

Paxlovid™ (nirmatrelvir/ritonavir) – Emergency use authorization

- On December 22, 2021, the [FDA announced](#) the [emergency use authorization \(EUA\) approval](#) of Pfizer's [Paxlovid \(nirmatrelvir/ritonavir\)](#), 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 authorized for initiation of treatment in patients requiring hospitalization due to severe or critical COVID-19.
 - Paxlovid is not authorized for pre-exposure or post-exposure prophylaxis for prevention of COVID-19.
 - Paxlovid is not authorized for use 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 (ie, anti-infectives).
- Paxlovid is the first oral drug to receive EUA for the treatment of COVID-19.
- Paxlovid contains two drugs: nirmatrelvir, a SARS-CoV-2 main protease (Mpro: also referred to as 3C-like protease [3CLpro] or nsp5 protease) inhibitor, and ritonavir, a human immunodeficiency virus (HIV)-1 protease inhibitor and CYP3A inhibitor.
 - Nirmatrelvir inhibition of SARS-CoV-2 Mpro renders the virus incapable of processing polyprotein precursors, preventing viral replication.
 - Ritonavir inhibits the CYP3A-mediated metabolism of nirmatrelvir, resulting in increased plasma concentrations of nirmatrelvir.
- The EUA was based on EPIC-HR, a randomized, double-blind, placebo-controlled study in 2,246 non-hospitalized symptomatic (≤ 5 days) adult subjects with a laboratory confirmed diagnosis of SARS-CoV-2 infection. It enrolled adults ≥ 18 years of age with one risk factor for progression to severe disease or were > 60 years of age regardless of comorbidities and who had no prior history of COVID-19 and were unvaccinated. Patients received Paxlovid twice daily for 5 days or placebo.
 - The primary efficacy endpoint was the proportion of subjects with COVID-19 related hospitalization or death from any cause through day 28.
 - A total of 0.8% of Paxlovid-treated patients vs. 6.3% of placebo-treated patients met the primary endpoint (hospitalization or death). The relative risk reduction was 88% (95% CI: 75%, 94%).
 - For all cause mortality, there were 0 patients in the Paxlovid group vs. 12 patients in the placebo group at day 28.
- Paxlovid is contraindicated:
 - In patients with a history of clinically significant hypersensitivity reactions to its active ingredients (nirmatrelvir or ritonavir) or any other components of the product
 - With drugs that are highly dependent on CYP3A for clearance, or drugs that are potent CYP3A inducers.

- Additional warnings and precautions for Paxlovid include risk of serious adverse reactions due to drug interactions, hepatotoxicity, and risk of HIV-1 resistance development.
- The most common adverse reactions (incidence $\geq 1\%$ and ≥ 5 subject difference) with Paxlovid use were dysgeusia, diarrhea, hypertension, and myalgia.
- The recommended dose of Paxlovid is 300 mg nirmatrelvir (two 150 mg tablets) with 100 mg ritonavir (one 100 mg tablet) with all three tablets taken together orally twice daily for 5 days.
 - The 5-day treatment course of Paxlovid should be initiated as soon as possible after a diagnosis of COVID-19, and within 5 days of symptom onset.
 - Nirmatrelvir must be co-administered with ritonavir to achieve the desired therapeutic effect.
 - Completion of the full 5-day treatment course and continued isolation in accordance with public health recommendations are important to maximize viral clearance and minimize transmission of SARS-CoV-2.
- Pfizer is ready to deliver Paxlovid immediately and the federal government will manage distribution.
 - Pfizer plans to supply 10 million treatment courses to the U.S. government, with delivery fulfillment to be completed in 2022.
 - Paxlovid will be available as 30 tablets divided in 5 daily-dose blister cards. Each daily blister card contains 4 nirmatrelvir tablets (150 mg each) and 2 ritonavir tablets (100 mg each). The NDC number is 0069-1085-30.
 - It is anticipated that the drug cost will be covered at this time by the federal government.



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