



What doctors wish patients knew about COVID-19 oral antivirals

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The federally declared COVID-19 public health emergency has ended, but the SARS-CoV-2 virus is still circulating. Previously, there was a rise in cases due to the Omicron variant followed by its subvariants XBB.1.5, EG.5 and FL.1.5.1, among others. And while there is an ongoing need for people to stay up to date on their COVID-19 vaccine, two antiviral oral treatments are available. Yet patient confusion remains about who is eligible and how these treatments work.

Two oral antivirals—Paxlovid and molnupiravir—are available for treatment of COVID-19. Treatment with these oral antivirals must begin within five days of symptom onset to maintain product efficacy.

Paxlovid—a combination of nirmatrelvir tablets and ritonavir—is the first oral antiviral pill to be approved by the Food and Drug Administration for the treatment of mild to moderate COVID-19 in adults who are at high risk for progression to severe illness, including hospitalization or death. It is also authorized for use in children 12 or older who are at risk of severe outcomes from COVID-19. About 250,000 courses of Paxlovid are being administered per week.

Molnupiravir is also authorized for adult outpatients with mild to moderate COVID-19 who are at high risk for progression to severe COVID-19, including hospitalization or death.

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.

In this installment, AMA member Elisa Choi, MD, an internist and infectious diseases physician, 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 as 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 said, noting that when this antiviral “enters the bloodstream, it blocks the ability of the SARS-CoV-2 virus to replicate.”

“For Paxlovid, it is currently approved for use in all adult patients and authorized 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

“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, these two medications really only cover 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,” she said.

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“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.

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," 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."

Breastfeeding is also not recommended during treatment with molnupiravir and for four days after the final dose.

"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 discussed."

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 against COVID-19

“I can't stress enough that these oral antivirals are not a substitute for getting a COVID-19 vaccine. ... 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.”

Those who are 6 months or older are eligible to receive the updated COVID-19 vaccine and should get it as soon as possible. This is a universal recommendation, similar to the flu vaccine.

For those 5 or older, a single dose of the updated vaccine is all they need, regardless of previous vaccination status and even if they've never had any previous COVID-19 vaccinations. This is because anyone 5 or older likely has some COVID-19 immunity, either through previous vaccination, infection or both.

Meanwhile, those who are immunocompromised need a three-dose prime and at least one updated shot. They can also get additional doses if their physician recommends it. Younger children—6 months to 4 years old—may need a multi-dose regimen, with two doses of Moderna, or three doses of Pfizer. The updated vaccine may be an addition to or part of that initial series.

“Those are the first steps to take, even before thinking about anything related to the antivirals because the vaccines work and are very safe,” Dr. Choi said. “The COVID-19 vaccines ... 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.”

“In no way are these antivirals a substitute for the biggest priority right now, which is getting as many people vaccinated ... as completely as possible against COVID-19,” she said.

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