1. Therapy for patients with COVID-19 is primarily supportive in nature with a focus on treatment of pneumonia, respiratory failure, ARDS, sepsis and septic shock. If there is clinical evidence or concern for pneumonia or sepsis, antibiotic therapy should be initiated as delineated in the CT Children's **pneumonia** and **septic shock clinical pathways**.

2. *Antiviral therapy:*
    a. *Remdesivir*: Remdesivir is an antiviral drug that inhibits viral replication by acting as an adenosine triphosphate analog and competing for incorporation into RNA chains resulting in delayed chain termination and inhibiting viral RNA synthesis.
        i. Remdesivir is FDA approved for those who are ≥ 12 years of age **and** ≥ 40 kg. It is only available by Emergency Use Authorization (EUA) for the treatment of patients weighing 3.5 kg to <40 kg, OR patients <12 years old weighing at least 3.5 kg, with positive results of SARS-CoV-2 and are hospitalized. Non-hospitalized patients are not discussed in this algorithm.
        ii. Emergency Use Authorization:
            1. Utilize **Health Care Provider FAQs** and **Patient/Family FAQs** available on **Remdesivir | Gilead.**
            2. Provide patient/family the Patient/Family FAQ sheet and explain that the drug is not FDA approved, but available through the emergency use authorization. Patient and families have the option to refuse treatment. Providers should discuss potential risks and benefits, and that the full extent of these risks and benefits are unknown. Providers should discuss alternative treatments that are available (and those associated risks and benefits).
            3. Please note that providers need to report any serious adverse effects within 7 days (see **Health Care Provider FAQs**)
            4. Additional EUA information including educational information in Spanish is available at: https://www.gilead.com/remdesivir

    b. *Baricitinib:* Baricitinib is a Janus kinase (JAK) inhibitor and interferes with viral entry. Benefits of baricitinib were shown in clinical trial ACTT-2 comparing baricitinib in combination with remdesivir to remdesivir alone, and in clinical trial COV-BARRIER comparing treatment with baricitinib to placebo in hospitalized patients.
        i. Baricitinib has now obtained Emergency Use Authorization (EUA) for treatment of suspected/laboratory confirmed COVID-19 in patients 2 years of age or older, who require supplemental oxygen, invasive mechanical ventilation, or ECMO. As of July 2021, baricitinib no longer needs to be given with remdesivir.
        ii. Emergency Use Authorization:
            1. Utilize **Health Care Provider FAQs** and **Patient/Family FAQs** available

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2. Provide patient/family the Patient/Family FAQ sheet and explain that the drug is not FDA approved, but available through the emergency use authorization. Patient and families have the option to refuse treatment. Providers should discuss potential risks and benefits, and that the full extent of these risks and benefits are unknown. Providers should discuss alternative treatments that are available (and those associated risks and benefits).
3. Please note that providers need to report any serious adverse effects within 7 days (see **Health Care Provider FAQs**)
4. Additional EUA information including educational information in Spanish is available at: Lilly's COVID-19 Baricitinib Treatment | Eli Lilly and Company

3. *Corticosteroids:* The safety and efficacy of dexamethasone or other corticosteroids for COVID-19 treatment have not been sufficiently evaluated in pediatric patients. Importantly, the RECOVERY trial did not include a significant number of pediatric patients. As mortality rates are significantly lower among pediatric patients with COVID-19 than among adult patients with the disease, caution is warranted when extrapolating the results of this trial to patients aged less than 18 years old. Nevertheless, newer data in the adult literature suggest benefit of using dexamethasone in those who require a low level of oxygen support rather than reserving its use only for those who require a higher level of support. As such, utilization of dexamethasone should be considered for patients who are on supplemental oxygen.

4. *Hydroxychloroquine*: To date, data regarding the benefit of hydroxychloroquine in COVID-19 positive patients with symptomatic disease is lacking, with increased rates of toxicity noted in the adult population. In addition, co-administration of remdesivir and chloroquine phosphate or hydroxychloroquine sulfate is not recommended based on in vitro data demonstrating an antagonistic effect of chloroquine on the intracellular metabolic activation and antiviral activity of remdesivir. As such, we are no longer recommending the use of hydroxychloroquine for the treatment of COVID-19 positive patients.

5. *Antibiotics*: Based on the study in adults by Zhou, *et. al.,* approximately 15% of hospitalized patients with COVID-19 infections developed a secondary bacterial infection (pneumonia or bacteremia with a positive culture). If there is clinical evidence or concern for pneumonia or sepsis, antibiotic therapy should be initiated as delineated in the CT Children's **pneumonia** and **septic shock clinical pathways**.

6. *Cytokine Storm Syndrome*: Clinical signs of cytokine storm syndrome (CSS) have been recognized in some patients with COVID-19 infections, including fever, hepatomegaly, splenomegaly, acute respiratory distress syndrome (ARDS), and

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coagulopathy. In addition, these patients have demonstrated laboratory abnormalities such as lymphopenia, thrombocytopenia and elevation of CRP, coagulation times, D-dimer, hepatic transaminases, ferritin, and soluble IL-2. The ideal treatment of COVID-19 induced CSS continues to be investigated, but there is increasing evidence that the IL-6 inhibitor tocilizumab and the IL-1 inhibitor anakinra can be beneficial in these patients. We recommend monitoring for laboratory evidence of CSS in patients with COVID-19. If there is clinical or laboratory evidence suggestive of CSS, we recommend rapid initiation of one of these medications. The Rheumatology Service should be consulted for all patients with signs of CSS. They can provide assistance in management and consideration of these medications or of alternative therapies (such as emapalumab, a gamma interferon blocker) if tocilizumab or anakinra are unavailable.

7. *Azithromycin*: The study by Gautret, *et. al.,* showed that monotherapy with hydroxychloroquine led to a similar proportion of negative testing at day 6 of illness compared to combination therapy of azithromycin and hydroxychloroquine. Therefore, *routine* use of azithromycin is not recommended.

8. *Angiotensin-Converting Enzyme (ACE) Inhibitors, Angiotensin II Receptor Blockers (ARBs), and other Related Agents:* Theoretical concerns exist regarding the use of ACE inhibitors and ARBs, which may continue to increase viral entry into cells leading to a more severe disease course. At this time, there are no clinical or epidemiological data to confirm or dispel this hypothesis. A joint statement by Heart Failure Society of America, American College of Cardiology, and American Heart Association recommends continuation of these medications for patients for whom they are currently prescribed for indications known to be beneficial, such as heart failure or hypertension.

9. *Nonsteroidal Anti-inflammatory Drugs (NSAIDs):* It has been hypothesized that NSAIDs may worsen COVID-19. There are no data suggesting an association between COVID-19 clinical outcomes and NSAID use. A meta-analysis of 11 observational studies showed that there was no increased risk with exposure to NSAIDs.

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This pathway is subject to change, based on evolving recommendations from the CDC and CT DPH.
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References

1. Murthy S, Gomersall CD, Fowler RA. Care for critically patients with COVID-19. *JAMA.* 2020 Mar;doi:10.1001/jama.2020.3633[Epub ahead of print].
2. Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19). https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html
3. Gao J, Tian Z, Yang X. Breakthrough: chloroquine phosphate has shown apparent efficacy has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. *Biosci Trends.* 2020 Mar;14(1):72-73.
4. Colson P, Rolain JM, Lagier JC, et. al. Chloroquine and hydroxychloroquine as available weapons to fight COVID-19. *Int J Antimicrob Agents.* 2020 Mar; doi:10.1016/j.ijantimicag.2020.105932 [Epub ahead of print].
5. 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. *Int J Antimicrob Agents.* 2020 Mar; doi:10.1016/j.ijantimicag.2020.105949 [Epub ahead of print].
6. Zhai P , Ding Y, Wu X, Long J, Zhong Y, Li Y. The epidemiology, diagnosis and treatment of COVID-19. *Int J Antimicrob Agents.* 2020 Mar; doi:10.1016/j.ijantimicag.2020.105955 [Epub ahead of print].
7. Chu CM, Cheng VC, Hung IF, et. al. Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings. *Thorax.* 2004 Mar;59 (3): 252-256.
8. Cao B, Wang Y, Wen D, et. al. A trial of lopinavir–ritonavir in adults hospitalized with severe COVID-19. *N Engl J Med.* 2020 Mar 18; doi:10.1056/NEJMoa2001282 [Epub ahead of print].
9. Gilead Sciences Update On The Company's Ongoing Response To COVID-19. https://www.gilead.com/purpose/advancing-global-health/covid-19
10. Cron RQ, Chatham WW. The rheumatologist's role in COVID-19. *J Rheumatol*. 2020 Mar; doi:10.3899/jrheum200334 [Epub ahead of print].
11. HFSA/ACC/AHA Statement Addresses Concerns Re: Using RAAS Antagonists in COVID-19. https://www.acc.org/latest-in-cardiology/articles/2020/03/17/08/59/hfsa-acc-aha-statement-addresses-concerns-re-using-raas-antagonists-in-covid-19
12. Vaduganathan, M, Vardeny O, Michel T,et al. Renin-angiotensin-aldosterone system inhibitors in patients with COVID-19. *N Engl J Med.* 2020 Mar; doi:10.1056/NEJMsr2005760 [Epub ahead of print].
13. 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. *Lancet*. 2020 Mar;395:1054–62.
14. 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 Mar; doi:10.1001/jamainternmed.2020.0994 [Epub ahead of print].
15. Xia W, Shao J, Guo Y, et. al. Clinical and CT features in pediatric patients with COVID-19 infection: different points from adults. *Pediatr Pulmonol.* 2020 Mar; doi:10.1002/ppul.24718 [Epub ahead of print].
16. Pan C, Chen L, Cong Lu C, *et. al.* Lung Recruitability in SARS-CoV-2 Associated Acute Respiratory Distress Syndrome: A Single-center, Observational Study. *Am J Respir Crit Care Med.* 2020 Mar; doi:10.1164/rccm.202003-0527LE [Epub ahead of print].
17. NIH Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. https://www.covid19treatmentguidelines.nih.gov/

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