Provider Health Alert
December 28, 2021

New COVID-19 Oral Anti-Viral Treatments: Paxlovid and Molnupiravir

Background

The Food & Drug Administration has issued two new emergency use authorizations (EUA) for oral anti-viral treatments: one on Dec. 22, 2021 for Pfizer's Paxlovid and one on Dec. 23, 2021 for Merck's Molnupiravir. Both anti-viral treatments received their EUA for use in patients with mild-to-moderate symptomatic COVID-19 with symptoms onset within 5 days.

In light of the Omicron variant, these new oral anti-viral treatments are a valuable addition to the current available monoclonal antibody (mAb) treatment as Bamlanivimab plus estesevimab and REGEN-COV are not effective against the Omicron variant. Additionally, although mAb sotrovimab remains effective against the Omicron variant when given within 10 days of symptoms onset, supplies are limited at this time.

Even as COVID-19 treatments are being authorized, vaccines remain the most important prevention against severe outcome from COVID-19. COVID-19 treatments are not a replacement for COVID-19 vaccinations and boosters, and providers should continue to encourage patients to get vaccinated and get their booster to protect against COVID-19.

Paxlovid

On December 14, 2021, Pfizer had announced the results from an analysis of 2,246 adults who received either Paxlovid or placebo. 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 EUA authorizes it for treatment of mild-to-moderate COVID-19 in adults and pediatrics patient 12 years of age and older weighing at least 40 kg with:

- a positive result of COVID-19 viral testing **AND**
- who are at high risk for progression to severe COVID-19, including hospitalization or death.

It is given twice a day for 5 days. Paxlovid 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 belongs (i.e., anti-infectives). It is not authorized for the pre-exposure or post-exposure prevention of

COVID-19 or for initiation of treatment in those requiring hospitalization due to severe or critical COVID-19.

Paxlovid includes nirmatrivir, a SARS-COVID-19 main protease and ritonavir, an HIV-1 protease inhibitor and CYP3A inhibitor. Given this, Paxlovid is contraindicated with many commonly prescribed prescription and over the counter drugs, and has some warnings and precautions.

Health Care Providers should review the Paxlovid EUA and fact sheet for healthcare, prior to prescribing Paxlovid, for a complete list of contraindicated drugs, further details on administration, dosing, warnings, and precautions.

Molnupiravir

On December 16, 2021, Merck published the Phase 3 results from the MOVe-OUT trial, a double-blind, randomized placebo-control trial of 1,433 patients. Molnupiravir is a nucleoside analogue that inhibits SARS-CoV-2 replication by viral mutagenesis. 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% and absolute risk reduction of 3.0%. One death was reported in the Molnupiravir groups and 9 in the placebo group through day 29.

Molnupiravir EUA authorizes it for use treatment of mild-to-moderate COVID-19 in adults (18 years of age or older) with:

- a positive result of COVID-19 viral testing **AND**
- who are at high risk for progression to severe COVID-19, including hospitalization or death, **AND**
- for **whom an alternative COVID-19 treatment option** authorized by the FDA are not accessible or clinically appropriate.

It is dosed twice a day for 5 days. There are no identified contraindications, but the use of Molnupiravir is not recommended during pregnancy or breastfeeding. Based on findings from animal reproduction studies, Molnupiravir may cause fetal harm when administered to pregnant individuals. Given this, females of childbearing potential are advised to use a reliable method of birth control during treatment with Molnupiravir and for four days after the final dose. Breastfeeding is also not recommended during treatment and for 4 days after the last dose of Molnupiravir. Males of reproductive potential who are sexually active with females of childbearing potential are advised to use a reliable method of birth control during treatment and for at least three months after the final dose. Molnupiravir 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 Molnupiravir belongs (i.e., anti-infectives).

Molnupiravir is not authorized for use in patients younger than 18 years of age because it may affect bone and cartilage formation and growth. Molnupiravir is not authorized for the pre-exposure or post-exposure prevention of COVID-19 or for initiation of treatment in those requiring hospitalization due to severe or critical COVID-19.

Health Care Providers should review the Molnupiravir EUA and fact sheet for health care providers for further details on administrations, dosing, warnings, precautions and consideration of the potential risks/benefits prior to prescribing Molnupiravir.

Expected Quantity

The federal government will be allocating Paxlovid and Molnupravir to states, and the California Department of Public Health (CDPH) will allocate these therapeutics to jurisdictions based on new COVID-19 cases and an equity measure formula that will be based on zip-code-level Healthy Places Index (HPI) Scores.

Within each jurisdiction, Paxlovid and Molnupravir will be distributed to selected pharmacies who can dispense medications. During the initial weeks of allocation, when supplies of Paxlovid and Molnupravir remain scarce, only a few pharmacies in each jurisdiction will be receiving product. Patients will require a prescription for both Paxlovid and Molnupravir, and should be directed to sites, noted below, that have received an allocation.

Overall supply in the initial weeks that the drugs are available is expected to be extremely limited. The U.S. Department of Health and Human Services has announced that only 64,970 treatment courses of Paxlovid will be available to the entire United States, with 6,180 courses allocated to California. The U.S. Department of Health and Human Services is allocating 28,920 courses of Molnupiravir to California in late December. Further federal allocations are not expected again until early January 2022.

In the setting of likely increasing COVID-19 cases due to Omicron around the state, demand for FDA authorized outpatient COVID-19 treatments, including Molnupiravir and Paxlovid, may exceed available supply.

Allocation and Distribution

Given the limited amount of Paxlovid and Molnupiravir available, product scarcity is expected. At this time, limited supplies of both Molnupravir and Paxolvid will be available through several retail pharmacies that are listed below. Prescriptions for both medications can be sent to these pharmacies for eligible patients. Due to the limited supply, providers should review patient risk and prioritize prescribing to patients who are highest risk for severe outcomes.

Prioritization of Patients for Therapeutics

Patients should only receive Paxlovid or Molnupiravir if they have symptomatic disease meeting the criteria as defined by the NIH:

- *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 (SpO2) ≥94% on room air at sea level.

Additionally, the National Institutes of Health (NIH) treatment guidelines listing priority groups for treatment were written for use of anti-SARS-CoV-2 monoclonal antibodies, but the same framework can be used for oral anti-virals to prioritize patients getting therapeutics when product is limited:

- 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 additional prioritization of 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

Ethical Considerations

As supplies of Paxlovid and Molnupiravir are expected to be limited, the overall aim in distribution and use of Paxlovid and Molnupiravir should be to achieve the greatest overall clinical benefit to patients infected with COVID-19, avoid bias, and mitigate healthcare disparities.

Clinicians are likely to find that they do not have adequate Paxlovid and Molnupiravir supply for all eligible patients initially. This situation will be challenging for patients and family members, clinicians, and hospital staff, and CDPH guidance for Hospitals Regarding Allocation of Scarce Medications for COVID-19 can be reviewed as institutional guidance to support and augment clinical judgement when allocations are scarce.

Retail Pharmacies In Contra Costa County receiving an allocation of Paxlovid and Molunpiravir:

- CVS 9565, 14830 Highway 4, Discovery Bay
- CVS 4323, 4028 Lone Tree Way, Antioch
- CVS 9875, 230 Atlantic Ave, Pittsburg
- Safeway Pharmacy 1215, 660 Bailey Rd, Pittsburg
- Walgreens 13026, 2700 Willow Pass Rd, Bay Point
- CVS 9545, 1123 S California Blvd, Walnut Creek
- CVS 9815, 738 Bancroft Rd, Walnut Creek
- Rite Aid 05913, 1905 Monument Blvd, Concord
- Safeway Pharmacy 0955, 2600 Willow Pass Rd, Concord
- CVS 9827, 5408 Ygnacio Valley Rd, Concord
- CVS 9989, 6668 Alhambra Ave, Martinez
- CVS 9938, 3625 Mt Diablo Blvd, Lafayette
- CVS 9203, 580 Moraga Rd, Moraga
- CVS 9086, 670 El Cerrito Plz, El Cerrito
- CVS 9299, 1617 Canyon Drive, Pinole
- CVS 16837, 4500 Macdonald Ave, Richmond
- CVS 3078, 2151 Meeker Ave, Richmond
- Walgreens 2506, 1150 Macdonald Ave, Richmond
- Walgreens 13796, 14280 San Pablo Ave, San Pablo
- Walgreens 4491, 15650 San Pablo Ave, San Pablo
- CVS 9296, 3420 Camino Tassajara, Danville
- CVS 9800, 650 San Ramon Valley Blvd, Danville
- Walgreens 16090, 11440 Windemere Pkwy, San Ramon

As allocations change, additional pharmacies and providers maybe added as an allocation site. Prior to prescribing, Health Care Providers should follow up with the pharmacy to ensure that the pharmacy has adequate supply.

Additionally, allocated pharmacies may change in the county. To review any updates to pharmacy allocated Paxlovid and Molunpiravir. To find COVID-19 antiviral distributors near you, please also visit the U.S. Department of Health and Human Services' Therapeutics Locator: https://covid-19-therapeutics-locator-dhhs.hub.arcgis.com/

For more information and updates please visit our COVID-19 Healthcare Provider website at https://cchealth.org/covid19/providers/ and our general COVID-19 website: https://www.coronavirus.cchealth.org/ for updated information.

Updated 3/14/2022 with new allocation sites

Additional Resources:

Paxlovid Resources:

- Patient Hand out: https://www.fda.gov/media/155051/download
- Paxlovid Fact Sheet for Healthcare providers : https://www.fda.gov/media/155050/download
- EUA: https://www.fda.gov/media/155049/download
- FDA announcements: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-first-oral-antiviral-treatment-covid-19
- Clinical Trail information: https://clinicaltrials.gov/ct2/show/NCT04960202

Molnupiravir Resources:

- Patient Hand out: https://www.fda.gov/media/155055/download
- Molnupiravir Healthcare Providers: https://www.fda.gov/media/155054/download
- FDA announcements: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-additional-oral-antiviral-treatment-covid-19-certain
- Merck Announcement: https://www.merck.com/news/merck-and-ridgeback-announce-publication-of-phase-3-study-of-molnupiravir-an-investigational-oral-antiviral-covid-19-treatment-in-the-new-england-journal-of-medicine/
- Clinical Trial Information: https://clinicaltrials.gov/ct2/show/NCT04575597

Other Resources:

- COVID-19 mAB treatment guidelines when Omicron is Predominant variant: https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-anti-sars-cov-2-mabs-and-rdv-and-omicron/
- CDPH COVID-19 Treatments webpage: https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/COVID-19/Treatments.aspx
- CDPH Get the Facts on Treatment: https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/COVID-19/Get-the-Facts-on-Treatments.aspx
- NIH statement on patient prioritization for COVID-19 therapies : https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-patient-prioritization-for-outpatient-therapies/
- NIH COVID-19 Clinical Spectrum: https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum/
- CDC Science Brief Underlying Conditions Related with Higher Risk of Severe COVID-19: https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/underlying-evidence-table.html
- Risk Factors Associated with In Hospital Mortality: https://pubmed.ncbi.nlm.nih.gov/33301018/
- Underlying Medical Conditions Associated with Severe COVID-19 among Children: https://pubmed.ncbi.nlm.nih.gov/34097050/
- CDPH Guidance for Hospitals Regarding Allocation of Scarce COVID-19 Medications: https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/COVID-19/GuidanceForHospitalsRegardingAllocationOfScarceMedicationsForCOVID19.aspx