Important Dosage Information for Patients with Renal Impairment

Nirmatrelvir tablets; Ritonavir tablets (PAXLOVID™)

PAXLOVID is approved 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.[1]

PAXLOVID has not been approved, but has been authorized for emergency use by FDA under an EUA, 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 or death.[2]

The emergency use of PAXLOVID is only authorized for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products during the COVID-19 pandemic under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization revoked sooner.[2]

Full Prescribing Information

Fact Sheet for Healthcare Providers

Fact Sheet for Patients, Parents, and Caregivers

FDA Emergency Use Authorization Letter*

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WARNING: SIGNIFICANT DRUG INTERACTIONS WITH PAXLOVID

See full prescribing information for complete boxed warning.

- **PAXLOVID includes ritonavir, a strong CYP3A inhibitor, which may lead to greater exposure of certain concomitant medications, resulting in potentially severe, life-threatening, or fatal events.**
- **Prior to prescribing PAXLOVID:**
    1. **Review all medications taken by the patient to assess potential drug-drug interactions with a strong CYP3A inhibitor like PAXLOVID and**
    2. **Determine if concomitant medications require a dose adjustment, interruption, and/or additional monitoring**
- **Consider the benefit of PAXLOVID treatment in reducing hospitalization and death, and whether the risk of potential drug-drug interactions for an individual patient can be appropriately managed.**

Systemic exposure of nirmatrelvir increases in renally impaired patients with increase in the severity of renal impairment. For more information, see the Full Prescribing Information and the full authorized Fact Sheet for Healthcare Providers.

Dosage Adjustments for Patients with Renal Impairment

Renal Function	eGFR*	PAXLOVID dose
Normal renal function or mild renal impairment	eGFR ≥60 to <90 mL/min	2 x 150 mg nirmatrelvir tablets + 100 mg ritonavir tablet — **300 mg nirmatrelvir with 100 mg ritonavir, with all 3 tablets taken together twice daily for 5 days**
Moderate renal impairment	≥30 to <60 mL/min	150 mg nirmatrelvir tablet + 100 mg ritonavir tablet — **150 mg nirmatrelvir with 100 mg ritonavir, with both tablets taken together twice daily for 5 days**
Severe renal impairment	<30 mL/min	**PAXLOVID is not recommended (the appropriate dose has not been determined).**

**eGFR=estimated glomerular filtration rate based on the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) formula*

Prescriptions should specify the numeric dose of each active ingredient within PAXLOVID.
Providers should counsel patients about renal dosing instructions.

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.

Healthcare providers should consult the Full Prescribing Information and the full EUA Fact Sheet for Healthcare Providers before prescribing PAXLOVID.

Clinical Pharmacology Data in Patients with Renal Impairment

The pharmacokinetics of nirmatrelvir in patients with renal impairment following administration of a single oral dose of nirmatrelvir 100 mg (0.33 times the approved recommended dose) co-administered with ritonavir 100 mg are presented in the following table. Compared to healthy controls with no renal impairment, the C_{max} and AUC of nirmatrelvir in patients with mild renal impairment was 30 % and 24 % higher, in patients with moderate renal impairment was 38 % and 87 % higher, and in patients with severe renal impairment was 48 % and 204 % higher, respectively.

Impact of Renal Impairment on PAXLOVID Pharmacokinetics

	Normal Renal Function (n=8)	Mild Renal Function (n=8)	Moderate Renal Function (n=8)	Severe Renal Function (n=8)
C_{max} (µg/mL)	1.60 (31)	2.08 (29)	2.21 (17)	2.37 (38)
AUC_{inf} (µg*hr/mL)	14.46 (20)	17.91 (30)	27.11 (27)	44.04 (33)
T_{max} (hr)	2.0 (1.0 – 4.0)	2.0 (1.0 – 3.0)	2.50 (1.0 – 6.0)	3.0 (1.0 – 6.1)
$T_{1/2}$ (hr)	7.73 ± 1.82	6.60 ± 1.53	9.95 ± 3.42	13.37 ± 3.32

Values are presented as geometric mean (geometric % CV) except median (range) for T_{max} and arithmetic mean ± SD for $t_{1/2}$.

Resources to Help Identify and Manage Drug-Drug Interactions with PAXLOVID (nirmatrelvir tablets; ritonavir tablets)

Pfizer Medical Resources

- Full Prescribing Information
- Fact Sheet for Healthcare Providers
- PAXLOVID Medical Information Page, which includes a drug interaction tool
- Potentially Significant Drug Interactions, Including Contraindicated Drugs Resource

Third-party Resources*

- NIH Guideline on Drug-Drug Interactions Between Ritonavir-Boosted Nirmatrelvir (PAXLOVID) and Concomitant Medications
- The University of Liverpool COVID-19 Drug Interactions website

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References

1. PAXLOVID™ [Prescribing Information]. Pfizer Inc. New York, NY; 2023.
2. PAXLOVID™ (nirmatrelvir tablets; ritonavir tablets) Emergency Use Authorization Fact Sheet for Healthcare Providers. Pfizer Inc.