What doctors wish patients knew about COVID-19 oral antivirals

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Since its emergence, the Omicron variant of SARS-CoV-2 has led to a significant increase in COVID-19 cases. This rise in COVID-19 cases has strained hospitals and emergency departments across the United States, increasing the demand for treatments. While there is an ongoing need for people to get vaccinated—and boosted—against COVID-19, two antiviral oral treatments are available in limited supplies, but patient confusion still remains about who is eligible and how these treatments work.

Last month, the two oral antivirals—Paxlovid (PDF) and molnupiravir (PDF)—were authorized for outpatients with mild to moderate COVID-19 under emergency use authorization (EUA) from the Food and Drug Administration (FDA). Treatment with these oral antivirals must begin within five days of symptom onset to maintain product efficacy. Learn what COVID-19 treatments are FDA authorized, and what works.

The AMA’s What Doctors Wish Patients Knew™ series provides physicians with a platform to share what they want patients to understand about today’s health care headlines, especially throughout the COVID-19 pandemic.

In this installment, AMA member Elisa Choi, MD, an internist and infectious disease specialist, discusses what patients need to know about COVID-19 antiviral pills.

There are two options

“The first one is a combination of pills more commonly known Paxlovid,” said Dr. Choi. “It’s a combination of nirmatrelvir tablets and a pharmacologic boosting pill called ritonavir.”

“There's also a second pill called molnupiravir,” she added, noting that when this antiviral enters the bloodstream, it blocks the ability of the SARS-CoV-2 virus to replicate.”

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“For Paxlovid, it is currently authorized for use in all adult patients and in pediatric patients who are 12 years or older who weigh at least 88 pounds,” said Dr. Choi. “Molnupiravir is only authorized in adult patients who are 18 or older because molnupiravir has potential to affect bone and cartilage growth, which can be detrimental to the pediatric population.”

They prevent hospitalization or death

While data is still limited, “in one study that was cited in the EUA, Paxlovid was found to reduce the proportion of people with COVID-19 related hospital admission or death by about 88% compared to the placebo treatment arm,” said Dr. Choi. “And that is for those patients who received the treatment within five days of the onset of symptoms.”

“The second medication, molnupiravir, has a lower efficacy rate compared to Paxlovid,” she said. “The rate of reduced hospitalization or death was about 30% compared to the placebo group.”

The pills are not for pre-exposure

“Both of these oral antivirals are used only for treatment of patients who have confirmed COVID-19 infection,” said Dr. Choi. “These are not for any prophylaxis—either as a pre-exposure or post-exposure—and are only for treatment of symptoms.”

“Even with COVID-19 infection, the EUA for these two medications really only covers those who are non-hospitalized, symptomatic adults who have mild to moderate COVID-19 illness” and who are at high risk for progression to severe COVID-19, including hospitalization or death, she said.

Severe COVID-19 needs different care

“The studies were looking at patients who were considered mild to moderate COVID-19 symptoms,” said Dr. Choi, adding that “if a patient has severe COVID symptoms, they probably will need a higher level of care.”

“Paxlovid and molnupiravir are not indicated for somebody who has severe COVID-19 as these medications are intended for outpatient care,” she said. For those with severe COVID-19 infection, “they likely will need oxygen support or more intense clinical monitoring.”
“By necessity, those patients with severe COVID-19 infection will need a high level of care that will likely require hospital admission and would not be managed as outpatients,” Dr. Choi added.

**Paxlovid is three tablets**

As a combination of pills, Paxlovid “comes as both nirmatrelvir and ritonavir tablets,” said Dr. Choi. “For a full dose of Paxlovid, it would be two tablets of nirmatrelvir, which would equal a total of 300 milligrams taken together with one tablet of ritonavir.”

“It would be three tablets total and they would be taken by mouth two times a day for a total duration of five days,” she said, noting that “hopefully when people review the prescriptions, the directions are clear about that because many people may not be used to taking a medication in combination with a pharmacologic booster pill, which is what Paxlovid is.”

“The ritonavir is acting as a pharmacologic boosting medication for the nirmatrelvir,” Dr. Choi added.

**Molnupiravir is four capsules**

“The second antiviral, molnupiravir, is a dose of 800 milligrams total,” said Dr. Choi. That means a patient is taking “four capsules of 200 milligrams each.”

“For molnupiravir, the four capsules are taken by mouth every 12 hours or twice a day for five days and not longer,” she said.

**Some side effects are expected**

“What appears to be the most common side effects with Paxlovid are altered taste or potentially loss of taste,” said Dr. Choi. “There also is the gastrointestinal side effect of diarrhea, and there can be myalgia, which means muscle aches.”

“For molnupiravir, similarly it does have some gastrointestinal side effects, namely diarrhea and nausea as well as some reported adverse side effects of dizziness.”

**Share what medications you’re taking**
“Paxlovid, because it has that boosting medication ritonavir as one of its components, creates potential drug interactions,” said Dr. Choi. “For anybody who receives a prescription for Paxlovid, they should make sure that their physician reviews all of the patient’s other medications that they are taking.”

“That includes over-the-counter medications and supplements or other non-prescription medications that they take, to check for any drug interactions,” she added, noting “it’s easiest to do that through certain drug interaction tools for which physicians will have access.”

“Many patients don’t think to mention medications that they’re taking that are non-prescription or that may be supplements, but everything should be mentioned to their physicians,” said Dr. Choi.

**Supplies are limited**

“The demand is just outstripping the supply for these oral antivirals right now due to the quickly spreading Omicron variant of COVID-19,” said Dr. Choi, noting that “most of the access for these medications are being directed by the state health departments to specific local health departments, pharmacies, clinics, hospitals and physician offices.”

“Not all physicians will be able to get these medications on demand for their patients—there’s a lot of state-to-state variability,” she said.

**Consult your doctor if pregnant**

“Molnupiravir is not recommended for use during pregnancy because of a potential for fetal harm in pregnant persons,” said Dr. Choi. “The nuance there, though, is if the patient’s physician has determined that the benefit of being treated with the molnupiravir would outweigh the risk for the patient, then there ought to be a discussion of the potential benefits versus the potential risks, of taking this medication in the pregnant patient with COVID-19 infection.”

“While molnupiravir is generally not recommended during pregnancy, this is an evolving area and treatments for COVID-19 infection are limited,” she added. “There needs to be good communication about the risks and benefits of molnupiravir, with clear documentation by the physician that those risks and benefits were discussed with the patient.”

“For Paxlovid, at this juncture, there isn’t that same prohibition against use in pregnancy,” said Dr. Choi. “Patients who are pregnant should, regardless, discuss the risks and benefits of any treatments for COVID-19 infection with their physicians so that the currently available evidence can be
Not everyone should take these pills

“For patients who are younger than 18, molnupiravir is not authorized at this point and should not be considered as a therapeutic option for pediatric patients with mild to moderate COVID-19,” said Dr. Choi. “Pediatric patients under the age of 12 or who weigh less than 88 pounds should not be prescribed Paxlovid.”

“Other groups of patients who will need to be careful about using these antivirals are those who have severe liver impairment or liver disease,” she said. “The other caution is for people who have severe kidney disease, at least until more medical data and evidence are acquired.”

Get vaccinated and boosted

“I can’t stress enough that these oral antivirals are not a substitute for getting a COVID-19 vaccine. We have so much more vaccine available than antivirals, currently, and prevention is always preferable to treatment,” said Dr. Choi. “If people haven’t been fully COVID-19 vaccinated, they need to get up to date with their COVID-19 vaccines,” which means two doses of a mRNA vaccine and a booster shot.

“If they have received the primary series of COVID-19 vaccine but have not received their COVID-19 booster vaccine, they need to get their booster dose” when eligible,” she said. “Those are the first steps to take, even before thinking about anything related to the antivirals because the vaccines work and are very safe.”

“The COVID-19 vaccines and boosters work against the Omicron variant, and they will help prevent a person who gets infected with COVID-19 from suffering severe enough illness that they will need hospitalization, or—worst case—die,” said Dr. Choi. “In no way are these antivirals a substitute for the biggest priority right now, which is getting as many people vaccinated and boosted as completely as possible against COVID-19.”

Visit the AMA COVID-19 resource center for clinical information, guides and resources, and updates on advocacy and medical ethics.