June 28, 2022

IMPORTANT PRESCRIBING INFORMATION

Subject: Updated contraindications related to drug interactions associated with PAXLOVID (nirmatrelvir tablets; ritonavir tablets).

Dear Healthcare Provider,

The purpose of this letter is to make you aware of the updates to contraindications related to drug interactions with use of PAXLOVID for the treatment of COVID-19.

PAXLOVID contains two different drugs (nirmatrelvir tablets; ritonavir tablets) that are co-packaged in a daily blister card for oral use.

Use of PAXLOVID, a strong CYP3A inhibitor, in patients receiving concomitant medications metabolized by CYP3A may increase the plasma concentrations of those concomitant medications.

Use of concomitant medications that inhibit or induce CYP3A may increase or decrease concentrations of PAXLOVID, respectively.

These interactions may lead to:
- Clinically significant adverse reactions, potentially leading to severe, life-threatening, or fatal events from greater exposures of concomitant medications.
- Clinically significant adverse reactions from greater exposures of PAXLOVID.
- Loss of therapeutic effect of PAXLOVID and possible development of viral resistance.

Drugs listed below are contraindicated with PAXLOVID. The list below is not considered a comprehensive list of all drugs that may be contraindicated with PAXLOVID. New drugs added to the list of contraindications have been italicized.

- Alpha₁-adrenoreceptor antagonist: alfuzosin
- Analgesics: pethidine
- Antianginal: ranolazine
- Antiarrhythmic: amiodarone, dronedarone, flecainide, propafenone, quinidine
- Anti-gout: colchicine
- Antipsyhotics: lurasidone, pimozide, clozapine
- Benign prostatic hyperplasia agents: silodosin
- Cardiovascular agents: eplerenone, ivabradine
- Ergot derivatives: dihydroergotamine, ergotamine, methylergonovine
- HMG-CoA reductase inhibitors: lovastatin, simvastatin
- Immunosuppressants: voclosporin
- Microsomal triglyceride transfer protein inhibitor: lomitapide
- Migraine medications: eletriptan, ubrogepant
- Mineralocorticoid receptor antagonists: finerenone
- **Opioid antagonists**: naloxegol
- PDE5 inhibitor: sildenafil (Revatio®) when used for pulmonary arterial hypertension (PAH)
- Sedative/hypnotics: triazolam, oral midazolam
- **Serotonin receptor 1A agonist/serotonin receptor 2A antagonist**: flibanserin
- **Vasopressin receptor antagonists**: tolvaptan
- Anticancer drugs: apalutamide
- Anticonvulsant: carbamazepine, phenobarbital, primidone, phenytoin
- **Cystic fibrosis transmembrane conductance regulator potentiators**: lumacaftor/ivacaftor
- Antimycobacterials: rifampin
- Herbal products: St. John’s Wort (hypericum perforatum)

Additional new drugs, that are not contraindicated with PAXLOVID but which also have potentially significant drug interactions with PAXLOVID, have also been added to Table 1 in the PAXLOVID EUA Fact Sheet for Healthcare Providers. The drugs listed in Table 1 of the Fact Sheet are a guide and not considered a comprehensive list of all possible drugs that may interact with PAXLOVID.

**HEALTHCARE PROVIDER ACTION**

- When prescribing PAXLOVID, the healthcare provider should consult other appropriate resources such as the prescribing information for the concomitant drug for comprehensive information on dosing or monitoring with concomitant use of a strong CYP3A inhibitor.

- See the current EUA Fact Sheet for Healthcare Providers (www.COVID19oralRx.com) for clinically significant drug interactions, including **contraindicated** drugs. Consider the potential for drug interactions prior to and during PAXLOVID therapy; review concomitant medications during PAXLOVID therapy and monitor for the adverse reactions associated with the concomitant medications.

- Inform patients that PAXLOVID may interact with some drugs and is **contraindicated** for use with some drugs; therefore, patients should be advised to report to their healthcare provider the use of any prescription or non-prescription medications or herbal products.

- Consider referring to PAXLOVID Patient Eligibility Screening Checklist Tool available for Prescribers (https://www.fda.gov/media/158165/download).

**Indication & Authorized Use:**

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.

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.
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/hcp/clinical-care/underlyingconditions.html

Healthcare providers should consider the benefit-risk for an individual patient.

**Limitations of Authorized Use:**

- 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 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).

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.

**Reporting Adverse Events and Medication Errors:**

Under the EUA, all serious adverse events and all medication errors potentially related to PAXLOVID must be reported within 7 calendar days from the healthcare provider's awareness of the event.

Serious adverse event reports and medication error reports should be submitted to FDA’s MedWatch program using one of the following methods:
- Complete and submit the report online: www.fda.gov/medwatch/report.htm, or
- Complete and submit a postage-paid Form FDA 3500 (https://www.fda.gov/media/76299/download) and return by mail (MedWatch, 5600 Fishers Lane, Rockville, MD 208529787, or by fax (1-800-FDA-0178), or
- Call 1-800-FDA-1088 to request a reporting form. Please provide a copy of all FDA MedWatch forms to Pfizer via fax (1-866-635-8337), telephone (1-800-438-1985) or website www.pfizersafetyreporting.com

The PAXLOVID EUA Fact Sheet for Healthcare Providers is available at www.COVID19oralRx.com or by scanning the QR Code below:

![QR Code](image)

Sincerely,

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