



Patient group	Current Potential Therapy Options	Notes
<p>Mild disease:</p> <p>Not requiring hospitalization</p> <p>OR</p> <p>Hospitalized patient with (SPO2 > 94%), and NO radiographic evidence of pneumonia</p>	<p>Supportive care</p>	<ul style="list-style-type: none"> • Infectious Diseases consult required for all hospitalized patients with confirmed COVID19
<p>Moderate disease:</p> <p>Hospitalized patients with hypoxia (SPO2 ≤ 94 %)</p> <p>OR</p> <p>Radiographic evidence of pneumonia</p>	<p>Hydroxychloroquine 400 mg PO q 12 hrs. x 2 doses then 12 hours later start 400 mg PO daily for 5-10 days</p> <p>If discharged, discontinue hydroxychloroquine.</p>	<ul style="list-style-type: none"> • Infectious Diseases consult required for all hospitalized patients with confirmed COVID19 • Check EKG prior to hydroxychloroquine initiation for QT prolongation. Risk is increased when used with other QT prolonging drugs. • Recheck EKG once after drug initiation and manage clinically. • Review potential medication interactions and other possible side effects
<p>Severe disease with respiratory failure but <u>no other end organ damage:</u></p> <p>Patient requiring mechanical ventilation</p> <p>AND</p> <p>Not on pressors, CrCl > 30 ml/min, ALT < 5x upper limit of normal</p>	<p>Hydroxychloroquine 400 mg PO q 12 hrs. x 2 dose then 12 hours later start 400 mg PO daily for 5-10 days.</p> <p>Initiate process for obtaining compassionate use remdesivir</p>	<ul style="list-style-type: none"> • Infectious Diseases consult required for all hospitalized patients with confirmed COVID19 • Remdesivir not to be used concomitantly with hydroxychloroquine or other antivirals • Check EKG prior to initiation of hydroxychloroquine for QT prolongation. Risk is increased when used with other QT prolonging drugs. • Recheck EKG once after drug initiation and manage clinically. • Review potential medication interactions and other possible side effects
<p>Severe disease with respiratory failure and <u>other end organ damage:</u></p> <p>Patient requiring mechanical ventilation</p> <p>AND</p> <p>Requiring pressors or CrCl < 30 ml/min or receiving HD or CVVH or ALT > 5x upper limit of normal</p>	<p>Not eligible for remdesivir compassionate use but may be eligible for the remdesivir or sarilumab clinical trial</p> <p>Start hydroxychloroquine</p> <p>Hydroxychloroquine 400 mg PO q 12 hrs. x 2 doses then 12 hours later start 400 mg PO daily for 5-10 days.</p>	<ul style="list-style-type: none"> • Infectious Diseases consult required for all hospitalized patients with confirmed COVID19 • Check EKG prior to initiation of hydroxychloroquine for QT prolongation. Risk is increased when used with other QT prolonging drugs. • Recheck EKG once after drug initiation and manage clinically. • Review potential medication interactions and other possible side effects
<p>Evidence of cytokine release syndrome</p> <p>Worsening of respiratory function with evidence of CRS including elevations of IL-6, fibrinogen, d-dimer, CRP</p>	<p>Consider Tocilizumab or sarilumab clinical trial.</p>	<ul style="list-style-type: none"> • Infectious Diseases consult required for all hospitalized patients with confirmed COVID19

Medications:

Hydroxychloroquine (Plaquenil®):

- May start in patient with moderate disease
- May start in patients with severe disease while awaiting remdesivir
- May start in patient with severe diseases who do not qualify for remdesivir

Dosing:

400 mg PO q 12 hours x 2 doses then 12 hours later start

400 mg PO q daily for 5 - 10 days (depending on clinical improvement)

- Pregnancy Category: D
- Renal and hepatic dose adjustments not recommended
- If GI discomfort, can change 400 mg daily to 200 mg BID
- Tablet can be crushed

Monitoring:

- Check EKG prior to hydroxychloroquine initiation for QT prolongation.
- Risk is increased when used with other QT prolonging drugs.
- Recheck EKG once after drug initiation and manage clinically.

Drug interaction Resources:

https://liverpool-covid19.s3.eu-west-2.amazonaws.com/landing-page/Covid_InteractionDetailsClass_Web_2020_Mar12.pdf

https://liverpool-covid19.s3.eu-west-2.amazonaws.com/landing-page/Covid_InteractionSummary_Web_2020_Mar12.pdf

Potential Side Effects: Cardiomyopathy, hypoglycemia, bone marrow suppression, dermatitis

Remdesivir:

- Consultation with Infectious Diseases required for obtainment/utilization
- May be requested from Gilead for compassionate use in critically ill patients that are:
 - Hospitalized
 - Have confirmed SARS-CoV-2 (COVID-19) by PCR
 - Intubated

Exclusions for compassionate use include:

- Evidence of multi-organ failure
- Pressor requirement to maintain blood pressure
- ALT levels > 5 X ULN
- Creatinine Clearance <30 mL/min or dialysis or Continuous Veno-Venous Hemofiltration
- **Remdesivir cannot be used in conjunction with any other potentially active agents (ex:hydroxychloroquine)**

Dosing per protocol

Drug interaction Resources:

https://liverpool-covid19.s3.eu-west-2.amazonaws.com/landing-page/Covid_InteractionDetailsClass_Web_2020_Mar12.pdf

https://liverpool-covid19.s3.eu-west-2.amazonaws.com/landing-page/Covid_InteractionSummary_Web_2020_Mar12.pdf

Potential Side Effects: Nausea, vomiting, elevated aminotransferase, headache, constipation, phlebitis, pain in extremity

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ACE inhibitors (angiotensin converting enzyme inhibitors) and ARBs (angiotensin-receptor blockers):¹³

- It is strongly recommended that patients **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 the infections.
- **Patients should NOT be started on an ACE inhibitor or an ARB for the treatment of COVID-19**

Agents NOT recommended at this time	
Corticosteroids ¹⁵	Per WHO guidelines, given the lack of effectiveness and possible harm, especially delayed viral clearance, routine corticosteroids should be avoided unless they are indicated for other reasons such as exacerbation of asthma, COPD and refractory septic shock.
Lopinavir/ritonavir (Kaletra) ^{16,17}	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.
Darunavir/cobicistat (Prezcobix) ¹⁸⁻¹⁹	Currently being evaluated in a clinical trial but no in vitro or in vivo data exist to support use at this time.
Oseltamivir	SARS-CoV-2, the virus that causes COVID-19, does not use neuraminidase as part of the viral replication cycle so oseltamivir is unlikely to be of therapeutic value, and supplies of the drug should be preserved for patients with influenza.
IVIG	IVIG remains on critical national shortage. The benefit in patient with COVID-19 is unclear.
Ribavirin	Role unclear, doses required for optimal antiviral activity often exceed limit of patient tolerability. Risk of toxicity likely outweighs potential clinical benefit.
Nitazonaxide ²⁰	Displays inhibitory activity against the virus in vitro however no clinical data in humans exists.

References:

1. Chen N et al. 'Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study.' Lancet; 395(10223):507-513.
2. Colson P, Rolan JM, Lagier JC, Brouqui, Raoult D. Chloroquine and hydroxychloroquine as available weapons to fight COVID-19. Int J Antimicrob Agent 2020 (epub ahead of print).
3. De Wit, E et al. 'Prophylactic and therapeutic remdesivir (GS-5734) treatment in the rhesus macaque model of MERS-CoV infection.' Proceeding of the National Academy of Sciences of the United States of America. First published February 13, 2020 <https://doi.org/10.1073/pnas.1922083117>.
4. Lai C-C, et al. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. Int J Antimicrob Agents 2020; In press. <https://doi.org/10.1016/j.ijantimicag.2020.105924>
5. Liverpool COVID-19 Crush/Chew/Liquid Guide "Covid__Swallowing_2020_Mar13 (1).Pdf." Accessed March 16, 2020. <https://www.covid19-druginteractions.org/>.
6. Liverpool COVID-19 Interactions." Drug Interactions database for COVID-19 Therapeutics. Accessed March 16, 2020. <https://www.covid19-druginteractions.org/>.
7. Multicenter collaboration group of Department of Science and Technology of Guangdong Province and Health Commission of Guangdong Province for chloroquine in the treatment of novel coronavirus pneumonia. [Expert consensus on chloroquine phosphate for the treatment of novel coronavirus pneumonia]. Zhonghua Jie He He Hu Xi Za Zhi 2020; 43:E019.
8. Sheahan TP et al. 'Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERS-CoV.' Nature Communications 11, 222 (2020). <https://doi.org/10.1038/s41467-019-13940-6>.
9. Wang M, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Research 2020;30:269-271.
10. WHO Clinical Management of Severe Acute Respiratory Infection when Novel Coronavirus (2019 – nCoV) Infection is suspected. <https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html>
11. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA. Published February 24, 2020.

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12. Xueting Y, 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. Doi: 10/1093/cid/ciaa237.
13. Fang Lei. Are Patients with Hypertension and Diabetes Mellitus at increased risk for COVID-19 infection? *The Lancet* Published: March 11, 2020 DOI: [https://doi.org/10.1016/S2213-2600\(20\)30116-8](https://doi.org/10.1016/S2213-2600(20)30116-8)
14. Young BE, Ong SWX, Kalimuddin S, et al. Epidemiologic Features and Clinical Course of Patients Infected with SARS-CoV-2 in Singapore. *JAMA*. Published online March 16, 2020. doi:10.1001/jama.2020.3204 (<https://jamanetwork.com/journals/jama/fullarticle/2762688>).
15. WHO Clinical Management of Severe Acute Respiratory Infection when Novel Coronavirus (2019 – nCoV) Infection is suspected.
16. Vastag B. Old drugs for a new bug: influenza, HIV drugs enlisted to fight SARS. *JAMA* 2003, 290(13):1695-1696.
17. Chan KS, Lai ST, Chu CM, Tsui E, Tam CY, Wong MM, Tse MW, Que TL, Peris JS. Treatment of severe acute respiratory syndrome with lopinavir/ritonavir: a multicenter retrospective match cohort study. *Hong Kong Med J*. 2003;9(6):399-406.
18. Multicenter collaboration group of Department of Science and Technology of Guangdong Province and Health Commission of Guangdong Province for chloroquine in the treatment of novel coronavirus pneumonia. [Expert consensus on chloroquine phosphate for the treatment of novel coronavirus pneumonia]. *Zhonghua Jie He He Hu Xi Za Zhi* 2020; 43:E019.
19. Colson P, Rolan JM, Lagier JC, Brouqui, Raoult D. Chloroquine and hydroxychloroquine as available weapons to fight COVID-19. *Int J Antimicrob Agent* 2020 (epub ahead of print).
20. Gamino-Arroyo E, Guerrero ML, McCarthy S, et al. Efficacy and Safety of Nitazoxanide in Addition to Standard of Care for the Treatment of Severe Acute Respiratory Illness. *Clin Infect Dis*. 2019 Nov 13;69(11):1903-1911.