Direct Healthcare Professional Communication

Date: 28/8/2022

PAXLOVID Conditional Marketing Approval (CMA) dosing and dispensing in moderate renal impairment, and risk of serious adverse reactions due to drug interactions

Dear Healthcare Professional,

Pfizer, in agreement with the Saudi Food and Drug Authority would like to inform you of the following:

Summary

- **Dosing of Paxlovid in renal impairment: the CMA dosing and dispensing requirements for patients with moderate renal impairment, and the potential for drug-drug interactions associated with PAXLOVID (Nirmatrelvir tablets; ritonavir tablets). PAXLOVID contains two different drugs that are co-packaged in a daily blister card for oral use.**

Further information on the safety concern and the recommendations

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.

Renal impairment

No dose adjustment is needed in patients with mild renal impairment.

In patients with moderate renal impairment, the dose of Paxlovid should be reduced to nirmatrelvir/ritonavir 150 mg/100 mg (1 tablet of each) twice daily for 5 days. The remaining tablet of nirmatrelvir should be disposed of in accordance with local requirements.

Paxlovid is not recommended in patients with severe renal impairment or with renal failure as the appropriate dose has not yet been determined.

Each daily blister card contains a morning and evening dose, with each dose consisting of 300 mg Nirmatrelvir (two oval, pink 150 mg tablets) and 100 mg ritonavir (one ovaloid, white 100 mg tablet) as shown in Figure A below, which is incongruent with the moderate renal impairment dose.

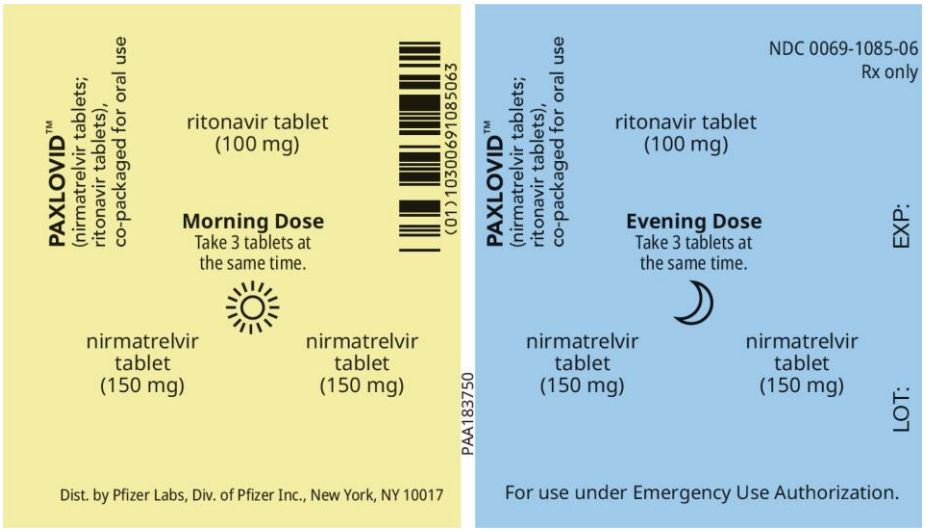

Figure A: Blister card containing morning and evening dose for normal renal function or <u>mild</u> renal impairment

Each daily blister card contains more Nirmatrelvir tablets than are needed for dosing in patients with moderate renal impairment. **It is critical that all prescriptions specify the numeric dose for each active ingredient within PAXLOVID as follows:**

- **PAXLOVID 150 mg Nirmatrelvir with 100 mg ritonavir for patients with moderate renal impairment, or**
- **PAXLOVID 300 mg Nirmatrelvir with 100 mg ritonavir for patients with normal renal function or mild renal impairment**

Patients with moderate renal impairment should be instructed to take only one 150-mg Nirmatrelvir tablet with one 100-mg ritonavir tablet together twice daily for 5 days.

Risk of Serious Adverse Reactions Due to Drug Interactions:

Use of PAXLOVID, a CYP3A inhibitor, in patients receiving concomitant medications metabolized by CYP3A may increase the plasma concentrations of those concomitant medications.

Use of concomitant medications that inhibit or induce CYP3A may increase or decrease concentrations of PAXLOVID, respectively.

These interactions may lead to:

- Clinically significant adverse reactions, potentially leading to severe, life-threatening, or fatal events from greater exposures of concomitant medications.
- Clinically significant adverse reactions from greater exposures of PAXLOVID.
- Loss of therapeutic effect of PAXLOVID and possible development of viral resistance.

See the current **SUMMARY OF PRODUCT CHARACTERISTICS** for Healthcare Providers for clinically significant drug interactions, including **contraindicated** drugs. Consider the potential for drug interactions prior to and during PAXLOVID therapy; review concomitant medications during PAXLOVID therapy and monitor for the adverse reactions associated with the concomitant medications.

Prescribers and pharmacists should inform patients that PAXLOVID may interact with some drugs and is **contraindicated** for use with some drugs; therefore, patients should be advised to report to their healthcare provider the use of any prescription or non-prescription medication or herbal products.

Indication & Authorized Use:

Paxlovid is 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

For information on medical conditions and factors associated with increased risk for progression to severe COVID-19, see the Centers for Disease Control and Prevention (CDC) website:

https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html.

Healthcare providers should consider the benefit-risk for an individual patient.

Patients requiring hospitalization due to severe or critical COVID-19 after starting treatment with PAXLOVID may complete the full 5-day treatment course per the healthcare provider's discretion.

Further information

See more safety information, including adverse events, and use the Interactions Finder to search for interactions with other medicinal products and other forms of interaction

Call for reporting

Suspected adverse reactions should be reported to:

- The National Pharmacovigilance Centre (NPC) at Saudi Food and Drug Authority (SFDA)
  SFDA Call Center: 19999
  Toll Free Phone: 8002490000
  E-mail: npc.drug@sfda.gov.sa
  Website: http://ade.sfda.gov.sa/

- Pharmacovigilance Department in the company
  E-mail: SAU.AEReporting@pfizer.com

Company Contacts

For more information, please contact Pfizer Medical Information: MedInfoMEandAfrica@pfizer.com

Sincerely,