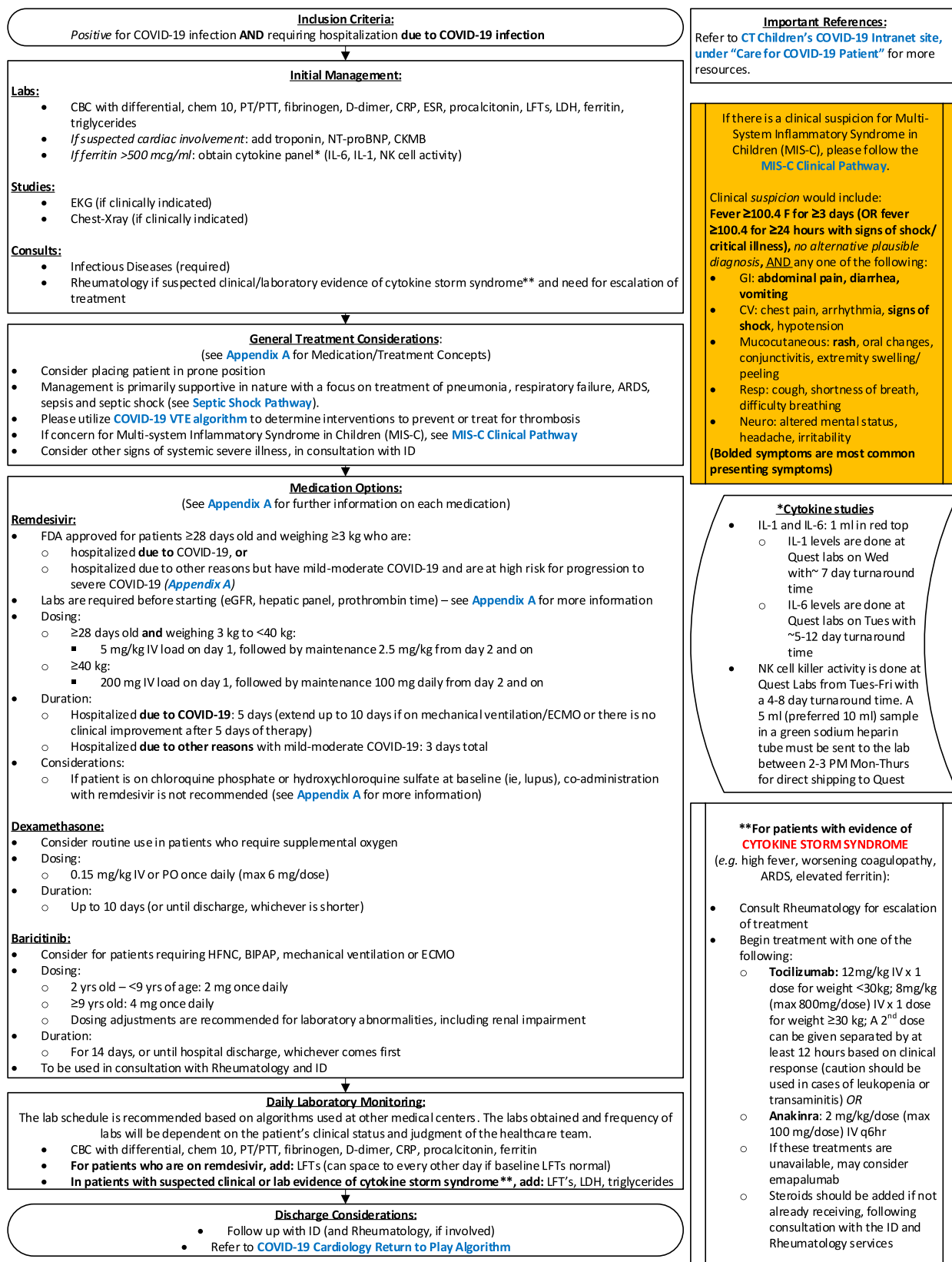


# CLINICAL PATHWAY: Inpatient Therapies for COVID-19

THIS PATHWAY  
SERVES AS A GUIDE  
AND DOES NOT  
REPLACE CLINICAL  
JUDGMENT.



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

LAST UPDATED: 05.09.22



**CLINICAL PATHWAY:**  
**Inpatient Therapies for COVID-19**  
**Appendix A: Medication and Treatment Concepts**

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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 fully FDA approved for patients 28 days of age and older, **and** weighing at least 3 kg, who are:
      1. Hospitalized **due to** COVID-19 illness, **or**
      2. Hospitalized **due to other reasons** but have mild-moderate COVID-19 and are at high risk for progression to severe disease, including hospitalization and death.
    - ii. Dosing:
      1. The recommended dose for those who weigh at least 40 kg is a single loading dose of 200 mg IV on day 1, followed by once daily maintenance doses of 100 mg IV from day 2 and on.
      2. The recommended dose for those 28 days and older, weighing 3 kg to less than 40 kg is a single loading dose of 5 mg/kg IV on day 1, followed by once daily maintenance doses of 2.5 mg/kg IV on day 2 and on.
    - iii. Duration:
      1. The total recommended treatment duration for hospitalization patients **due to COVID-19** requiring invasive mechanical ventilation and/or ECMO is 10 days.
      2. The recommended treatment for hospitalized patients **due to COVID-19** not requiring invasive mechanical ventilation and/or ECMO is 5 days. If there is no clinical improvement by 5 days, the duration may be extended up to 5 additional days (for a total treatment duration of 10 days).
      3. The recommended treatment for hospitalized patients **due to other reasons** with mild-moderate COVID-19 and at risk for progression to severe COVID-19 is 3 days total.
    - iv. Lab monitoring:
      1. Prior to starting IV remdesivir, obtain eGFR, hepatic lab testing, and prothrombin time. Monitor while receiving treatment as clinically appropriate.
    - v. Cautions:
      1. Remdesivir is contraindicated in patients with a history of clinically significant hypersensitivity reactions to remdesivir or any of its components
      2. Remdesivir is not recommended in patients with eGFR less than 30 ml per minute.
      3. Remdesivir may cause transaminase elevations. Consider stopping remdesivir if ALT levels increase to greater than 10 times the upper limit of normal. Stop remdesivir if ALT elevation is accompanied by signs and symptoms of liver inflammation .



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4. Co-administration of remdesivir and chloroquine phosphate or hydroxychloroquine sulfate is not recommended based on data from cell culture experiments (potential antagonistic effect of chloroquine on the intracellular metabolic activation and antiviral activity of 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
    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



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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 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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