Emergency Use Authorization (EUA) for PAXLOVID

Center for Drug Evaluation and Research (CDER) Review Memorandum

Identifying Information

Application Type (EUA or Pre-EUA)	EUA
EUA Application Number(s)	000105
Date of Memorandum	January 26, 2024
Sponsor (entity requesting EUA or pre-EUA consideration), point of contact, address, phone number, fax number, email address	Pfizer Inc. 235 East 42nd Street New York, NY 10017-5755 Karen Baker- Director Global Regulatory Affairs – Brand Hospital Products Email: (b) (6) Phone: (b) (6)
Original Authorization	December 22, 2021
OND Division / Office	Division of Antivirals (DAV)/Office of Infectious Diseases (OID)
Proprietary Name	PAXLOVID
Established Name/Other names used during development	Nirmatrelvir (PF-07321332) tablets; Ritonavir tablets
Dosage Forms/Strengths	300 mg nirmatrelvir (two 150 mg tablets) with 100 mg ritonavir (one 100 mg tablet) all taken together orally twice daily for 5 days.
Therapeutic Class	Nirmatrelvir is a SARS-CoV-2 main protease (Mpro: also referred to as 3CLpro or nsp5 protease) inhibitor that has demonstrated activity against SARS-CoV-2. Ritonavir is an HIV-1 protease inhibitor and is not active against SARS-CoV-2 Mpro. Ritonavir inhibits the CYP3A-mediated metabolism of nirmatrelvir, thereby providing increased plasma concentrations of nirmatrelvir.
Intended Use or Need for EUA	Treatment of mild-to-moderate coronavirus disease 2019 (COVID-19)
Intended Population(s)	Adults and pediatric patients (12 years of age and older weighing at least 40 kg) with mild-to-moderate coronavirus disease 2019 (COVID-19) and who are at high risk for progression to severe COVID-19, including hospitalization or death

Abbreviations: DAV, Division of Antivirals; EUA, emergency use authorization; OID, Office of Infectious Diseases; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Background

On October 30, 2023, Pfizer announced that PAXLOVID labeled and packaged in accordance with the approved New Drug Application 217188 (NDA-labeled PAXLOVID) would be available beginning November 1, 2023.[1] At that time, the Administration for Strategic Preparedness and Response (ASPR) in the U.S. Department of Health and Human Services also announced its transition from and winding down of the U.S. government's distribution of PAXLOVID that is labeled and packaged in accordance with the Emergency Use Authorization (EUA-labeled PAXLOVID).[2]

On November 1, 2023, and to facilitate this transition, the Agency revised the EUA for PAXLOVID to authorize NDA-labeled PAXLOVID for the treatment of mild-to-moderate COVID-19 in pediatric patients (12 years of age and older weighing at least 40 kg), who are at high risk for progression to severe COVID-19, including hospitalization and death.

To ensure continued patient access to PAXLOVID during this transition, the EUA for PAXLOVID continued to authorize EUA-labeled PAXLOVID for the treatment of adults and pediatric patients (12 years of age and older weighing at least 40 kg) who are at high risk for progression to severe COVID-19, including hospitalization or death.

During this transition, FDA committed to an ongoing review of data from Pfizer or other parties regarding the supply of EUA-labeled PAXLOVID and NDA-labeled PAXLOVID at the point of dispensing (to ensure that sufficient supplies of the commercial product are available to meet the public health need) and communicated our intent to consider further revisions to the EUA at an appropriate time.[3]

In early January, 2024, Pfizer contacted FDA staff requesting to meet to discuss additional revisions to the EUA to facilitate the transition to NDA-labeled Paxlovid. On January 17, 2024, FDA held a teleconference with Pfizer to discuss its request to revise the EUA for PAXLOVID. Thereafter, on January 18, 2024, Pfizer formally submitted a written request to FDA requesting that the Agency revise the EUA for PAXLOVID to no longer authorize EUA-labeled PAXLOVID, effective January 26, 2024. Pfizer's request is based on information related to the commercial availability of NDA-labeled PAXLOVID.

Summary and Rationale for EUA Revision

In support of the request, Pfizer provided the Agency with information regarding the amount of NDA-labeled PAXLOVID manufactured to date as well as estimates of additional NDA-labeled PAXLOVID to be manufactured through the first half of 2024. Pfizer also reported considerable growth in its distribution network for NDA-labeled PAXLOVID. However, Pfizer also noted certain challenges of particular relevance to the Agency's assessment of Pfizer's request to revise the EUA for Paxlovid, which Pfizer is still working to address.

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[1] https://www.pfizer.com/news/announcements/pfizers-covid-19-oral-antiviral-treatment-transitioninggovernment-distribution

[2] For more information, please refer to the COVID-19 treatments transition operational guide at: https://aspr.hhs.gov/COVID-19/Therapeutics/Pages/COVID19-Tx-Transition-Guide.aspx

[3] See generally section 564(g) of the Federal Food, Drug & Cosmetic Act and FDA's guidance titled Emergency Use Authorization of Medical Products and Related Authorities (January 2017).

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Second, Pfizer stated that (b) (4) % of the US population has access to NDA-labeled PAXLOVID. This indicates substantial growth in the distribution network since November 1, but also means that some areas are not yet served. Pfizer indicated that expansion is still ongoing. Pfizer's assessment is based on (b) (4)

These challenges preclude a determination that the NDA-labeled PAXLOVID is sufficiently available to warrant an immediate end to availability of the EUA-labeled product at this time. Specifically, the Agency has concerns that Pfizer's request to revise the Paxlovid EUA, as proposed, is likely to cause an acute lack of availability of PAXLOVID at many points of dispensing.

However, Pfizer's current and projected estimates on the availability of NDA-labeled PAXLOVID do provide reasonable assurances to the Agency that NDA-labeled PAXLOVID will be sufficiently available at points of dispensing in approximately 6 weeks' time. In these unique circumstances, the Agency finds it important to provide the public with information in the revised LOA on the timing of the transition plan from the use of EUA-labeled PAXLOVID to NDA-labeled PAXLOVID.

To minimize disruption to the availability of treatment while the transition to the use of NDA-labeled PAXLOVID is completed, the Division of Antivirals and the Office of Infectious Diseases recommends revising the Letter of Authorization to include a footnote to the description of "Category A" of the currently authorized presentations, which will state the following:

> PAXLOVID in Category A that has been distributed prior to the reissuance of this letter is authorized for emergency use, consistent with the terms and conditions of this authorization, through the currently labeled or extended expiry, as applicable, or through March 8, 2024, whichever is earlier. Individuals who are dispensed Paxlovid in Category A on or prior to March 8, 2024, in accordance with the terms and conditions of this authorization, and who have initiated treatment on or prior to that date, may complete their course of treatment even if completion of treatment were to occur after March 8, 2024. Such EUA-labeled product remains authorized for patient use in these circumstances.

Regulatory Conclusion and Associated Actions:

The Division of Antivirals and Office of Infectious Diseases recommend revisions to EUA 105 as outlined above in order to best protect public health.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

GLEN HUANG
01/26/2024 03:50:45 PM

STEPHANIE B TROY
01/26/2024 03:52:25 PM

WENDY W CARTER
01/26/2024 04:37:31 PM

DEBRA B BIRNKRANT
01/26/2024 04:38:49 PM

JOHN J FARLEY
01/26/2024 05:16:07 PM