

Dear Providers,

Two recently FDA authorized oral medications for the treatment of outpatients with mild-to-moderate COVID-19 at risk for progression to severe disease will be available in California by the end of December. These include:

- [Paxlovid](#) (nirmatrelvir tablets and ritonavir tablets, co-packaged for oral use) is an oral protease inhibitor. Pfizer [announced](#) the results from a trial of 2,246 adults who received either Paxlovid or placebo. All patients had not received a COVID-19 vaccine and had not been previously infected with COVID-19. In the study, Paxlovid significantly reduced the proportion of people with COVID-19 related hospitalization or death from any cause by 88% compared to placebo among patients treated within five days of symptom onset. Paxlovid has received an EUA authorizing use for the treatment of mild-to-moderate COVID-19 in patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death.
- [Molnupiravir](#) is a nucleoside analogue that inhibits SARS-CoV-2 replication by viral mutagenesis. Merck [announced](#) results from a trial of 1,433 patients. Enrolled participants had not received a COVID-19 vaccination and had at least one risk factor associated with poor disease outcomes and symptom onset within five days prior to study enrollment. The risk of hospitalization for any cause or death through day 29 was lower with molnupiravir (6.8%) than with placebo (9.7%), for a relative risk reduction of 30%. Molnupiravir is authorized for treatment of mild-to-moderate COVID-19 in adults with positive results of direct SARS-CoV-2 viral testing who are at high risk for progressing to severe COVID-19, including hospitalization or death, and for whom alternative COVID-19 treatment options authorized by FDA are not accessible or clinically appropriate.

### **Instructions to Providers**

Both oral antivirals may only be prescribed for an individual patient by physicians, advanced practice registered nurses, and physician assistants that are licensed or authorized under state law to prescribe drugs in the therapeutic class to which Paxlovid and molnupiravir belong (i.e., anti-infectives).

Providers should carefully review the fact sheet for healthcare providers (available both for [Paxlovid](#) and [molnupiravir](#)) before prescribing either medication to ensure that the patient's condition warrants treatment, that there are no drug interactions, and that there are contraindications to therapy.

The use of molnupiravir is not recommended during pregnancy. Advise individuals of childbearing potential to use effective contraception correctly and consistently, as applicable, for the duration of treatment as described in the FDA fact sheets. Paxlovid may lead to a risk of HIV-1 developing resistance to HIV protease inhibitors in individuals with uncontrolled or undiagnosed HIV-1 infection.

Unfortunately, supply of both oral antivirals is expected to be limited. Providers should communicate with [pharmacies](#) that will be receiving these drugs to ensure that supply exists before sending patients to pick up prescriptions.

Patients meeting the below criteria may be eligible for treatment with Paxlovid or molnupiravir:

- Patients who are symptomatic with mild to moderate COVID-19 AND
- Have positive results of direct SARS-CoV-2 viral testing AND
- Are at high risk for progressing to severe COVID-19 and/or hospitalization

The [definition](#) of mild and moderate disease and defined by NIH is below:

- *Mild Illness*: Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have shortness of breath, dyspnea, or abnormal chest imaging.
- *Moderate Illness*: Individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation (SpO<sub>2</sub>) ≥94% on room air at sea level.

Neither oral option is authorized for treatment in patients requiring hospitalization due to severe or critical COVID-19.

For a complete list of risk factors for disease progression, including information on the relative risk of severe disease, see the CDC webpage “[Underlying Medical Conditions Associated with High Risk for Severe COVID-19](#)”.

Treatment should be prioritized in unvaccinated or incompletely vaccinated individuals and vaccinated individuals who are not expected to mount an adequate immune response (e.g., individuals who are immunocompromised or on immunosuppressive medications or individuals aged ≥65 years).

If supply remains limited after applying the above criteria, CDPH recommends additionally prioritizing high-risk patients with moderate illness as defined above in the following order:

1. Immunocompromised or on immunosuppressive medications
2. Incompletely vaccinated AND > 65 years of age with risk factors for severe disease
3. > 65 years of age with risk factors for severe disease

Molnupiravir is only authorized for use if alternative COVID-19 treatment options authorized by FDA are not accessible or are not clinically appropriate. In cases where Paxlovid or sotrovimab are not available for treatment and the patient is at high risk, consideration should be given to [Remdesivir IV daily for three days](#) or molnupiravir can be considered.

### **Supply and Availability**

Supply of these products is expected to be extremely limited. While further allocations from the federal government are expected in early January 2022, the current availability is as follows for the state:

- Paxlovid: 6,180 full treatment courses allocated to California
- Molnupiravir: 28,920 full treatment courses allocated to California

Allocation of both oral antivirals will be to pharmacies and providers able to dispense the medication. The number of courses allocated to each county is determined using the overall COVID-19 cases in that county combined with an equity measure based on the [Healthy Places Index](#) (HPI).

A list of all pharmacies that will be receiving products will be posted on the CDPH website and is available [here](#).

Best wishes,

The CDPH COVID-19 Therapeutics Team