Molnupiravir has been FDA-authorized for emergency use to treat mild-to-moderate COVID-19 among nonhospitalized, nonpregnant adults since December 2021.

**CLINICAL INFORMATION**

**Eligibility:** The molnupiravir EUA covers adults 18 years of age and older 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. If it is decided to give molnupiravir, treatment should begin as soon as possible after diagnosis and within 5 days of symptom onset.

**Dosing:** A course of molnupiravir consists of 800 mg (four 200 mg capsules) taken orally every 12 hours for 5 days.

**Clinical Decision-Making:** In ambulatory adult patients with mild-to-moderate COVID-19 at high risk for progression to severe disease who have no other treatment options, IDSA guidelines suggest molnupiravir be initiated within 5 days of symptom onset (conditional recommendation, low certainty of evidence). NIH guidelines also suggest molnupiravir only when other antiviral options cannot be used (class CIII recommendation).

HHS's COVID-19 Therapeutics Decisionmaking Aid offers a path to evaluate treatment options:
Consider one of the following therapeutics, if available\(^1\)\(^2\):

- **Nirmatrelvir/ritonavir** within 5 days of symptom onset
  - eGFR 60 mL/min or greater: 300mg nirmatrelvir taken with 100mg ritonavir twice daily for 5 days
  - eGFR ≥30-≤60: 150mg nirmatrelvir taken together with 100mg ritonavir twice daily for 5 days; evaluate concomitant use of CYP3A inducers and medications with high dependency on CYP3A for clearance as these may be contraindicated per Paxlovid™ EUA

- **sotrovimab** 500mg IV within ASAP 10 days of symptom onset (sotrovimab EUA)

- **Remdesivir** 200mg IV x 1 dose on day 1, 100mg IV x1 on days 2-3 begun ASAP and within 7 days of symptom onset

If none of the above therapeutics are available for patient treatment within 5 days of symptom onset and patient is age 18 or greater

- **Consider molnupiravir**
  - Authorized only in patients ages 18 and older
  - Within 5 days of symptom onset
  - Molnupiravir 800mg by mouth every 12h for 5 days
  - Prescribers must review and comply with the mandatory requirements outlined in the molnupiravir EUA

\(^1\) Refer to the NIH COVID-19 Treatment Guidelines Panel’s Statement on the Use of Anti-SARS-CoV-2 Monoclonal Antibodies or Remdesivir for the Treatment of Covid-19 in Nonhospitalized patients when Omicron is the Predominant Circulating Variant; Remdesivir is only approved for hospitalized individuals with COVID-19. Outpatient treatment is based on information from the literature (Dec 22, 2021 Early Remdesivir to Prevent Progression to Severe Covid-19 in Outpatients; DOI: 10.1056/NEJMoa2116846)

\(^2\) COVID-19 convalescent plasma with high titers of anti-SARS-CoV-2 antibodies is authorized for the treatment of COVID-19 in patients with immunosuppressive disease in either the outpatient or inpatient setting (COVID-19 Convalescent Plasma EUA)
NIH’s COVID-19 Treatment Guidelines Panel offers a prioritization scheme based on four key elements: age, vaccination status, immune status and clinical risk factors:

| Risk Group 1 | 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 (see Immunocompromising Conditions below); or Unvaccinated individuals at the highest risk of severe disease (anyone aged ≥75 years or anyone aged ≥65 years with additional risk factors). |
| Risk Group 2 | 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). |
| Risk Group 3 | Vaccinated individuals at high risk of severe disease (anyone aged ≥75 years or anyone aged ≥65 years with clinical risk factors). **Note:** Vaccinated individuals who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients in this situation within this tier should be prioritized for treatment. |
| Risk Group 4 | Vaccinated individuals at risk of severe disease (anyone aged ≥65 years or anyone aged <65 with clinical risk factors). **Note:** Vaccinated individuals who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients in this situation within this tier should be prioritized for treatment. |

**SAFETY**

**Pregnancy:** FDA’s Fact Sheet for Health Care Providers states: “Based on findings from animal reproduction studies, molnupiravir may cause fetal harm when administered to pregnant individuals ... therefore, molnupiravir is not recommended for use during pregnancy.”

NIH’s COVID-19 Treatment Guidelines Panel states: “When other therapies are not available, pregnant people with COVID-19 who are at high risk of progressing to severe disease, particularly those who are beyond the time of embryogenesis (i.e., >10 weeks’ gestation), may reasonably choose molnupiravir therapy after being fully informed of the risks.

FDA and NIH both recommend that prescribing clinicians should document that a discussion with the patient of the risks and benefits occurred and that the patient chose this therapy after the discussion occurred.

**Interactions With Other Therapeutics:** No clinical drug-drug interaction studies of molnupiravir have been conducted, but no drug-drug interactions are expected based on available information.
SUPPLY & ACCESS

Distribution: Molnupiravir is currently available in limited quantities in the U.S. and is being allocated by the federal government to health departments in states, territories and jurisdictions as well as select community health centers.

For allocation details, refer to HHS’s weekly distribution summaries; for information intended for health providers, see HHS’s COVID-19 Therapeutics Locator; for provider-specific distribution information, view HHS’s COVID-19 Public Therapeutics Locator. Contact your state, territorial or jurisdictional health department for further local information.

CODING, BILLING & REPORTING

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<thead>
<tr>
<th>Drug Name</th>
<th>Dosage</th>
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Billing: Molnupiravir has been added to the Medicaid and Children’s Health Insurance Program formularies as a payable pharmacy benefit.

Reporting: Providers are required to report federally purchased course administration daily by 11:59 p.m. ET via HHS’s Health Partner Order Portal.

FURTHER INFORMATION

Real-Time Learning Network Molnupiravir Literature Reviews
FDA Molnupiravir EUA Fact Sheet for Health Care Providers
NIH Treatment Guidelines Panel Statement on Patient Prioritization
NIH Treatment Guidelines Panel Statement on High-Risk, Nonhospitalized Patients
University of Liverpool COVID-19 Prescribing Resources
University of Liverpool COVID-19 Drug Interactions