Indian Health Service
National Pharmacy and Therapeutics Committee
Medication Update

June 5, 2023

FDA Approves First Oral Antiviral for Treatment of COVID-19 in Adults

On May 25th, 2023, the U.S. Food and Drug Administration (FDA) approved the oral antiviral Paxlovid® (nirmatrelvir tablets and ritonavir tablets, co-packaged for oral use) for the treatment of mild-to-moderate COVID-19 in adults at high risk for progression to severe COVID-19, including hospitalization or death. **Paxlovid® is the fourth drug—and first oral antiviral pill—approved by the FDA to treat COVID-19 in adults.**

Paxlovid®®, manufactured and packaged under the emergency use authorization (EUA) and distributed by the U.S. Department of Health and Human Services, will continue to be available to ensure ongoing access for adults, as well as treatment of eligible children 12-18 years of age who are not covered by the May 25th approval. Paxlovid® is not approved or authorized for use as a pre-exposure or post-exposure prophylaxis for prevention of COVID-19.

Safety and Efficacy Data:

The efficacy of Paxlovid® was primarily supported by the final results of the EPIC-HR clinical trial. EPIC-HR was a randomized, double-blind, placebo-controlled clinical trial studying Paxlovid® for the treatment of non-hospitalized symptomatic adults with a laboratory confirmed diagnosis of SARS-CoV-2 infection. Patients were adults 18 years of age and older with a pre-specified risk factor for progression to severe disease or were 60 years and older regardless of pre-specified chronic medical conditions. All patients had not received a COVID-19 vaccine and had not been previously infected with COVID-19. Paxlovid® significantly reduced the proportion of people with COVID-19 related hospitalization or death from any cause through 28 days of follow-up by 86% compared to placebo among patients treated within five days of symptom onset and who did not receive COVID-19 therapeutic monoclonal antibody treatment. In this analysis, 977 patients received Paxlovid®, and 989 patients received placebo, and among these patients, 0.9% who received Paxlovid® were hospitalized due to COVID-19 or died from any cause during 28 days of follow-up compared to 6.5% of the patients who received the placebo.

Benefit of Paxlovid® was also observed in patients with prior immunity to the virus that causes COVID-19. Among patients in EPIC-HR who were antibody-positive at trial enrollment, the risk of COVID-19-related hospitalization or death from any cause during 28 days of follow-up was 0.2% among the 490 patients treated with Paxlovid® compared with 1.7% of the 479 patients receiving placebo. EPIC-SR was another clinical trial that enrolled vaccinated patients with at least one risk factor for progression to severe COVID-19. Although not statistically significant, among these vaccinated patients, there was a reduction in the risk of COVID-19 related hospitalization or death from any cause.

EPIC-HR and EPIC-SR were randomized controlled trials and provide information about COVID-19 rebound. Data from these two trials showed that rebound in SARS-CoV-2 (RNA or virus) shedding or COVID-19 symptoms occurred in a subset of patients and happened in both the patients receiving Paxlovid® and the placebo. Based on the data currently available to the FDA, there is not a clear association between Paxlovid® treatment and COVID-19 rebound.

Because of the importance of reducing the risk of significant drug-drug interactions with Paxlovid®, the approved label and authorized Fact Sheet for Health Care Providers for the Paxlovid® EUA come with a boxed warning with instructions for prescribers. Prescribers should review all medications taken by the patient to

assess for potential drug-drug interactions and determine if other medicines that a patient may be taking require a dose adjustment, interruption and/or additional monitoring. Prescribers should consider the benefit of Paxlovid® treatment in reducing hospitalization and death, and whether the risk of potential drug-drug interactions for an individual patient can be appropriately managed.

In conjunction with the May 25th approval, the FDA is providing all prescribers with important information for prescribing Paxlovid® properly and safely, such as dosing instructions, potential side effects and information regarding drugs that may cause drug-drug interactions with Paxlovid®. The most common side effects of taking Paxlovid® include impaired sense of taste and diarrhea. Patients should discuss with their health care provider whether Paxlovid® is right for them.

Clinician Resources:

- Fact Sheet: Healthcare Providers
- Fact Sheet: Patients, Parents and Caregivers
- Paxlovid®® Eligibility Screening Checklist
- Paxlovid®® Drug Interaction Checker
- COVID-19 Test to Treat Locator
- Frequently Asked Questions: FDA EUA for Paxlovid®® (FDA)

References:
1. U.S. Food and Drug Administration. FDA Approves First Oral Antiviral for Treatment of COVID-19 in Adults. Published online May 25, 2023
2. Department of Health and Humans Services. Administration for Strategic Preparedness and Response. Paxlovid (nirmatrelvir co-packaged with ritonavir). Available online.