**THERAPEUTIC OPTIONS:** There are no FDA-approved antiviral agents for the treatment of COVID-19. The following are based on in-vitro or in-vivo studies suggesting potential benefit and are subject to availability. All Severity Categories are for Patients with Confirmed SARS-CoV-2 by PCR*

### Moderate - Severe Symptoms: Remdesivir, all EUA requirements must be followed

**Inclusion Criteria:**  Patients must be hospitalized
- SpO2 ≤94% on room air
- Requiring supplemental oxygen

**Exclusion Criteria:**
- ALT or AST levels > 5x ULN
- CrCl < 30 mL/min at initiation, though this may be considered on a risk vs benefit assessment
- Improving on current regimen or imminent death

**Abnormal chest imaging consistent with COVID-19 AND One of the following:**
- Rapidly worsening gas exchange
- Mechanical ventilation or shock

**PLUS one of the following:**
- Ferritin > 300 ng/mL with doubling within 24 hours
- Ferritin > 600 ng/mL at presentation and LDH > 250
- CRP > 7 mg/dL

**Severe Symptoms:**

- Not requiring invasive mechanical ventilation and/or ECMO: **Remdesivir** 200 mg IV loading dose on day 1, followed by 100 mg IV once daily x 4 days

**Mechanically Ventilated and/or on ECMO:**
- **Remdesivir** 200 mg IV loading dose on day 1, followed by 100 mg IV once daily x 9 days

**Patient Pregnant or < 18 years of age, additional option:**
- Compassionate use request: [http://rdvcu.gilead.com/](http://rdvcu.gilead.com/)

**Adjunctive therapy in patients with any O2 requirement:**
- **Dexamethasone** 150 mcg/kg, max dose 6 mg po or IV daily x 10 days

### Severe or Immediately Life-Threatening: Convalescent Plasma **Investigational Use Only**

**Severe disease is defined as one or more of the following:**
- shortness of breath (dyspnea)
- respiratory frequency ≥ 30/min
- blood oxygen saturation ≤ 93%
- partial pressure of arterial oxygen to fraction of inspired oxygen ratio < 300
- lung infiltrates > 50% within 24 to 48 hours

**Life-threatening disease is defined as one or more of the following:**
- respiratory failure
- septic shock
- multiple organ dysfunction or failure

**Use of COVID-19 Convalescent Plasma, a blood product, should be a joint decision between ID and Critical Care providers and requested using this workflow:**

[https://www.uscovidplasma.org/#workflow](https://www.uscovidplasma.org/#workflow)

This is a part of the “Expanded Access Pathway for Use of Investigational COVID-19 Convalescent Plasma” outlined by the FDA. MCE, MCGC, and MCSA are registered through the Mayo Clinic

After obtaining a participant ID #, place the following orders in PowerChart:
1. “Convalescent Plasma”
2. “Transfusion Blood Products” -> ☑ “Transfuse Plasma” (below FFP) and enter comment = “Convalescent Plasma”

**Recommended Confirmed Sars-CoV-2 Positive Hospitalized Patient Tests**

<table>
<thead>
<tr>
<th>Baseline laboratory:</th>
<th>CMP, CBC with differential, D-dimer, PT, aPTT, CRP, fibrinogen, ferritin, LDH, PCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily laboratory:</td>
<td>BMP, CBC with differential</td>
</tr>
<tr>
<td>Every 2-3 days:</td>
<td>PT, aPTT, D-dimer, fibrinogen</td>
</tr>
</tbody>
</table>

**Baseline EKG**

**RESTRICTIONS AND WARNINGS**

**Hydroxychloroquine:** ID CONSULT REQUIRED for use in COVID-19
- Coadministration of remdesivir and hydroxychloroquine is not recommended based on an antagonistic effect on the antiviral activity of remdesivir. The FDA has withdrawn the EUA for use in COVID-19. Record QTc via baseline EKG or telemetry and avoid other non-critical QTc-prolonging agents if QTc >500.
- Avoid Use in pts with a history of CHF or arrhythmias.

**Remdesivir:** ID CONSULT REQUIRED
- Use is restricted to the following:
  - Infectious Disease physicians (confirmed or presumptive positive COVID-19 patients)*
  - Critical Care providers (confirmed COVID-19 patients) when the patient meets the criteria outlined in MCHS COVID-19 Inpatient Treatment Guideline

**Tocilizumab:** Use is restricted to the following:
- Infectious Disease physicians (confirmed or presumptive positive COVID-19 patients)*
- Critical Care providers (confirmed COVID-19 patients) when the patient meets the criteria outlined in MCHS COVID-19 Inpatient Treatment Guideline

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§ See the Appendix for additional treatment considerations and Emergency Use Authorization (EUA) requirements
COVID-19 ANTICOAGULATION GUIDELINE

This document is based on expert clinical guidance and current available evidence, which is still evolving. This guidance should be used in conjunction with latest evidence, patient-specific characteristics and should not supersede clinical judgment.

Background: Patients hospitalized with COVID-19 are at increased risk for thromboembolism due to immobility and inflammation which may cause injury to vascular endothelium. There is clinical evidence to suggest that COVID-19 is associated with increased coagulopathy including elevated D-dimer, fibrinogen, prothrombin time, and fibrin degradation products such as LDH.

Indication for therapeutic anticoagulation prior to admission (atrial fibrillation, recent venous thromboembolism (DVT/PE), mechanical heart valve)?

- If severe COVID, consider switching oral anticoagulant to therapeutic enoxaparin or heparin infusion
- Heparin products have known anti-inflammatory and potential anti-viral properties which may be beneficial in COVID-19

INTERMEDIATE-INTENSITY VTE PROPHYLAXIS DOSING:

- CrCL ≥ 30 mL/min: enoxaparin 0.5 mg/kg SubQ BID
- CrCL 15 - 29 mL/min: enoxaparin 0.5 mg/kg SubQ daily
- CrCL < 15 mL/min: heparin 7500 units SubQ TID

D-dimer level ≥ 3 mcg/mL?

- Any decision to increase the intensity of anticoagulation should take into account patient specific bleeding risk.

STANDARD VTE PROPHYLAXIS DOSING:

BMI < 40 kg/m²:
- CrCL ≥ 30 mL/min: enoxaparin 40 mg SubQ daily
- CrCL 15 - 29 mL/min: enoxaparin 30 mg SubQ daily
- CrCL < 15 mL/min: heparin 5000 units SubQ TID

BMI ≥ 40 kg/m²:
- CrCL ≥ 30 mL/min: enoxaparin 40 mg SubQ BID
- CrCL 15 - 29 mL/min: enoxaparin 40 mg SubQ daily
- CrCL < 15 mL/min: heparin 7500 units SubQ TID

High clinical suspicion or confirmed VTE?

Consider increasing intensity of anticoagulation if recurrent clotsting of vascular access devices despite VTE prophylaxis.

Consider the possibility of pulmonary thromboembolism in patients with sudden onset of oxygenation deterioration, reduced blood pressure, tachycardia with imaging not consistent with worsening COVID-19 pneumonia. Evaluate for elevated BNP, troponin, and/or markedly elevated D-dimer. If unable to obtain confirmatory CTA, consider bedside cardiac ultrasound to evaluate for right ventricular strain or thrombus.

VTE TREATMENT DOSING:

- CrCL ≥ 30 mL/min: enoxaparin 1 mg/kg SubQ q12hr
- CrCL < 30 mL/min: heparin IV continuous infusion protocol

DISCHARGE Considerations for Anticoagulation:

- If VTE confirmed or treated empirically discharge with oral therapeutic anticoagulation for 3 months
- Severely ill COVID-19 patients may experience continued thrombotic risk post-hospital discharge, consideration for VTE prophylaxis in appropriately selected patients (IMPROVE VTE9 score ≥ 4 or ≥ 2 AND D-dimer > 2x ULN) without high bleed risk (gastric ulcer, dual antiplatelet, recent bleed)

IMPROVE VTE Risk factor Score

- Previous VTE: 3
- Thrombophilia: 2
- Lower limb paresis: 2
- Cancer history: 2
- ICU stay: 1
- Immobilized ≥ 1d: 1
- Age ≥ 60 y: 1

If decision for discharge VTE prophylaxis consider: Rivaroxaban 10 mg PO daily for 14 – 30 days (caution CrCL < 30; avoid CrCL < 15 mL/min)
Anticoagulation References:


Therapeutic Options References:

5. https://rdvcu.gilead.com/
APPENDIX A: Additional Treatment Considerations and Requirements

GENERAL CONSIDERATIONS:
• High risk of drug interactions exists with any of the suggested therapies for management. Please see link below for table of drug interactions, especially those receiving immunosuppressive therapy.
  http://www.covid19-druginteractions.org/

HYDROXYCHLOROQUINE (PLAQUENIL):
Mechanism: immunomodulator and antiviral
Administration: hydroxychloroquine tablets can be crushed

Warnings and Adverse Effects:
• QTc prolongation, ventricular arrhythmia, atrioventricular heart block
• Cardiomyopathy (AHA: may either cause direct myocardial toxicity or exacerbate underlying myocardial dysfunction)
• Neutropenia and thrombocytopenia
• Neuropathy and myopathy
• Dermatologic reactions
• Retinal toxicity (retinopathy and vision changes)
• Hypoglycemia
• GI upset: nausea, vomiting, diarrhea

Pregnancy considerations: limited human data: probably compatible. Use of higher doses probably represents an increased risk to the fetus, magnitude of risk is unknown.

REMDESVIR:
EMERGENCY USE AUTHORIZATION REQUIREMENTS (link to full Fact Sheet for Healthcare Providers: https://www.fda.gov/media/137566/download)

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: https://www.fda.gov/media/137565/download) 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.

These bullet points must be documented in the provider’s progress note

Laboratory Requirements:
Prior to initiation of therapy:
• Estimated glomerular filtration rate (eGFR)
• Hepatic laboratory testing

Daily: Hepatic laboratory testing while receiving remdesivir

Recommended Daily Labs: CBC, BMP

Completion of FDA MedWatch Form to report all medication errors and adverse events occurring during remdesivir treatment is mandatory.
• The prescribing health care provider and/or the provider’s designee are/is responsible for mandatory reporting of all medication errors and adverse events within 7 calendar days from the onset of the event.
  www.fda.gov/medwatch/report.htm
**Remdesivir Warnings and Adverse Effects:**

**Infusion-Related Reactions**
- Hypotension
- Nausea / Vomiting
- Diaphoresis
- Shivering

**Increased Risk of Transaminase Elevations**
- **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.

**TOCILIZUMAB (ACTEMRA):**

**Mechanism:** humanized monoclonal antibody; interleukin 6 (IL-6) receptor antagonist; used for cytokine storm related to COVID-19

**Administration:** infuse over 60 min in dedicated IV line

**Warnings and Adverse Effects:**
- Serious and potentially fatal infections including reactivation of latent TB (if benefit outweighs risk in treatment of COVID-19, prescriber may defer TB testing)
- Neutropenia and thrombocytopenia (platelet and ANC cutoffs may be lower than package label recommendations in the setting of COVID-19)
- Hypersensitivity reactions including anaphylaxis
- Hepatic injury (if benefit outweighs risk in treatment of COVID-19, prescriber may initiate therapy despite elevated AST/ALT)
- Gastrointestinal perforation

**Pregnancy considerations:** limited human data; probably compatible. Patient should be advised of limited data if tocilizumab is to be used in pregnant patient. Pregnancy registry available, providers encouraged to call.