COVID-19 Treatment Guidelines*

January 22, 2021

Note: Because COVID-19 is a novel virus, there is very limited evidence to support effective treatments. This guideline outlines currently available information and is authorized by the CommonSpirit Health System P&T Committee.

Information is changing rapidly, please check for updates frequently. Revisions for this version are underlined.

SARS-CoV-2 (COVID-19) infection based on positive PCR or antigen** and clinical syndrome

Evaluate for clinical trial enrollment, depending on site availability and patient qualifications

Based on currently available information:

- **Fluid management.** Conservative fluid strategies should be encouraged, including aggressive conversion to PO, eliminating unnecessary intravenous medications, and concentration of IV fluids when feasible.

- **Prone positioning.** Consider prone positioning early in treatment course for patients with mild to moderate hypoxia.

- **Anticoagulation.** Systemic anticoagulation may be associated with improved outcomes among patients hospitalized with COVID-19.1

  - All patients with COVID should at least be on prophylactic dose of enoxaparin (preferred) or SQ heparin unless contraindicated.

  - In critically ill patients with COVID-19, the CHEST guidelines (published 6/23/2020) suggest current standard dose anticoagulant thromboprophylaxis over intermediate (LMWH BID or increased weight-based dosing) or full treatment dosing, per existing guidelines.2 At the time of writing there were no randomized trials assessing enhanced anticoagulation compared to standard anticoagulation in patients with COVID-19.

  - Anecdotally, it has been found that some patients may need anticoagulation beyond standard prophylactic dosing due to a hypercoagulable state (e.g., elevated D-dimer). Some institutions are using augmented anticoagulation (e.g., enoxaparin SQ 40 mg BID) to treat these patients. In ICU patients, some institution are using full anticoagulation based on patient presentation. Prophylactic and therapeutic anticoagulation has been shown to lower mortality when compared to no anticoagulation.3

- **NIH’s recommendations** for pharmacologic management of patients with COVID-19 based on disease severity4

<table>
<thead>
<tr>
<th>Disease Severity</th>
<th>NIH Panel Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not hospitalized, mild to moderate COVID-19</td>
<td>There are insufficient data to recommend either for or against any specific antiviral or monoclonal antibody therapy. The monoclonal antibodies, bamlanivimab or casirivimab plus imdevimab, are available through EUAs for outpatients who are at high risk for disease progression. Use in hospitalized patients is not authorized. Dexamethasone should not be used (AIII).</td>
</tr>
<tr>
<td>Hospitalized but does not require supplemental oxygen</td>
<td>Dexamethasone should not be used (AIIa). There are insufficient data to recommend either for or against the routine use of remdesivir. For patients at high risk of disease progression, the use of remdesivir may be appropriate. Use one of the following options: Dexamethasone plus remdesivir (e.g., for patients who require increasing amounts of supplemental oxygen) (BIII) Dexamethasone (e.g., when combination therapy with remdesivir cannot be used or is not available) (BII) Remdesivir (e.g., for patients who require minimal supplemental oxygen) (BIIa)</td>
</tr>
<tr>
<td>Hospitalized and requires supplemental oxygen (Does not require oxygen delivery through a high-flow device, noninvasive ventilation, invasive mechanical ventilation, or ECMO)</td>
<td>Dexamethasone (AII)</td>
</tr>
<tr>
<td>Hospitalized and requires oxygen delivery through a high-flow device or noninvasive ventilation</td>
<td>Dexamethasone plus remdesivir (BIII)</td>
</tr>
<tr>
<td>Hospitalized and requires invasive mechanical ventilation or ECMO</td>
<td>Dexamethasone (AI)</td>
</tr>
</tbody>
</table>

Rating recommendations: A=strong, B=moderate, C=optional.
Rating evidence: I=At least one randomized trial with clinical outcomes or valid laboratory endpoints, II=At least one well-designed non-randomized trials or observational cohort studies, III=expert opinion.

*Most data available is for adult patients, extrapolation to children can be considered but with lower certainty of effects and outcomes.

**Clinical diagnosis and strong epidemiological links may be considered. Supportive treatment can be considered in absence of testing confirmation.
Remdesivir (Veklury)\(^9\)

- **Availability**
  - Remdesivir is now FDA approved for treatment of COVID-19 requiring hospitalization in patients > 12 yrs old weighing at least 40 kg. Remdesivir is available for purchase from Amerisource Bergen (via online or telephone).
  - For pediatric patients under 12 years of age and weighing 3.5 to less than 40 kg, remdesivir is only available via the Emergency Use Authorization (EUA); it is required that criteria be followed.

- **Evidence and Recommendations**
  - The NIH trial suggests the patients with greatest benefit are those on supplemental oxygen and not intubated at initiation.\(^6\)
  - Current evidence also suggests that remdesivir does not show proven benefit for patients who are mechanically ventilated or on ECMO.
  - The benefit seen is shortened time to recovery (10 days vs. 15 days in placebo). It has not shown an effect on mortality.
  - The SOLIDARITY trial has been released prior to peer review. No mortality benefit was seen, particularly in patients on a ventilator.\(^7\) A more thorough review of the impact of this trial will occur once it has been peer reviewed.
  - Guidelines: Organizations have reviewed the same data and published conflicting recommendations
    - **The World Health Organization (WHO)** has issued a conditional recommendation against the use of remdesivir in hospitalized patients, regardless of disease severity, as there is currently no evidence that remdesivir improves survival and other outcomes in these patients.\(^8\)
    - **The Infectious Disease Society of America (IDSA)** has issued a conditional recommendation for hospitalized patients with severe COVID-19 to suggest remdesivir over no antiviral treatment (moderate certainty of evidence).\(^9\)
      - In patients on supplemental oxygen but not on mechanical ventilation or ECMO, the IDSA panel makes a conditional recommendation for treatment with five days of remdesivir rather than 10 days of remdesivir (low certainty of evidence).
      - In patients on mechanical ventilation or ECMO, the IDSA panel gives a conditional recommendation that the treatment duration can be 10 days of remdesivir (low certainty of evidence). The benefit from remdesivir for patients on mechanical ventilation or ECMO is unsubstantiated.

- **Dosing**
  - Data from Gilead indicates that treatment should be limited to a 5 day treatment course or until hospital discharge (whichever comes first).\(^10\)
  - Adults and children weighing ≥ 40 kg\(^5\)
    - **Day 1:** Single loading dose of 200 mg infused IV over 30 to 120 minutes
    - **Days 2 to 5:** Once daily maintenance doses of 100 mg infused IV over 30 to 120 minutes for 4 days
  - Pediatric patients weighing between 3.5 kg and <40 kg\(^2\) (use lyophilized powder formulation only)
    - **Day 1:** Single loading dose of 5 mg/kg infused IV over 30 to 120 minutes
    - **Days 2 to 5:** Once daily maintenance doses of 2.5 mg/kg infused IV over 30 to 120 minutes for 4 days.

- **Use Criteria (based on currently available information)**
  - Facilities may use more restrictive criteria.
  - **Inclusion Criteria (must meet all)**
    - COVID + or strong epidemiologic link
    - Requiring at least 2 liters of oxygen to maintain O\(_2\) Sat of 94%
    - Patient must be on oxygenation orders to maintain O\(_2\) Sat of 94% that includes orders to titrate down oxygen requirements
    - Symptoms of COVID for no more than 10 days. In general, starting treatment earlier is better.
  - **Exclusion Criteria (at the time of remdesivir initiation).**
    - Consider excluding patients with COVID-19 who require invasive mechanical ventilation or ECMO. In the final remdesivir report, patients receiving mechanical ventilation or ECMO at enrollment did not see a statistically significant improvement in recovery time (0.98, 95% CI 0.70 to 1.36).\(^4\)
    - Consider discontinuing remdesivir if ALT levels increase to greater than 10 times the upper limit of normal. Discontinue remdesivir if ALT elevation is accompanied by signs or symptoms of liver inflammation.\(^5\)
    - Incidental COVID positive cases without COVID symptoms found while screening.

- **Pregnant patients**
  - For pregnant patients, the same criteria for remdesivir therapy should be used as for non-pregnant patients.\(^11\) Per the NIH guidelines, remdesivir should not be withheld from pregnant patients if it is otherwise indicated.\(^4\) Available data from published case reports and compassionate use of remdesivir in pregnant women are insufficient to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. In nonclinical reproductive toxicity studies, remdesivir demonstrated no adverse effect on embryo-fetal development when administered to pregnant animals.\(^2\) In a study evaluating compassionate use of remdesivir in pregnant women with severe COVID-19, recovery rates were high and the rate of serious adverse events was low.\(^13\)
  - **Precautions, Adverse Reactions and Monitoring**
    - In all patients, before initiating VEKLURY and during treatment as clinically appropriate, perform renal and hepatic laboratory testing and assess prothrombin time.\(^5\)
    - Caution should be used when using remdesivir in patients with eGFR less than 30 mL/min. The package insert advises against use in these patients, however, risk versus benefit should be considered given lack of specific data on possible toxicity. Recent data suggests remdesivir may be safely used for short courses in patients with eGFR less than 30 mL/min or on hemodialysis.\(^14,15\)
COVID Convalescent Plasma (CCP)

- The FDA has issued an Emergency Use Authorization (EUA) to permit the use of COVID-19 convalescent plasma to treat hospitalized patients with COVID-19.\(^6\)
- EUA procedures must be followed when administering CCP including documenting the discussion regarding risks and benefits in the medical record and reporting any adverse reactions.
- CCP’s place in therapy remains unclear at this time. Recommend only starting within the first 3 days of hospitalization in patients who are older or with co-morbid conditions. After this time, patients likely have their own COVID-19 antibodies.\(^7,\ 8\)
- The NIH’s COVID-19 Treatment Guidelines Panel states that there are insufficient data to recommend either for or against the use of CCP for the treatment of COVID-19. CCP should not be considered the standard of care for the treatment of patients with COVID-19. Prospective, well-controlled, adequately powered randomized trials are needed to determine whether CCP is effective and safe for the treatment of COVID-19.\(^4\)
- There are supply limitations for obtaining CCP that both limits the overall availability and potential timing of administration.
- Evidence
  - In the Mayo Clinic study, there were 3082 adult patients at high-risk for progression to severe or life-threatening COVID-19 included. Death within 30 days after plasma transfusion occurred in 115 of 515 patients (22.3%) in the high-titer group, 549 of 2006 patients (27.4%) in the medium-titer group, and 166 of 561 patients (29.6%) in the low-titer group. The association of anti–SARS-CoV-2 antibody levels with the risk of death from Covid-19 was moderated by mechanical ventilation status. A lower risk of death within 30 days in the high-titer group than in the low-titer group was observed among patients who had not received mechanical ventilation before transfusion (relative risk, 0.66; 95% confidence interval [CI], 0.48 to 0.91), and no effect on the risk of death was observed among patients who had received mechanical ventilation (relative risk, 1.02; 95% CI, 0.78 to 1.32).\(^9\)
  - In a study evaluating 464 adults (≥18 years) admitted to hospital with confirmed moderate COVID-19, Convalescent plasma was not associated with a reduction in progression to severe COVID-19 or all cause mortality.\(^10\)
  - In a study evaluating 228 patients assigned to receive convalescent plasma and 105 to receive placebo, no significant differences were observed in clinical status or overall mortality between patients treated with convalescent plasma and those who received placebo. The median time from the onset of symptoms to enrollment in the trial was 8 days, and hypoxemia was the most frequent severity criterion for enrollment.\(^11\)
  - If available, CCP is supplied through the blood bank and not pharmacy.
  - For patients who have received CCP, it is advised to wait at least 90 days to receive a COVID-19 vaccine to avoid interference of the treatment with the vaccine-induced immune response.
  - For additional information, please see the memo entitled, “UPDATE: COVID Convalescent Plasma Emergency Use Authorization,” sent on 9/10/2020 and located on the CommonSpirit Health COVID-19 SharePoint sites.
  - Recommended language for CCP initiation.
    - I spoke with _(patient/power of attorney)_ to provide information about convalescent plasma for _(patient)_.
    - I offered them the “Fact Sheet for Patients and Parents/Caregivers” for COVID-19 convalescent plasma to read and review.
    - I stated the therapy has been approved by an emergency use authorization (EUA) process and has not fully been FDA reviewed or approved.
    - I shared potential risks from the therapy including transmission of blood borne pathogens such as HIV and hepatitis C, allergic and transfusion related reactions, posttransfusion purpura. Additionally theoretical risks including a phenomenon called antibody-dependent enhancement of infection such as is seen in dengue or attenuation of an immune response that may make patients more susceptible to re-infection.
    - I discussed there are other potential treatment options that are currently not FDA approved to treat COVID-19.
    - (When applicable) Discussed with patient that pregnancy is not an exclusion for convalescent plasma treatment, but the therapy has not been fully evaluated in pregnant patients.
    - Offered opportunity to ask questions and all questions were answered.
    - _(patient/power of attorney)_ voiced understanding and agreed to proceed with treatment for _(patient)_.
Baricitinib in Combination with Remdesivir

- The FDA issued an EUA for baricitinib (an oral Janus kinase (JAK) inhibitor), in combination with remdesivir, for suspected or laboratory confirmed COVID-19.
- **Patient population:** Hospitalized adults and pediatric patients two years of age or older requiring supplemental oxygen, invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).
- **Evidence:**
  - In a clinical trial of hospitalized patients with COVID-19, the combination of baricitinib with remdesivir reduced time to recovery within 29 days after initiating treatment compared to patients who received a placebo with remdesivir. It is unknown how many patient received steroid therapy during the baricitinib studies.
  - The safety and effectiveness of this investigational therapy for use in the treatment of COVID-19 continues to be evaluated.
  - There are insufficient data for the NIH Panel to recommend either for or against the use of baricitinib in combination with remdesivir for the treatment of COVID-19 in hospitalized patients in cases where corticosteroids can be used instead.
  - In the rare circumstances where corticosteroids cannot be used, the Panel recommends using baricitinib in combination with remdesivir for the treatment of COVID-19 in hospitalized, nonintubated patients who require oxygen supplementation (BII).
  - The Panel recommends against the use of baricitinib in the absence of remdesivir, except in a clinical trial (AII).
  - Baricitinib is available for COVID patients admitted to the hospital. Baricitinib is available from select specialty pharmacies for rheumatoid arthritis only.
- **Dose:**
  - Adults and pediatric patients 9 years of age and older: 4 mg orally once daily for 14 days or until hospital discharge (whichever comes first)
  - Pediatric patients 2 year to less than 9 years of age: 2 mg orally once daily for 14 days or until hospital discharge (whichever comes first)

Bamlanivimab

- The FDA granted emergency use authorization (EUA) to bamlanivimab based on trial data showing that a one-time infusion of the treatment reduced the need for hospitalization or emergency room visits in high-risk COVID-19 patients. It was not authorized for hospitalized patients nor for those who require oxygen therapy due to COVID-19 as it could worsen clinical outcomes for such patients.
- **Patient eligibility** Eligible patients have a COVID-19 positive test with symptom onset within 10 days
  - Mild to moderate COVID-19 in adults and pediatrics patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.
  - High risk is defined as patients who meet at least one of the below criteria:
    - body mass index (BMI) ≥35
    - chronic kidney disease
    - diabetes
    - immunosuppressive disease
    - currently receiving immunosuppressive treatment
    - ≥65 years of age
    - Are ≥65 years of age AND have
      - cardiovascular disease, OR
      - hypertension, OR
      - chronic obstructive pulmonary disease
    - Are 12 – 17 years of age AND have
      - BMI ≥85th percentile for their age and gender based on CDC growth charts OR
      - sickle cell disease, OR
      - congenital or acquired heart disease, OR
      - neurodevelopmental disorders, for example, cerebral palsy, OR
      - a medical-related technological dependence, (e.g., tracheostomy) OR
      - asthma other chronic respiratory disease that requires daily medication for control
  - The NIH has determined that bamlanivimab should not be considered the standard of care for the treatment of patients with COVID-19. At this time, there are insufficient data to recommend either for or against the use of bamlanivimab for the treatment of outpatients with mild to moderate COVID-19.
  - The Infectious Diseases Society of America (IDSA) COVID-19 Guidelines suggests against the routine use of bamlanivimab among ambulatory patients with COVID-19 (conditional recommendation, very low certainty of evidence).
  - **Suggested use criteria** for adult patients (age 18 years or older) to allow judicious use of medication while it is on federal allocation
    - The patient must have a positive COVID-19 test, be symptomatic with mild to moderate disease (within 7 days of symptom onset) and meet at least 1 to 2 high risk criteria listed below to qualify for bamlanivimab therapy
      - Body mass index (BMI) ≥35
      - Chronic kidney disease
      - Diabetes
      - Immunosuppressive disease or currently receiving immunosuppressive treatment
      - ≥65 years of age
Casirivimab and Imdevimab

The FDA issued an EUA for casirivimab and imdevimab to be administered together for the treatment of mild to moderate COVID-19.

Patient population:
- Adults and pediatric patients (12 years of age or older weighing at least 40 kilograms) with positive results of direct SARS-CoV-2 viral testing and who are at high risk for progressing to severe COVID-19.

High risk is defined as patients who meet at least one of the below criteria:
- Body mass index (BMI) ≥35
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease
- Currently receiving immunosuppressive treatment
- ≥65 years of age
- Are ≥55 years of age AND have cardiovascular disease, OR hypertension, OR chronic obstructive pulmonary disease
- Are 12 – 17 years of age AND have BMI ≥85th percentile for their age and gender based on CDC growth charts OR, sickle cell disease, OR congenital or acquired heart disease, OR neurodevelopmental disorders, for example, cerebral palsy, OR a medical-related technological dependence, (e.g., tracheostomy) OR asthma other chronic respiratory disease that requires daily medication for control

Casirivimab and imdevimab are not authorized for patients who are hospitalized due to COVID-19 or require oxygen therapy due to COVID-19. Treatment with these monoclonal antibodies may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

Evidence:
- In a clinical trial of patients with COVID-19, casirivimab and imdevimab, administered together via IV infusion, were shown to reduce COVID-19-related hospitalization or emergency room visits in patients at high risk for disease progression within 28 days after treatment when compared to placebo.
- The safety and effectiveness of this investigational therapy for use in the treatment of COVID-19 continues to be evaluated.
Casirivimab and Imdevimab  
Suggested use criteria for adult patients (age 18 years or older) to allow judicious use of medication while it is on federal allocation.
- The patient must have a positive COVID-19 test, be symptomatic with mild to moderate disease (within 7 days of symptom onset) and meet at least 1 to 2 high risk criteria listed below to qualify for bamlanivimab therapy.
  - Body mass index (BMI) ≥35
  - Chronic kidney disease
  - Diabetes
  - Immunosuppressive disease or currently receiving immunosuppressive treatment
  - ≥65 years of age
  - ≥55 years of age AND have cardiovascular disease, OR hypertension, OR chronic obstructive pulmonary disease/other uncontrolled chronic respiratory disease
- Exclusion criteria
  - Hospitalized patients
  - Patients who require new oxygen therapy or an increase in oxygen therapy due to COVID-19 (it could worsen clinical outcomes for such patients)
- For children (age 12 to 17), use patient eligibility criteria in the bamlanivimab EU (see above)
- Allocation. The federal government will determine appropriate allocation to state health departments based on COVID-prevalence rates.
- Dose: 1200 mg of casirivimab and 1200 mg of imdevimab administered as a single intravenous infusion over at least 60 minutes as soon as possible after positive viral test for SARS-CoV-2 and within 10 days of symptom onset. Clinically monitor patients during infusion and observe patients for at least 1 hour after infusion is complete. It is recommended to have anaphylaxis kits readily available.
  - At this time, the NIH has determined there are insufficient data to recommend either for or against the use of casirivimab plus imdevimab for the treatment of outpatients with mild to moderate COVID-19. The casirivimab plus imdevimab combination should not be considered the standard of care for the treatment of patients with COVID-19.
  - Casirivimab and imdevimab are not considered a hazardous drugs.
  - For patients who have received casirivimab and imdevimab, it is advised to wait at least 90 days to received a COVID-19 vaccine to avoid interference of the treatment with the vaccine-induced immune response.
  - There is no data to support preference for bamlanivimab or the combination of casirivimab and imdevimab at this time for the identified patient population.

Medication Considerations
- Anticoagulation (supplemental to information on page 1). All patients on therapeutic anticoagulation at home (e.g., atrial fibrillation) should remain on therapeutic anticoagulation. Utilize therapeutic dosing if a thromboembolism is suspected. Consider renal function on choice and dosing of anticoagulants. Mechanical thromboprophylaxis should be used when pharmacological thromboprophylaxis is contraindicated.
  - Monitoring
    - Consider Xa monitoring in patients that may be overweight (>120 kg), underweight or fluctuating renal function.
    - Consider TEG monitoring in critically ill patients or patients with evidence of thrombosis.
    - If fibrinogen <0.5 g/L or if platelet count less than 25 x10^9/L, consider holding anticoagulation.
    - At hospital discharge, data is sparse for appropriate duration and intensity of anticoagulation requirements in patients with COVID. If a patient requires anticoagulation while inpatient, evaluate if continued anticoagulation would be appropriate.
  - Steroids (supplemental to information on page 1). Recommendations are based on the results of the RECOVERY trial.
    - Patients with severe ARDS may require higher steroid doses.
    - Oral dexamethasone is preferred over IV if a patient can take oral medications.
    - If needed, equivalent glucocorticoid dose may be substituted if dexamethasone unavailable. Equivalent total daily doses of alternative glucocorticoids to dexamethasone 6 mg daily are methylprednisolone 32 mg and prednisone 40 mg.
    - Consider screening patients at high risk for infections exacerbated by corticosteroids (e.g., Strongyloides, TB). Treat as indicated. Patients from tropical areas are at risk of Strongyloides.
  - Ivermectin. The NIH has determined that currently there are insufficient data to recommend either for or against the use of Ivermectin for the treatment of COVID-19. Results from adequately powered, well-designed, and well-conducted clinical trials are needed to provide more specific, evidence-based guidance on the role of Ivermectin for the treatment of COVID-19. Most of the studies reported to date evaluating Ivermectin had incomplete information and significant methodological limitations, which make it difficult to exclude common causes of bias. There is currently a nation-wide shortage of Ivermectin.
  - Hyperglycemia management. Monitor blood glucose for all COVID or PUI patients. Treat hyperglycemia proactively. Well controlled blood glucose has been associated with better outcomes in COVID patients.
  - Influenza vaccination. Although data are lacking on influenza vaccination for persons with COVID-19, on the basis of practice for other acute respiratory infections, the NIH Panel recommends that persons with COVID-19 should receive an inactivated influenza vaccine (BIII).
Medication Considerations (continued)

- **Aviptadil.** The FDA has granted an Expanded Access Protocol for treatment of Respiratory Failure in COVID-19 with aviptadil, a synthetic form of vasoactive intestinal peptide. It has very limited availability and may not be available at this time.
  - The treatment is available to patients who have exhausted standard therapies and are not eligible for the current Phase 2/3 clinical trial of aviptadil due to confounding medical conditions and specifically makes the treatment available to pregnant women. This is still only investigational but expanded access program is now open.
  - Facilities must apply for Expanded Access and may or may not be accepted. Anecdotally, this is a cumbersome process to undergo. As of today, no CommonSpirit Health facility has obtained this medication.
  - To apply for the aviptadil expanded access program (EAP), a facility would identify a physician sponsor and access the EAP portal at https://www.neurorxpharma.com/. If enrollment is successful, please notify your respective CommonSpirit Health IRB.
  - Follow IDSA guidelines for community-acquired pneumonia (CAP) and ventilator-acquired pneumonia (VAP) treatment. Discontinuation of empiric antibiotics is warranted if no bacterial pathogen is isolated and no other source of infection is suspected.

- **ACE Inhibitors.** Persons with COVID-19 who are prescribed ACE inhibitors or ARBs for cardiovascular disease (or other indications) should continue these medications (AII). The COVID-19 Treatment Guidelines Panel (the Panel) recommends against the use of ACE inhibitors or ARBs for the treatment of COVID-19, except in a clinical trial (AIII). 4

- **Statins.** Persons with COVID-19 who are prescribed statin therapy for the treatment or prevention of cardiovascular disease should continue these medications (AIII). The Panel recommends against the use of statins for the treatment of COVID–19, except in a clinical trial (AIII). 4

- **Inhaled epoprostenol.** In mechanically ventilated adults with COVID-19, severe ARDS and hypoxemia despite optimizing ventilation and other rescue strategies, the Surviving Sepsis Campaign suggests a trial of inhaled pulmonary vasodilator (e.g., epoprostenol) as a rescue therapy. If no rapid improvement in oxygenation is observed, the treatment should be tapered off. This is a weak recommendation, with very low quality evidence. 32


**Medications Without Sufficient Evidence to Recommend for COVID-19 Treatment**

Many medications are being trialed anecdotally for treatment of COVID-19. There are continued claims without substantiated clinical efficacy. The below of medications do not have sufficient evidence to recommend in the absence of another clinical indication.

- **Treatment with hydroxychloroquine/chloroquine.** The NIH panel recommends against chloroquine or hydroxychloroquine for the treatment of COVID–19, except in a clinical trial (AII). The FDA has withdrawn the EUA for hydroxychloroquine and chloroquine. 33 The NIH and WHO have terminated their randomized, controlled studies assessing hydroxychloroquine due to lack of efficacy. 34 Trials have shown no benefit of hydroxychloroquine for patients with COVID–19. 35–37

- **Hydroxychloroquine and azithromycin.** Do not use for COVID–19. 4

- **Prophylaxis with hydroxychloroquine.** Prophylaxis should not be utilized based on results from a large, US based, randomized, placebo controlled trial. 38

- **Kaletra (lopinavir-ritonavir).** In a recent in vivo study, it did not show benefit compared to standard of care. 39 The NIH recommends against the use of this therapy at this time. Additional studies are ongoing, including those with combination therapy.

- **Triple therapy with ribavirin, lopinavir-ritonavir and interferon beta–1b** does not have enough evidence to support routine use outside of a clinical trial. The limited data currently available is in patients with mild to moderate disease. 40

- **IL-6 inhibitors** (e.g., tocilizumab (Actemra)). Use is not recommended outside of a clinical trial. 41 Published data to support use for COVID-19-related ARDS did not show benefit. A trial assessing sarilumab (Kevzara) also showed no benefit. Currently, the NIH and IDSA has not determined the place in therapy for IL-6 inhibitors (both currently do not recommend). A recent study which has not yet been peer reviewed, showed potentially positive results. 42 Recommendations will be made once the study has been peer reviewed and evaluated by national societies.

- **Ribavirin.** There is no evidence to support ribavirin monotherapy as a treatment for COVID–19 at this time.

- **Alteplase.** For a known PE or stroke, use continues to be recommended.

- **Many medications are being trialed anecdotally for treatment of COVID–19.** There are continued claims without substantiated clinical efficacy. The below of medications do not have sufficient evidence to recommend in the absence of another clinical indication.

- **Ascorbic acid.** Do not use IV ascorbic acid.

- **IL-1 inhibitors (e.g., anakinra) (insufficient data).**

- **Melatonin**

- **Pioglitazone**

- **Zinc**

- **Thiamine**

- **IVIG.** Do not use.

- **Interferons.** Do not use.

- **Famotidine**

- **Acetazolamide**

- **Acalabrutinib**

- **Quercetin**

- **Colchicine**

- **Oseltamivir**

- **Vitamin D**

- **Fenofibrate**

- **Fluvoxamine**

For non–medication related treatment strategies for critical care patients, please see the CommonSpirit Health Critical Care COVID–19 Clinical Guidelines.
References


