COVID-19 Ambulatory Care Treatment Guidelines*

January 11, 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

Supportive treatment plus the following:

- **Home pulse oximetry** and oxygenation monitoring program for patients with moderate disease (including patients requiring home aerosol bronchodilation treatment)
- **Home Care Services** / Care Coordination / Advanced Directives
- **Anticoagulation.**
  - Systemic anticoagulation may be associated with improved outcomes in hospitalized patients with COVID-19.[1] Prophylactic and therapeutic anticoagulation has been shown to lower mortality when compared to no anticoagulation.[2]
  - 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.
  - 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.
  - **COVID-19 late sequelae complications.** Guideline for testing and evaluation coming soon.
- **NIH's recommendations** for pharmacologic management of patients with COVID-19 based on disease severity[4]

Disease Severity	NIH Panel Recommendations
Not hospitalized, mild to moderate COVID-19	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).
Hospitalized but does not require supplemental oxygen	**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.
Hospitalized and requires supplemental oxygen (Does not require oxygen delivery through a high-flow device, noninvasive ventilation, invasive mechanical ventilation, or ECMO)	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) (BI) • **Remdesivir** (e.g., for patients who require minimal supplemental oxygen) (BIIa)
Hospitalized and requires oxygen delivery through a high-flow device or noninvasive ventilation	Use one of the following options: • **Dexamethasone** (AI) • **Dexamethasone plus remdesivir** (BIII)
Hospitalized and requires invasive mechanical ventilation or ECMO	Dexamethasone (AI)

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 sudies, 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.

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Bamlanivimab[5]

- 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**[6] Eligible patients have a COVID-19 positive test with symptom onset within 10 days
  - Mild to moderate COVID-19 in adults and pediatric 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 ≥55 years of age AND have
        - cardiovascular disease, OR
        - hypertension,
        - 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.[4]
- 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).[7]
- **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 EUA (see above)
- **Allocation**. The federal government will determine appropriate allocation to state health departments based on COVID -prevalence rates.
- **Dose and Setting:** Bamlanivimab should be administered as a single 700 mg IV infusion post-dilution (0.9% normal saline) via an infusion pump or gravity. The infusion is intended for administration in an outpatient setting over 1 hour with at least an additional hour of observation upon completion for anaphylaxis or infusion-related reactions.
- For patients who have received bamlamivimab, 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.
- The **bamlanivimab patient fact sheet** (http://pi.lilly.com/eua/bamlanivimab-eua-factsheet-patient.pdf) must be provided to patients and caregivers.
- The **bamlanivimab provider fact sheet** contains additional pertinent information (http://pi.lilly.com/eua/bamlanivimab-eua-factsheet-hcp.pdf)
- Clinical trial are ongoing to gather additional data on efficacy and safety
- **Recommended language for bamlanivimab initiation**
  - I spoke with _(patient/healthcare proxy)_ to provide information about bamlanivimab for _(patient)_
  - I offered them the "Fact Sheet for Patients and Parents/Caregivers" for bamlanivimab 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 anaphylaxis and infusion related reactions. Infusion-related reactions may include fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, dizziness.
  - I discussed there are other potential treatment options to treat COVID-19.
  - (When applicable) Discussed with patient that pregnancy is not an exclusion for bamlanivimab, but the therapy has not been fully evaluated in pregnant patients
  - Offered opportunity to ask questions and all questions were answered
  - _(patient/healthcare proxy)_voiced understanding and agreed to proceed with treatment for _(patient)_

Casirivimab and Imdevimab [8]

- 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,
        - 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 therapydue to COVID-19**. Treatment with these monoclonal antibodies may be associated with worse clinical outcomes whenadministered 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.
  - **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.
    - 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.
    - 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.[4]
    - The **casirivimab and imdevimab patient fact sheet** (https://www.regeneron.com/sites/default/files/treatment-covid19-eua-fact-sheet-for-patient.pdf and https://www.regeneron.com/sites/default/files/treatment-covid19-eua-fact-sheet-for-patient-spanish.pdf) must be provided to patients and caregivers (available in English and Spanish).
    - 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

- **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.[9-10]
- **Influenza vaccination.** Visits for routine influenza vaccination should be deferred for asymptomatic and pre-symptomatic persons who have tested positive for SARS-CoV-2, the virus that causes COVID-19, for 10 days from their positive test result. For symptomatic persons with suspected or confirmed COVID-19, visits for routine vaccination should be deferred until criteria have been met for them to discontinue isolation: at least 10 days after symptom onset AND 24 hours with no fever without the use of fever-reducing medications AND COVID-19 symptoms are improving, AND the person is no longer moderately to severely ill.[11]
- **ACE Inhibitors**. Persons with COVID-19 who are prescribed ACE inhibitors or ARBs for cardiovascular disease (or other indications) should continue these medications (AIII). 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]
- **FDA website available on COVID-19:** https://www.fda.gov/health-professionals/coronavirus-disease-2019-covid-19-resources-health-professionals
- Additional medication-related information, please refer to the ASHP website: https://www.ashp.org/Pharmacy-Practice/Resource-Centers/Coronavirus

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 the use of chloroquine or hydroxychloroquine for the treatment of COVID-19, except in a clinical trial (AII).[4] The FDA has withdrawn the EUA for hydroxychloroquine and chloroquine.[12] The NIH and WHO have terminated their randomized, controlled studies assessing hydroxychloroquine due to lack of efficacy.[13] Trials have shown no benefit of hydroxychloroquine for patients with COVID-19.[14-16]
- **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.[17]
- **Kaletra (lopinavir-ritonavir).** In a recent in vivo study, it did not show benefit compared to standard of care.[18] The NIH recommends against the use of this therapy at this time.[4] Additional studies are ongoing, including those with combination therapy.
- **Ribavirin.** There is no evidence to support ribavirin monotherapy as treatment for COVID-19 at this time.
- **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.[19]
- **IL-6 inhibitors** (e.g., tocilizumab (Actemra)). Use is not recommended at this time outside of a clinical trial.[4] Published data to support use for COVID-19-related ARDS did not show benefit.[20] A trial assessing sarilumab (Kevzara) also showed no benefit.
- **Alteplase.** For a known PE or stroke, use continues to be recommended.
- **Ascorbic acid.** Do not use IV ascorbic acid.
- IL-1 inhibitors (e.g., anakinra) (insufficient data)[4, 21]
- Melatonin
- Pioglitazone
- Zinc
- Thiamine
- Ivermectin[4] In the study that examined this drug, there were clinical differences in the study populations and therapy standards have been updated.[22]
- IVIG. Do not use.
- Interferons. Do not use.
- Famotidine[23]
- Acetazolamide
- Acalabrutinib[24]
- Quercetin
- Colchicine[25]
- Oseltamivir
- Vitamin D
- Fenofibrate
- Fluvoxamine

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