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. 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 treatment algorithm will be updated to reflect new data as it becomes available.

### Confirmed positive COVID-19 patient

**Outpatient**
- Supportive care

**Pediatric inpatient admission**
- Pediatric Infectious Diseases consult for consideration of treatment with Remdesivir\(^2,3,4\)

**Pregnant woman inpatient admission**
- Early consideration for compassionate use access program of Remdesivir\(^2,3\)
- Consult Infectious Diseases
- Consult Rheumatology for consideration of anti-cytokine storm biologic therapy\(^6\)

**Adult inpatient admission**
- Discussion with patient/caregiver about treatment options\(^2,3,6\)
- Patient/caregiver prefers supportive care
- Patient/caregiver accepts Remdesivir\(^3,5\)
- Consult Infectious Diseases
- Consult Rheumatology for consideration of anti-cytokine storm biologic therapy\(^6\)

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1. If remdesivir was initiated at another VT hospital, the remaining doses should be transported with the patient for continuation of therapy.
2. **Remdesivir criteria of use**: Positive COVID-19 test, O2 sat < 94%, CrCl ≥ 30 ml/min, AST & ALT < 5x ULN, use of IV medication is clinically appropriate.
3. **Baricitinib criteria of use**: Positive COVID-19 test, Fever, Radiographic evidence of pneumonia, O2 < 94% on ambient air
4. See table 1 for information about remdesivir
5. See table 2 for information about consent and monitoring.
6. See table 3 for information about anti-cytokine storm agents, criteria of use, and exclusion criteria.

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Supply Source & Formulation

Dosing

Notes

Donated supply from US Government
Solution: adults and children weighing > 40kg.

Adults and children weighing > 40kg:
200 mg IV on day 1, then 100 mg IV daily for up to 10 days

Children 3.5kg - ≤40kg:
5mg/kg IV on day 1, then 2.5mg/kg IV daily for up to 10 days.

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 clinical improvement is seen at day 5.

10 days of therapy is recommended for intubated patients.

Infectious Diseases consult required.

Remdesivir is currently available in limited supply through an FDA Emergency Use Authorization (EUA) letter.

Current criteria for consideration of use as decided by the State of Vermont:
Positive COVID-19 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

Lyophilized powder:
children weighing 3.5 kg – ≤40kg

Pregnant women:
200 mg IV on day 1, then 100 mg IV daily for up to 10 days

Children 3.5kg - ≤ 40kg:
5mg/kg IV on day 1, then 2.5mg/kg IV daily for up to 10 days.

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 clinical improvement is seen at day 5.

10 days of therapy is recommended for intubated patients.

Infectious Diseases consult required.

Currently, Gilead prefers pregnant women in need of antiviral therapy access Remdesivir through the compassionate use access program over the US government donated supply.

The EUA stipulates that the lyophilized powder formulation of remdesivir should be used for children weighing 3.5kg – 40kg. There is limited supply of the lyophilized powder formulation in Vermont. If this supply is exhausted and not replaced by the US Government, further supply should be obtained through Gilead’s compassionate use program.

Remdesivir can be obtained through Gilead’s compassionate use program.
https://rdvcu.gilead.com/

Obtaining compassionate use remdesivir requires assistance by the investigational pharmacy and UVM IRB.

Gilead Compassionate Use Program
Pregnant women
children weighing 3.5 kg – ≤40kg

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. It is not FDA approved and does not have safety or efficacy profiles.

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. It is not FDA approved and does not have safety or efficacy profiles.


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### Consent

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
- $CrCl ≥ 30 ml/min$
- 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.
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](http://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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Table 2. Consent and Monitoring for US Government donated Remdesivir

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Tocilizumab 400mg IV x1 (Use order panel)

Rheumatology approval required. Call Rheumatology if patient has progressive respiratory decline with need for higher level of respiratory support, or needing transfer to the ICU.

Tocilizumab is an interleukin-6 (IL-6) receptor inhibitor, binding to soluble and membrane-bound IL-6 receptors. It is currently under investigation as an agent targeting cytokine storm as a result of COVID-19.

Tocilizumab has been shown to be safe in pregnancy

Contraindications: any known hypersensitivity to tocilizumab.

Baricitinib if CrCl > 60ml/min
4mg po daily x 7 days

If CrCl 30 – 59ml/min: 2mg po daily x 7 days
If CrCl <30ml/min do not use

Rheumatology approval required.

Baricitinib inhibits Janus kinase (JAK) enzymes, which are involved in stimulating hematopoiesis and immune cell function through a complex signaling pathway. Its role in the treatment of COVID-19 is evolving. The current thought is early administration of baricitinib could stave off cytokine storm.

If pill cannot be swallowed, medication can be dispersed in a small amount of liquid.

Criteria for consideration of use

Inclusion criteria:

- Positive COVID-19 test
- worsening respiratory decline with impending transfer to the ICU
- Onset of symptoms less than 1 week and hospitalization <48 hours
- Temperature > 38.3 C
- Labs
  - Ferritin > 1000 ng/mL
  - D-Dimer >1000 ng/mL
  - LDH >250 U/L
  - CRP > 70 mg/L or >40 mg/L and doubling within 48 hours
  - Lymphocyte count < 0.6 x 10^9/L
  - Likelihood of good clinical outcome based on age and other comorbidities

Exclusion criteria:

- Pregnant or breast feeding
- Already taking a JAKi or other biologic DMARD, anti-IL6 or anti-IL8 antibodies, or potent immunosuppressants, such as azathioprine and cyclosporine
- AST/ALT > 5x ULN
- Absolute lymphocyte count <500 cells/mL
- Absolute neutrophil count <1,000 cells/mL
- Hemoglobin <8g/dL
- Platelets < 50,000/mL
- CrCl < 30ml/min
- Malignancy and receiving immunosuppressant therapy
- Active or suspected bacterial or fungal, or viral infection other than SARS-CoV-2
- Symptoms of or known diagnosis of thromboembolism, phlebitis, or hypercoagulable state

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