



NEWS RELEASE

Statement from Pfizer Chairman and CEO Albert Bourla on Testing Positive for COVID-19

8/15/2022

NEW YORK, AUGUST 15, 2022 – Pfizer Inc. (NYSE: PFE) – I would like to inform the public that I have tested positive for COVID-19. I am grateful to have received four doses of the Pfizer-BioNTech vaccine and I am feeling well while experiencing very mild symptoms. I have started a course of PAXLOVID™ (nirmatrelvir [PF-07321332] tablets and ritonavir tablets), I am isolating in place as well as following all public health precautions.

We have come so far in the past two years in our efforts to battle this disease that I am confident that I will have a speedy recovery. I am incredibly grateful for the tireless efforts of my Pfizer colleagues who worked to make vaccines and treatments available for me and people around the world

About PAXLOVID™ (nirmatrelvir [PF-07321332] tablets and ritonavir tablets)

PAXLOVID is a SARS-CoV-2 main protease (Mpro) inhibitor (also known as SARS-CoV-2 3CL protease inhibitor) therapy. It was developed to be administered orally so that it can be prescribed early after infection, potentially helping patients avoid severe illness (which can lead to hospitalization and death). Nirmatrelvir [PF-07321332], which originated in Pfizer laboratories, is designed to block the activity of the Mpro, an enzyme that the coronavirus needs to replicate. Co-administration with a low dose of ritonavir helps slow the metabolism, or breakdown, of nirmatrelvir in order for it to remain active in the body for longer periods of time at higher concentrations to help combat the virus.

Nirmatrelvir is designed to inhibit viral replication at a stage known as proteolysis, which occurs before viral RNA replication. In preclinical studies, nirmatrelvir did not demonstrate evidence of mutagenic DNA interactions.

Current variants of concern can be resistant to treatments that work by binding to the spike protein found on the

surface of the SARS-CoV-2 virus. PAXLOVID, however, works intracellularly by binding to the highly conserved Mpro (3CL protease) of the SARS-CoV-2 virus to inhibit viral replication. Nirmatrelvir has shown consistent in vitro antiviral activity against the following variants: Alpha, Beta, Delta, Gamma, Lambda, Mu, and Omicron BA.1 and BA.2. PAXLOVID is generally administered at a dose of 300 mg (two 150 mg tablets) of nirmatrelvir with one 100 mg tablet of ritonavir, given twice-daily for five days. One carton contains five blister packs of PAXLOVID, as co-packaged nirmatrelvir tablets with ritonavir tablets, providing all required doses for a full five-day treatment course.

U.S. FDA Emergency Use Authorization Statement

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.

AUTHORIZED USE

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) for the emergency use of the unapproved product PAXLOVID 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.

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 use as 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).

PAXLOVID is not approved for any use, including for use for the treatment of COVID-19.

PAXLOVID is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of PAXLOVID under 564(b)(1) of the Food Drug and Cosmetic Act unless the authorization is terminated or revoked sooner.

IMPORTANT SAFETY INFORMATION

PAXLOVID is contraindicated in patients with a history of clinically significant hypersensitivity reactions (eg, toxic epidermal necrolysis [TEN] or Stevens-Johnson syndrome) to its active ingredients (nirmatrelvir or ritonavir) or any other components of the product.

Drugs listed in this section are a guide and not considered a comprehensive list of all drugs that may be contraindicated with PAXLOVID. The healthcare provider should consult other appropriate resources such as the prescribing information for the interacting drug for comprehensive information on dosing or monitoring with concomitant use of a strong CYP3A inhibitor such as ritonavir.

PAXLOVID is contraindicated with drugs that are highly dependent on CYP3A for clearance and for which elevated concentrations are associated with serious and/or life-threatening reactions:

- Alpha1-adrenoreceptor antagonist: alfuzosin
- Analgesics: pethidine, propoxyphene
- Antianginal: ranolazine
- Antiarrhythmic: amiodarone, dronedarone, flecainide, propafenone, quinidine
- Anti-gout: colchicine
- Antipsychotics: 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
- Sedative/hypnotics: triazolam, oral midazolam
- Serotonin receptor 1A agonist/serotonin receptor 2A antagonist: flibanserin

- Vasopressin receptor antagonists: tolvaptan

PAXLOVID is contraindicated with drugs that are potent CYP3A inducers where significantly reduced nirmatrelvir or ritonavir plasma concentrations may be associated with the potential for loss of virologic response and possible resistance. PAXLOVID cannot be started immediately after discontinuation of any of the following medications due to the delayed offset of the recently discontinued CYP3A inducer:

- Anticancer drugs: apalutamide
- Anticonvulsant: carbamazepine, primidone, phenytoin
- Cystic fibrosis transmembrane conductance regulator potentiators: lumacaftor/ivacaftor
- Herbal Products: St. John's Wort (*hypericum perforatum*)

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

Risk of Serious Adverse Reactions Due to Drug Interactions: Initiation of PAXLOVID, a CYP3A inhibitor, in patients receiving medications metabolized by CYP3A or initiation of medications metabolized by CYP3A in patients already receiving PAXLOVID, may increase plasma concentrations of medications metabolized by CYP3A. Initiation of 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

Consult Table 1 of the Fact Sheet for Healthcare Providers for clinically significant drug interactions, including contraindicated drugs. Drugs listed in Table 1 are a guide and not considered a comprehensive list of all possible drugs that may interact with PAXLOVID. 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.

Hypersensitivity reactions have been reported with PAXLOVID including urticaria, angioedema, dyspnea, mild skin eruptions, and pruritus. Cases of anaphylaxis, TEN, and Stevens-Johnson syndrome have also been reported with components of PAXLOVID (refer to NORVIR labeling). If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue PAXLOVID and initiate appropriate medications and/or supportive care.

Hepatotoxicity: Hepatic transaminase elevations, clinical hepatitis, and jaundice 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.

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.

Adverse events in the PAXLOVID group ($\geq 1\%$) that occurred at a greater frequency (≥ 5 subject difference) than in the placebo group were dysgeusia (6% and $< 1\%$, respectively), diarrhea (3% and 2%), hypertension (1% and $< 1\%$), and myalgia (1% and $< 1\%$). The proportions of subjects who discontinued treatment due to an adverse event were 2% in the PAXLOVID group and 4% in the placebo group.

The following adverse reactions have been identified during post-authorization use of PAXLOVID. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Immune System Disorders: Hypersensitivity reactions

Gastrointestinal Disorders: Abdominal pain, nausea

General Disorders and Administration Site Conditions: Malaise

Required Reporting for Serious Adverse Events and Medication Errors: The prescribing healthcare provider and/or the provider's designee is/are responsible for mandatory reporting of all serious adverse events and medication errors potentially related to PAXLOVID within 7 calendar days from the healthcare provider's awareness of the event.

Submit adverse event and medication error reports to FDA MedWatch using one of the following methods:

- Online: <https://www.fda.gov/medwatch/report.htm>
- Complete and submit a postage-paid **FDA Form 3500** and returning by mail/fax
- Call 1-800-FDA-1088 to request a reporting form

In addition, please provide a copy of all FDA MedWatch forms to: <http://www.pfizersafetyreporting.com/> or by fax (1-866-635-8337) or phone (1-800-438-1985).

PAXLOVID is an inhibitor of CYP3A and may increase plasma concentrations of drugs that are primarily metabolized by CYP3A. Co-administration of PAXLOVID with drugs highly dependent on CYP3A for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening events is contraindicated. Co-administration with other CYP3A substrates may require a dose adjustment or additional monitoring.

Nirmatrelvir and ritonavir are CYP3A substrates; therefore, drugs that induce CYP3A may decrease nirmatrelvir and ritonavir plasma concentrations and reduce PAXLOVID therapeutic effect.

Pregnancy: There are no available human data on the use of nirmatrelvir during pregnancy to evaluate for a drug associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Published observational studies on ritonavir use in pregnant women have not identified an increase in the risk of major birth defects. Published studies with ritonavir are insufficient to identify a drug associated risk of miscarriage. There are maternal and fetal risks associated with untreated COVID-19 in pregnancy.

Lactation: There are no available data on the presence of nirmatrelvir in human or animal milk, the effects on the breastfed infant, or the effects on milk production. A transient decrease in body weight was observed in the nursing offspring of rats administered nirmatrelvir. Limited published data reports that ritonavir is present in human milk. There is no information on the effects of ritonavir on the breastfed infant or the effects of the drug on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for PAXLOVID and any potential adverse effects on the breastfed infant from PAXLOVID or from the underlying maternal condition. Breastfeeding individuals with COVID 19 should follow practices according to clinical guidelines to avoid exposing the infant to COVID 19.

Contraception: Use of ritonavir may reduce the efficacy of combined hormonal contraceptives. Advise patients using combined hormonal contraceptives to use an effective alternative contraceptive method or an additional barrier method of contraception.

Pediatrics: PAXLOVID is not authorized for use in pediatric patients younger than 12 years of age or weighing less than 40 kg. The safety and effectiveness of PAXLOVID have not been established in pediatric patients. The authorized adult dosing regimen is expected to result in comparable serum exposures of nirmatrelvir and ritonavir in patients 12 years of age and older and weighing at least 40 kg as observed in adults, and adults with similar body weight were included in the trial EPIC-HR.

Systemic exposure of nirmatrelvir increases in renally impaired patients with increase in the severity of renal impairment. No dosage adjustment is needed in patients with mild renal impairment. In patients with moderate renal impairment (eGFR \geq 30 to $<$ 60 mL/min), reduce the dose of PAXLOVID to 150 mg nirmatrelvir and 100 mg ritonavir twice daily for 5 days. Prescriptions should specify the numeric dose of each active ingredient within PAXLOVID. Providers should counsel patients about renal dosing instructions. PAXLOVID is not recommended in patients with severe renal impairment (eGFR $<$ 30 mL/min based on CKD-EPI formula) until more data are available; the appropriate dosage for patients with severe renal impairment has not been determined.

No dosage adjustment of PAXLOVID is needed for patients with either mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment. No pharmacokinetic or safety data are available regarding the use of nirmatrelvir or ritonavir in subjects with severe hepatic impairment (Child-Pugh Class C); therefore, PAXLOVID is not recommended for use in patients with severe hepatic impairment.

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