria for consideration of use as decided by the State of Vermont:
  Positive COVID-19 test
  \(O_2\) sat ≤ 94%, or the need for supplemental \(O_2\), mechanical ventilation, or ECMO
  \(CrCl\) ≥ 30ml/min
  AST & ALT ≤ 5x upper limit of normal
  The use of IV medication is appropriate |
| **Notes** | **Remdesivir** should not be co-administered with strong inducers of CYP450, such as rifampin. Check for drug-drug interactions prior to prescribing. Concomitant use of hydroxychloroquine, chloroquine, and remdesivir is not recommended. |

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This document is subject to change. Updated by the UVMMC COVID-19 Therapeutics Working Group on 10/14/2020.
Table 2. Consent and Monitoring for US Government donated Remdesivir

Consent

Current criteria for consideration of use as decided by the State of Vermont:
Positive COVID-19 pcr test
O₂ sat ≤ 94%, or the need for supplemental O₂, mechanical ventilation, or ECMO
CrCl ≥ 30ml/min
AST & ALT ≤ 5x upper limit of normal
The use of IV medication is appropriate

Prior to administration:
1. It must be documented that the patient (or caregiver) received the EUA patient fact sheet and fact sheet has been explained to the patient. The patient fact sheet has been translated into eight languages as all are available on the UVMMC COVID-19 website.
2. Physician must document that he/she has read the EUA physician fact sheet.
3. It must be documented that the patient has been informed about alternative treatments.
4. It must be documented that the patient has been informed that remdesivir is not an FDA approved medication.

Use dotphrase ".remdesivirconsent" in H&P or progress note to document patient consent.

Monitoring

Daily laboratory monitoring:
Creatinine and creatinine clearance
AST, ALT
CBC
Electrolytes

Risk of infusion related reaction:
Infusion-related reactions have been observed during, and/or 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 hypersensitive to remdesivir.

Discontinue remdesivir if ALT ≥ 5x upper limit of normal. Remdesivir may be restarted when ALT ≤ 5x upper limit of normal. Discontinue remdesivir if ALT elevation is accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or INR.

Adverse Events or death must be reported to FDA Medwatch within 7 days of event. www.fda.gov/medwatch/report.htm and copied to Gilead at Safety_fc@gilead.com
Serious adverse events are defined in the EUA are:
Death
Inpatient hospitalization or prolongation of existing hospitalization
Persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
Congenital anomaly/birth defect
A medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly

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