

Paxlovid side effects, treatment timelines and more with John Farley, MD, MPH

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In today's COVID-19 Update, AMA Chief Experience Officer Todd Unger discusses what physicians and patients need to know about Paxlovid with John Farley, MD, MPH, director of the Office of Infectious Diseases in the Center for Drug Evaluation and Research's Office of New Drugs at the FDA.

Find more information on Paxlovid from the FDA.

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Speaker

- John Farley, MD, MPH, director, Office of Infectious Diseases in the Center for Drug Evaluation and Research, Office of New Drugs, FDA

Transcript

Unger: Hello, this is the American Medical Association's COVID-19 Update video and podcast. Today we're discussing what physicians and patients need to know about Paxlovid with Dr. John Farley, director of the Office of Infectious Diseases in the Center for Drug Evaluation and Research's Office of New Drugs at the FDA in Silver Spring, Maryland. I'm Todd Unger, AMA's chief experience officer in Chicago.

Dr. Farley, thank you so much for joining us again, heading to the way back machine because the last time that we talked was about Ivermectin and how it should not be used to treat COVID. Fortunately, this time we're talking about Paxlovid, which has been proven to help in the treatment of COVID. Let's start by talking about some of the benefits that we've seen from Paxlovid so far.

Dr. Farley: Thanks, Todd. And I appreciate the opportunity to participate in this AMA COVID-19 Update today. The benefit of a five-day treatment course of Paxlovid was demonstrated in the clinical trial that supported the emergency use authorization. That authorization was back in December 2021. The trial was called EPIC-HR and enrolled over 2000 non-hospitalized patients with mild-to-moderate COVID-19. And the results showed that among non-hospitalized patients at high risk of progression to severe disease, treatment with Paxlovid reduced the risk of hospitalization or death by 88%.

Unger: That's an incredible number. When we think about who Paxlovid should be given to, talk a little bit about that and the ideal timeframe to get maximum benefit.

Dr. Farley: Sure. Paxlovid was authorized for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients. Now, the pediatric patients had to be 12 years of age and older and weigh at least 40 kilograms. All patients with a positive result of a direct SARS-CoV-2 viral test and who are at high risk for progression to severe COVID-19, including hospitalization or death. And Paxlovid treatment should be initiated as soon as possible after diagnosis and within five days of symptom onset.

Unger: Is there anyone that Paxlovid should not be given to? Talk to us a little bit about contraindications that physicians should be aware of.

Dr. Farley: Sure. Paxlovid is in the protease inhibitor drug class. And I think the biggest challenge for health care providers is assessing and managing potential drug-drug interactions. Paxlovid contains nirmatrelvir and ritonavir, and ritonavir is a strong inhibitor of cytochrome P450.

Now, other drugs the patient may be taking for which there may be clinically relevant drug interactions fall into different categories. So there are some for which management strategies are not possible or the risks of holding the medication usually outweighs the benefit. There are many for which temporarily holding the medication during Paxlovid treatment, and perhaps for a few days after, may be clinically appropriate. And then there are others where either adjusting the concomitant medication dose or monitoring for side effects might be clinically appropriate. So for me, this challenge underscores the critical role that primary care providers play in the COVID response. You know your patient the best and are really in the best position to make a decision about their medication management during a COVID infection.

Now, there are a number of tools for health care providers focused on drug interaction management. FDA recently updated the health care provider fact sheet for Paxlovid and developed a Paxlovid

eligibility screening checklist that may be helpful in a busy practice setting. The NIH COVID-19 treatment guidelines panel just released more detailed information on Paxlovid drug interactions to guide providers. And lastly, the University of Liverpool has an online tool that provides even more detailed recommendations by drug.

Unger: What about side effects? What should physicians be telling patients to watch for or be aware of?

Dr. Farley: Sure. Like many medications, we observed rare hypersensitivity reactions in the trial. And if these occur, providers would need to discontinue Paxlovid and treat the hypersensitivity symptoms. Now, ritonavir can cause transaminase liver function test elevations and Paxlovid is not recommended for patients with severe hepatic impairment. For those managing patients with uncontrolled HIV infection, so these are HIV patients who do not have an undetectable viral load, Paxlovid use could lead to development of protease inhibitor resistance. Other side effects seen in the trial, and these are quite common with this protease inhibitor class, there are metallic taste on the tongue, as well as diarrhea and loose stools. And you should warn your patients about that.

Unger: Well, in addition to the side effects that you outline, there have been reports of people rebounding after receiving Paxlovid, where they test negative and they feel better quickly but then they test positive again in a couple days and risk infecting others or find themselves with a continuing symptomatic infection. Are you seeing this? And what do physicians need to be telling patients to watch out for if they do suspect that they're experiencing a rebound infection?

Dr. Farley: The FDA is working with the sponsor and other government agencies to better understand these reports of some patients developing recurrent COVID-19 symptoms after completing a treatment course of Paxlovid. What we know so far is that those patients reported with recurrent symptoms did not progress to needing hospital admission. In the Paxlovid clinical trial, we observed some patients who had one or more positive SARS-CoV-2 PCR tests after testing negative or an increase in the amount of SARS-CoV-2 detected by PCR after they completed their treatment course. Important to note is that this finding was observed in patients treated with the drug, as well as patients who received placebo. And the finding was not associated with an increased occurrence of hospitalization or death or the development of drug resistance. Lastly, health care providers and patients should refer to CDC recommendations regarding patient isolation and should wear a mask and isolate if they have any symptoms, regardless of whether or not they have been treated with an antiviral agent.

Unger: Well, based on that, do you expect any changes to dosing? And should physicians prescribe a second round if needed?

Dr. Farley: Based on what we observed in the clinical trial, we're still not sure whether this is part of the natural history of disease rather than drug-related. These reports don't change the conclusions from the Paxlovid clinical trial, which demonstrated a marked reduction in hospitalization and death,

nor is there data at this time that would support a general change in clinical management, such as a second course of treatment.

Unger: Dr. Farley, there has also been some confusion about what's needed prior to giving a Paxlovid prescription. Do patients need proof of a positive COVID test before they can be given Paxlovid? And if so, does it have to be a PCR test or will an at-home antigen test be enough?

Dr. Farley: Yeah. There are now many rapid antigen tests which are authorized for home use. And as a care provider, it's a good idea to encourage your patient to have a stock of these at home. I certainly do. Patients in the authorized population who report a positive home test result from a rapid antigen diagnostic test to their provider are eligible for Paxlovid under the EUA. A positive result on a PCR test also meets the requirement under the EUA to have a positive test result. But confirmation of a positive home rapid antigen test with additional direct SARS-CoV-2 viral testing like a PCR, that's not required.

Unger: We've also heard some patients report that physicians are requiring a renal function test prior to prescribing. Is this necessary?

Dr. Farley: Renal status is an important consideration, as a dose adjustment is recommended for moderate renal impairment. That's an EGFR between 30 and 60 milliliters per minute. And Paxlovid is not recommended at this time in patients with severe renal impairment. That's a GFR of less than 30 milliliters per minute. Of note, Paxlovid is now supplied in two different dose packs for the pharmacy, one for standard dosing and one for moderate renal impairment. So you can write that in a prescription.

Health care providers may rely on patient history and access to patient's health records to make an assessment regarding the likelihood of renal impairment. Providers may consider ordering a serum creatinine or calculating the estimated glomerular filtration rate for certain patients but that's based on assessment on a case-by-case basis. In my view, this again highlights the critical role primary care providers can play in the COVID-19 response, as you already know your patient's renal function status.

Unger: Dr. Farley, there was some talk early on about how Paxlovid was in short supply. The drug now seems to be widely available but many patients are still reporting that they're having trouble acquiring it and finding some physicians that are hesitant to prescribe. What can physicians do to help make this kind of access easier? And what would you tell physicians who might still have some concerns?

Dr. Farley: Sure. The Paxlovid supply has improved dramatically and it's now widely available at community pharmacies. The U.S. government maintains a web-based locator tool for COVID-19 therapeutics that lists community pharmacies that have Paxlovid in stock. They actually even tell you how many doses they have available. And there's a search icon there where one can enter the

patient's zip code, or the patient can enter it, and pharmacies are listed by proximity to the patient.

Unger: Paxlovid is currently authorized, as you mentioned before, through an EUA. Do we expect a full approval anytime soon? What do you think the next step is there?

Dr. Farley: For all the therapeutics authorized under EUA, our goal is to move toward full approval. But I don't have a timeline for Paxlovid that I can share at this time.

Unger: Any additional questions you'd like to address or confusion you want to clear up while we have the chance here?

Dr. Farley: I don't think so. You ask great questions, Todd.

Unger: Well, looking at the big picture, is Paxlovid a game-changer in COVID treatment? And what impact do you think or expect it will have on our pandemic response come the fall and winter, when we might see another surge?

Dr. Farley: I think Paxlovid and the other authorized or approved COVID-19 therapeutics are important tools to help reduce the risk of hospitalization for our high-risk patients and we're going to continue to need those. Time is of the essence with COVID-19 therapeutics and primary care providers are in the best position to use these tools, as patients can reach them easily, patients trust their provider and the provider knows their patients the best.

Unger: Where can physicians go to find out more detailed information about Paxlovid?

Dr. Farley: The FDA's EUA webpage will always have the most up-to-date information on Paxlovid and other authorized therapeutics.

Unger: Well, Dr. Farley, thank you so much for being here and providing all that important information about Paxlovid. That wraps up today's COVID-19 Update. We'll be back with another segment soon. For resources on COVID-19, make sure to visit [ama-assn.org/COVID-19](https://www.ama-assn.org/COVID-19). Thanks for joining us, and please take care.

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