

Ambulatory Treatment Guidance for COVID-19

This updated guidance is intended for use in management of adult and pediatric patients with COVID-19 in the ambulatory setting. There will be ongoing additions and modifications based on your questions and as the science evolves. These principles are based on a variety of published studies and guidelines from leading national organizations. For additional information on COVID-19 please also refer to ChristianaCare Infection Prevention website at [COVID-19 \(sharepoint.com\)](https://www.christianacare.com/COVID-19). For additional information regarding inpatient COVID management, please refer to [ChristianaCareInterimTreatmentGuidelinesforCOVID-19.pdf](#).

Admission Criteria for patients with COVID-19

Most patients with COVID-19 will not require hospitalization and can be managed with supportive care and measures in place for careful monitoring. Progression of dyspnea and/or hypoxemia are concerning signs that require further evaluation for acute management and/or hospitalization. Pulse oximetry is an important tool for monitoring patients but should not be considered a stand-alone parameter for determining need for admission. Dark skinned patients may have occult hypoxemia which is not detected by pulse oximetry. Disposition will be determined on a case-by-case basis taking into consideration underlying chronic conditions, the ability for self-care at home, and their ability to engage in monitoring.

Diagnostic Testing

Refer to the Infection Prevention website at [COVID-19 \(sharepoint.com\)](https://www.christianacare.com/COVID-19) for up to date information regarding testing.

Risk of Disease based on Age and Co-morbidities

Adults from 30-80 years of age account for most confirmed cases with most deaths occurring in persons aged 65 years or older. Risk factors for severe illness from COVID-19 include:

- Smoking tobacco or vaping
- People who live in a nursing home or long-term care facility
- Other high-risk conditions could include:
 - People with chronic lung disease or moderate to severe asthma
 - People with chronic kidney disease
 - People who have cardiovascular disease, including cardiomyopathy
 - People with diabetes
 - People who are on immunosuppressive therapy
 - People who are immunocompromised including cancer treatment
 - Obesity (BMI >30)
 - Transplant patients
 - Sickle cell disease
 - HIV infection

ChristianaCare Referral Process and COVID Scoring Tool for Ambulatory Antiviral Treatment Options

Given the limited availability of various treatment options, ChristianaCare utilizes a risk prediction Weighted Scoring Allocation as a tool to help identify potential high-risk patients with the primary goal to **prevent hospitalizations in high-risk patients with mild to moderate disease**. Characteristics of race, age, sex, sexual orientation, gender identity or expression, disability, ethnicity, national origin, ability to pay, insurance status, socioeconomic status, income derived from public assistance programs, citizenship or immigration status, perceived social worth and ability, perceived obstacles to care, and past use of resources shall not be considered as part of the primary allocation process. Factors such as prognosis for short term survival and existence of severe comorbid conditions will be considered when determining clinical appropriateness of these therapeutic interventions. The following bullet points describe the logistics for obtaining outpatient antiviral therapy for patients:

- If providers wish to use ChristianaCare pharmacies for EUA ordering, they must go through the Center for Virtual Health's COVID-19 Clinic.
- Providers are free to send their patients to other pharmacies, but it is important to know that they are taking on the responsibility of adhering to EUA guidelines for oral antivirals. Non-ChristianaCare pharmacies which have COVID antivirals can be found at this website: <https://healthdata.gov/Health/COVID-19-Public-Therapeutic-Locator/rxn6-qnx8/data>.
- Referrals directly from patients are accepted as we do not want to limit this resource only to patients who have providers referring them. Patients may call 302-428-2121 to request an evaluation for treatment, which may include monitoring and/or medication.
- For providers wishing to use ChristianaCare outpatient pharmacies, the PowerChart PowerForm referral tool has been updated to include clinical and demographic factors that influence patients' risk for hospitalization: severe immunodeficiency diagnoses; vaccination status; BMI; age; chronic conditions, and pregnancy. Data from the past two years indicate that all of these factors have been statistically significant drivers of hospitalization for symptomatic COVID-19 patients. In addition, these medications are most effective when given within days of symptom onset for patients who are COVID-19 positive.
- Moderate/high risk patients will be monitored and considered for treatment.
- Low-risk patients can be given self-care information and referred to other patient-facing workstreams in production.
- Form completion does not guarantee an immediate video visit. A video visit will occur if the patient is identified as clinically worsening by Twistle or having provider evaluation for treatment.
- The Center for Virtual Health's COVID-19 Clinic team will communicate back to the referring provider in a timely fashion. The COVID-19 Clinic will be responsible for either ordering monoclonal antibody or oral medications based on the clinical scenario.
- The Weighted Scoring scheme is below, and Center for Virtual Health will make decisions for patients based on score and product availability.

Severely immunocompromised **(6 points)**

(active cancer, organ transplant, stem cell transplant in last 2years, severe immunodeficiency, advanced or untreated HIV, >20mg pred for >2weeks)

Unvaccinated (no vaccines at all) **(4 points)**

Age 45-64 **(1 point)**

65-74 **(2 points)**

75-84 **(3 points)**

85+ **(4 points)**

Does not apply to pediatric patients

BMI greater than 30 **(1.5 points)**

Pregnant **(1 point)**

Any chronic risk factor – see above **(1 point)** (This is not additive. If you have hypertension or if you have 10 chronic conditions, patient gets 1 point.)

The following agents have been recommended by NIH and most of these bullet points are directly from the NIH guideline at [Statement on Therapies for High-Risk, Non-hospitalized Patients | COVID-19 Treatment Guidelines \(nih.gov\)](#). The vast majority of COVID cases currently are being caused by the Omicron variant of SARS-CoV-2. This variant is susceptible to several agents which are available at ChristianaCare. Remdesivir is FDA-approved, but the other agents are authorized for use under an EUA (Emergency use Authorization) - an FDA authorization for the emergency use of an unapproved product or unapproved use of an approved product in the US under certain circumstances including, but not limited to, when the Secretary of HHS declares that there is a public health emergency.

For non-hospitalized patients with mild to moderate COVID-19 who are at high risk of disease progression, the NIH Panel recommends using one of the following therapeutics (listed in order of preference):

- **Nirmatrelvir 300 mg with ritonavir 100 mg (Paxlovid)** orally twice daily for 5 days, initiated as soon as possible and within 5 days of symptom onset in those aged ≥ 12 years and weighing ≥ 40 kg **(Alla)**.
 - Paxlovid requires a dose reduction for patients with moderate renal impairment (eGFR ≥ 30 to < 60 mL/min): 150 mg nirmatrelvir (one 150 mg tablet) with 100 mg ritonavir (one 100 mg tablet), with both tablets taken together twice daily for 5 days
 - Paxlovid is not recommended in patients with severe renal impairment (eGFR < 30 mL/min)
 - Paxlovid is not recommended in patients with severe hepatic impairment (Child-Pugh Class C)

- Ritonavir-boosted nirmatrelvir (Paxlovid) has significant and complex drug-drug interactions, primarily due to the ritonavir component of the combination.
- Before prescribing ritonavir-boosted nirmatrelvir (Paxlovid), clinicians **should carefully review the patient's concomitant medications**, including over-the-counter medications and herbal supplements, to evaluate potential drug-drug interactions. See the [Panel's statement on the drug-drug interactions for ritonavir-boosted nirmatrelvir \(Paxlovid\)](#) for details. Additionally, the University of Liverpool's COVID-19 Drug Interaction Checker can be referenced here: [Liverpool COVID-19 Interactions \(covid19-druginteractions.org\)](https://covid19-druginteractions.org)
- **Remdesivir 200 mg IV** on Day 1, followed by **remdesivir 100 mg IV** daily on Days 2 and 3, initiated as soon as possible and within 7 days of symptom onset in those aged ≥12 years and weighing ≥40 kg (**BIIa**).
 - Remdesivir's FDA approval has been expanded to include use in adults and pediatric patients (12 years of age and older who weigh at least 40 kg).
 - Remdesivir is also authorized under EUA for treatment of pediatric patients weighing 3.5 kg to less than 40 kg or pediatric patients less than 12 years of age weighing at least 3.5 kg who are not hospitalized.
 - Remdesivir is not recommended in patients with eGFR < 30 mL/min due to accumulation of the excipient sulfobutylether-beta-cyclodextrin. However, the clinical significance of this accumulation is uncertain and significant toxicity with a short duration of therapy (e.g., 3 days) is unlikely. Therefore, providers should have a risk-benefit discussion with patients with severe renal impairment, as benefits may outweigh the risks in select patients.
 - Providers should consider discontinuation of remdesivir if ALT levels increase to greater than 10 times the upper limit of normal. Discontinuation is recommended if ALT elevation is accompanied by signs or symptoms of liver inflammation.
 - Because remdesivir requires IV infusion for 3 consecutive days, there may be logistical constraints to administering remdesivir in many settings.
 - Remdesivir should be administered in a setting where severe hypersensitivity reactions, such as anaphylaxis, can be managed. Patients should be monitored during the infusion and observed for at least 1 hour after infusion.
 - Please note that, even though recommended by NIH, ChristianaCare is not currently offering remdesivir as an option.
- **Bebtelovimab 175 mg** is a monoclonal antibody administered as a single IV injection (slow IV push) over at least 30 seconds, as soon as possible and within 7 days of symptom onset in those aged ≥12 years and weighing ≥40 kg, **ONLY** if none of the preferred therapies are available, feasible to deliver, or clinically appropriate (**CIII**).
 - The data that support the use of bebtelovimab are derived from in vitro studies that demonstrated its potent activity across a broad spectrum of variants of concern (VOCs) (**including both the BA.1 and BA.2**

subvariants of Omicron) and a Phase 2 randomized trial that showed no unexpected safety events and more rapid viral decay in patients at low risk for progression to severe disease. **Please note that sotrovimab is no longer recommended due to decreased activity against the Omicron BA.2 subvariant.**

- Although there are insufficient data on hospitalization and mortality outcomes in patients at high risk of disease progression who have received bebtelovimab, the agent has a mechanism of action similar to other anti-SARS-CoV-2 mAbs that have demonstrated a reduction in hospitalization or death in high-risk patients in Phase 3 trials.
- Therefore, the laboratory and Phase 2 clinical data for bebtelovimab, coupled with the aggregate evidence for this class of agents, support the use of bebtelovimab in high-risk patients when other options are not available, feasible to deliver, or clinically appropriate.
- Bebtelovimab should be administered in a setting where severe hypersensitivity reactions, such as anaphylaxis, can be managed.
Patients should be monitored during the infusion and observed for at least 1 hour after infusion.
- **Molnupiravir 800 mg** orally twice daily for 5 days, initiated as soon as possible and within 5 days of symptom onset in those aged ≥ 18 years **ONLY** when none of the above options can be used (**CIIa**).
 - The FDA EUA states that **molnupiravir is not recommended for use in pregnant patients due to concerns about the instances of fetal toxicity** observed during animal studies. However, when other therapies are not available, pregnant people with COVID-19 who are at high risk of progressing to severe disease may reasonably choose molnupiravir therapy after being fully informed of the risks, particularly those who are beyond the time of embryogenesis (i.e., >10 weeks' gestation). The prescribing clinician should document that a discussion of the risks and benefits occurred, and that the patient chose this therapy.
 - There are no data on the use of molnupiravir in patients who have received COVID-19 vaccines, and the risk-to-benefit ratio is likely to be less favorable because of the lower efficacy of this drug.
- **Ambulatory Continuation of VTE Prophylaxis and Treatment for discharged COVID-19 patients:**
 - VTE prophylaxis should be considered at discharge for patients with COVID-19 who are at high risk of VTE and with a low risk of bleeding.
 - VTE treatment should be considered at discharge for patients that were treated inpatient for confirmed or highly suspected VTE.
 - Recommendations can be found at the following link:
<http://intranet/sites/PharmacyServices/AntimicrobialStewardsh>

- **Investigational Over the Counter and Alternative Medications**
 - Some over the counter and alternative medications have been hypothesized to be beneficial in the management of COVID-19. In the absence of demonstrated benefit, ChristianaCare does NOT recommend routine use of these alternative treatment approaches.
 - Azithromycin, ivermectin and hydroxychloroquine are specifically not recommended for the treatment or prophylaxis of COVID-19.
 - Oseltamivir is not effective for COVID-19.

- **Maintenance Medications:**
 - All patients should remain on their regularly prescribed medications. Optimal control of chronic disease is critical. If patient is prescribed Paxlovid for COVID-19, be aware that the ritonavir component (pharmacologic booster) has many drug interactions. Temporary interruption of certain maintenance medications may be recommended by your care team. There is no evidence to support stopping inhaled or systemic steroids, immunosuppressive medications, biologic agents, or ACEi/ARB therapy to lessen the risk of developing COVID-19 infection.
 - Patients that are chronically on immunosuppressive medications, biologic agents, systemic steroids, or chemotherapeutic medications should have the continuation of these medications addressed with the prescribing physician in the setting of an infection.

- **Steroids:** Oral steroids should be avoided as a treatment option specifically for COVID-19 patients in the ambulatory setting. These may be considered for alternative diagnoses such as exacerbations of chronic lung disease. Inhaled steroids can be continued.

- **Acetaminophen vs. NSAIDs:** Acetaminophen and NSAIDs may be used for fever control. Early reports of NSAIDs being associated with worsening of COVID-19 have not been substantiated.

- **MDI and Nebulizer Treatment:**
 - Nebulized formulations of medications carry a higher risk of aerosolization of particles. If possible, patients should utilize MDI's for acute management of symptoms.
 - For COVID-19 patients who require nebulized formulations of medications (due to lack of efficacy or availability of MDI's) for ongoing control they should be advised to use them in an isolated section of their home, preferably a garage or patio, and minimize exposure to other family members to that location.

- Practices can do nebulizer treatments if the patient is not a candidate for MDI with spacer and if the patient has known pulmonary disease (e.g. asthma, COPD). However, the practices should not indiscriminately use nebulizers for patients who present with new, undifferentiated respiratory conditions, which could conceivably be COVID. Nebulized formulations in healthcare setting should be administered only in an isolated setting with clear procedures regarding specialized PPE utilization for high risk aerosolization. Gloves, a fit-tested N95 or RAPR, eye protection (safety glasses or face shield), and a patient contact gown should be donned prior to initiating nebulizer treatment. In addition, the door should remain closed while performing the neb treatment. It is not necessary to leave the room vacant for an hour, and the exam room should be cleaned with PDI wipes, to include all horizontal surfaces.
- **CPAP:** Patients on CPAP with COVID-19 infection should discuss options with you and their Sleep Medicine physician. When using CPAP, COVID patients should be separated from other family members.

References:

1. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at <https://www.covid19treatmentguidelines.nih.gov/>. Accessed [March 31, 2022].
2. U.S. Food and Drug Administration. (2021). *Fact Sheet for Healthcare Providers: Emergency Use Authorization for PAXLOVID* [Fact Sheet]. <https://www.fda.gov/media/155050/download>
3. U.S. Food and Drug Administration. (2022). *Fact Sheet for Healthcare Providers: Emergency Use Authorization for Remdesivir* [Fact Sheet]. [EUA 046 Veklury \(remdesivir\) FS for HCPs \(01212022\) \(fda.gov\)](https://www.fda.gov/oc/2022/03/eua-046-veklury-remdesivir-fs-for-hcps-01212022)
4. U.S. Food and Drug Administration. (2022). *Fact Sheet for Healthcare Providers: Emergency Use Authorization for Bebtelovimab* [Fact Sheet]. [Bebtelovimab Health Care Provider Fact Sheet 03302022 \(fda.gov\)](https://www.fda.gov/oc/2022/03/bebtelovimab-health-care-provider-fact-sheet-03302022)
5. U.S. Food and Drug Administration. (2021). *Fact Sheet for Healthcare Providers: Emergency Use Authorization for Molnupiravir* [Fact Sheet]. <https://www.merck.com/eua/molnupiravir-hcp-fact-sheet.pdf>