GUIDANCE FOR TREATMENT OF COVID-19 IN ADULTS AND CHILDREN

Patient population:

Adults and pediatric patients with COVID-19 infection, who are admitted on an inpatient floor or to the intensive care unit.

Key points:

Details regarding isolation/precautions, personal protective equipment, patient movement, family/visitor policy, and cleaning/disinfection can be found here.

Clinical symptoms:

Range from asymptomatic, uncomplicated upper respiratory tract viral infection to pneumonia, acute respiratory distress syndrome (ARDS), sepsis, and septic shock (Table 1)

Diagnosis:

See current COVID-19 testing recommendations.

Multisystem Inflammatory Syndrome in Adults (MIS-A) CDC case definition is available here

Multisystem Inflammatory Syndrome in Children (MIS-C) case definition and management considerations are available here

Treatment:

Based on data from several randomized control trials, Remdesivir may provide a modest benefit in a subgroup of patients hospitalized with COVID-19. See further details regarding patient populations (see below) and <u>Table 2</u>.

Table 1. **Potential** Treatment Recommendations by Severity of Disease

Patients who are receiving outpatient oral antiviral therapy for COVID-19 (molnupiravir or ritonavir-boosted nirmatrelvir (Paxlovid)) and admitted should complete their course using their own supply (Michigan Medicine does not have these medications). Consult Infectious Diseases for patients admitted for worsening COVID-19 infection who started oral antivirals as an outpatient.

Disease severity Potential Treatment Recommendations			
Disease severity			
	(per ID consult discretion based on details in <u>Table 2</u>)		
Multisystem Inflammatory Syndrome in	MIS-A therapeutic management considerations are available here		
Adults (MIS-A)			
Multisystem Inflammatory Syndrome in	MIS-C management considerations are available <u>here</u>		
Children (MIS-C)			
No supplemental oxygen	Supportive care		
	Remdesivir (3 days) may be an option in certain high-risk patients (see eligibility		
	criteria in Table 2) who have mild to moderate symptoms of COVID-19.		
Low flow supplemental oxygen	Supportive care		
	• <u>Dexamethasone</u> (Exceptions: Minimal supplemental oxygen (1-2 L) with <7 days		
	of symptoms or pediatric bronchiolitis—uncertain benefit)		
	Remdesivir (5 days)		
High flow supplemental oxygen or non-	Supportive Care		
invasive mechanical ventilation	Dexamethasone (Uncertain benefit for pediatric bronchiolitis)		
	• <u>Tocilizumab</u>		
	Remdesivir (5 days)		
l	Supportive care		
Mechanical ventilation or ECMO	oupportive date		
Mechanical ventilation or ECMO	Dexamethasone (Uncertain benefit for pediatric bronchiolitis)		



Table 2: Therapeutic agents dosing, duration, and details for treatment of COVID-19

The second second desires desiring, defraction, and dectains for treatment of covid-15			
Therapeutic Agents	Dosing & Duration	Comments	
Remdesivir (5-day regimen) Patients not hypoxic and those requiring mechanical ventilation or ECMO will not meet the below criteria because existing data does not demonstrate that remdesivir confers a clinical benefit in these patients (clinical recovery or mortality). Exceptions to the below criteria may be considered on an individualized basis. Guidelines for Use: Patients should meet criteria a & b. a. Laboratory confirmed SARS-CoV-2 infection by PCR from nasopharyngeal or respiratory sample b. Severe COVID-19 on admission or during hospitalization: Requires supplemental oxygen, high-flow nasal cannula*, or non-invasive mechanical ventilation* *HFNC and NIMV are included as possible indications for remdesivir, but it is uncertain if remdesivir confers a clinical benefit among patients requiring this level of O2 support Patients <28 days or <3 kg Remdesivir is not FDA approved in this population. Consult Pediatric Infectious Diseases to discuss use.	Adult dosing: 200 mg IV load, then 100 mg IV q24h Pediatric dosing ≥28 days of age: 3 kg to <40 kg: 5 mg/kg IV load, then 2.5 mg/kg q24h ≥40 kg: 200 mg IV load, then 100 mg IV q24h Duration: 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	 Please page 30780 (adult) or 36149 (pediatrics) for approval prior to first dose of remdesivir between 7 AM and 11 PM (7 days a week). ID consult is recommended for the following reasons: To discuss remdesivir use in pediatric patients <28 days or <3 kg with severe COVID-19 Question about whether remdesivir should be initiated/continued Patient does not meet criteria for remdesivir but unique clinical circumstances warrant ID evaluation for treatment Patient/family request CrCl <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 & benefit likely outweighs risk Increased LFTs: daily monitoring of hepatic function is recommended. The risk of hepatotoxicity with a baseline AST/ALT >5x ULN is not known due to patient exclusion from clinical trials; weigh benefit versus risk Pregnancy: Use of remdesivir should not be withheld in pregnant patients if otherwise indicated per criteria on this page. 	



There were a second	MICHIGAN MEDICINE UNIVERSITY OF MICHIGAN	C
i nerapeutic Agents	Dosing & Duration	Comments
Therapeutic Agents Dexamethasone Patients 18 years and older: 1. Recommended in patients with COVID-19 who require mechanical ventilation or ECMO 2. Recommended for patients on supplemental oxygen. The benefit of dexamethasone is uncertain in adults on minimal levels of supplemental oxygen (1-2L) with <7 days of symptoms. Decisions should be individualized in such patients with consideration of disease severity in conjunction with risks and benefits of glucocorticoid therapy. This recommendation is based on the RECOVERY RCT, NIH and IDSA treatment guidelines for patients with COVID-19 (see references) Patients <18 years: Corticosteroids are not recommended for treatment of children with viral bronchiolitis. For children with asthma or croup triggered by SARS-CoV-2 infection, corticosteroids should be used per the usual standards of care for those indications. For other pediatric patients requiring mechanical ventilation or high levels of oxygen support (e.g., high flow oxygen or noninvasive ventilation), NIH guidelines now endorse use of corticosteroids for COVID-19. However, patients <18 years were not represented in the RECOVERY RCT. It is not known if the benefit of dexamethasone will extend to children with COVID-19 who require oxygen, or if there is even the potential for harm, as seen in adults who did not require oxygen. Recommend consultation with Pediatric Infectious Diseases.	Adult dosing: 6 mg PO or IV q24h Pediatric dosing*: 0.15 mg/kg/dose IV q24h (max: 6 mg/dose) Duration: Maximum 10 days, or until discharge Shorter duration is reasonable to consider in patients who have improved rapidly or are experiencing adverse events from steroids. The median duration of therapy in the RECOVERY trial was 6 days. *Pediatric dosing is based on extrapolation from the adult dose and the RECOVERY protocol but has not been established for COVID-19	Weigh risks/benefits of use on a case-by-case basis in patients with: Active bacterial or fungal infection Diabetic ketoacidosis Baseline immunosuppression Not recommended in the following patients: Not requiring supplemental oxygen. (In RECOVERY, those had a trend towards worse outcomes). No longer COVID-19 PCR positive, but remain intubated. (In RECOVERY, patients were randomized after admission; the risk/benefit of alternative approaches later in the disease course is unknown). Pregnancy, breastfeeding: Consult OB for gestational age of viability. Alternatives may be prednisone 40 mg PO daily or hydrocortisone 80 mg IV BID. Dexamethasone is a CYP3A4 substrate, as such drug interactions should be assessed prior to use. Alternatives less prone to interactions are prednisone 40 mg PO daily, or hydrocortisone 80 mg IV BID. Potential adverse events: Increased risk for infection Hyperglycemia Peripheral edema Increased appetite Insomnia, irritability, delirium 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 (<40 kg: 0.8 mg/kg) daily or prednisone 40 mg



[- 	MICHIGAN MEDICINE UNIVERSITY OF MICHIGAN	T -
Therapeutic Agents	Dosing & Duration	Comments
Note the eligibility criteria below. This 3-day regimen is indicated for patients with mild-moderate COVID-19 (not hypoxic), based on the PINETREE study (doi: 10.1056/nejmoa2116846). Eligibility Criteria Patients with mild or moderate COVID-19 who meet criteria #1-3 AND one of criteria #4-8 1. No requirement for supplemental oxygen (or no increase from baseline supplemental oxygen) 2. Symptoms ≤7 days 3. Patient ≥28 days of age AND ≥3 kg	Adult dosing: 200 mg IV load, then 100 mg IV q24h Pediatric dosing (≥28 days of age): 3 kg to <40 kg: 5 mg/kg IV load, then 2.5 mg/kg q24h ≥40 kg: 200 mg IV load, then 100 mg IV q24h Duration: 3 days or until hospital discharge whichever comes first.	 Please page 30780 (adult) or 36149 (pediatric) for approval prior to first dose of remdesivir between 7 AM and 11 PM (7 days a week). Patients <28 days or <3 kg: Remdesivir is not FDA approved in this population. Consult Pediatric Infectious Diseases to discuss use. TO ORDER: Choose the 'New Starts' Remdesivir order panel but change duration of the maintenance (100 mg) dose to 2 days. CrCl <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 & benefit likely outweighs risk Increased LFTs: daily monitoring of hepatic function is recommended. The risk of hepatotoxicity with a baseline AST/ALT >5x ULN is not known due to patient exclusion from clinical trials; weigh benefit versus risk ** The CDC definition of 'up-to-date': received primary series and the most recent recommended booster dose.



Dosing & Duration

Therapeutic Agents

Tocilizumab

 ID APPROVAL NEEDED, ID consult is recommended for all patients with critical COVID

Recommend **Tocilizumab** (*in addition to dexamethasone*) in patients:

- 1. Newly on mechanical ventilation (<48 hours)
- 2. On high flow supplemental oxygen or noninvasive mechanical ventilation

Tocilizumab is <u>NOT</u> recommended in the following scenarios:

- Patients requiring lower levels of respiratory support than high flow support, noninvasive ventilation, or mechanical ventilation.
- 2. High concern for systemic bacterial or fungal co-infection
- 3. Receiving mechanical ventilation for longer than 48 hours
- Patients who significantly improve with the initiation of enhanced oxygen support or corticosteroids; monitoring such patients for 12-24 hours is reasonable
- 5. Unlikely to survive >48 hours
- 6. Receiving baricitinib* (see comment)

Patients <18 years:

Recommendations are primarily based on preliminary findings from the REMAP-CAP and RECOVERY trials (see references 14 and 16). Pediatric patients were not represented in these trials. It is not known if the benefit will extend to children with COVID-19. However, it is reasonable to consider tocilizumab for children who require mechanical ventilation or high levels of oxygen support (e.g., high-flow oxygen or noninvasive ventilation) who do not have rapid (e.g., within 24 hours) improvement in oxygenation after initiation of dexamethasone. Recommend consultation with Pediatric Infectious Diseases.

** Dose rounding currently built into Epic order. Doses should be rounded to nearest available full vial

(80 mg, 200 mg, 400 mg vials)**

Adult Dosing (≥18 years):

8 mg/kg (max: 800 mg/dose)

Pediatric Dosing (2 to 17 years):

<30 kg:

12 mg/kg

≥30 kg:

8 mg/kg

(max: 800 mg/dose)

Duration:

One dose

There are no data to inform risk vs. benefit of a second dose. Based on local experience a second dose is <u>NOT</u> recommended.

Pregnancy and Nursing Mothers:

Comments

- Maternal-Fetal Medicine at Michigan Medicine has endorsed the use of tocilizumab in pregnancy
- Tocilizumab may be harmful to newborns, and mothers should stop breastfeeding if receiving tocilizumab but may resume after discontinuation and discussion with provider
- *Tocilizumab benefit has been shown in studies with concomitant corticosteroid therapy. The combination of tocilizumab + baricitinib has not been rigorously studied and both the safety and efficacy of this combination is unclear. Thus, when tocilizumab is administered, it should be in combination with dexamethasone or an equivalent corticosteroid. Prior use of baricitinib is not a contraindication to using tocilizumab

Serious adverse events:

- Gastrointestinal perforation
- Anemia
- Hepatitis
- Infusion reaction
- Neutropenia
- Infection

Healthcare Providers must review FDA <u>Fact</u> <u>Sheet for Health Care Providers</u>

Healthcare Providers must provide recipients with the <u>Fact Sheet for Patients/Caregivers</u> and communicate the following information to the recipients:

- 1. FDA has authorized emergency use of Tocilizumab for patients 2 years and older with COVID-19, which is not an FDA-approved indication for use
- The patient or caregiver has the option to accept or refuse administration of Tocilizumab
- 3. The significant known and potential risks and benefits of Tocilizumab and the extent to which such risks and benefits are unknown
- 4. Information on available alternative treatments and the risks and benefits of those alternatives.

Do not use (therapies without any supportive evidence and/or associated with potential harm): hydroxychloroquine, hydroxychloroquine + azithromycin, lopinavir/ritonavir, nitazoxanide, oseltamivir, baloxavir, interferon, ribavirin, IVIG



Antibiotic Management for Pneumonia in PUI and Confirmed COVID-19 Patients

Recommendations:

- 1. In patients admitted with suspected COVID-19 pneumonia (testing pending), decisions whether to initiate antibiotic therapy should be based on guidance provided in the institutional pneumonia treatment and procalcitonin usage guidelines.
- 2. Continuation/initiation of antibiotic therapy *solely* due to confirmation of COVID-19 pneumonia is not indicated as described below.
- 3. In patients with confirmed COVID-19 pneumonia, community-onset bacterial co-infection is uncommon, even in critically ill patients, and elevated procalcitonin levels are not reliably associated with bacterial infection, especially in the setting of concomitant renal dysfunction. Empiric antibiotic therapy should generally be discontinued once a patient is confirmed COVID-19 positive but may be indicated in patients with leukocytosis and/or hemodynamic instability. De-escalation/discontinuation of antibiotics should be considered based on clinical and microbiological data. Note that an extended duration of fevers is typical in COVID-19 patients.
- 4. In patients who test negative for COVID-19 pneumonia, antibiotic therapy should be based on guidance provided in the institutional pneumonia treatment and procalcitonin usage guidelines.

Reports thus far have not identified unusual associations between COVID-19 infection and bacterial co-infection. Additionally, no unique association with resistant pathogens, including MRSA or *Pseudomonas*, has been made.

In an observational analysis by Somers et al of 154 patients with severe COVID-19 infection requiring mechanical ventilation at Michigan Medicine:

• 40% developed a bacterial superinfection, with 32% developing bacterial pneumonia. The median time to development of infection was 8-10 days after initiation of mechanical ventilation.

In a review of studies reporting bacterial co-infections in patients with COVID-19, Lansbury et al reported that the proportion of co-infection in ICU patients was 14%, compared to a proportion of 4% in studies which grouped ICU and floor-status together. Timing of onset of infection was not reported. Similarly, Vaughn et al reported that 3.5% of all patients hospitalized with COVID-19 had a community-onset bacterial co-infection and that 11% of patients admitted directly to the ICU had a community-onset bacterial co-infection¹¹.

In the study of adult patients by Zhou et al.:

- 15% of hospitalized COVID-19 patients developed a secondary bacterial infection (definition: clinical symptoms or signs of pneumonia or bacteremia with a positive culture).
- The median time to secondary bacterial infection was 17 days (13 to 19 days).
- Of all COVID-19 patients in their cohort, 79% had a WBC <10.
- Only 1% of survivors developed a secondary bacterial infection, yet the median duration of fever in survivors was 12 days and cough persisted for 19 days. Thus, 'just in case' treatment of bacterial infection can result in prolonged durations of therapy.

Data in pediatric patients are limited, but one small study (Xia et al.) suggests that procalcitonin may be higher in children with COVID-19, regardless of suspected bacterial superinfection. Decisions about antibiotic management for children should continue to be guided by clinical judgment.

Adult pneumonia treatment guidelines are summarized here, and adult and pediatric pneumonia treatment guidelines are available in their entirety at:

- Pneumonia Treatment (Adult)
- Pneumonia Treatment (Pediatrics)
- Procalcitonin Use Guidelines



Procalcitonin

• Although PCT levels should not be used in isolation to decide whether to initiate antibiotics in patients with suspected bacterial pneumonia, bacterial co-infection is unlikely in a confirmed COVID-19 patient with a low procalcitonin (<0.25), and antibiotics can be safely withheld¹¹. In addition, PCT levels >0.25 are not uncommon in patients with COVID-19 pneumonia, and do not appear to be a reliable marker of bacterial superinfection. Importantly, patients with CKD and AKI have falsely elevated PCT levels, and as such PCT is not reliable in such settings. Procalcitonin should also NOT be routinely used to extend treatment duration.

Adult Pneumonia Treatment Summary Recommendations

Indication	1 st Line Empiric Therapy	Duration of Therapy
	(see guidelines for alternatives)	
Pathway A – Inpatient	Ampicillin-sulbactam 3 g IV q6h	Uncomplicated pneumonia:
community-acquired with no	+ Azithromycin 500 mg IV/PO x1 day, then 250	5 days for patients who defervesce within
risk factors	mg q24h x4 days	72 hours and have no more than 1 sign
		of CAP instability at the time of antibiotic
		discontinuation
Pathway B	Cefepime 2 g IV q8h	Uncomplicated pneumonia:
-Community onset	(+ Tobramycin IV if admitted to ICU)	7 days
pneumonia with risk factors	+ Vancomycin* IV (see nomogram)	
for drug resistant pathogens		
(see risk factors below)	*Discontinue vancomycin if no evidence of MRSA	
	colonization/infection (negative MRSA nasal swab	
	or respiratory culture).	
Pathway C	Cefepime 2 g IV q8h	Uncomplicated pneumonia:
Hospital-acquired	(+ Tobramycin IV if admitted to ICU)	7 days
Pneumonia	+ Vancomycin* IV (see <u>nomogram</u>)	
Ventilator-associated	*Discontinue vancomycin if no evidence of MRSA	
pneumonia	colonization/infection (negative MRSA nasal swab	
	or respiratory culture).	

PATHWAY B RISK FACTORS

 History of infection or colonization with Pseudomonas spp., MRSA, or pathogens resistant to standard CAP therapy (ampicillin-sulbactam or ceftriaxone) within previous 12 months

OR

- Immunocompromised, defined as:
 - AIDS (CD4 <200)
 - Neutropenia (ANC <1000)
 - Kidney or liver or heart transplant recipient within previous 1 year
 - o Solid organ transplant recipient treated for rejection within previous 6 months
 - Lung transplant recipient
 - o Allogeneic stem cell transplant within previous 1 year or those with chronic GVHD
 - O Autoimmune disorders on biologic agents (TNFα inhibitors, rituximab, etc.)

OR

- Severe community-acquired pneumonia (septic shock OR requiring mechanical ventilation OR high clinical concern for needing ICU care³),
 AND meeting 1 of the following criteria:
 - o Hospitalization for at least 48 hours AND use of any intravenous antibiotic, fluoroquinolone, or linezolid within previous 90 days

Concomitant use of NSAIDs and/or ACE-I/ARBs:

There are conflicting theories regarding the risk and benefit of non-steroidal anti-inflammatory drugs (NSAIDs) or angiotensin converting enzyme inhibitors/ angiotensin II receptor blockers (ACE-I/ARBs) in patients with COVID-19 infection. Currently, there are no robust data demonstrating beneficial or adverse outcomes with use of these drugs in COVID-19 infections or specifically in COVID-19 infected patients taking these medications for cardiovascular disease. The American Heart Association, American College of Cardiology, and Heart Failure Society of America do not recommend stopping ACE-I or ARBs in COVID-19 infected patients. In addition, a clinical trial (NCT04312009) is investigating whether adjunctive ARB therapy can improve outcomes in COVID-19 patients. Pending this data, we do not endorse stopping or starting such therapies solely because of COVID-19 infection.



References:

- 1. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. <u>Lancet. 2020 Mar 28;395(10229):1054-1062</u>.
- 2. Beigel JH, et al. Remdesivir for the Treatment of Covid-19 —Final Report. N Engl J Med. 2020 Oct 8;NEJMoa2007764.
- 3. Goldman JD, et al. Remdesivir for 5 or 10 Days in Patients With Severe Covid-19. N Engl J Med 2020 [Online ahead of print]
- 4. Group RC, Horby P, Lim WS, et al. Dexamethasone in hospitalized patients with COVID-19—preliminary report. N Engl J Med. 2020 Jul 17;NEJMoa2021436.
- 5. NIH COVID-19 Treatment Guidelines, https://www.covid19treatmentguidelines.nih.gov/antiviral-therapy
- 6. IDSA COVID-19 Treatment Guidelines, https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/
- 7. Lansbury L, et al. Co-infections in people with COVID-19: a systematic review and meta-analysis. <u>J Infect. 2020</u> Aug;81(2):266-275.
- 8. Committee on Drugs, American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. Pediatrics 2001;108:776–89.
- Vaughn VM, Gandhi T, et al. Empiric Antibacterial Therapy and Community-onset Bacterial Co-infections in Patients Hospitalized with COVID-19: A Multihospital Cohort Study. Clin Infect Dis. 2020 Aug 21;ciaa1239.
- Pan H, Peto R, et al. Repurposed antiviral drugs for COVID-19 interim WHO Solidarity trial results. medRxiv 2020.10.15.2029817; doi: https://doi.org/10.1101/2020.10.15.20209817
- Agarwal A, Mukherjee A, et al. Convalescent plasma in the management of moderate covid-19 in adults in India:open label phase II multicentere randomized controlled trial (Placid Trial). BMJ 2020;371:m3939
- 12. Chen P et al. SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19. NEJM. 2020 Oct 28;NEJMoa2029849.
- Weinreich DM et al. REGN-COV2, a neutralizing cocktail, in outpatients with COVID-19. <u>NEJM 2020 Dec 17;NEJM 0a2035002</u>.
- Effectiveness of Tocilizumab, Sarilumab, and Anakinra for critically ill patients with COVID-19 The REMAP-CAP COVID-19 Immune Modulation Therapy Domain Randomized Clinical Trial. medRxiv 2021: https://www.medrxiv.org/content/10.1101/2021.06.18.21259133v2.
- Libster R et al. Early High-Titer Plasma Therapy to Prevent Severe Covid-19 in Older Adults <u>NEJM. 2021 Jan 6;NEJMoa2033700.</u>
- 16. RECOVERY Collaborative Group. Tocilizumab in patients admitted to hospital with 3 COVID-19 (RECOVERY): preliminary results of a 4 randomised, controlled, open-label, platform trial. MedRxiv 2021: https://www.medrxiv.org/content/10.1101/2021.02.11.21249258v1
- Marconi VC et al. Efficacy and safety of baricitinib in patients with COVID-19 infection: Results from the randomised, double-blind, placebo-controlled, parallel-group COV-BARRIER phase 3 trial. MedRxiv 2021: https://www.medrxiv.org/content/10.1101/2021.04.30.21255934v2



Antimicrobial Subcommittee Approval: 1	12/2022	Originated:	03/2020
P&T Approval: 0	01/2023	Last Revised:	03/2023

Revision History:

- 3/16/20: Removed testing recommendations added link to testing document
- 3/17/20: Added tocilizumab, adjusted pediatric hydroxychloroquine dosing
- 3/19/20: Revised tocilizumab criteria, added pneumonia guidance
- 3/20/20: Revised tocilizumab dosing to weight based due to changes in Epic dose rounding capabilities, added limited data for corticostaroids in ARDS
- 3/24/20: Added guidance on azitrhomycin, revised tocilizumab dosing, added clincial study enrollment appendix
- 3/25/20: Revised criteria for HCQ use.
- 3/26/20: Revised tocilizumab criteria & included sarilumab study caveat
- 3/27/20: Removed study flow diagram
- 3/31/20: Removed recommendation for routine HCQ, removed nitazoxanide and lopinavir/ritonavir options, revised ACE/ARB/NSAID recommendations, recommendations re: combination HCQ/Azithromycin, revised pregnancy/breastfeeding recommendations and Remdesivir compassionate use criteria, deleted Tocilizimab re-dosing
- 4/2/20: Added suggested labs, revised remdesivir clinical trial information
- 4/3/20: Added hyperlink to Appendix A review of HCQ data
- 4/6/20: Revised testing guidance hyperlink
- 4/7/20: Revised tocilizumab criteria
- 4/10/20: Revised tocilizumab criteria
- 4/15/20: Revised tocilizumab criteria
- 5/15/20: Revised tocilizumab criteria, revised remdesivir comments
- 6/3/20: Revised secondary infection information, revised remdesivir obtainment information
- 7/10/20: Added dexamethasone section
- 8/3/20: Added remdesivir criteria
- 9/15/20: Added convalescent plasma section
- 10/5/20: Removed tocilizumab, updated remdesivir comments, updated convalescent plasma comments
- 10/14/20: Revised remdesivir criteria
- 10/28/20: Revised Table 1, revised remdesivir section
- 11/19/20: Revised remdesivir comments
- 12/3/20: Revised remdesivir criteria
- 12/8/20: Added neutralizing antibodies section, revised remdesivir criteria.
- 12/17/20: Revised neutralizing antibodies criteria
- 12/23/20: Revised neutralizing antibodies criteria
- 1/5/21: Revised neutralizing antibodies criteria
- 1/13/21: Revised neutralizing antibodies criteria
- 1/17/21: Added tocilizumab section
- 1/27/21: Updated convalescent plasma criteria
- 2/25/21: Revised tocilizumab criteria, added new reference
- 3/15/21: Added bamlanivimab + etesevimab to mAb section
- 3/22/21: Added criteria and comments for tocilizumab, updated vancomycin nomogram hyperlink
- 4/7/21: Removed bamlanivimab monotherapy from mAb section
- 5/26/21: Revised mAb criteria
- 6/9/21: Revised casirivimab + imdevimab dosing and provider fact sheet
- 6/29/21: Revised mAb product availability
- 8/10/21: Added Post-exposure Prophylaxis hyperlink
- 8/25/21: Removed convalescent plasma section, revised tocilizumab section, revised alternative to tocilizumab section, updated pneumonia treatment recommendation
- 10/14/21: Revised tocilizumab section, removed alternatives to tocilizumab section, revised mAb product availability
- 12/13/21 Revised bamlanivimab + etesevimab dosing and criteria
- 12/24/21: Removed bamlanivimab + etesevimab & casirivimab + imdevimab, revised mAb criteria
- 1/4/22: Revised remdesivir 3-day and 5-day sections, revised mAb criteria
- 1/10/22: Revised remdesivir 3-day section
- 1/13/22: Removed serostatus criteria for mAb
- 2/28/22: Revised remdesivir 3-day criteria, revised mAb criteria
- 3/15/22: Added MIS-A and MIS-C hyperlinks, updated mAb and remdesivir criteria
- 3/21/22: Removed sotrovimab, added bebtelovimab
- 5/13/22: Revised mAb criteria
- 5/16/22: Revised mAb and remdesivir 3-day criteria
- 5/24/22: Revised pediatric recommendations
- 10/31/22: Removed mAb criteria, adjusted remdesivir 3-day criteria
- 12/6/22: Revised pediatric recommendations
- 3/21/23: Revised pediatric recommendations

The recommendations in this guide are meant to serve as treatment guidelines for use at Michigan Medicine facilities. If you are an individual experiencing a medical emergency, call 911 immediately. These guidelines should not replace a provider's professional medical advice based on clinical judgment, or be used in lieu of an Infectious Diseases consultation when necessary. As a result of ongoing research, practice guidelines may from time to time change. The authors of these guidelines have made all attempts to ensure the accuracy based on current information, however, due to ongoing research, users of these guidelines are strongly encouraged to confirm the information contained within them through an independent source. If obtained from a source other than med.umich.edu/asp, please visit the webpage for the most up-to-date document