

CMMC Guideline for the Treatment of COVID 19 Adult Patients

Please see the following Flowchart for those patients who are SARS-CoV2 Positive.
Treatment with Medications for suspected patients is not indicated at this time

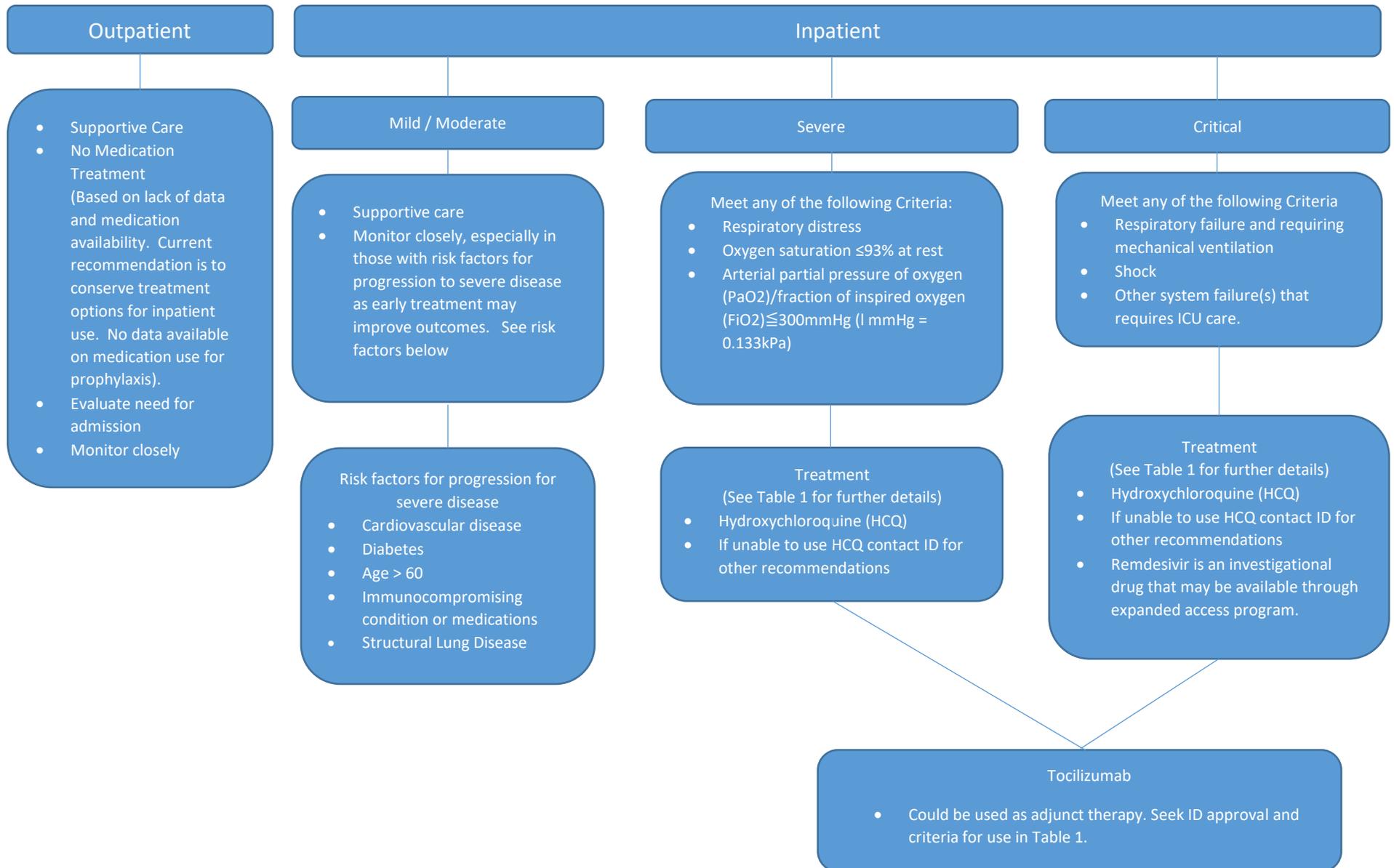


Table 1.

Currently there is no FDA approved Treatment for COVID 19.

The following Medications are either Investigational drugs or being used off-label and have the most promising data to date, and are currently available (treatment is subject to change as availability and more data emerge)

Medication	Dose	Special Considerations and Monitoring
Hydroxychloroquine (HCQ)	<ul style="list-style-type: none"> • 400 mg PO Q12 hours for 24 hours, then 200 mg PO Q12 hours for 4 days • If no clinical improvement is seen on treatment day 5, may continue 200 mg Q12 hours for up to an additional 5 days. • Treatment is only for the duration of the patient's hospitalization. • If patient clinically improves prior to end of treatment duration, consider stopping drug early to conserve medication supply. 	<ul style="list-style-type: none"> • Availability is extremely limited and highly variable • Get consent from Patient for off-label use of this medication • Oral suspension able to be compounded by pharmacy • Use with caution in those with QT prolongation and monitor QTc • Special Patient populations <ul style="list-style-type: none"> ○ Exclude pregnant and nursing mothers unless the theoretical benefits outweigh the risks. Thorough discussion of the risks and theoretical benefits of the treatment is required • The combination of azithromycin and HCQ has not been well studied and it is still unclear if it adds additional benefit. Both medications are known to cause QTc prolongation • See attached for more extensive information on use, adverse events, and monitoring at CMMC
Remdesivir	200mg IV on day 1 followed by 100mg once daily for 5 to 10 days	<ul style="list-style-type: none"> • Investigational drug, not commercially available • Check Gilead website for updates, plan is for it to be made available thru expanded access programs • https://rdvcu.gilead.com/
Tocilizumab	<p>4 – 8 mg/kg (max single dose of 800mg)</p> <p>Possible additional dose 12 hours later decided on case by case basis in conjunction with Infectious Disease</p>	<ul style="list-style-type: none"> • Product availability is extremely limited and highly variable • Consider its use as adjunct to supportive care with HCQ • There is limited data about its benefit from uncontrolled studies. Tocilizumab is an IL-6 inhibitor. It reduces IL-6 production which is a key cytokine produced in COVID-19. • Before use evaluate the patient for the following: <ul style="list-style-type: none"> ○ Patient has ARDS or impending respiratory failure despite other treatment and supportive care and elevated Ferritin level > 1000 ng/ml. Ferritin is used as a surrogate marker for cytokine storm. Ideally an IL-6 level would be checked but is currently a send out at CMMC and turnaround time is too lengthy to justify its use. In addition patient should have 1 or more of the following predictors of severe disease: <ul style="list-style-type: none"> ▪ CRP > 35 mg/L ▪ D-dimer > 1 ng/mL ▪ Lymphopenia ▪ LDH > 200 U/L ▪ Increased troponin without cardiac disease • Warnings/Precautions <ul style="list-style-type: none"> ○ Can cause serious and potentially fatal infections including reactivation of latent and new infections. Test for latent tuberculosis before therapy. ○ Hepatic or renal impairment might preclude use ○ Do not use in pregnancy

Table 2.
Miscellaneous Medications

Medication	Available Information
Corticosteroids	<ul style="list-style-type: none"> • Recommendations from the CDC and WHO are that corticosteroids should be avoided because of the potential for prolonged viral replication, unless indicated for other reasons (refractory shock) • Available data is inconsistent, currently there is not enough evidence to promote its use for treatment of COVID-19
Angiotensin-Converting Enzyme Inhibitors (ACEI) and Angiotensin II Receptor Blockers (ARBs)	<ul style="list-style-type: none"> • Concerns have been raised about the use of ACEI and ARBs in COVID-19 Patients. This is based upon the fact that SARS-CoV-2 bind to their target cells through angiotensin converting enzyme 2 (ACE2) and the hypothesis that because ACE2 is increased in patients treated with ACE inhibitors and ARBs this might facilitate infection with COVID-19 • There is proposed hypothetical benefit of ARBs as having a protective effect in COVID 19 patients • American Heart Association (AHA), American College of Cardiology (ACC), Heart Failure Society of America, and European Society of Cardiology all recommend to continue use of ACEI and ARBs in patients currently prescribed them
Non-steroidal anti-inflammatory drugs (NSAIDS)	<ul style="list-style-type: none"> • Concerns have been raised about the use of NSAIDS in COVID-19 Patients. This is based upon the fact that SARS-CoV-2 bind to their target cells through angiotensin converting enzyme 2 (ACE2) and the hypothesis that because ACE2 is increased by Ibuprofen this might facilitate infection with COVID-19. • Currently there is no scientific evidence to support this. • Acetaminophen is preferred over NSAID use whenever possible.
Nebulized medications	<ul style="list-style-type: none"> • SARS-CoV-2 is an easily transmitted virus spread through respiratory droplets because of this the use of nebulized medications has the potential to increase viral transmission • When possible use Metered dose inhalers, if not available use appropriate personal protective equipment (PPE) and limit those present in the room to only those that are necessary.
Statins	<ul style="list-style-type: none"> • At this time there is no evidence to support the addition of statin therapy in the treatment of COVID-19 patients

References

This protocol was adapted from UW Medicine and Maine Medical Center treatment guidelines for COVID-19

1. Arabi YM, Mandourah Y, Al-Hameed F, et al. Corticosteroid Therapy for Critically Ill Patients with Middle East Respiratory Syndrome. *Am J Respir Crit Care Med* 2018; 197:757-67.
2. Alhazzani W, Moller MH, Arabi YM, et al. *Crit Care Med* 2020; accepted manuscript. Available at: <https://www.sccm.org/getattachment/Disaster/SSC-COVID19-Critical-Care-Guidelines.pdf?lang=en-US>.
3. Auyeung TW, Lee JS, Lai WK, et al. The use of corticosteroid as treatment in SARS was associated with adverse outcomes: a retrospective cohort study. *J Infect* 2005;51:98-102.
4. Chen RC, Tang XP, Tan SY, et al. Treatment of severe acute respiratory syndrome with glucocorticoids: the Guangzhou experience. *Chest* 2006; 129:1441-52.
5. Colson P, Rolain J-M, Raoult D. Chloroquine for the 2019 novel coronavirus SARS-CoV-2. *International Journal of Antimicrobial Agents* 2020;55:105923.
6. Fang L, Karakiulakis G, Roth M. Are Patients With Hypertension and Diabetes Mellitus at Increased Risk for COVID-19 Infection? *Lancet Respir Med* 2020;S2213-2600(20)30116-8. doi:10.1016/S2213-2600(20)30116-8.
7. FDA advises patients on use of non-steroidal anti-inflammatory drugs (NSAIDs) for COVID-19. FDA website. Accessed March 26, 2020. Available at: <https://www.fda.gov/drugs/drug-safety-and-availability/fda-advises-patients-use-non-steroidal-anti-inflammatory-drugs-nsaids-covid-19>
8. Gautret P, Lagier JC, Parola P, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial.
9. Gordon CJ, Tchesnokov EP, Feng JY, et al. The antiviral compound remdesivir potently inhibits RNA-dependent RNA polymerase from Middle East respiratory syndrome coronavirus. *J Biol Chem* 2020;24:013056.
10. Ho JC, Ooi GC, Mok TY, Chan JW, et al. High-dose pulse versus nonpulse corticosteroid regimens in severe acute respiratory syndrome. *Am J Respir Crit Care Med* 2003;168:1449-56
11. Qin C, Zhou L, Hu Z, et al. Dysregulation of immune response in patients with COVID-19 in Wuhan, China . *Clin Infect Dis* 2020;accepted manuscript. DOI:10.1093/cid/ciaa248.
12. Shang L, Zhao J, Hu Y, Du R, Cao B. On the use of corticosteroids for 2019-nCoV pneumonia: *Lancet*. 2020 Feb 29;395(10225):683-684.
13. Sun ML, Yang JM, Sun YP, et al. [Inhibitors of RAS Might Be a Good Choice for the Therapy of COVID-19 Pneumonia]. *Zhonghua Jie He He Hu Xi Za Zhi* 2020;43:219-222. doi:10.3760/cma.j.issn.1001-0939.2020.03.016
14. Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, Shi Z, Hu Z, Zhong W, Xiao G. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro: *Cell Res*. Mar;30(3):269-271.
15. Wu C, Chen X, Cai Y, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. *JAMA Intern Med* 2020;13.
16. Xu X H, Mingfeng, Li, Tiantian, et al. Effective Treatment of Severe COVID-19 Patients with Tocilizumab. *ChinaXiv:20200300026* 2020.
17. Yao X, Ye F, Zhang M, et al. In Vitro Antiviral Activity and Projection of Optimized Dosing Design of Hydroxychloroquine for the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). *Clin Infect Dis* 2020;9.
18. Zhang G HC, Luo L, Fang F, et al. Clinical features and outcomes of 221 patients with COVID-19 in Wuhan, China. doi: 101101/2020030220030452 *J Med Rxiv* 2020.