Montefiore Health System Guidelines for Therapeutic Remdesivir Access

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**Background**

Remdesivir is an antiviral drug being studied for the treatment of COVID-19. Results from the NIH ACTT1 trial show that those who received remdesivir had significantly shorter duration of hospitalization and lower mortality than those receiving placebo. Based on this observed benefit, the FDA issued an Emergency Use Authorization (EUA) for remdesivir, and the federal government has distributed much of Gilead's existing limited supply of remdesivir to hospitals across the US. However, the supply of remdesivir will remain extremely limited pending ramp up of manufacturing in the coming weeks.

Until production has expanded, there are a number of pathways to access the limited supply of remdesivir at the Montefiore Health System (MHS):

1. Montefiore Moses and Einstein campuses will be study sites for the ACTT2 trial studying outcomes in patients who receive remdesivir alone, or remdesivir plus baricitinib, beginning May 11, 2020.
2. The Moses and Einstein campuses have been granted limited access to remdesivir through Gilead’s Expanded Access Program (EAP).
3. For pregnant patients and pediatric patients (<18 years old), remdesivir can be requested through direct application to Gilead for its Individual Compassionate Use Program, on a case-by-case basis.
4. MHS has been issued a limited supply of remdesivir under the EUA program

Data is just emerging on how best to use remdesivir in patients with COVID-19. However, many patients with COVID-19 will not benefit from this treatment either due to mild/moderate, generally self-limited disease or, due to disease that is so severe, damaging, or late into the course that an antiviral such as this is unlikely to help. Additionally, there is emerging data on the optimal length of treatment with remdesivir for those most likely to benefit; more data will be available in the next few weeks.

Given these limitations, and the desire of the MHS to responsibly, maximally, and most equitably manage the remdesivir EUA stock and benefit the health and outcomes of its patients with COVID-19, the following algorithm for remdesivir access and specific guidelines are implemented as the basis for release of EUA remdesivir within MHS hospitals.
Therapeutic Triage Algorithm for COVID-19

NOTE: remdesivir by EUA is a nonpreferred and last option for remdesivir access due to limited supply; all other options must be explored first

* http://studies.montecovid.net
ACTT2 Trial Criteria (Montefiore Moses and Einstein)

The NIH ACTT2 trial is a study of the combination of remdesivir plus randomized, double-blinded baricitinib or a matching placebo. All patients receive remdesivir; half receive baricitinib in addition, while the other half receive placebo.

Patients eligible for ACTT2 meet ALL of the following criteria:

1. Admitted, symptomatic, and willing to consent
2. Male or non-pregnant female adults ≥ 18 years of age
3. Lab-confirmed SARS-CoV-2 by PCR or other commercial or public health assay:
   a. PCR+ or antigen+ in sample collected < 72 hours prior to randomization; OR
   b. PCR+ or antigen+ in sample ≥72 hours prior, documented inability to obtain repeat sample (e.g. lack of supplies, limited testing capacity, results > 24 hrs) AND progressive disease.
4. Illness of any duration, and at least one of the following:
   a. Radiographic infiltrates by imaging (chest x-ray, CT scan, etc.), OR
   b. SpO2 ≤ 94% on room air OR
   c. Requiring supplemental oxygen, OR
   d. Requiring mechanical ventilation or ECMO.
5. Women of childbearing potential agree to either abstinence or at least one primary form of contraception not including hormonal contraception through Day 29.
6. Agrees to not participate in another COVID-19 treatment trial through Day 29.

Patients are excluded from ACTT2 if they meet ANY of the following criteria:

1. ALT or AST > 5 times the upper limit of normal.
2. eGFR < 30 ml/min (including patients receiving hemodialysis or hemofiltration).
3. Neutropenia (ANC <1000).
4. Lymphopenia (ALC <200).
5. Pregnancy or breast feeding.
6. Anticipated discharge or transfer within 72 hours.
7. Allergy to any study medication.
8. Cytotoxic or biologic treatments (e.g., anti-interleukin-1 [IL-1], anti-IL-6 [tocilizumab or sarilumab], or T-cell or B-cell targeted therapies (e.g., rituximab), tyrosine kinase inhibitors including baricitinib, or interferon within 4 weeks prior.
9. TNF inhibitors within 2 weeks prior.
10. Received convalescent plasma or IVIG for COVID-19.
11. Corticosteroids (>10 mg/day prednisone or equivalent) within 2 weeks of screening.
12. Use of probenecid that cannot be discontinued.
13. Current active tuberculosis (TB) or, if known, latent TB treated <4 weeks (history only, no screening required).
14. Suspected serious, active bacterial, fungal, viral, or other infection (besides COVID-19) that in the opinion of the investigator could constitute a risk with baricitinib.
15. Received any live vaccine (live attenuated) within 4 weeks before screening, or intend to receive a live vaccine (or live attenuated) during study.
16. History of VTE (DVT or PE) within 12 weeks prior or history of recurrent (>1) VTE (DVT/PE).

**Instructions for enrolling patient in ACTT2:**

1. Review criteria to ensure inclusions are met without exclusions.
2. Discuss the trial with the patient and/or legal representative to determine interest in enrolling (and willingness to potentially transfer hospitals if not at a study site). Please note that neither transfer nor enrollment is guaranteed, and that only study staff can officially consent any patient for a study.
3. Contact the study team by email (COVID-NIH-AdaptiveTreatmentTrial-StudyTeam-Moses@montefiore.org for Moses; COVID-NIH-AdaptiveTreatmentTrial-StudyTeam-Weiler@montefiore.org for Weiler), or call the Principal Investigator (Dr. Barry Zingman; 718-920-2647) or a study coordinator (718-920-5224) to ask about the potential for ACTT2 enrollment for the patient.

4. If patient is confirmed to be a potential candidate and requires transfer, contact the Montefiore transfer office at 718-920-8000.

5. A member of the study team will assist in assessing eligibility at Moses or Weiler (after transfer, if applicable).
Remdesivir Access via Individual Compassionate Use Protocol

Patients eligible for remdesivir individual compassionate use meet the following criteria:

1. Age <18 years old OR pregnant
2. Confirmed SARS-CoV-2 by PCR or antigen
3. Hospitalized with SaO2 < 94 % on room air or requiring supplemental O2
4. Liver function tests (ALT) levels less than 5x the upper limit of normal

Patients are excluded from EAP remdesivir if they meet ANY of the following criteria:

1. Requiring significant vasopressor or inotropic support
2. Requiring veno-arterial (VA) ECMO
3. Creatinine Clearance less than 30 mL/min or if the patient is on dialysis or Continuous Veno-Venous Hemofiltration
4. Note any investigational agents for COVID-19 such as lopinavir/ritonavir, chloroquine would need to be stopped prior to the initiation of remdesivir

Instructions for accessing Remdesivir Individual Compassionate Use Protocol:

1. Review criteria to ensure all criteria are met
2. Obtain an Infectious Disease consult (required to ensure clinical appropriateness and duration)
3. If ID approves, the consultant will contact an ID pharmacist to begin the process
4. An ID Pharmacist will review and assist clinician in submitting the request
5. If approved by Gilead and FDA, pharmacy will process the order for remdesivir in Epic/EHR
Remdesivir Access via Expanded Access Program (EAP)

Patients eligible for EAP remdesivir meet ALL of the following criteria:

1. Hospitalized non-pregnant female or male >18 years old
2. Lab-confirmed SARS-CoV-2 by PCR or antigen
3. Requiring invasive mechanical ventilation (ETT or tracheostomy)
4. ALT <5x ULN

Patients are excluded from EAP remdesivir if they meet ANY of the following criteria:

Exclusion Criteria

1. Evidence of multiorgan failure including but not limited to coagulopathy (significant thrombocytopenia), hepatic failure (elevated bilirubin), renal failure (low urine output or eGFR < 30mL/min), or significant cardiomyopathy (low cardiac output)
2. Use of more than 1 pressor for septic shock
3. Renal failure (eGFR < 30mL/min or HD or CVVHD)
4. Eligible for enrollment in a randomized clinical trial involving remdesivir for treatment of COVID-19 at the medical facility where the patient is admitted
5. Known hypersensitivity to the study drug or its metabolites

Instructions for accessing Remdesivir EAP:

1. Review criteria to ensure inclusion criteria are met, without exclusions
2. Request ID consult (required to ensure clinical appropriateness and duration)
3. If ID approves, the consultant will contact an ID pharmacist
4. Pharmacy will review and process remdesivir order in Epic/EHR.
Remdesivir Access via Emergency Use Authorization (EUA)

Patients eligible for EUA remdesivir meet ALL of the following criteria:

1. Adult ≥18 years old, currently hospitalized, with progressively symptomatic COVID-19 disease.
2. Have a positive SARS-CoV-2 PCR or antigen in the last 72 hours, or have a negative/pending PCR or antigen but are diagnosed clinically with COVID-19 by the Infectious Diseases consult service and have no other reasonable explanation for the progressive, symptomatic disease under care.
3. Have signs of moderate-severe lower respiratory tract infection as demonstrated by BOTH of the following:
   a. Bilateral infiltrates or ground glass opacities on chest imaging
   b. Need for oxygen supplementation or ventilation:
      i. O2 by nasal cannula, non-rebreather mask, high-flow device, non-invasive ventilation, mechanical ventilation, or ECMO.
4. If requiring oxygen supplementation or ventilation by high-flow device, non-invasive ventilation, mechanical ventilation or ECMO, they have received one or more of these treatments for ≤7 consecutive days.
5. They do not qualify for or they (or their legal representative) have been asked and declined enrollment in other mechanisms to obtain remdesivir at their hospital site (as available) including randomized controlled trials (such as ACTT), expanded access, and individual compassionate use.
6. They do not have contraindications to remdesivir including:
   a. eGFR <30 ml/min or need for hemodialysis or hemofiltration
   b. ALT or AST >5x the upper limit of normal
   c. Remdesivir allergy that cannot be managed medically
Patients eligible for EUA remdesivir, as above, will be treated with the following regimens according to degree of oxygen requirement:

1. O2 by nasal cannula or non-rebreather mask  
   a. 200 mg IV load then 100 mg IV q24H x up to a maximum of 5 days total.  
   b. Remdesivir is discontinued if discharge occurs or need for supplemental oxygen ceases prior to day 5.
2. O2 by high-flow device, non-invasive ventilation, mechanical ventilation, or ECMO  
   a. 200 mg IV load then 100 mg IV q24H for up to a maximum of 10 days total.  
   b. Remdesivir is discontinued if discharge occurs or need for supplemental oxygen ceases prior to day 10.

Instructions for accessing Remdesivir EUA:

1. Review criteria to ensure all criteria are met.  
2. Request ID consult (required to ensure clinical appropriateness and duration)  
3. If ID approves, the consultant will contact an ID pharmacist  
4. Pharmacy will review and process remdesivir order in Epic/EHR.