



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

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## Questions related to Paxlovid's approval or EUA

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

**A.** On May 25, 2023, FDA approved a New Drug Application (NDA) for [Paxlovid](#) for the treatment of mild-to-moderate coronavirus disease (COVID-19) in adults who are at high risk for progression to severe COVID-19, including hospitalization or death. FDA has determined Paxlovid is safe and effective when used in accordance with the FDA-approved labeling.

Paxlovid is not FDA-approved for use as pre-exposure or post-exposure prophylaxis for prevention of COVID-19.

### **Q. Now that Paxlovid is an approved drug, is the EUA continuing, and what does the EUA authorize?**

**A.** Yes. The [EUA](#) authorizes 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) who are at high risk for progression to severe COVID-19, including hospitalization or death.

The EUA continues to authorize Paxlovid for emergency use to treat certain eligible pediatric patients, a patient population that is not covered under the approved NDA for Paxlovid at this time. Paxlovid also remains authorized under EUA to ensure continued access for all eligible patients to the U.S. government's supply of Paxlovid, including adult patients who are the subject of the approved NDA, pending commercial launch of the approved product.

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.

The use of Paxlovid under the EUA must be consistent with the terms and conditions of the authorization.

### **Q. Does the authorized Paxlovid provide the same clinical benefit as the approved Paxlovid, once the approved Paxlovid is available?**

**A.** Yes. The authorized Paxlovid contains the same tablets (nirmatrelvir tablets and ritonavir tablets) as the Paxlovid that is now FDA-approved. Since Paxlovid was initially authorized for emergency use, Pfizer has also been required, as a condition under the EUA, to comply with the same good manufacturing practices that apply to approved products. Based on these considerations, it is FDA's expectation that patients being treated with Paxlovid for COVID-19 will receive the same clinical benefit as long as the product is used in accordance with the labeling, regardless of whether the authorized or approved Paxlovid is dispensed.

Paxlovid is FDA-approved for the treatment of mild-to-moderate COVID-19 in certain adults. Paxlovid is authorized for emergency use, but not FDA-approved, for the treatment of mild-to-moderate COVID-19 in certain pediatric patients.

**Q. Why does the EUA authorize Paxlovid for its approved patient population, specifically for the treatment of mild-to-moderate COVID-19 in high-risk adults?**

**A.** Although different presentations of PAXLOVID are now FDA-approved for the treatment of mild-to-moderate COVID-19 in certain adults, there are not sufficient quantities of the approved PAXLOVID available for distribution to this population in its entirety at the time of reissuance of this EUA. To ensure continued access to the U.S. government's supply for Paxlovid and fully meet the public health need before commercial launch of the approved product, the EUA continues to include the patient population now approved under the NDA for Paxlovid.

The use of Paxlovid under the EUA must be consistent with the terms and conditions of the authorization.

**Q. Paxlovid is approved and authorized only for certain patients at "high risk". What does "high risk" mean?**

**A.** Determining whether a patient is at high risk for progression to severe COVID-19, including hospitalization or death, is based on the provider's assessment of the individual patient being considered for treatment with COVID-19 and that patient's medical history.

Resources providing information on conditions that place a patient with mild-to-moderate COVID-19 at high risk for disease progression, including hospitalization or death, can be found at the Centers for Disease Control and Prevention site: [Underlying Medical Conditions Associated with Higher Risk for Severe COVID-19: Information for Healthcare Professionals](#) and at [NIH's COVID-19 Treatment Guidelines: Clinical Spectrum of SARS-CoV-2 Infection](#).

**Q. Why is pediatric use not approved for Paxlovid and only authorized under the EUA?**

**A.** The clinical development of Paxlovid for pediatric use is ongoing.

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

**A.** For questions on how to obtain Paxlovid, please contact [COVID19therapeutics@hhs.gov](mailto:COVID19therapeutics@hhs.gov). Information about Paxlovid's distribution can be [found here](#).

## **Efficacy and Safety Considerations**

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

**A.** Yes. The primary data supporting the approval as well as the 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 through 28 days of follow-up by 86% 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, 977 patients received Paxlovid, and 989 patients received placebo, and among these patients, 0.9% who received Paxlovid were hospitalized due to COVID-19 or died from any cause during 28 days of follow-up compared to 6.5% of the patients who received placebo. Of the people who received Paxlovid, no patients died through 24 weeks after receipt compared to 15 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](#) and approved [Prescribing Information](#).

**Q. Are there data supporting the benefit of Paxlovid for high-risk patients with mild-moderate COVID-19 regardless of prior/acquired immunity?**

**A.** Benefit of Paxlovid was observed in patients with prior immunity to the virus that causes COVID-19. Among patients in EPIC-HR who were antibody positive at trial enrollment, the risk of COVID-19-related hospitalization or death from any cause during 28 days of follow-up was 0.2% among those treated with Paxlovid compared with 1.7% of those receiving placebo. EPIC-SR was another clinical trial that enrolled vaccinated patients with at least one risk factor for progression to severe COVID-19. Among these vaccinated patients, there was a reduction in the risk of COVID-19 related hospitalization or death from any cause with use of PAXLOVID versus placebo, although not statistically significant.

**Q. Does Paxlovid retain activity against currently circulating Omicron variants?**

**A.** Yes. Based on virology data, Paxlovid retains activity against currently circulating Omicron variants.

**Q. Does Paxlovid cause COVID-19 rebound?**

**A.** EPIC-HR, described above, and EPIC-SR, another trial that enrolled vaccinated patients with at least one risk factor for progression to severe COVID-19 or unvaccinated patients with no risk factors for progression to severe COVID-19, were both randomized placebo-controlled trials. These trials provide useful data to assess COVID-19 rebound. Data from these two trials showed that rebound in SARS-CoV-2 (RNA or virus) shedding or self-reported COVID-19 symptoms occurred in a subset of patients and happened at similar rates in both the patients receiving Paxlovid and placebo. Based on the data currently available to FDA, there is not a clear association between Paxlovid treatment and COVID-19 rebound.

**Q. Are there potential side effects of Paxlovid?**

**A.** Yes. Paxlovid consists of nirmatrelvir and ritonavir, and ritonavir interacts with many 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.

Because of the importance of reducing the risk of significant drug-drug interactions with Paxlovid, the approved [Prescribing Information](#) and authorized [Fact Sheet for Health Care Providers](#) for the Paxlovid EUA include a boxed warning with instructions for providers to review all medications taken by the patient to assess for potential drug-drug interactions and determine if other medicines that a patient may be taking require a dose adjustment, interruption and/or additional monitoring.

The most common side effects of taking Paxlovid include impaired sense of taste (for example, a metallic taste in the mouth) and diarrhea.

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.

See Warnings and Precautions in the FDA-approved [Prescribing Information](#) and the Fact Sheet for [Health Care Providers](#) for additional information on risks associated with Paxlovid.

#### **Q. Why was a boxed warning included in the Paxlovid prescribing information?**

**A.** Paxlovid includes ritonavir, a strong CYP3A inhibitor, which may lead to greater exposure of certain other medications the patient may be taking, resulting in potentially severe, life-threatening, or fatal events due to drug-drug interactions. Such interactions can be avoided by appropriate handling of the patient's other medications when starting treatment with Paxlovid or, in some situations when adjustments of the patient's other medication may not be feasible, choosing an alternative COVID-19 treatment for the individual patient. Since the authorization of Paxlovid under EUA, FDA has reviewed new data related to the risk of drug-drug interactions. These data were discussed by FDA during the recent [Antimicrobial Drugs Advisory Committee](#) on March 16, 2023.

- FDA identified more than 250 cases of serious adverse events assessed as possibly or probably related to Paxlovid drug-drug interactions. Many of these cases reported hospitalization, and a fatal outcome was reported in a few cases.
- FDA determined that greater than 50% of Paxlovid-eligible Medicare and VA patients were taking medications that were identified as having a drug-drug interaction with Paxlovid. FDA noted that most of these potential drug-drug interactions could be prevented or managed with dose modification, interruption, and/or additional monitoring.
- FDA determined that most Paxlovid prescriptions were written by a broad range of health care providers, who may not be familiar with managing potential drug-drug interactions associated with ritonavir, which is more commonly prescribed by infectious disease physicians and other specialists who may have more experience managing ritonavir drug-drug interactions.

Drug-drug interactions are not unique to Paxlovid and are almost always manageable risks. Prior to prescribing Paxlovid, health care providers must: 1) review all medications taken by the patient to assess potential drug-drug interactions with a strong CYP3A inhibitor like Paxlovid and 2) determine if

medications require a dose adjustment, interruption, and/or additional monitoring if taken at the same time as Paxlovid.

There are resources for health care providers to identify and manage potential drug-drug interactions with Paxlovid. These include: the approved [prescribing information](#), [the Fact Sheet for Health Care Providers](#) and the [Prescriber Patient Eligibility Screening Checklist](#) available on the FDA EUA webpage. Other resources include: the [NIH COVID-19 Treatment Guidelines](#), the [IDSA COVID-19 Treatment Guidelines](#) and the [University of Liverpool COVID-19 Drug Interactions online checker](#).

## Provider Considerations When Prescribing Paxlovid

### **Q. Who may prescribe Paxlovid?**

**A.** 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 certain conditions that are listed in the EUA. For more information on this topic, please refer to the section titled [Questions for Pharmacist Prescribers](#) below.

### **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, even if symptoms are mild, and within five days after symptoms start.

More information about administration is available in the in the FDA-approved [Prescribing Information](#) and the [Fact Sheet for Health Care Providers](#).

### **Q: Is a positive result from a direct SARS-CoV-2 viral test required prior to prescribing Paxlovid to a patient who is at high risk for severe COVID-19?**

**A:** No. FDA recognizes that, in rare instances, individuals with a recent known exposure (e.g., a household contact) who develop signs and symptoms consistent with COVID-19 may be diagnosed by their health care provider as having COVID-19 even if they have a negative direct SARS-CoV-2 viral test result. In such instances, their health care provider may determine that treatment with Paxlovid for COVID-19 is appropriate if the patient reports mild-to-moderate symptoms of COVID-19 and is at high-risk for progression to severe COVID-19, including hospitalization or death, and the terms and conditions of the authorization are met, as detailed in the Letter of Authorization for Paxlovid and the authorized [Fact Sheet for Healthcare Providers](#).

The agency continues to recommend that providers use direct SARS-CoV-2 viral testing to help diagnose COVID-19.



**Q. I am traveling soon. May I receive Paxlovid under the EUA prior to travel in case I become sick with COVID-19?**

**A.** Individuals being considered for Paxlovid treatment must meet the eligibility requirements under the EUA at the time of prescription. Providers must determine that patients have signs and symptoms consistent with mild-to-moderate COVID-19, assess risk for disease progression, assess renal and hepatic function, and review all medications taken by the patient to assess for potential drug-drug interactions and determine if other medicines that a patient may be taking require a dose adjustment, interruption and/or additional monitoring.

**Q. What if I have questions about the expiration date on the Paxlovid carton or container?**

**A.** FDA has authorized an extension to the expiration date (shelf-life) for certain lots of Paxlovid. To find the extended expiration date, enter the lot number found on the side of the carton or bottom of the blister pack at [this website](#) or talk with the pharmacist or provider.

Information on the authorized shelf-life extensions for Paxlovid may also be found [on FDA's website](#).

### Questions for pharmacist prescribers

**Q. Are pharmacists permitted to prescribe Paxlovid?**

**A.** The EUA authorizes state-licensed pharmacists to prescribe Paxlovid for an individual patient, subject to the terms and conditions of the EUA (e.g., eligible patient populations), 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.

**Q. What do state-licensed pharmacist prescribers need to do to determine whether a patient may be eligible to receive Paxlovid?**

**A.** State-licensed pharmacist prescribers have the same requirements as all other prescribers to assess an adult or pediatric patient (12 years of age and older weighing at least 40 kg), who is being considered for treatment with Paxlovid, to determine that they have a diagnosis of mild-to-moderate COVID-19 and are at high risk for progression to severe COVID-19, including hospitalization or death.

A review of reported symptoms should be completed to determine that patients have signs and symptoms consistent with mild-to-moderate COVID-19, and not severe COVID-19. Patients reporting shortness of breath or difficulty breathing should be immediately referred for further medical assessment to determine whether their illness has progressed to the severe stage, which may require hospitalization. Paxlovid is not authorized or approved for the treatment of severe COVID-19.

Definitions for mild and moderate illness are provided in [NIH's COVID-19 Treatment Guidelines: Clinical Spectrum of SARS-CoV-2 Infection](#).

State-licensed pharmacist prescribers may determine whether an individual patient is at high risk for severe COVID-19 by obtaining a medical history from the patient or by accessing the patient's medical records. Resources 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: Underlying Medical Conditions Associated with Higher Risk for Severe COVID-19: Information for Healthcare Professionals and at NIH's COVID-19 Treatment Guidelines: Clinical Spectrum of SARS-CoV-2 Infection.

**Q. How do state-licensed pharmacist prescribers assess for potential drug interactions?**

**A.** All prescribers are expected to utilize available health records or patient history to obtain a complete list of all medications (prescribed and non-prescribed) that the patient is taking. State-licensed pharmacists may also consult with a health care provider in an established provider-patient relationship with the individual patient to obtain a comprehensive list of medications the patient is taking. Resources to identify potential drug interactions include the approved Prescribing Information, the [Fact Sheet for Health Care Providers](#) and the [Prescriber Patient Eligibility Screening Checklist](#) available on the [FDA EUA webpage](#). Other resources include: the [NIH COVID-19 Treatment Guidelines](#), the [IDSA COVID-19 Treatment Guidelines](#) and the [University of Liverpool COVID-19 Drug Interactions](#).

Should an adjustment to another medication be needed due to a potential drug interaction, the state-licensed pharmacist should refer the individual patient for clinical evaluation with a physician, advanced practice registered nurse, or physician assistant licensed or authorized under state law to prescribe drugs.

**Q. How do state-licensed pharmacist prescribers assess renal and hepatic function?**

**A.** State-licensed pharmacist prescribers must have access to sufficient information from health records to assess renal and hepatic function. Health records include access to an electronic health record system containing this information in progress notes or laboratory records, reviewing a printed health record such as a laboratory report provided by the patient, or reviewing information in electronic health records the patient may have access to through a phone app or other means. Health records within the



past 12 months are generally acceptable, provided there is no patient self-report or other information suggestive of kidney or liver disease. State-licensed pharmacists may also consult with a health care provider in an established provider-patient relationship with the individual patient to obtain this information. If sufficient information is not available to assess renal and hepatic function, 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.

Physicians, advanced practice registered nurses, and physician assistants may rely on patient history and access to the patient's health records to make an assessment regarding the likelihood of renal impairment. These providers may consider ordering a serum creatinine or calculating the estimated glomerular filtration rate (eGFR) for certain patients after assessment on a case-by-case basis.

**Q. Will state-licensed pharmacists be able to prescribe both the standard and renal doses of Paxlovid?**

**A.** Yes, the EUA authorizes state-licensed pharmacists to prescribe both the standard and renal doses of Paxlovid, subject to the terms and conditions on pharmacist prescribing as detailed in the EUA, provided the pharmacist has adequate information to assess renal function and the patient is otherwise eligible to receive Paxlovid.

## General EUA-related questions

**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. 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.

**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](http://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.