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	March 12, 2024
Sponsor (entity requesting EUA or pre-EUA consideration), point of contact, address, phone number, fax number, email address	Pfizer Inc. 66 Hudson Boulevard East New York, NY 10001 Nestor Duci – Senior Manager Global Regulatory Sciences 445 Eastern Point Road, Groton, CT 06340 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)	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

In November 2023, Pfizer began to make available PAXLOVID labeled and packaged in accordance with the approved New Drug Application 217188 (NDA-labeled PAXLOVID).[1] At that time, the Administration for Strategic Preparedness and Response (ASPR) in the U.S. Department of Health and Human Services also began to transition from the U.S. government's distribution of PAXLOVID that is labeled and packaged in accordance with the Emergency Use Authorization (EUA-labeled PAXLOVID).[2]

Additionally, on November 1, 2023, FDA implemented certain revisions to the PAXLOVID EUA to facilitate this transition while retaining certain aspects of the authorization in order to ensure continued patient access to PAXLOVID during this time.[3]

In early January 2024, Pfizer provided to FDA updated information on the commercialization of NDA-labeled PAXLOVID in support of additional revisions to the EUA. On January 29, 2024[4], based on the information provided, and to further facilitate the transition to NDA-labeled PAXLOVID, FDA revised the Letter of Authorization to include a footnote to the description of "Category A"[5] of the authorized presentations, which stated 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.

Thereafter, on February 8, 2024, Pfizer requested that FDA further revise the PAXLOVID EUA to remove reference to EUA-labeled PAXLOVID and its authorized uses.

Summary and Rationale for EUA Revision

Since FDA's revision to the PAXLOVID EUA in January 2024, Pfizer continued to provide updated metrics to the Agency on the availability of NDA-labeled PAXLOVID. As of March 1,

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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] As part of its ongoing assessment of the appropriateness and circumstances of the EUA, FDA will consider the availability of the presentations of Paxlovid that are packaged and labeled in accordance with the approved NDA 217188. See generally section 564(g) of the Federal Food, Drug & Cosmetic Act. See also FDA's guidance titled Emergency Use Authorization of Medical Products and Related Authorities (January 2017). For more information, please also refer to CDER's Summary Review, dated November 1, 2023 at: https://www.fda.gov/media/173586/download?attachment.

[4] For more information, please refer to the CDER's Summary Review, dated January 29, 2024 at: https://www.fda.gov/media/175805/download?attachment

[5] The presentations of PAXLOVID described in Category A of the Product Description section of the Letter of Authorization (LOA) were those that were labeled and packaged in accordance with EUA 105 ("EUA-labeled PAXLOVID").

2024, Pfizer stated that over (b) (4) dose packs of NDA-labeled PAXLOVID had been distributed to a broad network of retail pharmacies or other points of dispensing with approximately (b) (4) % of the US population living near at least one of these distribution points.[6] Pfizer also stated that it has already manufactured (b) (4) dose packs of NDA-labeled PAXLOVID and expects to have manufactured a total of (b) (4) dose packs of NDA-labeled PAXLOVID by the end of 2024.

Based on the information above, the Office of Infectious Diseases (OID) and the Division of Antivirals (DAV) in CDER's Office of New Drugs have determined that sufficient quantities of the NDA-labeled PAXLOVID have been made available to meet the current public health need. Further, based on the information above, OID and DAV have determined that Pfizer will continue to be able to meet the public health need for the foreseeable future.

Therefore, consistent with the January 29, 2024 reissuance of the Letter of Authorization for the PAXLOVID EUA, EUA-labeled PAXLOVID will no longer be authorized for emergency use. OID and DAV recommend revising the PAXLOVID EUA on March 13, 2024 to remove all references to EUA-labeled PAXLOVID, all uses previously authorized for EUA-labeled PAXLOVID, and any terms and conditions previously applicable to that product. By March 13, 2024, any individual who had been dispensed Paxlovid in Category A on or prior to March 8, 2024, in accordance with the terms and conditions of this authorization, and who had initiated treatment on or prior to that date, will have completed their course of treatment. Corresponding revisions will also be made to the authorized Fact Sheet for Health Care Providers and Fact Sheet for Patients, Parents and Caregivers.

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.

[6] Pfizer's assessment is based on (b) (4)

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