

December 22, 2021

Pfizer, Inc.
Attention: Karen Baker
Director, Global Regulatory Affairs
235 East 42nd Street
New York, NY 10017-5755

RE: Emergency Use Authorization 105

Dear Ms. Baker:

This letter is in response to Pfizer, Inc.'s (Pfizer) request that the Food and Drug Administration (FDA or Agency) issue an Emergency Use Authorization (EUA) for the emergency use of PAXLOVID (nirmatrelvir co-packaged with ritonavir) for the treatment of mild-to-moderate coronavirus disease 2019 (COVID-19) in certain adults and pediatric patients pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3).

On February 4, 2020, pursuant to Section 564(b)(1)(C) of the Act, the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes coronavirus disease 2019 (COVID-19).¹ On the basis of such determination, the Secretary of HHS on March 27, 2020, declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic, pursuant to Section 564 of the Act (21 U.S.C. 360bbb-3), subject to terms of any authorization issued under that section.²

PAXLOVID is comprised of nirmatrelvir, a SARS-CoV-2 main protease (Mpro: also referred to as 3CLpro or nsp5 protease) inhibitor, co-packaged with ritonavir, an HIV-1 protease inhibitor and CYP3A inhibitor. Ritonavir, which has no activity against SARS-CoV-2 on its own, is included to inhibit the CYP3A-mediated metabolism of nirmatrelvir and consequently increase nirmatrelvir plasma concentrations to levels anticipated to inhibit SARS-CoV-2 replication. PAXLOVID is not approved for any use, including for use for the treatment of COVID-19.

Based on the totality of scientific evidence available to FDA, including data from the clinical trial EPIC-HR (NCT04960202), a Phase 2/3 randomized, double blind, placebo-controlled clinical trial, it is reasonable to believe that PAXLOVID may be effective for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing

¹ U.S. Department of Health and Human Services, *Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act*, 21 U.S.C. § 360bbb-3. February 4, 2020.

² U.S. Department of Health and Human Services, *Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act*, 21 U.S.C. § 360bbb-3, 85 FR 18250 (April 1, 2020).

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, as described in the Scope of Authorization (Section II), and when used under the conditions described in this authorization, the known and potential benefits of PAXLOVID outweigh the known and potential risks of such product.

Having concluded that the criteria for issuance of this authorization under Section 564(c) of the Act are met, I am authorizing the emergency use of PAXLOVID for the treatment of mild-to-moderate COVID-19 in certain adults and pediatric patients, as described in the Scope of Authorization section of this letter (Section II) and subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of PAXLOVID for the treatment of COVID-19, when administered as described in the Scope of Authorization (Section II), meets the criteria for issuance of an authorization under Section 564(c) of the Act, because:

1. SARS-CoV-2 can cause a serious or life-threatening disease or condition, including severe respiratory illness, to humans infected by this virus;
2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that PAXLOVID may be effective 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, as described in the Scope of Authorization (section II), and that, when used under the conditions described in this authorization, the known and potential benefits of PAXLOVID outweigh the known and potential risks of such product; and
3. There is no adequate, approved, and available alternative to the emergency use of PAXLOVID 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.³

II. Scope of Authorization

I have concluded, pursuant to Section 564(d)(1) of the Act, that the scope of this authorization is limited as follows:

- Distribution of the authorized PAXLOVID will be controlled by the United States (U.S.) Government for use consistent with the terms and conditions of this EUA. Pfizer will supply PAXLOVID to authorized distributor(s)⁴, who will distribute to

³ No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

⁴ “Authorized Distributor(s)” are identified by Pfizer as an entity or entities allowed to distribute authorized PAXLOVID.

healthcare facilities or healthcare providers as directed by the U.S. Government, in collaboration with state and local government authorities as needed;

- PAXLOVID may only be used by healthcare providers to treat 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 risk⁵ for progression to severe COVID-19, including hospitalization or death;

Limitations on Authorized Use

- PAXLOVID is not authorized for initiation of treatment in patients requiring hospitalization due to severe or critical COVID-19.⁶
- PAXLOVID is not authorized for use as pre-exposure or as post-exposure prophylaxis for prevention of COVID-19.
- PAXLOVID is not authorized for use for longer than 5 consecutive 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).⁷
- The use of PAXLOVID covered by this authorization must be in accordance with the authorized Fact Sheets.

Product Description

PAXLOVID consists of two 150 mg tablets of nirmatrelvir that are co-packaged with one 100 mg tablet ritonavir.

Nirmatrelvir is supplied as an oval, pink, immediate-release, film-coated tablet debossed with “PFE” on one side and “3CL” on the other side.

Ritonavir is supplied as a white, film-coated, ovaloid tablet debossed with the "a" logo and the code NK.

The authorized storage and handling information for PAXLOVID is included in the authorized Fact Sheet for Healthcare Providers.

⁵ For information on medical conditions and factors associated with increased risk for progression to severe COVID-19, see the Centers for Disease Control and Prevention (CDC) website: <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html>.

⁶ Patients requiring hospitalization due to severe or critical COVID-19 after starting treatment with PAXLOVID may complete the full 5-day treatment course per the healthcare provider’s discretion.

⁷ The term “State” includes any State or Territory of the United States, the District of Columbia, and the Commonwealth of Puerto Rico. See section 201(a)(1) of the Act.

PAXLOVID is authorized for emergency use with the following product-specific information required to be made available to healthcare providers and to patients, parents, and caregivers, respectively, through Pfizer’s website www.COVID19oralRX.com (referred to as the “authorized labeling”):

- Fact Sheet for Healthcare Providers: Emergency Use Authorization (EUA) for PAXLOVID
- Fact Sheet for Patients, Parents and Caregivers: Emergency Use Authorization (EUA) of PAXLOVID for Coronavirus Disease 2019 (COVID-19)

I have concluded, pursuant to Section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of PAXLOVID, when used for the treatment of COVID-19 and used in accordance with this Scope of Authorization (Section II), outweigh the known and potential risks.

I have concluded, pursuant to Section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that PAXLOVID may be effective for the treatment of COVID-19 when used in accordance with this Scope of Authorization (Section II), pursuant to Section 564(c)(2)(A) of the Act.

Having reviewed the scientific information available to FDA, including the information supporting the conclusions described in Section I above, I have concluded that PAXLOVID (as described in this Scope of Authorization (Section II)) meets the criteria set forth in Section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of PAXLOVID under this EUA must be consistent with, and may not exceed, the terms of the Authorization, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section III). Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS's determination under Section 564(b)(1)(C) described above and the Secretary of HHS's corresponding declaration under Section 564(b)(1), PAXLOVID is authorized 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, as described in the Scope of Authorization (Section II) under this EUA, despite the fact that it does not meet certain requirements otherwise required by applicable federal law.

III. Conditions of Authorization

Pursuant to Section 564 of the Act, I am establishing the following conditions on this authorization:

Pfizer and Authorized Distributors⁸

- A. Pfizer and authorized distributor(s) will ensure that PAXLOVID is distributed and the authorized labeling (i.e., Fact Sheets) will be made available to healthcare facilities and/or healthcare providers as described in Section II of this Letter of Authorization.

⁸ Supra at Note 4.

- B. Pfizer and authorized distributor(s) will ensure that appropriate storage is maintained until the product is delivered to healthcare facilities and/or healthcare providers.
- C. Pfizer and authorized distributor(s) will ensure that the terms of this EUA are made available to all relevant stakeholders (e.g., U.S. government agencies, state and local government authorities, authorized distributors, healthcare facilities, healthcare providers) involved in distributing or receiving PAXLOVID. Pfizer will provide to all relevant stakeholders a copy of this Letter of Authorization and communicate any subsequent amendments that might be made to this Letter of Authorization and its authorized accompanying materials (i.e., Fact Sheets).
- D. Pfizer may request changes to this authorization, including to the authorized Fact Sheets for PAXLOVID. Any request for changes to this EUA must be submitted to the Office of Infectious Diseases/Office of New Drugs/Center for Drug Evaluation and Research. Such changes require appropriate authorization prior to implementation.⁹
- E. Pfizer may develop and disseminate instructional and educational materials (e.g., materials providing information on product administration and/or patient monitoring) that are consistent with the authorized emergency use of PAXLOVID as described in this Letter of Authorization and authorized labeling, without FDA’s review and concurrence, when necessary to meet public health needs. Any instructional and educational materials that are inconsistent with the authorized labeling for PAXLOVID are prohibited. If the Agency notifies Pfizer that any instructional and educational materials are inconsistent with the authorized labeling, Pfizer must cease distribution of such instructional and educational materials. Furthermore, as part of its notification, the Agency may also require Pfizer to issue corrective communication(s).
- F. Pfizer will report to FDA serious adverse events and all medication errors associated with the use of PAXLOVID for its authorized use that are reported to Pfizer using either of the following options.

Option 1: Submit reports through the Safety Reporting Portal (SRP) as described on the [FDA SRP](#) web page.

Option 2: Submit reports directly through the Electronic Submissions Gateway (ESG) as described on the [FAERS electronic submissions](#) web page.

⁹ The following types of revisions may be authorized without reissuing this letter: (1) changes to the authorized labeling; (2) non-substantive editorial corrections to this letter; (3) new types of authorized labeling, including new fact sheets; (4) new carton/container labels; (5) expiration dating extensions; (6) changes to manufacturing processes, including tests or other authorized components of manufacturing; (7) new conditions of authorization to require data collection or study; (8) new strengths of the authorized product, new product sources (e.g., of active pharmaceutical ingredient) or of product components. For changes to the authorization, including the authorized labeling, of the type listed in (3), (6), (7), or (8), review and concurrence is required from the Counter-Terrorism and Emergency Coordination Staff/Office of the Center Director/CDER and the Office of Counterterrorism and Emerging Threats/Office of the Chief Scientist.

Submitted reports under both options must state: “PAXLOVID use for COVID-19 under Emergency Use Authorization (EUA).” For reports submitted under Option 1, include this language at the beginning of the question “Describe Event” for further analysis. For reports submitted under Option 2, include this language at the beginning of the “Case Narrative” field.

- G. All manufacturing, packaging, and testing sites for both drug substance and drug product will comply with current good manufacturing practice requirements of Section 501(a)(2)(B) of the Act.
- H. Pfizer will submit information to the Agency within three working days of receipt of any information concerning significant quality problems with drug product distributed under this emergency use authorization for PAXLOVID that includes the following:
- Information concerning any incident that causes the drug product or its labeling to be mistaken for, or applied to, another article; or
 - Information concerning any microbiological contamination, or any significant chemical, physical, or other change or deterioration in the distributed drug product, or any failure of one or more distributed batches of the product to meet the established specifications.

If a significant quality problem affects unreleased product and may also impact product(s) previously released and distributed, then information must be submitted for all potentially impacted lots.

Pfizer will include in its notification to the Agency whether the batch, or batches, in question will be recalled.

If not included in its initial notification, Pfizer must submit information confirming that Pfizer has identified the root cause of the significant quality problems, taken corrective action, and provide a justification confirming that the corrective action is appropriate and effective. Pfizer must submit this information as soon as possible but no later than 45 calendar days from the initial notification.

- I. Pfizer will manufacture PAXLOVID to meet all quality standards and per the manufacturing process and control strategy as detailed in Pfizer’s EUA request. Pfizer will not implement any changes to the description of the product, manufacturing process, facilities and equipment, and elements of the associated control strategy that assure process performance and quality of the authorized product, without notification to and concurrence by the Agency as described under condition D.
- J. Through a process of inventory control, Pfizer and authorized distributor(s) will maintain records regarding distribution of PAXLOVID (i.e., lot numbers, quantity, receiving site, receipt date).

- K. Pfizer will establish a process for monitoring genomic database(s) for the emergence of global viral variants of SARS-CoV-2 and will provide reports to the Agency on a monthly basis summarizing any findings as a result of its monitoring activities and, as needed, any follow-up assessments planned or conducted. Updated data listings summarizing amino acid variability should be provided at least monthly for Mpro amino acid sequences, and at least every 2 months for Mpro cleavage site amino acid sequences. The data listings should include a cumulative list of amino acid polymorphisms detected in genomic database(s), highlighting changes/variants that are increasing in frequency from the previous month.
- L. FDA may require Pfizer to assess the activity of the authorized PAXLOVID against any global SARS-CoV-2 variant(s) of interest (e.g., variants that are prevalent or becoming prevalent that harbor substitutions in the target protein or in protein(s) that interact with the target protein). Pfizer will perform the required assessment in a manner and timeframe agreed upon by Pfizer and the Agency. Pfizer will submit to FDA a preliminary summary report immediately upon completion of its assessment followed by a detailed study report within 30 calendar days of study completion. Pfizer will submit any relevant proposal(s) to revise the authorized labeling based on the results of its assessment, as may be necessary or appropriate based on the foregoing assessment.
- M. Pfizer shall provide samples as requested of the authorized nirmatrelvir to the U.S. Department of Health and Human Services (HHS) for evaluation of activity against emerging global viral variants of SARS-CoV-2, including specific amino acid substitution(s) of interest (e.g., variants that are highly prevalent or that harbor substitutions in the target protein(s) or target cleavage sites) within 5 business days of any request made by HHS. Analyses performed with the supplied quantity of authorized nirmatrelvir may include, but are not limited to, cell culture potency assays, biochemical assays, and in vivo efficacy assays.
- N. Pfizer must provide the following information to the Agency:
1. Pfizer must conduct cell culture phenotypic analyses of recombinant SARS-CoV-2 viruses or replicons carrying specific amino acid changes potentially associated with reduced nirmatrelvir susceptibility in nonclinical or clinical studies, or polymorphisms emerging in novel SARS-CoV-2 variants. Specific amino acid changes that should be characterized include the following:
 - amino acid changes associated with reduced nirmatrelvir susceptibility in biochemical assays,
 - natural amino acid polymorphisms in Mpro that come in contact with or in close proximity (<5 Å) to bound nirmatrelvir,
 - amino acid changes associated with nirmatrelvir/ritonavir treatment emergence, treatment failure, or prolonged virologic shedding or rebound in clinical trials, and
 - amino acid polymorphisms identified in resistance surveillance analyses.Amino acid changes in both Mpro and Mpro cleavage sites should be considered in these analyses. Specific amino acid changes of interest for

phenotypic characterization in cell culture assays currently include Mpro substitutions Y54A, E55L, F140A, S144A, E166A, H172Y, Q189K, and A260V. When warranted due to technical challenges, alternative approaches to the requested cell culture assays will be considered on a case-by-case basis. Pfizer must submit a preliminary summary report no later than February 28, 2022 for any currently ongoing studies, and at least every 6 months thereafter as additional data accumulate.

2. Pfizer must evaluate the cell culture antiviral activity of nirmatrelvir against an authentic SARS-CoV-2 isolate representative of the Omicron variant. Pfizer must submit a summary report no later than February 28, 2022.
3. Pfizer must conduct studies characterizing potential nirmatrelvir resistance mechanisms in SARS-CoV-2 in cell culture, including selection and genotypic and phenotypic characterization of nirmatrelvir-resistant virus. Pfizer must submit a brief monthly progress report on these studies, a preliminary summary report no later than April 30, 2022, and a final report within 30 days of study completion.
4. Pfizer must complete analyses of SARS-CoV-2 shedding and nucleotide sequencing from the EPIC-HR clinical trial. Viral sequencing analyses should be conducted for all clinical samples with sufficient viral RNA levels, including samples collected at baseline, on-treatment and post-treatment, to identify and characterize the potential emergence or persistence of amino acid changes associated with PAXLOVID treatment. Pfizer must submit a summary of available data (including analysis-ready datasets) no later than February 28, 2022, and a final report and associated datasets (including analysis-ready datasets and raw fastq NGS data) no later than April 30, 2022.
5. Pfizer will submit the clinical study report containing data from all enrolled subjects in the EPIC-HR clinical trial no later than January 15, 2022.
6. Pfizer will provide results from a safety and pharmacokinetic study evaluating PAXLOVID as treatment of mild-to-moderate COVID-19 in patients with severe renal impairment (for both patients requiring and not requiring hemodialysis), with the study protocol submitted no later than March 31, 2022.
7. Pfizer will provide the audited final report of the rat PPND study, *An Oral (Gavage) Study of the Effects of PF-07321332 on Pre- and Postnatal Development, Including Maternal Function in Rats*, no later than April 30, 2022.

- O. Pfizer and authorized distributor(s) will make available to FDA upon request any records maintained in connection with this EUA.

Healthcare Facilities to Whom PAXLOVID Is Distributed and Healthcare Providers Administering PAXLOVID

- P. Healthcare facilities and healthcare providers will ensure that they are aware of the Letter of Authorization, and the terms herein, and that the authorized Fact Sheets are made

available to healthcare providers and to patients, parents, and caregivers, respectively, through appropriate means, prior to administration of PAXLOVID.

- Q. Healthcare facilities and healthcare providers receiving PAXLOVID will track all serious medication errors and adverse events that are considered to be potentially attributable to PAXLOVID use and must report these to FDA in accordance with the Fact Sheet for Healthcare Providers. Complete and submit a MedWatch form (www.fda.gov/medwatch/report.htm), or complete and submit FDA Form 3500 (health professional) by fax (1-800-FDA-0178) (these forms can be found via link above). Call [1-800-FDA-1088](tel:1-800-FDA-1088) for questions. Submitted reports must state, “PAXLOVID use for COVID-19 under Emergency Use Authorization” at the beginning of the question “Describe Event” for further analysis. A copy of the completed FDA Form 3500 must also be provided to Pfizer per the instructions in the authorized labeling.
- R. Healthcare facilities and healthcare providers will ensure that appropriate storage is maintained until the product is administered consistent with the terms of this letter and the authorized labeling.
- S. Through a process of inventory control, healthcare facilities will maintain records regarding the dispensing and administration of PAXLOVID for the use authorized in this letter (i.e., lot numbers, quantity, receiving site, receipt date), product storage, and maintain patient information (e.g., patient name, age, disease manifestation, number of doses administered per patient, other drugs administered).
- T. Healthcare facilities will ensure that any records associated with this EUA are maintained until notified by Pfizer and/or FDA. Such records will be made available to Pfizer, HHS, and FDA for inspection upon request.
- U. Healthcare facilities and providers will report therapeutics information and utilization data as directed by HHS.

Conditions Related to Printed Matter, Advertising, and Promotion

- V. All descriptive printed matter, advertising, and promotional materials relating to the use of PAXLOVID under this authorization shall be consistent with the authorized labeling, as well as the terms set forth in this EUA, and meet the requirements set forth in Section 502(a) and (n) of the Act, as applicable, and FDA implementing regulations. References to “approved labeling”, “permitted labeling” or similar terms in these requirements shall be understood to refer to the authorized labeling for the use of PAXLOVID under this authorization. In addition, such materials shall:
- Be tailored to the intended audience.
 - Not take the form of reminder advertisements, as that term is described in 21 CFR 202.1(e)(2)(i), 21 CFR 200.200 and 21 CFR 201.100(f).

- Present the same risk information relating to the major side effects and contraindications concurrently in the audio and visual parts of the presentation for advertising and promotional materials in audio-visual format.
- Be accompanied by the authorized labeling, if the promotional materials are not subject to Section 502(n) of the Act.
- Be submitted to FDA accompanied by Form FDA-2253 at the time of initial dissemination or first use.

If the Agency notifies Pfizer that any descriptive printed matter, advertising or promotional materials do not meet the terms set forth in conditions V-X of this EUA, Pfizer must cease distribution of such descriptive printed matter, advertising, or promotional materials in accordance with the Agency's notification. Furthermore, as part of its notification, the Agency may also require Pfizer to issue corrective communication(s).

- W. No descriptive printed matter, advertising, or promotional materials relating to the use of PAXLOVID under this authorization may represent or suggest that PAXLOVID is safe or effective when used for the treatment of COVID-19.
- X. All descriptive printed matter, advertising, and promotional material, relating to the use of PAXLOVID under this authorization clearly and conspicuously shall state that:
- PAXLOVID has not been approved, but has been authorized for emergency use by FDA under an EUA, 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; and
 - The emergency use of PAXLOVID is only authorized for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products during the COVID-19 pandemic under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization revoked sooner.

IV. Duration of Authorization

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products during the COVID-19 pandemic is terminated under Section 564(b)(2) of the Act or the EUA is revoked under Section 564(g) of the Act.

Sincerely,

--/S/--

Jacqueline A. O'Shaughnessy, Ph.D.
Acting Chief Scientist
Food and Drug Administration

Frequently Asked Questions on the Emergency Use Authorization for Paxlovid for Treatment of COVID-19

Q. What is an emergency use authorization (EUA)?

A. Under section 564 of the Federal Food, Drug & Cosmetic Act, after a declaration by the HHS Secretary based on one of four types of determinations, FDA may authorize an unapproved product or unapproved uses of an approved product for emergency use. In issuing an EUA, FDA must determine, among other things, that based on the totality of scientific evidence available to the agency, including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing a serious or life-threatening disease or condition caused by a chemical, biological, radiological, or nuclear agent; that the known and potential benefits of the product, when used to treat, diagnose or prevent such disease or condition, outweigh the known and potential risks of the product; and that there are no adequate, approved, and available alternatives. Emergency use authorization is NOT the same as FDA approval or licensure.

Q. What does this EUA authorize? What are the limitations of authorized use?

A. The [EUA](#) authorizes the emergency use of the unapproved product Paxlovid (nirmatrelvir co-packaged with ritonavir) for the treatment of mild-to-moderate coronavirus disease 2019 (COVID-19) in 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. Paxlovid is not approved for any use, including for the treatment of COVID-19.

Paxlovid is not authorized:

- for initiation of treatment in patients requiring hospitalization due to severe or critical COVID-19.
- for pre-exposure or post-exposure prophylaxis for prevention of COVID-19.
- for use longer than five consecutive days.

Q. How is high risk defined under the EUA?

A. Information about conditions that place a patient with mild-to-moderate COVID-19 at increased risk for disease progression or death can be found at the Centers for Disease Control and Prevention site: [People with Certain Medical Conditions](#). Health care providers should consider the benefit-risk for an individual patient.

Q. Are there potential side effects of Paxlovid?

A. Possible side effects of Paxlovid include dysgeusia (altered or impaired sense of taste), diarrhea, increased blood pressure, and myalgia (muscle aches).

Nirmatrelvir and ritonavir, which comprise Paxlovid, also interact with other medicines, which may lead to serious or life-threatening adverse reactions. Patients should tell their health care providers all of the medicines they are taking, including over-the-counter medications and herbal supplements, when deciding whether to take Paxlovid.

Liver problems have occurred in patients receiving ritonavir. Therefore, caution should be exercised when administering Paxlovid to patients with pre-existing liver diseases, liver enzyme abnormalities, or hepatitis. Patients should talk with their health care provider if they have a history of liver problems.

Paxlovid is not recommended for patients with severe kidney problems, and a different dose is needed for patients with moderate kidney problems. Patients should talk with their health care provider if they have a history of kidney problems.

Because nirmatrelvir is co-administered with ritonavir, there may be a risk of HIV-1 developing resistance to HIV protease inhibitors in individuals with uncontrolled or undiagnosed HIV-1 infection. Patients with HIV who are not on treatment with “undetectable” viral load should talk with their health care provider before taking Paxlovid.

There are limited clinical data available for Paxlovid. Serious and unexpected adverse events may occur that have not been previously reported with Paxlovid use.

Q: Is Paxlovid FDA-approved to prevent or treat COVID-19?

A. No. Paxlovid is not FDA-approved to prevent or treat any diseases or conditions, including COVID-19. Paxlovid is an investigational drug.

Q. How can Paxlovid be obtained for use under the EUA?

A. For questions on how to obtain Paxlovid, please contact COVID19therapeutics@hhs.gov.

Q. Who may prescribe Paxlovid under the EUA?

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

Q. When should Paxlovid be administered to a patient?

A. Patients should talk to their health care provider to determine whether, based on their individual circumstances, they are eligible to receive Paxlovid. Paxlovid treatment should be initiated as soon as possible after diagnosis of COVID-19 and within 5 days of symptom onset.

More information about administration is available in the [Fact Sheet for Health Care Providers](#).

Q. Does the EUA permit the use of Paxlovid for some hospitalized patients?

A. Yes, Paxlovid is authorized for the treatment of patients hospitalized with mild-to-moderate COVID-19, such as patients admitted for monitoring of drug-drug interactions. Paxlovid is also authorized for patients hospitalized for conditions other than COVID-19, provided the terms of the authorization are otherwise met. Paxlovid is also authorized for patients who require hospitalization due to severe or critical COVID-19 after starting treatment with Paxlovid. These patients should complete the full 5-day treatment course per the healthcare provider’s discretion.

Q. Are there data showing Paxlovid may provide benefit for treatment of mild-to-moderate COVID-19 for certain patients?

A. Yes. The primary data supporting this EUA for Paxlovid are from EPIC-HR, a randomized, double-blind, placebo-controlled clinical trial studying Paxlovid for the treatment of non-hospitalized symptomatic adults with a laboratory confirmed diagnosis of SARS-CoV-2 infection. Patients were adults 18 years of age and older with a prespecified risk factor for progression to severe disease or were 60 years and older regardless of prespecified chronic medical conditions. All patients had not received a COVID-19

vaccine and had not been previously infected with COVID-19. The main outcome measured in the [trial](#) was the proportion of people who were hospitalized due to COVID-19 or died due to any cause during 28 days of follow-up. 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 and who did not receive COVID-19 therapeutic monoclonal antibody treatment. In this analysis, 1,039 patients had received Paxlovid and 1,046 patients had received placebo and among these patients, 0.8% who received Paxlovid were hospitalized or died during 28 days of follow-up compared to 6% of the patients who received placebo. Of the people who received Paxlovid, no patients died within this time period compared to 12 people who received placebo.

Details on the clinical trial results can be found in Section 14 of the authorized [Fact Sheet for Health Care Providers](#).

Q. Are there reporting requirements for health care facilities and providers as part of the EUA?

A. Yes. As part of the EUA, FDA requires health care providers who prescribe Paxlovid to report all medication errors and serious adverse events considered to be potentially related to Paxlovid through FDA's [MedWatch Adverse Event Reporting](#) program. Providers can complete and submit the report [online](#); or download and complete the [form](#), then submit it via fax at 1-800-FDA-0178. This requirement is outlined in the EUA's [Fact Sheet for Health Care Providers](#). FDA MedWatch forms should also be provided to Pfizer.

Health care facilities and providers must report therapeutics information and utilization data as directed by the U.S. Department of Health and Human Services. Such information and data should be reported through HHS Protect, Teletracking, or National Health care Safety Network (NHSN).

Q. Do patient outcomes need to be reported under the EUA?

A. No, reporting of patient outcomes is not required under the EUA. However, reporting of all medication errors and serious adverse events considered to be potentially related to Paxlovid occurring during treatment is required.

Q. FDA has issued a number of EUAs including for therapeutics. If state laws impose different or additional requirements on the medical product covered by an EUA, are those state laws preempted?

A. As stated in FDA's [Emergency Use Authorization of Medical Products and Related Authorities Guidance](#), "FDA believes that the terms and conditions of an EUA issued under section 564 preempt state or local law, both legislative requirements and common-law duties, that impose different or additional requirements on the medical product for which the EUA was issued in the context of the emergency declared under section 564." The guidance explains the basis for FDA's views on this subject.

Q. Can health care providers share the patient/caregiver Fact Sheet electronically?

A. Under the authorization, Pfizer must make available the authorized Fact Sheets on its website at: www.COVID19oralRX.com. Health care facilities and health care providers must ensure that fact sheets are made available to patients, parents, and caregivers through "appropriate means" and electronic delivery of the Fact Sheet is an appropriate means.

FACT SHEET FOR PATIENTS, PARENTS, AND CAREGIVERS

EMERGENCY USE AUTHORIZATION (EUA) OF PAXLOVID FOR CORONAVIRUS DISEASE 2019 (COVID-19)

You are being given this Fact Sheet because your healthcare provider believes it is necessary to provide you with PAXLOVID for the treatment of mild-to-moderate coronavirus disease (COVID-19) caused by the SARS-CoV-2 virus. This Fact Sheet contains information to help you understand the risks and benefits of taking the PAXLOVID you have received or may receive.

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to make PAXLOVID available during the COVID-19 pandemic (for more details about an EUA please see “**What is an Emergency Use Authorization?**” at the end of this document). PAXLOVID is not an FDA-approved medicine in the United States. Read this Fact Sheet for information about PAXLOVID. Talk to your healthcare provider about your options or if you have any questions. It is your choice to take PAXLOVID.

What is COVID-19?

COVID-19 is caused by a virus called a coronavirus. You can get COVID-19 through close contact with another person who has the virus.

COVID-19 illnesses have ranged from very mild-to-severe, including illness resulting in death. While information so far suggests that most COVID-19 illness is mild, serious illness can happen and may cause some of your other medical conditions to become worse. Older people and people of all ages with severe, long lasting (chronic) medical conditions like heart disease, lung disease, and diabetes, for example seem to be at higher risk of being hospitalized for COVID-19.

What is PAXLOVID?

PAXLOVID is an investigational medicine used to treat mild-to-moderate COVID-19 in adults and children [12 years of age and older weighing at least 88 pounds (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 investigational because it is still being studied. There is limited information about the safety and effectiveness of using PAXLOVID to treat people with mild-to-moderate COVID-19.

The FDA has authorized the emergency use of PAXLOVID for the treatment of mild-to-moderate COVID-19 in adults and children [12 years of age and older weighing at least 88 pounds (40 kg)] with a positive test for the virus that causes COVID-19, and who are at high risk for progression to severe COVID-19, including hospitalization or death, under an EUA.

What should I tell my healthcare provider before I take PAXLOVID?

Tell your healthcare provider if you:

- Have any allergies
- Have liver or kidney disease
- Are pregnant or plan to become pregnant
- Are breastfeeding a child
- Have any serious illnesses

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Some medicines may interact with PAXLOVID and may cause serious side effects. Keep a list of your medicines to show your healthcare provider and pharmacist when you get a new medicine.

You can ask your healthcare provider or pharmacist for a list of medicines that interact with PAXLOVID. **Do not start taking a new medicine without telling your healthcare provider.** Your healthcare provider can tell you if it is safe to take PAXLOVID with other medicines.

Tell your healthcare provider if you are taking combined hormonal contraceptive.

PAXLOVID may affect how your birth control pills work. Females who are able to become pregnant should use another effective alternative form of contraception or an additional barrier method of contraception. Talk to your healthcare provider if you have any questions about contraceptive methods that might be right for you.

How do I take PAXLOVID?

- PAXLOVID consists of 2 medicines: nirmatrelvir and ritonavir.
 - Take 2 pink tablets of nirmatrelvir with 1 white tablet of ritonavir by mouth 2 times each day (in the morning and in the evening) for 5 days. **For each dose, take all 3 tablets at the same time.**
 - **If you have kidney disease, talk to your healthcare provider. You may need a different dose.**
- Swallow the tablets whole. Do not chew, break, or crush the tablets.
- Take PAXLOVID with or without food.
- Do not stop taking PAXLOVID without talking to your healthcare provider, even if you feel better.
- If you miss a dose of PAXLOVID within 8 hours of the time it is usually taken, take it as soon as you remember. If you miss a dose by more than 8 hours, skip the missed dose and take the next dose at your regular time. Do not take 2 doses of PAXLOVID at the same time.
- If you take too much PAXLOVID, call your healthcare provider or go to the nearest hospital emergency room right away.
- If you are taking a ritonavir- or cobicistat-containing medicine to treat hepatitis C or Human Immunodeficiency Virus (HIV), you should continue to take your medicine as prescribed by your healthcare provider.

Talk to your healthcare provider if you do not feel better or if you feel worse after 5 days.

Who should generally not take PAXLOVID?

Do not take PAXLOVID if:

- You are allergic to nirmatrelvir, ritonavir, or any of the ingredients in PAXLOVID.
- You are taking any of the following medicines:
 - Alfuzosin
 - Pethidine, piroxicam, propoxyphene
 - Ranolazine
 - Amiodarone, dronedarone, flecainide, propafenone, quinidine
 - Colchicine
 - Lurasidone, pimozone, clozapine
 - Dihydroergotamine, ergotamine, methylergonovine
 - Lovastatin, simvastatin
 - Sildenafil (Revatio®) for pulmonary arterial hypertension (PAH)
 - Triazolam, oral midazolam
 - Apalutamide
 - Carbamazepine, phenobarbital, phenytoin
 - Rifampin
 - St. John's Wort (*hypericum perforatum*)

Taking PAXLOVID with these medicines may cause serious or life-threatening side effects or affect how PAXLOVID works.

These are not the only medicines that may cause serious side effects if taken with PAXLOVID. PAXLOVID may increase or decrease the levels of multiple other medicines. It is very important to tell your healthcare provider about all of the medicines you are taking because additional laboratory tests or changes in the dose of your other medicines may be necessary while you are taking PAXLOVID. Your healthcare provider may also tell you about specific symptoms to watch out for that may indicate that you need to stop or decrease the dose of some of your other medicines.

What are the important possible side effects of PAXLOVID?

Possible side effects of PAXLOVID are:

- **Liver Problems.** Tell your healthcare provider right away if you have any of these signs and symptoms of liver problems: loss of appetite, yellowing of your skin and the whites of eyes (jaundice), dark-colored urine, pale colored stools and itchy skin, stomach area (abdominal) pain.
- **Resistance to HIV Medicines.** If you have untreated HIV infection, PAXLOVID may lead to some HIV medicines not working as well in the future.

- **Other possible side effects include:**

- altered sense of taste
- diarrhea
- high blood pressure
- muscle aches

These are not all the possible side effects of PAXLOVID. Not many people have taken PAXLOVID. Serious and unexpected side effects may happen. PAXLOVID is still being studied, so it is possible that all of the risks are not known at this time.

What other treatment choices are there?

Like PAXLOVID, FDA may allow for the emergency use of other medicines to treat people with COVID-19. Go to <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization> for information on the emergency use of other medicines that are authorized by FDA to treat people with COVID-19. Your healthcare provider may talk with you about clinical trials for which you may be eligible.

It is your choice to be treated or not to be treated with PAXLOVID. Should you decide not to receive it or for your child not to receive it, it will not change your standard medical care.

What if I am pregnant or breastfeeding?

There is no experience treating pregnant women or breastfeeding mothers with PAXLOVID. For a mother and unborn baby, the benefit of taking PAXLOVID may be greater than the risk from the treatment. If you are pregnant, discuss your options and specific situation with your healthcare provider.

It is recommended that you use effective barrier contraception or do not have sexual activity while taking PAXLOVID.

If you are breastfeeding, discuss your options and specific situation with your healthcare provider.

How do I report side effects with PAXLOVID?

Contact your healthcare provider if you have any side effects that bother you or do not go away.

Report side effects to **FDA MedWatch** at www.fda.gov/medwatch or call 1-800-FDA-1088 or you can report side effects to Pfizer Inc. at the contact information provided below.

Website	Fax number	Telephone number
www.pfizersafetyreporting.com	1-866-635-8337	1-800-438-1985

How should I store PAXLOVID?

Store PAXLOVID tablets at room temperature, between 68°F to 77°F (20°C to 25°C).

How can I learn more about COVID-19?

- Ask your healthcare provider.
- Visit <https://www.cdc.gov/COVID19>.
- Contact your local or state public health department.

What is an Emergency Use Authorization (EUA)?

The United States FDA has made PAXLOVID available under an emergency access mechanism called an Emergency Use Authorization (EUA). The EUA is supported by a Secretary of Health and Human Service (HHS) declaration that circumstances exist to justify the emergency use of drugs and biological products during the COVID-19 pandemic.

PAXLOVID for the treatment of mild-to-moderate COVID-19 in adults and children [12 years of age and older weighing at least 88 pounds (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, has not undergone the same type of review as an FDA-approved product. In issuing an EUA under the COVID-19 public health emergency, the FDA has determined, among other things, that based on the total amount of scientific evidence available including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that the product may be effective for diagnosing, treating, or preventing COVID-19, or a serious or life-threatening disease or condition caused by COVID-19; that the known and potential benefits of the product, when used to diagnose, treat, or prevent such disease or condition, outweigh the known and potential risks of such product; and that there are no adequate, approved, and available alternatives.

All of these criteria must be met to allow for the product to be used in the treatment of patients during the COVID-19 pandemic. The EUA for PAXLOVID is in effect for the duration of the COVID-19 declaration justifying emergency use of this product, unless terminated or revoked (after which the products may no longer be used under the EUA).

Additional Information

For general questions, visit the website or call the telephone number provided below.

Website	Telephone number
<p data-bbox="305 359 683 390">www.COVID19oralRx.com</p> 	<p data-bbox="1032 443 1305 531">1-877-219-7225 (1-877-C19-PACK)</p>

www.pfizermedinfo.com or call 1-800-438-1985 for more information.



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