Republic of the Philippines
Department of Health
**FOOD AND DRUG ADMINISTRATION**

20 June 2022

**PFIZER, INC.**
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**Second Amendment to the Emergency Use Authorization (EUA) for COVID-19 Drug Nirmatrelvir 150 mg Film-Coated Tablet + Ritonavir 100 mg Film-Coated Tablet *(Co-Packaged in Alu/Alu Push-Through Blister Pack)* [PAXLOVID] with Conditional Marketing Authorization[1]**

This refers to the request to amend the Emergency Use Authorization (EUA) for COVID-19 Drug Nirmatrelvir 150 mg Film-Coated Tablet + Ritonavir 100 mg Film-Coated Tablet *(Co-Packaged in Alu/Alu Push-Through Blister Pack)* [PAXLOVID] with Conditional Marketing Authorization (COVID-19 Drug [PAXLOVID]) to include indication for 12 years old and above.

After due consideration, the Food and Drug Administration (FDA) revises the EUA of the COVID-19 Drug [PAXLOVID] to reflect the requested change. In arriving at this decision, the FDA has taken into account similar regulatory actions of the National Regulatory Authorities of the United States of America, South Korea and Japan.

The foregoing change is made pursuant to the discretionary power of the Food and Drug Administration (FDA) under Section 6 of Executive Order (EO) No. 121, entitled "Granting Authority to the Director General of the Food and Drug Administration to Issue Emergency Use Authorization (EUA) for COVID-19 Drugs and Vaccines, Prescribing Conditions Therefor, and for Other Purposes," to revisit any issued Emergency Use Authorization (EUA) as may be appropriate to protect the general public health and safety.

The details of the COVID-19 Drug [PAXLOVID] are as follows:

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| **Product Name:** | Paxlovid 150mg/100mg film coated tablet |
| **Dosage Strength and Form:** | Nirmatrelvir 150 mg Film-Coated Tablet + Ritonavir 100 mg Film Coated Tablet (Co-Packaged in Alu/Alu Push-Through Blister Pack) |
| **Pharmacologic category:** | Drug |
| **Storage:** | Store below 25°C. Do not refrigerate or freeze. |

[1] We refer you to the EUA dated 10 March 2022 and Amended EUA dated 05 April 2022

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| **Shelf Life:** | 12 months |
| **Packaging:** | Alu/Alu push-through blister pack x 6 tablets [4 Nirmatrelvir tablets + 2 Ritonavir tablets] in Box of 30 tablets [20 Nirmatrelvir tablets + 10 Ritonavir tablets] |
| **Manufacturer:** | Listed in *Section III. Manufacturer* |
| **Indication:** | Indicated for the treatment of COVID 19 in adults and adolescents (12 years of age and older weighing at least 40 kg) who do not require supplemental oxygen and who are at increased risk for progression to severe COVID 19 |

After careful consideration of the application, with all its supporting documents and a review of local experts, the FDA has been satisfied that all the conditions for the issuance of an EUA exist as provided under Executive Order (EO) No. 121, s. 2020 entitled *"Granting Authority to the Director General of the Food and Drug Administration to Issue Emergency Use Authorization for COVID-19 Drugs and Vaccines, Prescribing Conditions Therefor, and for Other Purposes,"* particularly:

1. Based on the totality of evidence available to date, including data from adequate and well- known controlled trials, it is reasonable to believe that the drug or vaccine may be effective to prevent, diagnose, or treat COVID-19;
2. The known and potential benefits of the drug or vaccine, when used to diagnose, prevent, or treat COVID-19, outweigh the known and potential risks of the drug or vaccine as of date; and
3. There is currently no adequate, approved and available alternative to the product for diagnosing, preventing or treating COVID-19.

In issuing this EUA, reliance has been accorded to the emergency use authorization of mature and established National Regulatory Authorities of the United Kingdom, United States of America and Japan. Consideration has also been given to the emergency use authorization of the National Regulatory Authority of India. Under Section 5 of EO No. 121, the Director General of the FDA has been granted power to implement recognition processes of established regulatory authorities.

While this EUA is not a marketing authorization or a Certificate of Product Registration (CPR), conditional marketing involving wholesale and retail of the COVID-19 the drug product by FDA licensed establishments shall be authorized provided that such entities comply with the responsibilities enumerated in this Letter.

While the evaluation process was facilitated, strict conditions on the authorization granted in this Letter shall be imposed as follows:

## I. Scope

Pfizer, Inc. shall deliver the COVID-19 Drug [PAXLOVID] only to the following FDA licensed establishments:

1. Drug outlets (government or private hospital pharmacies and community drug outlets), excluding Retail Outlets for Non-Prescription Drugs (RONPDs) in which the COVID-19 Drug [PAXLOVID] shall be dispensed; and
2. Distributor-wholesalers which shall strictly supply only to establishments identified in the preceding paragraph.

The COVID-19 Drug [PAXLOVID] shall be dispensed only by pharmacists registered with the Professional Regulation Commission (PRC).

The COVID-19 Drug [PAXLOVID] shall be used only for COVID-19 according to the approved indication stated herein, and in accordance with the COVID-19 management and treatment program.

Considering the investigational nature of the COVID-19 drug under EUA, online selling of the COVID-19 Drug [PAXLOVID] shall not be allowed.

FDA licensed establishments, and healthcare providers, which may include physicians, nurses, pharmacists and healthcare workers, as used in this EUA refer to those responsible in the receipt, storage, prescription, dispensation, and administration of the COVID-19 Drug [PAXLOVID], in accordance with the COVID-19 management and treatment program of the DOH.

## II. Posology and Method of Administration

Nirmatrelvir must be co-administered with Ritonavir. Each Nirmatrelvir is a pink film coated tablet which contains 150 mg of Nirmatrelvir, while each Ritonavir-film coated tablet contains 100 mg of Ritonavir.

The recommended dosage in adult and adolescent patients (12 years of age and older weighing at least 40 kg) is 300 mg Nirmatrelvir (two 150 mg tablets) with 100 mg Ritonavir (one 100 mg tablet) all taken together orally twice daily for 5 days. Paxlovid should be given as soon as possible after positive results of direct SARS-CoV-2 viral testing and within 5 days of onset of symptoms.

COVID-19 Drug PAXLOVID is not recommended for women with childbearing potential, pregnant and lactating women.

## III. Storage and Supply Chain Management

In the absence of agreement with the DOH or NTF, Pfizer, Inc. shall ensure that appropriate storage, transport, distribution, handling and supply chain is maintained until the product is delivered to FDA licensed establishments and dispensed by healthcare providers consistent with the terms of this letter, and ensure that a contingency plan is in place.

## IV. Pharmacovigilance

Pfizer, Inc. shall have a comprehensive pharmacovigilance system for the COVID-19 Drug [PAXLOVID] following system or protocol for a registered drug and biologic

product as stated in the FDA Circular No. 2020-003. Submission of serious and non-serious adverse reaction reports is mandatory.

Pfizer, Inc. shall ensure compliance with the Risk Management Plan (RMP) along with the Philippine-specific Annex. Additional pharmacovigilance activities such as interventional and non-interventional studies (ongoing or new studies, or additional activities) shall be implemented as stated in the RMP. The RMP must be updated whenever there is a significant change which may affect the benefit-risk profile of the drug or when an important milestone is reached.

Pfizer, Inc. shall submit monthly adverse drug reaction and safety reports collated from pharmacies or drug outlets and physicians/patients as planned and discussed in the RMP submitted to the Pharmacovigilance Section of the Center for Drug Regulation and Research (CDRR). For this purpose, Pfizer, Inc. shall establish a system of tracking and tracing the adverse drug reactions submitted by the pharmacies or drug outlets to which the COVID-19 Drug [PAXLOVID] were delivered.

## V. Responsibility of FDA Licensed Establishments and Healthcare Providers

Under FDA Circular No. 2020-036 or the *Guidelines for the Issuance of Emergency Use Authorization for Drugs and Vaccines for COVID-19*, the pharmacovigilance obligations and post-authorization commitments imposed in the Letter shall be shared to the fullest extent possible and applicable by the national procurer and health program implementors. In addition to the requirements of the COVID-19 management and treatment program, FDA licensed establishments and healthcare providers shall have the following responsibilities.

A. FDA licensed drug wholesalers and retailers:

1. Receive the COVID-19 Drug [PAXLOVID], and ensure appropriate storage and supply chain management in accordance with Good Distribution and Storage Practices.
2. Ensure dispensation of the COVID-19 Drug [PAXLOVID] is consistent with the terms of this Letter, latest product information and the COVID-19 management and treatment program; and
3. Ensure that healthcare providers of the COVID-19 Drug [PAXLOVID] are aware of this Letter of Authorization and the terms herein and any subsequent amendments thereof, instructed about the means which they

are to obtain and dispense the COVID-19 Drug [PAXLOVID], and provided with approved fact sheets.

B. On the other hand, healthcare providers shall:

1. Participate and comply with the terms and training required by the DOH for the COVID-19 management and treatment program;
2. Provide fact sheets to the recipients and caregivers, and provide necessary information for receiving the dosing regimen;
3. Report any Adverse Drug Reaction (ADR) on the use of the COVID-19 Drug [PAXLOVID];
4. Monitor and comply with drug management requirements (e.g. obtaining, tracking and handling drug) of the DOH; and
5. Keep patient records associated with this EUA, and ensure that the same are maintained until notified by FDA. Such records shall be made available to DOH and FDA for inspection upon request.
6. Prior to prescription of the COVID-19 Drug [PAXLOVID], PRC registered physicians shall:
    a. Discuss the benefits and risks of the use of the COVID-19 Drug [PAXLOVID] with the patient,
    b. Screening and advise patients included in the special population such as pregnant, breastfeeding or lactating women, women with child bearing potential, and the immunocompromised;
    c. Obtain written informed consent and a positive RT PCR test result for COVID-19 from the patient prior to prescription of the drug under EUA.
7. Furthermore, pharmacists shall dispense the COVID-19 Drug [PAXLOVID] upon presentation of a valid prescription, All prescriptions of the COVID-19 Drug [PAXLOVID] dispensed shall be recorded in the prescription record book indicating therein, among other things, the name and address of the patient, name of prescribed drug, dosage strength, quantity of drug and name of the dispensing pharmacist. The records shall be open for inspection upon request.

C. Notwithstanding the foregoing, Pfizer, Inc. has the ultimate responsibility for monitoring the safety and quality of the COVID-19 Drug [PAXLOVID]. Pfizer, Inc. shall ensure that the FDA licensed establishments and healthcare providers comply with the requirements of this EUA as well as the COVID-19 management and treatment program. Pfizer, Inc. must keep an up to date distribution record of all the wholesalers and retailers to which the COVID-19 Drug [PAXLOVID] has

been delivered. The distribution records should be immediately provided to FDA upon request.

## VI. Validity

Unless otherwise revoked, this EUA shall be valid only within the duration of the declared public health emergency due to COVID-19, or upon issuance of a marketing authorization/Certificate of Product Registration.

In the event that the declared public health emergency is lifted, or when a COVID-19 drug or vaccine is registered with the FDA, this EUA shall have a provisional validity for a period of one (1) year from date of lifting of the declaration or registration of the drug or vaccine for the sole purpose of exhausting remaining products.

This EUA is subject to revocation, suspension or cancellation due to violations of pharmacovigilance obligations and post authorization commitments, as well as any violation of the EO No. 121, and RA No. 3720 as amended by RA No. 9711, FDA Circular No. 2020-036, and other rules and regulations issued thereunder.

For strict compliance.