Mount Sinai Health System Treatment Guidelines for SARS-CoV-2 Infection (COVID-19)[1,2]

Illness Severity	Current Potential Therapy Options	Notes
Not hospitalized or Asymptomatic	Supportive care	Given the potential harm, hydroxychloroquine with or without azithromycin should not be prescribed. **Do not use in ambulatory setting.**[3]
Mild disease Hospitalized patient with (SpO2 > 94%) AND Radiographic evidence of pneumonia	Supportive care **Consider:** **Remdesivir[4,5] clinical trial**	Given the potential harm with insufficient evidence of benefit, hydroxychloroquine with or without azithromycin should not be prescribed for COVID-19.
Moderate disease Hospitalized patients with hypoxia (SpO2 ≤ 94 % on RA) AND Radiographic evidence of pneumonia	Supportive care **Consider:** • **Convalescent Plasma** • **Remdesivir EUA[6]* or clinical trial**	* On May 1, 2020, the FDA issued an EUA for the use of remdesivir in hospitalized patients. Remdesivir is not recommended in adult and pediatric patients with an eGFR < 30 mL/min or with an ALT/AST > 5 times with upper limit of normal. **Remdesivir EUA** **Healthcare providers must document in the medical record that the patient/caregiver has been given information consistent with the "Fact Sheet for Patients and Parents/Caregivers" and have been informed that remdesivir is not FDA-approved but it's use is authorized under an EUA.**
Severe disease with respiratory failure with no other end organ damage: Patient requiring high flow, NRB, BIPAP or within 24-48 hours of intubation (progressive hypoxemia) AND Radiographic evidence of bilateral pneumonia	Supportive care **Consider:** • **Convalescent plasma** • **Remdesivir EUA** • **Mesenchymal stem cells (MSH only)** • **Tocilizumab† (IL6-receptor monoclonal antibody (MOAB)** **Clinical trials:** • **Remdesivir clinical trials** • **Gimsilumab (anti-GM-CSF) clinical trial**	**†Can consider tocilizumab in patients with the below clinical parameters.** • **RR ≥ 30** • **PaO2/FiO2 < 300** • **CRP ≥ 150 OR D-dimer ≥ 2.5** **Use of tocilizumab excludes patients from enrollment in the gimsilumab clinical trial.** **ID Attending Physician approval and subsequent in-person consultation required for use in COVID-19 at all times. Please note this is off-label use and a MOAB consent form will need to be completed and the discussion regarding off-label use needs to be documented in the EMR.** Avoid use in patients with platelets < 50,000 or ANC < 1000 Use caution in patients on chronic corticosteroids (> 10 mg of prednisone or equivalent) as lower gastrointestinal perforations have been noted in patients on concurrent corticosteroids, NSAIDs, and/or methotrexate and in patients with diverticulitis. Use of tocilizumab and any immunomodulatory agent places patients at higher risk for infection and likely is additive to the increased risk of infection with high dose corticosteroids.
Severe disease with respiratory failure requiring ICU care and other end organ damage: Patient requiring mechanical ventilation with or without pressor support	Supportive care **Consider** • **Convalescent plasma** • **Remdesivir EUA** • **Mesenchymal stem cells (MSH only)** **Clinical trials** • **Remdesivir[4,5] clinical trial** • **Gimsilumab (anti-GM-CSF) clinical trial**	

Medications **NOT** currently recommended for the treatment of SARS-CoV-2 (COVID-19):

ACE inhibitors and ARBs[7]	**It is strongly recommended that those patients prescribed ACE inhibitors and ARBs for preexisting conditions should be continued on their ACE inhibitor and ARB therapy.** Currently, there is no scientific or clinical evidence that taking ACE inhibitors or ARBs increases the risk of acquiring COVID-19 or that use may increase the severity of illness for those acquiring infections.
Azithromycin[8]	Azithromycin with or without hydroxychloroquine is NOT recommended to treat COVID-19.
Darunavir-based treatments	Currently no evidence to support use of darunavir-based treatments for COVID-19.
Hydroxychloroquine[3,8-11]	Hydroxychloroquine is NOT recommended for pre-exposure and or post-exposure prophylaxis or in patients with a confirmed diagnosis of SARS-CoV-2 infection. There is insufficient data to support any benefit in persons with COVID-19 and potential harms include cardiac arrhythmias and methemoglobinemia. A pre-print NIH-funded cohort study from the VA hospitals noted increased mortality in patients treated with hydroxychloroquine. Use of hydroxychloroquine for COVID-19 requires ID Attending approval. Patients prescribed hydroxychloroquine for preexisting rheumatologic conditions should be continued on their current dose.
Ivermectin[12]	Displays inhibitory activity against virus *in vitro* however no clinical data in humans exists.
IVIG	IVIG remains on critical national shortage. There is insufficient evidence to recommend the use of IVIG for COVID 19 outside of labeled indications.
Lopinavir/ritonavir (Kaletra)®[13,14]	Lopinavir inhibits the protease activity of coronavirus in SARS. Two retrospective matched cohorts of lopinavir/ritonavir (used in combination with ribavirin and corticosteroids) in SARS demonstrated a potential role in clinical outcomes, especially when used in the early stages of diseases. Due to risk of adverse events and drug-drug interactions, along with lack of data in SARS-CoV-2 at present time, not currently recommended.
Nitazoxanide[15]	Displays inhibitory activity against the virus *in vitro* however no clinical data in humans exists.
Oseltamivir	SARS-CoV-2 does NOT use neuraminidase as part of the viral replication cycle so oseltamivir is unlikely to be of therapeutic value.
Ribavirin	Role unclear, doses required for optimal antiviral activity often exceed limit of patient tolerability. Risk of toxicity outweighs potential clinical benefit.
Zinc	There are no clinical data suggesting zinc improves outcomes in patients with COVID-19.

Medications:

Gimsilumab:

- Gimsilumab is available as part of a clinical trial for patients > 18 years old.
- Consult Infectious Diseases for enrollment consideration if patient meets above criteria.
- Clinical Trial Exclusions: eGFR < 30 mL/min, ANC <2000, Platelets <50,000, AST or ALT > 5 x ULN

Remdesivir[4-6]:

- Remdesivir is currently available for compassionate use for pregnant patients and patients less than 18 years of age.
- Email COVIDGILEAD@mssm.edu for trial enrollment consideration in a clinical trial or for compassionate use.
- If tocilizumab administered to patient, **must wait 24 hours after tocilizumab** administration to give remdesivir for inclusion in a clinical trial.
- Clinical Trial Exclusions: eGFR < 50 mL/min, AST or ALT > 5 x ULN

On May 1, 2020, the FDA issued an EUA for the use of remdesivir in hospitalized patients with suspected (pending laboratory confirmation) and confirmed COVID-19 who are hypoxic (SpO2 ≤ 94% on room air).

Documentation:
Healthcare providers must document in the medical record that the patient/caregiver has been given information consistent with the "Fact Sheet for Patients and Parents/Caregivers" and have been informed that remdesivir is not FDA-approved but its use is authorized under an EUA.

Remdesivir EUA dosing:
Patients ≥ 40 kg: 200 mg IV on day 1 then 24 hours later start 100 mg IV q 24h for 4 days (the duration can be extended for up to a total of 10 days if lack of clinical improvement)
In patients requiring mechanical ventilation or ECMO the duration can be extended for up to 5 days (i.e., up to a total of 10 days)

Caution:
- **Hepatic function tests should be checked prior to initiating remdesivir and daily.** Elevation in transaminases have been observed in clinical trials including in both healthy volunteers and patients with COVID-19. Hepatic function tests should be checked prior to initiating remdesivir and daily.
- **Remdesivir should be discontinued if AST or ALT > 5 times the upper limit of normal or if there is signs and symptoms of liver inflammation (e.g., increased bilirubin, alkaline phosphatase, or INR)**
- **Adverse events should be reported to FDA Medwatch.**

Tocilizumab (Actmera®)

- Not FDA-approved for the treatment of COVID-19-related cytokine release syndrome though case reports and case series exist[1,2]
- **ID Attending Physician approval and subsequent in-person consultation required for use in COVID-19 at all times.**
- **A MOAB consent form will need to be completed and the discussion regarding off-label use needs to be documented in the EMR.**
- Use of tocilizumab and any immunomodulatory agent places patients at higher risk for infection and likely is additive to the increased risk of infection with high dose corticosteroids.

Dosing:
Patients ≥30 kg: 8 mg/kg (actual body weight) **IV** x single dose (maximum dose: 800 mg)

162 mg **subcutaneous** (SC) pre-filled syringe to be injected into left and right leg – total of **TWO syringes to be injected one time**

Caution:
- Interaction: Tocilizumab may **reduce levels** of **apixaban** and **rivaroxaban** but does NOT interfere with enoxaparin or heparin
- Associated with lower gastrointestinal perforations in patients on **concomitant steroids (> 10 mg prednisone daily or equivalent), NSAIDS, and/or methotrexate and in patients with diverticulitis**
- Avoid use in patients with **platelets <50,000 and those with ANC <1,000**

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References:

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