

Emergency Use Authorization (EUA) for PAXLOVID
 Center for Drug Evaluation and Research Review Memorandum

Identifying Information

Application Type (EUA or Pre-EUA)	EUA
EUA Application Number(s)	000105
Date of Memorandum	July 6, 2022
Sponsor (entity requesting EUA or pre-EUA consideration), point of contact, address, phone number, fax number, email address	Pfizer Inc. 235 East 42nd Street New York, NY 10017-5755 Karen Baker- Director Global Regulatory Affairs – Brand Hospital Products Email: [REDACTED] (b) (6) Phone: [REDACTED] (b) (6)
Original Authorization	December 22, 2021
OND Division / Office	Division of Antivirals (DAV)/Office of Infectious Diseases (OID)
Proprietary Name	PAXLOVID
Established Name/Other names used during development	Nirmatrelvir (PF-07321332) tablets; Ritonavir tablets
Dosage Forms/Strengths	300 mg nirmatrelvir (two 150 mg tablets) with 100 mg ritonavir (one 100 mg tablet) all taken together orally twice daily for 5 days.
Therapeutic Class	<u>Nirmatrelvir</u> is a SARS-CoV-2 main protease (Mpro: also referred to as 3CLpro or nsp5 protease) inhibitor that has demonstrated activity against SARS-CoV-2. <u>Ritonavir</u> is an HIV-1 protease inhibitor and is not active against SARS-CoV-2 Mpro. Ritonavir inhibits the CYP3A-mediated metabolism of nirmatrelvir, thereby providing increased plasma concentrations of nirmatrelvir.
Intended Use or Need for EUA	Treatment of mild-to-moderate coronavirus disease 2019 (COVID-19)
Intended Population(s)	Adults and 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

Abbreviations: DAV, Division of Antivirals; EUA, emergency use authorization; OID, Office of Infectious Diseases; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Rationale for Revisions to EUA Fact Sheets and Other Documents

On December 22, 2021, the United States Food and Drug Administration (FDA or Agency) authorized PAXLOVID (nirmatrelvir co-packaged with ritonavir) for the treatment of mild-to-moderate COVID-19 in adults and pediatric 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. PAXLOVID is not currently approved for any use, including treatment of COVID-19.

At the time FDA initially issued the Emergency Use Authorization (EUA), the Agency limited the prescribing of PAXLOVID for an individual patient to 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).¹ This limitation was included to ensure appropriate prescribing of PAXLOVID under the EUA, which requires appropriate patient assessment to confirm the patient meets the eligibility criteria for receiving PAXLOVID. Prescribing of PAXLOVID also requires an assessment of renal and hepatic function and potential drug interactions, which may necessitate clinical management of other medications. This may include a temporary discontinuation, dose modification and/or increased therapeutic monitoring of other medications.

While there were limited supplies of PAXLOVID at the time it was initially authorized, supply has increased substantially and there is now ample supply of PAXLOVID. As of June 26, 2022, the United States Government (USG) has distributed approximately 3.9 million treatment courses of PAXLOVID and approximately 1.8 million treatment courses have been administered for the treatment of COVID-19 under its EUA.²

As part of its ongoing review of the circumstances and appropriateness of the EUA for PAXLOVID³, which included inter-Agency consultation within the USG and consideration of input received from other stakeholders, the Agency recommends revising the EUA for PAXLOVID to authorize the prescribing of PAXLOVID by state-licensed pharmacists in certain circumstances. Specifically, as revised, state-licensed

¹ Under the Ninth Amendment to the Secretary's PREP Act Declaration, a pharmacist is only allowed to order COVID-19 therapeutics under the terms of the FDA EUA issued for that product. For example, if the EUA includes a condition that the product 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 the belongs, the Ninth Amendment to the Secretary's PREP Act Declaration would not permit pharmacists to order the product. See <https://www.federalregister.gov/documents/2021/09/14/2021-19790/ninth-amendment-to-declaration-under-the-public-readiness-and-emergency-preparedness-act-for-medical>

² <https://aspr.hhs.gov/COVID-19/Therapeutics/orders/Pages/default.aspx>

³ See generally section 564(g) of the Federal Food, Drug and Cosmetic Act.

pharmacists may prescribe PAXLOVID for an individual patient under the following conditions:

- Sufficient information is available, such as through access to health records less than 12 months old or consultation with a health care provider in an established provider-patient relationship with the individual patient, to assess renal and hepatic function; and
- Sufficient information is available, such as through access to health records, patient reporting of medical history, or consultation with a health care provider in an established provider-patient relationship with the individual patient, to obtain a comprehensive list of medications (prescribed and non-prescribed) that the patient is taking to assess for potential drug interaction.

The Agency believes that authorizing state-licensed pharmacists to prescribe PAXLOVID as described above may provide more timely treatment for some patients who are eligible to receive PAXLOVID for the treatment of COVID-19.

State-licensed pharmacists are not authorized to prescribe PAXLOVID when sufficient information consistent with the above is not available at the time of patient assessment. In such instances, the state-licensed pharmacist should refer the individual patient to a physician, advanced practice registered nurse, or physician assistant licensed or authorized under state law to prescribe drugs for further clinical evaluation. The state-licensed pharmacist should also refer the individual patient to a physician, advanced practice registered nurse, or physician assistant licensed or authorized under state law to prescribe drugs when an adjustment to another medication is needed due to a potential drug interaction, or when PAXLOVID is not an appropriate therapeutic option based on the authorized Fact Sheet for Healthcare Providers or due to potential drug interactions for which recommended monitoring would not be feasible. Referral in such instances will ensure appropriate clinical management of the individual, including consideration of other therapeutics approved or authorized by FDA for the same uses as PAXLOVID.

Based on the above, the letter of authorization and the Fact Sheet for Healthcare Providers will be revised as described below:

Summary of Revisions to the Letter of Authorization:

Section 2 (Scope of Authorization) will be revised to state the following:

"PAXLOVID may 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.

PAXLOVID may also be prescribed for an individual patient by a state-licensed pharmacist under the following conditions:

- *Sufficient information is available, such as through access to health records less than 12 months old or consultation with a health care provider in an established provider-patient relationship with the individual patient, to assess renal and hepatic function; and*
- *Sufficient information is available, such as through access to health records, patient reporting of medical history, or consultation with a health care provider in an established provider-patient relationship with the individual patient, to obtain a comprehensive list of medications (prescribed and non-prescribed) that the patient is taking to assess for potential drug interaction.*

Summary of Revisions to the Fact Sheet for Healthcare Providers:

Section 1 of the Fact Sheet for Healthcare Providers, under “LIMITATIONS OF AUTHORIZED USE”, will be revised to authorize prescribing of PAXLOVID by state-licensed pharmacists under certain conditions. The following language will be added to this section, with similar revisions made to the highlights section of the Fact Sheet for Healthcare Providers:

PAXLOVID may 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.

PAXLOVID may also be prescribed for an individual patient by a state-licensed pharmacist under the following conditions:

- *Sufficient information is available, such as through access to health records less than 12 months old or consultation with a health care provider in an established provider-patient relationship with the individual patient, to assess renal and hepatic function; and*
- *Sufficient information is available, such as through access to health records, patient reporting of medical history, or consultation with a health care provider in an established provider-patient relationship with the individual patient, to obtain a comprehensive list of medications (prescribed and non-prescribed) that the patient is taking to assess for potential drug interaction.*

The state-licensed pharmacist should refer an individual patient for clinical evaluation (e.g., telehealth, in-person visit) with a physician, advanced practice registered nurse, or physician assistant licensed or authorized under state law to prescribe drugs, if any of the following apply:

- *Sufficient information is not available to assess renal and hepatic function.*
- *Sufficient information is not available to assess for a potential drug interaction.*
- *Modification of other medications is needed due to a potential drug interaction.*

- *PAXLOVID is not an appropriate therapeutic option based on the authorized Fact Sheet for Healthcare Providers or due to potential drug interactions for which recommended monitoring would not be feasible.*

Regulatory Conclusion and Associated Actions:

The Division of Antivirals and Office of Infectious Diseases recommends revisions to EUA 105 as outlined above in order to best protect public health.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

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