MUNSON HEALTHCARE

Treatment Considerations in Adults and Children with Laboratory Confirmed SARS-CoV-2 (COVID-19)

Developed in collaboration by the MHC Antimicrobial Stewardship Committee and Infectious Diseases Section

Purpose:

The purpose of this document is to provide guidance for the management of patients with laboratory confirmed and suspected SARS-CoV-2 infection, the virus that causes COVID-19. Given the rapidly evolving nature of data on COVID-19, this document is subject to change.

Clinical symptoms:

COVID-19 causes a range of symptoms including fever, cough, shortness of breath, and ranges from uncomplicated upper respiratory tract viral infection to pneumonia, acute respiratory distress syndrome (ARDS), sepsis, and septic shock.

Supportive care: Appropriate treatment of concomitant pneumonia, respiratory failure, ARDS, sepsis, septic shock.

Table of Contents:

Table 1: Outpatient treatment of mild COVID-19 (symptomatic, not requiring oxygen or increase in baseline oxygen)		
	Paxlovid (ritonavir-boosted nirmatrelvir)	**Molnupiravir**
Preference per NIH Guidelines	→	
Core Criteria	• Mild to moderate COVID-19 (symptomatic COVID, NOT requiring oxygen or increase from baseline supplemental oxygen) • Patient tests positive for SARS-CoV-2 (PCR, other NAAT, or antigen, including home test) • Outpatient or not hospitalized for COVID-19 (can administer in emergency department, observation, or outpatient setting) • At high risk for disease progression and hospitalization or death (see risk factors below)	
FDA Provider Fact Sheet	Paxlovid – Fact sheet for Providers	Molnupiravir – Fact sheet for Providers
FDA Patient/Caregiver Fact Sheet	Paxlovid - Patients and caregivers	Molnupiravir – Patients and caregivers
Availability	Pharmacies with Paxlovid	Pharmacies with molnupiravir
Age/Weight	≥12 YO & ≥40 kg	≥18 YO (no weight criteria)
Start within (x) days of symptoms: (symptom onset date is day ZERO)	5 days	5 days
Duration of therapy, route	5 days, oral	5 days, oral
First line/alternative	First Line	Alternative (last line)
Relative risk reduction in hospitalization or death	88%	30%
Further Criteria	First line for mild-moderate COVID-19 at high risk for progression to severe disease with at least 1 of the CDC risk factors below (not an inclusive list): • Age ≥65 years of age • Adults with BMI >25 kg/m^2, or if 12 to 17 years of age, have BMI ≥85th percentile for their age and gender based on CDC growth charts • Pregnancy (Paxlovid or Remdesivir x 3 days preferred, Molnupiravir contraindicated) • Chronic kidney disease • Diabetes • Immunosuppression • Cardiovascular disease or hypertension • Chronic lung diseases • Sickle cell disease • Neurodevelopmental disorders or other conditions that confer medical complexity • Having a medical-related technological dependence (for example, tracheostomy, gastrostomy, or positive pressure ventilation [not related to COVID 19])	Same high-risk criteria as Paxovid Alternative **ONLY** if patient cannot get Paxlovid due to drug interactions, impaired kidney/liver function, or supply.
Contraindications **(not including allergy)**	Renal impairment eGFR < 30 mL/min Child-Pugh Class C liver disease Certain drug interactions (See below)	Contraindicated in Pregnancy. Males of reproductive age should use reliable contraception during treatment and 3 months after last dose; females, during treatment and 4 days after last dose.
Drug Interactions (Paxlovid only)	FDA Paxlovid eligibility screening checklist and drug interaction checking: https://www.fda.gov/media/158165/download Paxlovid drug interaction checker: Liverpool COVID-19 Drug Interaction Website A guide to drug interactions with Paxlovid can be found at: MI Medicine Tool	
Management of Disease Relapse (Paxlovid only)	There have been reports of relapse (a positive test with symptoms after testing negative) in patients receiving Paxlovid. The prevalence of relapse during the Omicron surge is currently unknown. At this time, there are no data to support a 2nd course of Paxlovid if symptoms recur. For more information, see this message from the FDA.	

[1] **Severe immunocompromise**: Solid organ transplant, bone marrow transplant, hematologic malignancy, on b-cell depleting therapy (i.e., on rituximab)

[2] **Moderate immunocompromise**: Primary immunodeficiency, active malignancy and receiving chemotherapy, autoimmune diseases requiring immunosuppressive therapy (hydroxychloroquine or sulfasalazine alone is not sufficient), advanced or untreated HIV infection

[3] **Up-to-date with vaccines**: a person has received all recommended COVID-19 vaccines, including any booster dose(s) when eligible

Table 2: Inpatient treatment of mild/moderate to severe COVID-19

Severity of illness	Consideration
Inpatients	
Mild illness • Symptomatic, not requiring oxygen or increase in baseline oxygen	• **Supportive care** • Remdesivir x 3 days (200 mg day 1, then 100 mg daily on days 2-3). Started within 7 days of symptom onset. • Not recommended: Dexamesthasone, tocilizumab, or baricitinib
Moderate illness • Presence of hypoxia requiring supplemental oxygen, but not high-flow or mechanical ventilation.	• **Supportive care** • Dexamethasone 6 mg daily for up to 10 days (or until discharge if sooner). • Remdesivir x 5 days • Not recommended: Paxlovid, Molnupiravir • If patient is started on Paxlovid or Molnupiravir and progresses to moderate, or severe disease, it is reasonable to stop these therapies and initiate the next level of care.
Severe illness • Severe pneumonia requiring high-flow nasal cannula, CPAP, BiPAP, or mechanical ventilation	• **Supportive care** • Dexamethasone 6 mg daily for up to 10 days. Consideration can be made to use higher Dexamethasone doses. See Dexamethasone section for more details. • Tocilizumab x 1 (If unavailable, suggested alternative is Baricitinib). Strong recommendation to wait until blood cultures are negative for 48 hours before initiating tocilizumab. • Note: if remdesivir is started and the patient progresses to severe disease, it is reasonable to continue remdesivir, but should be based on clinical judgement. • Not recommended to be started in response to meeting severe illness criteria: ○ Remdesivir, Paxlovid, Molnupiravir
See individual drug summaries in Table 3 for specific information in special populations (e.g. pediatrics & pregnancy) **Risk factors for severe disease:** Age ≥65 years, chronic cardiovascular, pulmonary, hepatic, renal, hematologic, or neurologic conditions, immunocompromised, pregnant women, residents of nursing homes or long-term care facilities.	

Table 3: Dosing and additional considerations for treatment options for the management of COVID-19

Antiviral therapy & mechanism	Dosing & Duration	Comments
Remdesivir Nucleoside inhibitor with broad antiviral activity; inhibits viral RNA synthesis by polymerase	Adult: ≥40 kg: 200mg IV on day 1, then 100mg IV q24h x 4 days Pediatric: 3.5 - 40 kg: 5 mg/kg IV load, then 2.5 mg/kg IV q24h x 4 days ≥40 kg: 200 mg IV load, then 100 mg IV q24h x 4 days Typical duration is 5 days, or until hospital discharge whichever comes first. Patients started on remdesivir and progress to requiring higher level of oxygen support (i.e. mechanical ventilation) should still complete a course of remdesivir. Per the PINETREE study, for patients with mild illness who are not hypoxic, a duration of 3 days is appropriate (200 mg x1, then 100 mg on day 2-3).	• FDA approved for patients ≥ 12 years old and ≥ 40 kg. • The following criteria must be met prior to initiation: 1. Laboratory confirmed SARS-CoV-2 infection by PCR from nasopharyngeal or respiratory sample 2. Radiographic evidence of pulmonary infiltrates (CXR or CT). 3. SpO2 ≤ 94% on room air or requires low-flow supplemental oxygen ≤ 6 L/min. (5-day duration) 4. Not currently receiving high-flow nasal cannula (>6 liters), non-invasive mechanical ventilation (excluding home CPAP), or mechanical ventilation. 5. Consideration for ≤ 7 days of symptoms (not a hard exclusion). Antivirals work better earlier in the disease course. Of note, per the PINETREE study, patients with mild symptoms within 7 days of symptom onset but not hypoxic can be treated with a 3-day duration (without dexamethasone). • For patients < 12 years old and weighing 3.5 - 40 kg, remdesivir is available through FDA Emergency Use authorization (EUA). 1. The healthcare provider must review the Fact sheet for Health care providers prior to prescribing. 2. The healthcare provider must communicate information consistent with the Fact Sheet for Patients and Parents/caregivers prior to the patient receiving remdesivir, AND must document in the patient's chart that the patient/caregiver has been: i. Given the Fact Sheet for patients and parents/caregivers. ii. Informed of alternatives to receiving remdesivir, & iii. Informed that remdesivir is an unapproved drug that is authorized for use under EUA. • Baseline AST/ALT should be < 5 x ULN (or < 200). This is not an absolute contraindication, but these patients were excluded from clinical trials. • eGFR < 30 mL/min is NOT a contraindication to remdesivir. The risk of cyclodextrin accumulation to a toxic level with 5 days of therapy is small and benefit of remdesivir likely outweighs this small risk. • Adverse events include increased liver enzymes, injection site reactions, bradycardia, and potential to have drug-drug interactions with medications metabolized through cytochrome system. • Pregnancy & Breastfeeding: limited studies exist for remdesivir use in pregnant women. Remdesivir should be used during pregnancy only if the potential benefit justifies

Antiviral therapy & mechanism	Dosing & Duration	Comments
		the potential risk for the mother and the fetus. There is no information regarding the presence of remdesivir in human breastmilk, the effects on the breastfed infant, or the effects on milk production.
Dexamethasone	Adult dosing: 6 mg daily, maximum 10 days or until discharge from the hospital. Consider 20 mg daily x 5 days followed by 10 mg daily x 5 days as an option for patients with severe disease receiving ≥10 L/min HFNC, noninvasive positive pressure ventilation (e.g. BIPAP), or invasive mechanical ventilation. Shorter duration is reasonable in patients who rapidly improve. Durations >10 days are generally not recommended, but may be reasonable on a case by case basis for critically ill patients.	• NIH Guidelines recommends using dexamethasone (at a dose of 6 mg per day for up to 10 days) for the treatment of COVID-19 in patients who are mechanically ventilated (AI) and in patients who require supplemental oxygen but who are not mechanically ventilated (BI). • Higher doses have been studied in the CoDEX trial (JAMA 2020) and the COVID STEROID 2 Trial (JAMA 2021). Given high mortality in critically ill patients receiving ≥10 L HFNC, noninvasive positive pressure ventilation, or invasive mechanical ventilation, it is reasonable to use 20mg daily x 5 days followed by 10 mg daily x 5 days in this population (CoDEX dosing). Use caution with higher dexamethasone doses in combination with tocilizumab or baricitinib. Note: stress ulcer prophylaxis should be considered for patients receiving dexamethasone doses >6 mg daily. • The NIH Panel recommends **against** using dexamethasone for the treatment of COVID-19 in patients who do not require supplemental oxygen (AI). • Unclear benefit in patients on low level supplemental oxygen (1-2 L) with < 7d of symptoms. • In the setting of a dexamethasone shortage, an equivalent total daily dose of an alternative glucocorticoid to dexamethasone 6 mg daily can be used (e.g., methylprednisolone 32 mg daily or prednisone 40 mg daily). • Pregnancy & Breastfeeding: Given the potential benefit of decrease in maternal mortality and the low risk of fetal adverse effects for this short course of therapy, the NIH Guidelines recommend using dexamethasone in pregnant women with COVID-19 who are mechanically ventilated (AIII) or who require supplemental oxygen but who are not mechanically ventilated (BIII).
Tocilizumab Guidance based on REMAP-CAP & RECOVERY randomized controlled trials, in accordance with NIH & IDSA COVID-19 Treatment guidelines.	Adult Dosing (≥18 years): >40-65 kg: 400 mg >65-90 kg: 600 mg >90 kg: 800 mg (max: 800 mg/dose) Pediatric Dosing (<18 years): <30 kg: 12 mg/kg ≥30 kg: 8 mg/kg (max: 800 mg/dose) Duration: One dose over 60 minutes	If supply is inadequate, a suggested alternative is Baricitinib. Strong recommendation to wait until blood cultures are negative for 48 hours before initiating tocilizumab. Recommend **Tocilizumab** (*in addition to* ***dexamethasone***) in: 1. Patients with rapidly increasing oxygen needs within 24 hours while on dexamethasone with either: a. HFNC > 6 L / min (FiO_2 >40%), noninvasive mechanical ventilation, or mechanical ventilation within 48 hours, OR b. Increased markers of inflammation (e.g. CRP > 7.5 mg/dL), in addition to rapidly increasing O_2 needs.

Antiviral therapy & mechanism	Dosing & Duration	Comments
	There are no data to inform risk vs. benefit of a second dose.	**Tocilizumab** is NOT recommended in the following scenarios: 1. Significant immunosuppression (e.g. ANC < 500) 2. Use of biologic immunomodulating drugs with increased risk of infection, or where opportunistic infection prophylaxis would be considered. (NOTE: COVID-19 monoclonal antibodies are NOT immunomodulating) 3. ALT > 5 x upper limit of normal 4. Platelet count <50,000 cells/µL 5. High concern for systemic bacterial or fungal co-infection 6. High-risk for GI perforation 7. Receiving mechanical ventilation for longer than 48 hours 8. Patients who significantly improve with the initiation of enhanced oxygen support or corticosteroids; monitoring such patients for 12-24 hours is reasonable 9. Unlikely to survive >48 hours **6.24.2021 – FDA issued an EUA for tocilizumab.** *Providers must provide FDA fact sheet for patients and document verbal consent in their note.* • Health Care Providers must review FDA Fact Sheet for Health Care Providers: https://www.fda.gov/media/150321/download • Health Care Providers must provide recipients with the Fact Sheet for Patients/Caregivers: https://www.fda.gov/media/150320/download Pregnancy and Nursing Mothers: • Tocilizumab is not currently recommended for the treatment of rheumatic and musculoskeletal diseases during pregnancy; however, given the increased risk of severe COVID-19 Disease in pregnancy, benefit of tocilizumab may outweigh the risk. • Tocilizumab may be harmful to newborns, and mothers should stop breastfeeding if receiving tocilizumab but may resume after discontinuation. Serious adverse events: • Gastrointestinal perforation, Anemia, Hepatitis, Infusion reaction, Neutropenia, Infection
Baricitinib Selective inhibitor of JAK 1&2 Non-formulary at MHC Should not be used in combo with tocilizumab	Adult 4 mg PO q24hr *renal adjustment for eGFR: ≥ 60 mL/min: 4 mg PO q24hr 30-59 mL/min: 2mg PO q24hr 15-29 mL/min: 1mg PO q24hr <15 mL/min (contraindicated) Duration: Maximum 14 days, or until discharge	• May 10, 2022: FDA approved Baricitinib for the treatment of COVID-19 in hospitalized adults requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO). • Criteria for Use ○ Can be considered in patients that meet criteria for tocilizumab, if tocilizumab is unavailable. ○ Not recommended in the following patients: ▪ Previously received tocilizumab ▪ Not requiring supplemental oxygen ▪ Requiring mechanical ventilation ▪ Patients with known active Tuberculosis

Antiviral therapy & mechanism	Dosing & Duration	Comments
Should be used in combination with dexamethasone, based on the results of the COV-BARRIER study.	Shorter duration is reasonable to consider in patients who have improved rapidly or are experiencing adverse events.	▪ Patients with AKI and eGFR < 15, or those with ESRD, or receiving dialysis. • Monitoring parameters: ○ Renal function (dosed based on eGFR) ○ Absolute lymphocyte count ○ Absolute neutrophil count ○ VTE prophylaxis present ○ AST/ALT ○ Platelets ○ Drug-drug interactions • Potential Adverse events: ○ Thromboembolic events: VTE, PE ○ Increased risk for infection
Paxlovid (nirmatrelvir/ritonavir)	Dosing: eGFR ≥60 mL/min: Nirmatrelvir 300 mg + ritonavir 100 mg twice daily x 5 days eGFR 30-59 mL/min: Nirmatrelvir 150 mg + ritonavir 100 mg twice daily x 5 days eGFR <30 mL/min: Not indicated Must be initiated with 5 days of symptoms onset. Day 0 is the first day of symptoms. Duration: 5 days	• Contraindicated in patients with eGFR < 30 and Child Pugh class C • Multiple drug interactions exist. Resources for Drug interaction checking. ○ https://www.covid19-druginteractions.org/ ○ U of M Paxlovid Drug interaction guidance • FDA fact sheet for HCP • FDA fact sheet for patients/caregivers
Bebtelovimab **Not recommended as of 11.15.2022 due to high circulation of BQ Omicron subvariants that are likely resistant to Bebtelovimab*	Dosing: 175 mg IV push over 30 seconds Observation for 1 hour	• FDA fact sheet for HCP • FDA fact sheet for patients/caregivers
Molnupiravir	Dosing: 800 mg twice daily x 5d Must be initiated with 5 days of symptoms onset. Day 0 is the first day of symptoms.	• Considered alternative when other therapies are unavailable (e.g. Paxlovid,) • Avoid in pregnancy • Men who are sexually active with a woman of reproductive age should use reliable contraception during treatment and 3 months after last dose; • Women of reproductive age should use reliable contraception during treatment and 4 days after last dose. • FDA fact sheet for HCP • FDA fact sheet for patients/caregivers

Table 4: Additional pharmacologic considerations

Medication	Recommendation
VTE Prophylaxis and Treatment	**VTE <u>Prophylaxis</u> recommendations for COVID-19 Patients** <u>For hospitalized, non-pregnant adults who require low-flow oxygen and are NOT receiving intensive care unit level of care</u> 1. The NIH recommends using prophylactic dose heparin who are not administered therapeutic heparin unless a contraindication exists. MHC dosing recommendations as follows: a. Enoxaparin 40mg SQ q24hrs (May be increased if BMI greater than 40 to 40mg q12hrs, or if BMI greater than 50 then 60mg q12hrs) i. For patients with a CrCl greater than or equal to 30mL/min b. Unfractionated Heparin 5,000 units SQ every 8 to 12 hours 2. The NIH recommends using therapeutic dose heparin for patients who have a D-dimer above the upper limit of normal, require low-flow oxygen, and have no increased bleeding risk or contraindications. MHC dosing recommendations as follows: a. Enoxaparin (1mg/kg every 12 hours for CrCl greater than or equal to 30mL/min) is preferred b. Unfractionated Heparin per VTE protocol i. Contraindications: platelet count less than 50, hemoglobin less than 8gm/dL, need for dual antiplatelet therapy, know bleeding within last 30 days requiring ED visit or hospitalization, known history of bleeding disorder, or an inherited/active acquired bleeding disorder. 3. In patients without VTE who are started on therapeutic dose heparin, treatment should continue for 14 days or until hospital discharge, whichever comes first. <u>For hospitalized, non-pregnant adults who are receiving intensive care unit level of care (with or without high-flow oxygen)</u> 1. The NIH recommends using prophylactic dose heparin who are not administered therapeutic heparin unless a contraindication exists. MHC dosing recommendations as follows: a. Enoxaparin 40mg SQ q24hrs (May be increased if BMI greater than 40 to 40mg q12hrs, or if BMI greater than 50 then 60mg q12hrs) i. For patients with a CrCl greater than or equal to 30mL/min b. Unfractionated Heparin 5,000 units SQ every 8 to 12 hours 2. The NIH DOES NOT recommend using intermediate dose (eg enoxaparin SQ 1mg/kg daily) and therapeutic dose anticoagulation for VTE prophylaxis in this patient population, except in a clinical trial. 3. For patients who start of therapeutic dose heparin while on low flow oxygen due to COVID 19 for VTE prophylaxis and then transfer to the ICU the NIH recommends switching to prophylactic dose heparin unless VTE is confirmed. <u>For Hospitalized Pregnant Adults:</u> 1. The NIH recommends using prophylactic dose heparin who are not administered therapeutic heparin unless a contraindication exists. MHC dosing recommendations as follows: a. Enoxaparin 40mg SQ q24hrs (May be increased if BMI greater than 40 to 40mg q12hrs, or if BMI greater than 50 then 60mg q12hrs) i. For patients with a CrCl greater than or equal to 30mL/min

	b. Unfractionated Heparin 5,000 units SQ ever 8 to 12 hours 2. Because pregnant patients have not been included in most clinical trials evaluating therapeutic anticoagulation in the setting of COVID-19, there is currently insufficient evidence to recommend either for or against therapeutic anticoagulation for pregnant patients with COVID-19 in the absence of a known VTE. **Duration of VTE prophylaxis for hospitalized COVID-19 patients:** 1. Hospitalized patients with COVID-19 should not routinely be discharged from the hospital while on CTE prophylaxis. Continuing anticoagulation with a FDA approved regimen for extended VTE prophylaxis after hospital discharge can be considered for patient who are at low risk for bleeding and high risk for VTE; per FDA labeling indications and supporting primary literature. **VTE treatment in hospitalized COVID-19 patients:** 1. Established guidelines should be used to treat patients with confirmed VTE, with advantages of LMWH in the inpatient setting and DOACs in the post-hospital discharge setting. A change from treatment-dose DOAC or vitamin K antagonists (VKA) to in-hospital LMWH should be considered especially for patients in critical care settings or with relevant concomitant medications, and dependent on renal function and platelet counts. Anticoagulant regimens should not change based solely on D-dimer levels. 2. A change of anticoagulant regimen (ie, from prophylactic or intermediate-dose to treatment-dose regimen) can be considered in patients without established VTE but deteriorating pulmonary status or ARDS 3. The duration of treatment should be at least 3 months
NSAIDS	Currently, no compelling evidence to support an association between NSAIDS and negative outcomes in patients with COVID-19.
Vitamin C	While this idea has been popular in mainstream media, there is currently no evidence to support low- or high-dose vitamin C in COVID-19 patients. There is a trial currently recruiting for high-dose vitamin C trial in COVID-19 patients in China slated to be complete in the fall of 2020 (NCT04264533).
Ivermectin	IDSA Guidelines recommend against the use of ivermectin. NIH Guidelines state insufficient data to recommend for or against the use of ivermectin. Although it has in vitro activity against some viruses, it has no proven therapeutic utility. Ivermectin does have some in vitro activity against SARS-CoV-2, but concentrations needed to obtain the in vitro IC50 are considerably higher than those achieved in human plasma and lung tissue. A randomized controlled trial in JAMA Internal medicine found no difference compared to standard of care. Further resources for providers, pharmacists and patients can be found on the MHC COVID-19 Provider page, under COVID-19 treatment guidelines.

Developed:	03/2020
Expedited P&T Approval:	03/19/20
Revision History:	**12/29/23:** added recommendation to wait until blood cultures are negative for 48 hours before initiating tocilizumab. **11/15/22:** Bebtelovimab removed from outpatient & ED treatment options due to high circulation of BQ omicron subvariants that are likely resistant to Bebtelovimab. **9/2/22:** Added FDA Paxlovid eligibility screening checklist & drug interaction checking link to table 1 **7/13/22:** Updated Bebtelovimab criteria for use **5/18/22:** FDA approved Baricitinib on May 10th, 2022 for patients with severe COVID-19 **5/11/22:** Added information about relapse after taking Paxlovid **3/30/22:** Removed sotrovimab from list of recommended therapies due to reduced activity against the BA.2 subvariant and high frequency of circulating BA.2 in Michigan. Paxlovid, Bebtelovimab, and Molnupiravir are still believed to be active against BA.2. **3/3/22:** Removed tiered prioritization from Table 1. Relocated remdesivir from Table 1 into the "inpatient" treatment recommendations for mild COVID-19 in Table 2. **3/1/22:** New VTE prophylaxis recommendations. **2/1/22:** Updated eligibility criteria for treatment of mild COVID-19 **1/21/22:** Added prioritization criteria & treatment consideration for mild COVID-19 in the inpatient and outpatient settings. Added recommendations for remdesivir 200 mg x1, then 100 mg daily on days 2 & 3 for patients with mild COVID-19. **1/10/22:** Added higher dose dexamethasone option (20 mg daily x 5 days followed by 10 mg daily x 5 days) as an consideration for patients with severe disease receiving in critically ill patients receiving ≥10 L/min HFNC, noninvasive positive pressure ventilation (e.g. BIPAP), or invasive mechanical ventilation. (note: stress ulcer prophylaxis recommended for patients on higher doses of dexamethasone). Added Paxlovid & Molnupiravir to outpatient recommendations with a link to MHC provider page for more detailed, updated information. **11/18/21:** Removed drug interaction between tocilizumab and direct oral anticoagulants (DOACs). Updated remdesivir section: patients started on remdesivir who progress to requiring HFNC or mechanical ventilation should complete the course of remdesivir. **10/19/21:** Added clarity to Tocilizumab exclusion: use of concomitant biologic immunomodulating drugs with increased risk of infection, or where opportunistic infection prophylaxis would be considered. (NOTE: COVID-19 monoclonal antibody is NOT immunomodulating). **9/3/21:** Updated outpatient treatment guidance. Removal of convalescent plasma. Updated tocilizumab shortage information, with suggested alternative of baricitinib. **8/24/21:** Updated tocilizumab shortage information **7/6/2021:** Updated tocilizumab emergency use authorization (EUA) information **4/7/2021:** Updated tocilizumab criteria for use **3/26/2021:** Added information & guidance on tocilizumab **12/23/20:** Added information & guidance on Baricitinib. Added clarity to remdesivir criteria for use. Updated VTE prophylaxis and treatment. **10/29/20:** Updated Remdesivir criteria for use: added criteria for ≤ 10 days of symptoms. Updated remdesivir FDA approval. Removed remdesivir exclusion of eGFR < 30 mL/min. Softened remdesivir contraindication when baseline AST/ALT > 5 x ULN. Updated dexamethasone and convalescent plasma information. **7/28/20:** Revised recommendations for remdesivir and dexamethasone. **6/24/20:** Removed HCQ and Tocilizumab. Updated Remdesivir information. Added dexamethasone for critically ill patients with further information to follow based on results of the RECOVERY Trial. **5/14/20:** Added Remdesivir Emergency Use Authorization (EUA) information. Added additional information about ivermectin, nitazoxanide. Updated VTE prophylaxis section. **4/17/20:** Downgraded recommendations for investigational therapies outside of a clinical trial per the IDSA COVID-19 treatment guidelines. Added information on convalescent plasma. Removed nitazoxanide and lopinavir/ritonavir. **4/9/20:** added recommendations for Vit C, Zn^{2+}, thiamine, & melatonin. Added recommendations for VTE prophylaxis. Added QTc prolongation risk stratification **4/2/20:** reduced HCQ dose. Added proposed mechanisms of action. **3/25/20:** removed azithromycin due to limited data. Added alt. HCQ dosing for outpatients. Added statement regarding ACEI/ARBs & NSAIDs. Updated Remdesivir compassion use program to Expanded Access. **3/20/20:** added recommendation to NOT use hydroxychloroquine prophylactically outside of clinical trial ongoing in Minnesota. **03/19/20:** Removed lopinavir/ritonavir. Added nitazoxanide for alternative in pregnancy. Added azithromycin in combination with hydroxychloroquine based on preliminary data[24]