Optum Rx®

Paxlovid® (nirmatrelvir; ritonavir) – New drug approval

- On May 25, 2023, the FDA announced the approval of Pfizer's Paxlovid (nirmatrelvir; ritonavir), for the treatment of mild-to-moderate coronavirus disease 2019 (COVID-19) in adults who are at high risk for progression to severe COVID-19, including hospitalization or death.
    - Paxlovid is not approved for use as pre-exposure or post-exposure prophylaxis for prevention of COVID-19.
- 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 continued access for adults, as well as treatment of eligible children ages 12 to 18 who are not covered by today's approval.
    - Paxlovid remains available for eligible children, 12 to 17 years of age (and weighing at least 40 kg), under the existing EUA. Pfizer continues to gather pediatric data from the ongoing clinical trial, EPIC-Peds and intends to submit a supplemental New Drug Application to support the FDA approval of Paxlovid in children at a future date.
- The efficacy of Paxlovid was established in EPIC-HR, a randomized, double-blind, placebo-controlled study in non-hospitalized symptomatic adult patients with a SARS-CoV-2 infection. Patients were randomized to receive Paxlovid or placebo every 12 hours for 5 days. The primary endpoint was the proportion of patients with COVID-19 related hospitalization or death from any cause through day 28. The efficacy analysis was conducted in all treated patients with onset of symptoms ≤ 5 days who at baseline did not receive nor were expected to receive COVID-19 therapeutic monoclonal antibody treatment (N = 1,966).
    - For the primary endpoint, the relative risk reduction in the analysis population for Paxlovid compared to placebo was 86% (95% CI: 72%, 93%).
    - Among the analysis population, 0.9% who received Paxlovid were hospitalized due to COVID-19 or died from any cause compared to 6.5% of the patients who received the placebo (reduction relative to placebo -5.6; 95% CI: -7.3, -4.0).
- The FDA approval of Paxlovid was further supported by the results from a secondary endpoint of EPIC-SR, a randomized, double-blind, placebo-controlled study in non-hospitalized symptomatic adult patients with a laboratory confirmed diagnosis of SARS-CoV-2 infection. The trial included previously unvaccinated patients with no risk factors for progression to severe disease or patients fully vaccinated against COVID-19 with at least 1 of the risk factors for progression to severe disease as defined in EPIC-HR. The primary endpoint was the difference in time to sustained alleviation of all targeted COVID-19 signs and symptoms through day 28.
    - The primary endpoint was not met. However, in an exploratory analysis of the subgroup of fully vaccinated patients with at least 1 risk factor for progression to severe disease, a non-statistically significant numerical reduction relative to placebo for the secondary endpoint of COVID-19 related hospitalization or death from any cause through day 28 was observed.
- Paxlovid carries a boxed warning for significant drug interactions with Paxlovid.
- Paxlovid is contraindicated:

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  - In patients with a history of clinically significant hypersensitivity reactions to the active ingredients (nirmatrelvir or ritonavir) or any other components
  - With co-administration with drugs highly dependent on CYP3A for clearance and for which elevated concentrations are associated with serious and/or life-threatening reactions
  - With co-administration with potent CYP3A inducers where significantly reduced nirmatrelvir or ritonavir plasma concentrations may be associated with the potential for loss of virologic response and possible resistance.

- Additional warnings and precautions for Paxlovid include hypersensitivity reactions, hepatotoxicity, and risk of HIV-1 resistance development.

- The most common adverse reactions (≥ 1% and greater incidence than in the placebo group) with Paxlovid use were dysgeusia and diarrhea.

- The recommended dosage for Paxlovid is 300 mg nirmatrelvir (two 150 mg tablets) with 100 mg ritonavir (one 100 mg tablet) with all 3 tablets taken together orally twice daily for 5 days.

  - The 5-day treatment course of Paxlovid should be initiated as soon as possible after a diagnosis of COVID-19 has been made, and within 5 days of symptom onset even if baseline COVID-19 symptoms are mild.
  - Should a patient require hospitalization due to severe or critical COVID-19 after starting treatment with Paxlovid, the patient should complete the full 5-day treatment course per the healthcare provider's discretion.

- At this time, the U.S. government will continue to oversee the distribution of Paxlovid, and U.S. residents eligible for Paxlovid will continue to receive the medicine at no charge until supply is depleted. At that time, commercial distribution of Paxlovid will begin.

  - New NDCs for the commercial product will be issued.
  - Pricing for the commercial product is to be determined.

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