MEDICINE

Paxlovid, Advertised for Mass Use, Has Contraindications With Hundreds of Drugs

COVID-19 treatment pill Paxlovid in boxes at Misericordia hospital in Grosseto, Italy, on Feb. 8, 2022. (Jennifer Lorenzini/Reuters)

By Marina Zhang

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One of the most robustly campaigned and well-known drugs for treating COVID is Paxlovid. Yet the drug's limited clinical studies and numerous drug interactions raise questions of safety for COVID patients.

Approved for Emergency Use Authorization (EUA) in December 2021 and promoted by the Food and Drug Administration (FDA), health officials, and politicians alike, Paxlovid is fast becoming the one-track drug for early COVID treatment.

Paxlovid's EPIC-HR clinical trial, sponsored by Pfizer, revealed that those who took the drug were 89 percent less likely to develop severe COVID than those who took a placebo. Those who took Paxlovid also had lower quantities of the SARS-CoV-2 virus detected after five days of treatment.

With such impressive results, the FDA made swift moves to promote the prescription of Paxlovid—extending to pharmacists the authority to prescribe Paxlovid beginning in July 2022.

This raised concerns and disapproval from some clinicians.

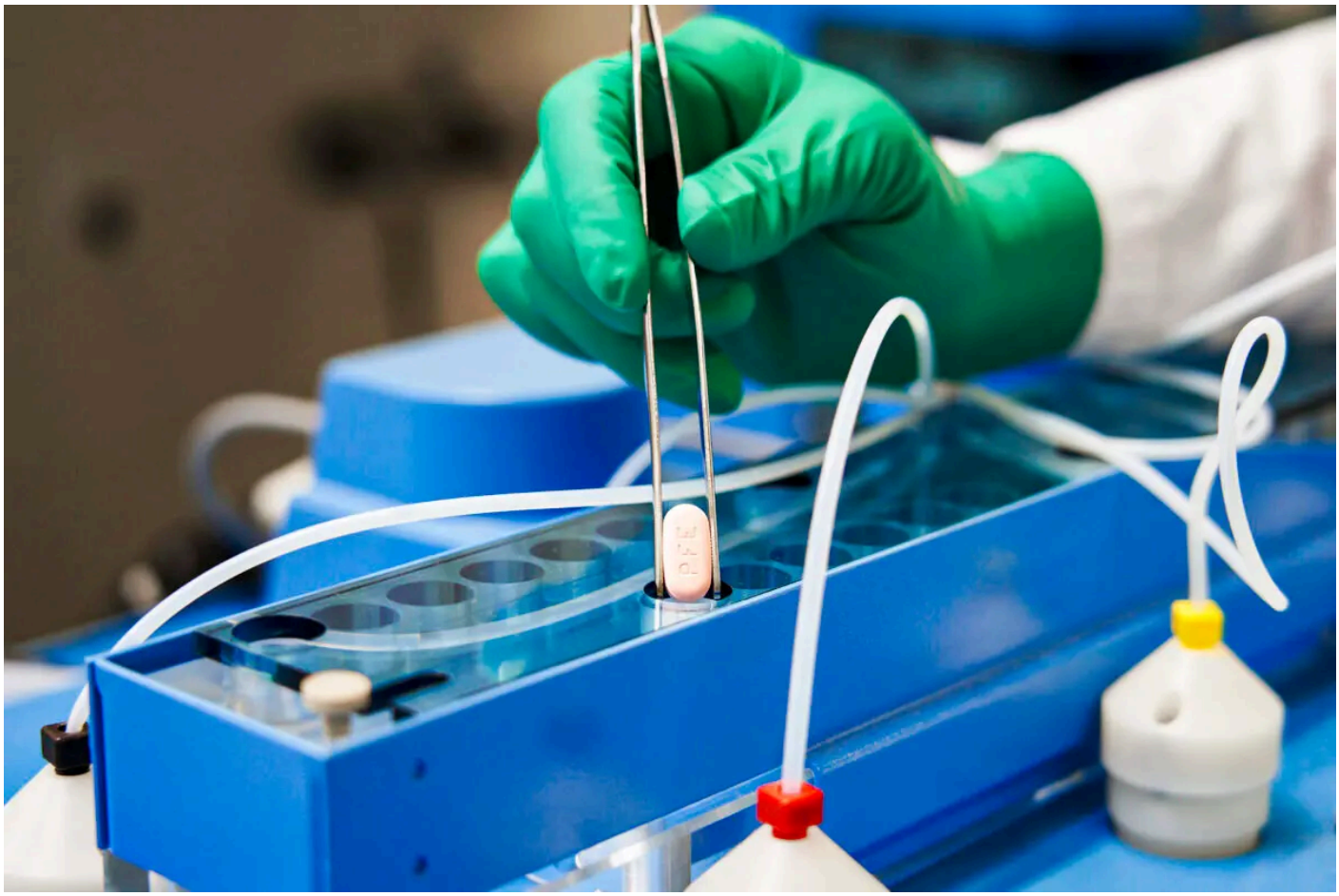
Though laws in some states allow pharmacists to prescribe a limited number of drugs, such as contraceptives and naloxone, prescribing medication is primarily the responsibility of doctors.

Diagnostic and interventional cardiologist Dr. Jack Askins from Wichita Heart Center told The Epoch Times that it was unprecedented for pharmacists to be given authority to prescribe EUA medication.

Physicians are familiar with their patient's medical histories, intolerances, allergies, and other medications the patient is taking and would be able to avoid potentially dangerous adverse effects from drug interactions. Though pharmacists can access medical records electronically, a study wrote that "pharmacists' access to patient information is not adequate for competent prescribing."

The FDA has required pharmacists who prescribe Paxlovid to have access to the patient's medical history and a list of all the drugs the patient is taking.

Pharmacists taking on the role of physicians through their authority to prescribe Paxlovid is only one aspect of clinicians' concerns about the drug; the more significant problem is a multitude of potential drug interactions.



A Pfizer technician handles the company's COVID-19 pill, known as Paxlovid, in a file photograph. (Pfizer via AP)

Drug Mechanism and Interactions

Askins wrote in his Substack article published Oct. 16, 2022, that he had "never seen a drug with that many drug interactions and potential incompatibilities."

Paxlovid can interact with at least 43 different classes of drugs and over 550 active drug ingredients. Some of these interactions can be

severe and potentially dangerous, some mild.

A single dose of Paxlovid contains three pills: two pink and one white. The pink pills are nirmatrelvir tablets, patented by Pfizer; the white pill is ritonavir, a medication for HIV.

Nirmatrelvir is an antiviral; it works early during COVID-19 infections by stopping the virus from replicating.

Nirmatrelvir targets a viral protein in the SARS-CoV-2 virus that is common to all coronaviruses. This viral protein, known as Mpro, helps to assemble the viral components into an infectious virus. Nirmatrelvir stops the action of Mpro by attaching itself to it so that the viral protein can no longer form functional viruses.

Ritonavir is also an antiviral, but it does not target coronaviruses. The job of ritonavir is to boost the actions of nirmatrelvir.

When ingested, ritonavir will bind and stop the action of an enzyme named cytochrome P4503A4 (CYP3A4) and prevent the body's own proteins from breaking down and metabolizing nirmatrelvir.

Problems arise from here.

Many classes of drugs work by blocking or activating the actions of CYP3A4. If a person takes these drugs while taking Paxlovid, the other drugs' effects can be neutralized or increased, both potentially dangerous.

According to a statement published by the FDA, Paxlovid interacts with various drugs, including cardiovascular drugs, narcotics, antipsychotics, anticoagulants, anti-HIV drugs, and many others.

"This contraindication list is significant because it means many patients with heart conditions, arrhythmias, high cholesterol, epilepsy, depression, and many other common diseases in supposedly high-risk COVID-19 patients cannot take the 'game-changer,'" emergency doctor Dr. John Hughes wrote to The Epoch Times.

A particularly paradoxical aspect of Paxlovid is that the clinical data shows it seems to work the best for older adults. However, people over 65 are also most at risk of drug interactions, as they are likely to be taking multiple prescription drugs.

This was demonstrated in a a recently published study that evaluated over 62,000 hospitalized COVID-19 patients in Paris. These hospitalized patients received a positive COVID test between January 2020 and November 2021. Given that Paxlovid was authorized and marketed in 2022, none of the patients received Paxlovid.

However, even if Paxlovid had been available, many would likely not have been able to use the medication, as half (50.7 percent) of the patients were on other medications that would contraindicate with the antiviral, or had organ deficiencies.

Askins noted that many of the anticoagulants and cardiovascular drugs he prescribes for his patients would interact with Paxlovid, and thus one of the drugs would need to be excluded.

“Some of the antiarrhythmic drugs can be dangerous if given concurrently with the Paxlovid,” Askins said.

In antiarrhythmic drugs with the active ingredient amiodarone, dronedarone, flecainide, propafenone, or quinidine, Paxlovid can increase the pharmacologic effects of these drugs. Since antiarrhythmic drugs slow down and reset heart rates, an enhanced effect of these drugs can lead to lower heart rates, reduced blood pressure, and cardiac arrest.

In certain anticoagulants with the active ingredient apixaban, dabigatran, or rivaroxaban, Paxlovid increases the risk of bleeding if used concomitantly.

Paxlovid can increase the effects of antipsychotics such as lurasidone and pimozide, both prescribed for schizophrenia, and may lead to potentially fatal cardiac arrhythmias.

Askins noted that Paxlovid also enhances the effects of fentanyl, a powerful opioid. Fentanyl's potency makes the drug extremely dangerous when overdosed, as it can cause death from reduced breathing.

The FDA has recommended that patients either go off their usual medications or take Paxlovid in conjunction with their medications, depending on the severity of the interactions. Patients' physicians should observe them for any adverse effects of taking Paxlovid.

In the FDA's statement "Fact Sheet for Healthcare Providers," the agency recommended that physicians follow patients' medical history; for prescribing pharmacists, only those with at least 12 months of a patient's medical history can prescribe.

However, Askins has become aware that some of his emergency department colleagues may prescribe Paxlovid without adequate knowledge of the potentially dangerous drug contraindications.

Hughes also said that some clinicians are unaware of Paxlovid drug interactions.

"Just last week, an elderly man with a serious heart arrhythmia on amiodarone came to my ER to get Paxlovid. But I couldn't prescribe it because of the medication he was on," Hughes wrote to The Epoch Times, "His cardiologist hadn't even paid attention to his medication list before sending him to the ER."

"For a disease killing almost nobody now, a severe drug interaction with heart and other common medications begs for a serious risk-benefit analysis," Hughes added.

Askins highlighted that the past two years of extensive green-lighting of experimental drugs by the FDA through EUAs have made experimental drugs and medical interventions a "new normal" for clinicians and patients.

"I think one of my big concerns about the last few years is this emergency use authorization," said Askins.

Before 2020, EUA was rarely implemented. But since the pandemic, the FDA has authorized EUAs at least 600 times on vaccinations, pharmaceuticals, medical equipment, and tests.

Apart from the drug interactions, Paxlovid is not recommended for people with liver or kidney insufficiency as it can cause toxicity.

Pharmacist Michael Lam said that Paxlovid's side effect of dysgeusia, known as "Paxlovid mouth," also seems to impact patients' drug adherence.

The ritonavir in the Paxlovid leaves a bitter or metallic taste in the mouth that can last for hours.

Lam took Paxlovid when he developed COVID and went off it after two days. "You take it two times a day," described Lam. "So it lasted like six hours in a day [during which] you have that bitterness in your mouth."

The Pfizer clinical trials showed that 5.6 percent of the people reported dysgeusia to describe the altered taste. However, Lam wondered if the actual proportion of people experiencing this side effect is higher.

Effectiveness: More Research Needed

Despite being the "go-to" drug for COVID-19, the actual effectiveness of Paxlovid is questionable.

The clinical study that granted Paxlovid's approval came from the abovementioned EPIC-HR study. The study was conducted with unvaccinated and previously uninfected COVID patients with a high risk of severe COVID disease.

Given that 68 percent of the American population has now been vaccinated and most people have been exposed to the virus through previous infections, the group studied in the Paxlovid trial does not represent most of the current population.

The study was conducted from July 2021 to December 2021, when the dominant COVID-19 strain was Delta, but the common strain now is Omicron, known to be the least pathogenic of all COVID-19 viral strains.

Pfizer later conducted another study from August 2021 to July 2022, likely coinciding with the Omicron wave.

This study was named EPIC-SR and was conducted on people with a "standard risk" of developing severe COVID. The study also accepted vaccinated people and would be the most reflective of the current population. Yet it did not meet its primary endpoint, which is sustained alleviation in COVID symptoms for four days after a five-day Paxlovid treatment.

The trial was terminated in June 2022, as even the secondary endpoint could not be met. The secondary endpoint was reduced relative risk of hospitalization and deaths, but standard risk patients have a very low risk of hospitalizations and deaths, and the study could not reach a statically significant outcome.

"That's what it was, basically a fail," said Lam. "In terms of efficacy, it is debatable for COVID."

Researchers conducting a study in Israel on the effects of Paxlovid for severe Omicron infections found that in the group that took Paxlovid, only patients who were 65 years of age or older had significantly lower rates of hospitalizations and deaths.

For people younger than 65, the study found no benefits. This finding raises further questions on the actual effectiveness of the drug.

Other studies conducted in Hong Kong and Israel also found that Paxlovid was associated with lower risks of hospitalization and death. In each of these studies, over 50 percent of the patients on Paxlovid were over 60 years of age (1, 2).

Therefore, more research is needed to determine the drug's effectiveness, especially in younger people.

Askins and Hughes also noted that politicians and health agency officials, including President Joe Biden and the head of the National Institute of Allergy and Infectious Diseases (NIAID), Dr. Anthony Fauci, experienced reinfections with COVID-19 after taking Paxlovid, highlighting the risk of possible rebounds.

The Centers for Disease Control and Prevention (CDC) issued a rebound warning on Paxlovid on May 24, 2022. Since then, studies that evaluate rebound incidence have dished out contradicting and varied results.

A Mayo Clinic study published in June 2022 reported that less than one percent of patients taking Paxlovid experienced rebound symptoms.

One pre-print (not yet peer-reviewed) report published in June 2022 described a 3.5 to 5.4 percent rebound rate in people who took Paxlovid.

Another pre-print study published in November 2022 found that of 127 patients treated with Paxlovid, 14 percent tested positive for COVID after a previous negative test, while in the group of patients who did not take Paxlovid, this number was 9 percent.

Additionally, among the people who took Paxlovid, around 19 percent reported a rebound in COVID symptoms. This number was 7 percent in the control group who did not take Paxlovid.

Nevertheless, Askins said that most of his emergency physician colleagues report that patients who take Paxlovid within the first five days of a COVID infection generally experience a symptom alleviation by the third or fourth day after starting the drug.

Lam and Hughes each noted that given Omicron is significantly less severe than previous Alpha and Delta strains, the question is if patients are getting better from the drug or because the disease is so mild. Most with Omicron “get better in three to four days regardless of whether they took anything for it,” stated Hughes.

Gastroenterologist Dr. Sabine Hazan has told The Epoch Times that, in her clinic, for people with a healthy constitution, rather than using medications, she would primarily focus on supplementing their immune system with vitamins C and D so patients can fight off the infection themselves.

Holistic and integrative medicine physician Dr. Saleeby Yusuf has recommended that COVID patients who turn to supplements should use pharmaceutical-grade versions rather than easily accessible supplements from supermarkets, as the pharmaceutical-grade versions would generally be more effective with greater bioavailability.

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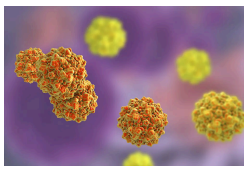

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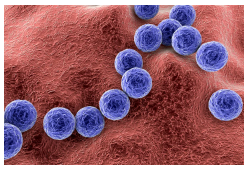

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