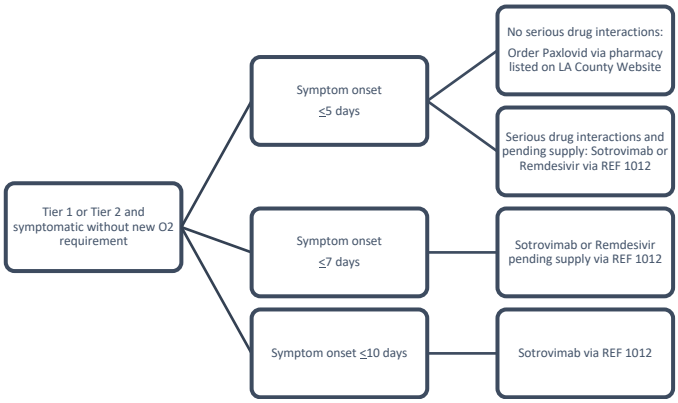
UCLA Health Outpatient Treatment Guidance v2
1/11/22

Background:
The National Institutes of Health (NIH) Covid-19 Treatment Panel[1] has recommended the use of several treatments for outpatients **with symptoms** of mild-moderate COVID-19 who are at **high risk for progression** to severe infection. While most of these treatments have been given Emergency Use Authorization (EUA) by the Food and Drug Administration (FDA), some have been considered for off-label use based on published data.

The following guidance is for **all available outpatient treatments** for mild-moderate Covid-19 infection.

A quick-view summary of the approach is as follows:



Criteria for treatment:
Patients must meet **all** the following criteria to be eligible for any outpatient treatment at UCLA:

- Not requiring any supplemental O2 or increase from baseline O2 requirements
- SARS-CoV-2 positive test ≤ 7 days prior (PCR preferred)
- Symptom onset ≤ 7 days prior
- At least one high-risk criterion

AND meet at least one high risk criteria as follows:

- Age ≥ 65 regardless of medical co-morbidities
- Diabetes
- Immunosuppressive disease or immunosuppressive therapy (see below)
- CKD (CrCl < 60 ml/min per Cockroft-Gault for > 3 months)
- Obesity (BMI ≥ 25 or if 12-17 years BMI ≥ 95th percentile (based on CDC growth chart))
- Neurologic diseases: cerebrovascular diseases, Down Syndrome or other neurodevelopmental disorders, or dementia
- Pregnancy if other risk factors and under maternal fetal medicine consultation (consider checking antibody status)
- Hemoglobin disorders (sickle cell, thalassemia)
- Cardiovascular disease (congenital heart disease, heart failure, CAD, cardiomyopathy, or pulmonary HTN), OR Hypertension
- Chronic lung disease (COPD/emphysema, moderate-severe asthma, CF, pulmonary fibrosis)
- Medical-related technological dependence (tracheostomy, gastrostomy, or positive pressure ventilation not related to COVID-19)
- Other CDC defined high risk criteria including history of smoking, history of cancer, liver disease, well controlled HIV, mental health disorders and substance use disorders

[1] https://www.covid19treatmentguidelines.nih.gov/

Individuals coming from a disadvantaged socioeconomic background are also considered given their increased risk of mortality in several studies.

Prioritization in times of scarcity

The following recommendations by the NIH will be implemented:

- Treatment of COVID-19 over post-exposure prophylaxis (PEP) of SARS-CoV-2 infection.
- Treatment of COVID-19 in unvaccinated or incompletely vaccinated individuals with clinical risk factors for severe illness and vaccinated individuals who are not expected to mount an adequate immune response (ie, Immunocompromising Conditions).

Tier 1	Unvaccinated individuals at the highest risk of severe disease (anyone aged ≥75 years or anyone aged ≥65 years with additional risk factors) OR Immunocompromised individuals not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying conditions, regardless of vaccine status (highest risk)
Tier 2a	Tier 2A - Unvaccinated individuals at risk of severe disease not included in Tier 1 (anyone aged ≥65 years or anyone aged <65 years with clinical risk factors based on criteria above)
Tier 2b	Tier 2B - Moderate-severe immunocompromise (per CDC criteria) not otherwise included in Tier 1, regardless of vaccine status and age
Tier 3	Vaccinated individuals at high risk of severe disease (anyone aged ≥75 years or anyone aged ≥65 years with clinical risk factors other than immunosuppression)
Tier 4	Tier 4 - Vaccinated individuals at risk of severe disease (anyone aged ≥65 years or anyone aged <65 with clinical risk factors)

Immunocompromising Conditions may be stratified as follows:

Tier 1 Immunocompromising Conditions:

- Patients who are within 1 year of receiving B-cell depleting therapies (e.g., rituximab, ocrelizumab, ofatumumab, alemtuzumab)
- Patients receiving Bruton tyrosine kinase inhibitors
- Chimeric antigen receptor T cell recipients
- Post-hematopoietic cell transplant recipients who have chronic graft versus host disease or who are taking immunosuppressive medications for another indication
- Patients with hematologic malignancies who are on active therapy
- Lung transplant recipients
- Patients who are within 1 year of receiving a solid-organ transplant (other than lung transplant)
- Solid-organ transplant recipients with recent treatment for acute rejection with T or B cell depleting agents
- Patients with severe combined immunodeficiencies
- Patients with untreated HIV who have a CD4 T lymphocyte cell count <50 cells/mm^3

Tier 2 Immunocompromising Conditions:

- Receiving active cancer treatment for non-hematologic malignancies (e.g. myelosuppressive chemotherapy)
- Solid organ transplant on immunosuppression (>1 year)

[1] https://www.covid19treatmentguidelines.nih.gov/

- HSCT <2 years (without GVHD/not taking immunosuppressive meds for another indication)
- Moderate primary immunodeficiency on treatment
- Untreated/advanced HIV, CD4 count <200 but >50 cells/mm3
- Active treatment with high-dose corticosteroids (>20mg daily for at least 2 weeks) or other drugs that may suppress your immune response (active, within the last month)

When the demand for this therapy may exceeds our ability to administer on any given day, the order time stamp and a point system, specifically prioritizing risk of disease severity and risk of exposure (including socioeconomic vulnerability), will be included in the allocation process. A lottery system may also be utilized if multiple individuals have the same risk for disease severity. We will review all referrals at 10:30am on each calendar day.

Selection of Therapies

Four* options will be considered depending on availability of treatment and contraindications:

- Sotrovimab (IV), a monoclonal antibody targeting the receptor binding domain of the spike protein
- Paxlovid (PO), a protease inhibitor: several drug interactions
- Molnupiravir (PO), nucleotide analogue, introduces errors in replication: contraindicated in pregnancy
- Remdesivir (IV), a nucleotide prodrug analogue targeting RNA polymerase

*Convalescent plasma in the outpatient setting is currently not available

	Sotrovimab	Paxlovid (nirmatrelavir/ritonavir)	Molnupiravir (Lagevrio)	Remdesivir
Standard Dose	500mg IV x 1	Nirmatrelvir 300mg (two 150 mg tablets) with 100 mg ritonavir (one 100mg tablet), with all three tablets taken together twice daily for 5 days with or without food	800mg (4 tablets) orally every 12 hours x 5 days with or without food	200mg IV day 1 100mg IV d2-3
Window	10 days from sx onset	5 days from sx onset	5 days from sx onset	7 days from sx onset
Efficacy	85% risk reduction	89% risk reduction	30% risk reduction	87% risk reduction
Drug Interactions	None	-Substrate and inhibitor of CYP3A4. -Review Appendix A, the drug EUA, and https://www.covid19-druginteractions.org/checker -Must discuss management of immunosuppression with Transplant team before prescribing	None	No significant interaction
Pregnancy/ Lactation	Limited data, generally considered safe	Limited data, must be approved by MFM	Contraindicated	Limited data, generally considered safe
Renal adjustment	No adjustment	-For eGFR ≥30 ml/min and ≤60 ml/min: decrease dose to 150 mg nirmatrelvir (one 150 mg tablet) and 100 mg ritonavir (one 100 mg tablet) twice daily x 5 days with or without food -Not recommended for eGFR < 30 ml/min	No adjustment	Discuss with pharmacy if eGFR <30
Hepatic adjustment	No adjustment	Not recommended in severe impairment	No adjustment	Not recommended if AST/ALT >10 x ULN

Patients must receive fact sheets and consent to treatment prior to administration.
Sotrovimab fact sheet (available in English and Spanish)
Paxlovid fact sheet (available in English and Spanish)
Molnupiravir fact sheet (English, Spanish)
Remdesivir fact sheet separate and specific to UCLA Health

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How to order/refer:
The referral process for these outpatient treatments will remain the same as it has been for monoclonal antibody therapies. A new referral order for outpatient Covid-19 therapies, which includes these criteria, is currently available on Care Connect as follows: **Referral for COVID-19 Outpatient Therapies** [REF1012].

Prescriptions for outpatient oral antivirals (Paxlovid (nirmatrelvir-ritonavir) and molnupiravir) for approved patients will be sent by the Outpatient Treatment Team to the UCLA Med Plaza Level 1 pharmacy or UCLA Santa Monica 16th Street pharmacy for curbside pickup or home delivery if supply is available. **Please note that UCLA does not have any supply at the moment.**

If you have patients whom we are not able to accommodate with oral therapies due to supply but fall under Tier 1 and Tier 2 categories, you can consider one of these outpatient pharmacies that carry oral antiviral therapies.

[1] https://www.covid19treatmentguidelines.nih.gov/