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# 5.01.074

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| **Section:** | Prescription Drugs | **Effective Date:** | April 1, 2024 |
| **Subsection:** | Anti-Infective Agents | **Original Policy Date:** | January 7, 2022 |
| **Subject:** | COVID-19 Oral Antiviral Agents | **Page:** | 1 of 6 |

***Last Review Date:*** March 8, 2024

# COVID-19 Oral Antiviral Agents

## Description

Molnupiravir
Paxlovid (nirmatrelvir and ritonavir)

**Background**
Coronavirus disease 2019 (COVID-19) is caused by the novel coronavirus SARS-CoV-2. SARS-CoV-2 is an RNA virus that is associated with acute respiratory tract illness in humans. Symptoms may be mild to severe and generally occur within 2 to 14 days of exposure to SARS-CoV-2. The clinical course of COVID-19 is variable, but severe outcomes, including death, have occurred. Between 20- 30% of patients hospitalized do require mechanical respiratory support (1).

The intent of this criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Molnupiravir has been granted an emergency use authorization (EUA) by the FDA. Molnupiravir is a prodrug that is metabolized by the virus into a nucleoside analog. The nucleoside analog is erroneously incorporated into the viral genome resulting in inhibition of replication. Paxlovid has full regular FDA-approval for use in adults 18 years and older, while use in pediatric patients 12 to 17 years of age is covered under the emergency use authorization (EUA). Paxlovid is a combination of nirmatrelvir and ritonavir. Nirmatrelvir targets the SARS-CoV-2 main protease (Mpro), inhibiting protein processing and leading to inhibition of replication. Ritonavir inhibits the metabolism of nirmatrelvir, allowing it to exert its therapeutic effect longer before being inactivated (2-4).

**Regulatory Status**
Indications granted by the FDA: (2-4)

1. Molnupiravir
    - Emergency Use Authorization: The U.S. Food and Drug Administration (FDA) has issued an EUA for the emergency use of the unapproved molnupiravir, a nucleoside analogue that inhibits SARS-CoV-2 replication by viral mutagenesis for the treatment of mild-to-moderate coronavirus disease 2019 (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. Molnupiravir is not FDA-approved for any use including for use for the treatment of COVID-19. Prior to initiating treatment with molnupiravir, carefully consider the known and potential risks and benefits.
        i. Limitations of authorized use:
            1. Molnupiravir is <u>not</u> authorized:
                a. For use in patients less than 18 years of age
                b. For initiation of treatment in patients requiring hospitalization due to COVID-19. Benefit of treatment with molnupiravir has not been observed in subjects when treatment was initiated after hospitalization due to COVID-19.
                c. For use longer than 5 consecutive days.
                d. For pre-exposure or post-exposure prophylaxis for prevention of COVID-19.

2. Paxlovid
    - FDA-approved indication: Paxlovid is indicated for the treatment of mild-to-moderate coronavirus disease 2019 (COVID-19) in adults who are at high risk for progression to severe COVID-19, including hospitalization or death.
        i. Limitations of use: Paxlovid is not approved for use as pre-exposure or post-exposure prophylaxis for prevention of COVID-19. (
    - Emergency Use Authorization: The U.S. Food and Drug Administration has issued an EUA for the emergency use of the unapproved Paxlovid which includes nirmatrelvir, a SARS-CoV-2 main protease (Mpro: also referred to as 3CLpro or nsp5 protease) inhibitor, and ritonavir, an HIV-1 protease inhibitor and CYP3A inhibitor, for the treatment of mild-to-moderate coronavirus disease 2019 (COVID-19) in pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct severe acute respiratory syndrome coronavirus

2(SARS-CoV-2) viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death.

i. Limitations of authorized use:
   1. Paxlovid is not authorized:
      a. For initiation of treatment in patients requiring hospitalization due to severe or critical COVID-19.
      b. For pre-exposure or post-exposure prophylaxis for prevention of COVID-19.
      c. For use longer than 5 consecutive days.

The EUA of molnupiravir does not allow use in pediatric patients less than 18 years of age (2).

Paxlovid is approved for use in adults 18 years of age or older, while the EUA of Paxlovid does not allow use in pediatric patients less than 12 years of age and weighing less than 40 kg (3,4).

**Related policies**

## Policy

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Molnupiravir and Paxlovid may be considered **medically necessary** if the conditions indicated below are met.

Molnupiravir and Paxlovid may be considered **investigational** for all other indications.

## Prior-Approval Requirements

***The medications in this policy have a Pre-PA allowance, the quantity that can be filled without a prior authorization (PA). Pre-PA quantity limit allows one 5-day fill every 30 days.***

**Age**

| | |
|---|---|
| Molnupiravir | 18 years of age or older |
| Paxlovid | 12 years of age or older |

**Diagnosis**

COVID-19 confirmed by direct SARS-CoV-2 viral testing

## Prior–Approval *Renewal* Requirements

Same as above

## Policy Guidelines

## Pre–PA Allowance

**Age**

| | |
|---|---|
| Molnupiravir | 18 years of age or older |
| Paxlovid | 12 years of age or older |

| Drug | Quantity Limit** | Additional Requirements |
|---|---|---|
| Molnupiravir 200mg | 40 capsules per 30 days | Max day supply of 5 days |
| Paxlovid [nirmatrelvir 300 mg (2 x 150mg) tablet and ritonavir 100mg] | 30 tablets per 30 days (1 carton containing 30 tablets divided in 5 daily-dose blister cards, with each daily-dose blister card containing 4 tablets of nirmatrelvir tablets and 2 tablets of ritonavir) | Max day supply of 5 days |
| Paxlovid (nirmatrelvir 150mg tablet and ritonavir 100mg) | 20 tablets per 30 days (1 carton containing 20 tablets divided in daily-dose blister cards, with each daily-dose blister card containing 2 tablets of nirmatrelvir and 2 tablets of ritonavir) | |

***Quantity sufficient to allow one 5-day fill every 30 days. If the request exceeds the Pre-PA quantity limit, the claim will reject with a message indicating a PA is needed.*

## Prior–Approval Limits

| Drug | Quantity Limit |
|---|---|
| Molnupiravir 200mg | Pre-PA allows for the FDA recommended maximum dosage |
| Paxlovid | Pre-PA allows for the FDA recommended maximum dosage |

| | |
|---|---|
| [nirmatrelvir 300 mg (2 x 150mg) tablet and ritonavir 100mg] | |
| Paxlovid (nirmatrelvir 150mg tablet and ritonavir 100mg) | |

**Duration** 30 days

## Prior–Approval *Renewal* Limits

Same as above

## Rationale

**Summary**

Molnupiravir and Paxlovid (nirmatrelvir and ritonavir) are antiviral agents granted authorization under an FDA emergency use agreement or full FDA approval for the treatment of mild-to-moderate COVID-19. These agents are not for use in patients that are hospitalized. The agents are to be started within 5 days of symptom onset and to be taken for no longer than 5 consecutive days (1-3).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of molnupiravir and Paxlovid while maintaining optimal therapeutic outcomes.

**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 on December 23, 2021
2. Molnupiravir [Emergency Use Authorization Fact Sheet for Health Care Providers]. Kenilworth, NJ: Merck & Co., Inc.; December 2021.
3. Paxlovid [package insert]. New York, NY: Pfizer Labs; May 2023
4. Paxlovid [Emergency Use Authorization Fact Sheet for Health Care Providers]. New York, NY: Pfizer; April 2022.

## Policy History

| Date | Action |
|---|---|
| January 2022 | Addition to PA |
| June 2022 | Addition of Paxlovid new strength/carton (nirmatrelvir 150mg tablet and ritonavir 100mg) |
| September 2023 | Annual review and reference update. Changed policy number to 5.01.074 |
| March 2024 | Annual review |

## Keywords

**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 8, 2024 and is effective on April 1, 2024.**