This letter is to inform you of the following:

- **Changes to the PAXLOVID pack.**
- **Updates to the contraindications section of the Data Sheet.**
- **Dosing instructions for patients with renal impairment.**

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25 January 2024

Dear Healthcare Professional,

Supply of PAXLOVID® (nirmatrelvir 150 mg/ritonavir 100 mg), film coated tablets, TT50-10969

The purpose of this letter is to make you aware of a newly available New Zealand pack for PAXLOVID (nirmatrelvir 150 mg/ritonavir 100 mg), the updated contraindications in the Data Sheet and a reminder about the dosing instructions for patients with renal impairment.

PAXLOVID is indicated for the treatment of coronavirus disease 2019 (COVID-19) in adults 18 years of age and older, who do not require initiation of supplemental oxygen due to COVID-19 and are at increased risk of progression to hospitalisation or death.

New Pack

Over the coming months, both the current international pack and a newly available New Zealand pack may be supplied. PAXLOVID tablets in the New Zealand pack are identical in every way (formulation, method of manufacture, testing, appearance, etc.) to the ones in the international pack that has been supplied.

The table below specifies the differences between the international pack and the New Zealand pack.

Table 1: Differences between the international pack and the New Zealand pack

	International Pack	New Zealand Pack
Carton		
Medicine classification and cautionary statements	Rx symbol is used	PRESCRIPTION ONLY MEDICINE KEEP OUT OF REACH OF CHILDREN
Sponsor details	Distributed by Pfizer Labs Division of Pfizer Inc. New York, NY 10017	Pfizer New Zealand Limited Auckland Medical Information: In New Zealand, go to www.pfizermedicalinformation.co.nz; or ph. 0800 736 363
Allergen statement	Not included	Contains sugars (as lactose)[1]
Storage	Store at room temperature 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F)	Store below 25°C
Other	For use under Emergency Use Authorisation. This is how the FDA has authorised PAXLOVID for use in the USA.	No statement is required. In New Zealand, Medsafe has granted PAXLOVID provisional consent for distribution under Section 23 of the medicines Act 1981.
Blister foil		
Sponsor details	Pfizer Labs, Div. of Pfizer Inc	Pfizer logo

[1] The level of lactose within this preparation should not routinely preclude the use of this medication in those with galactosaemia. See Section 4.4 Special warnings and precautions for use in the PAXLOVID Data Sheet.

Images of the international pack and the New Zealand pack are provided below.

Figure 1: Carton of the international pack (current)

Figure 2: Carton of the New Zealand pack (new)

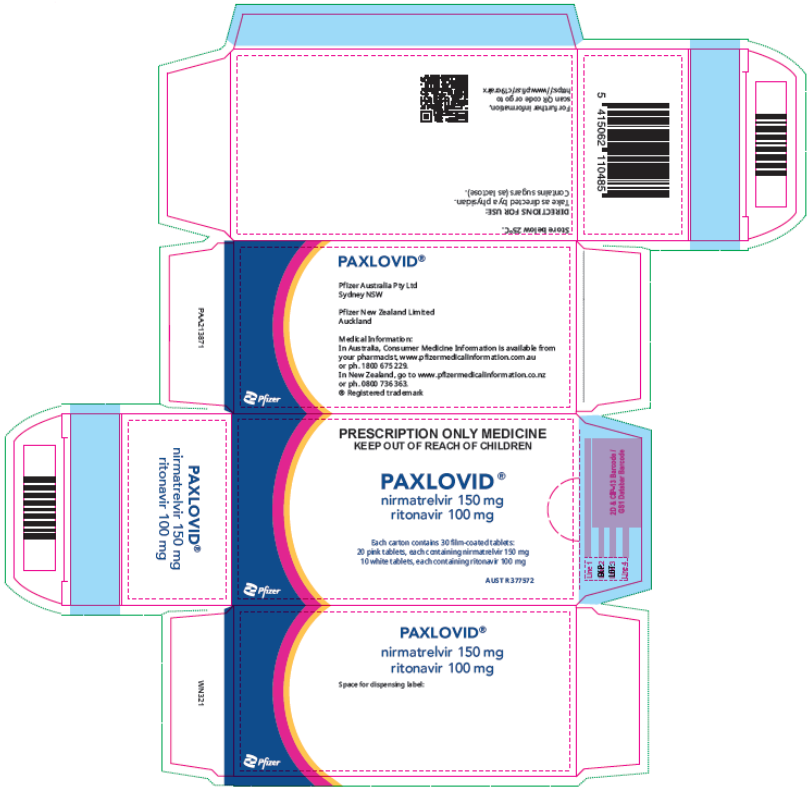


Figure 3: Blister card in the international pack containing morning and evening dose (current)

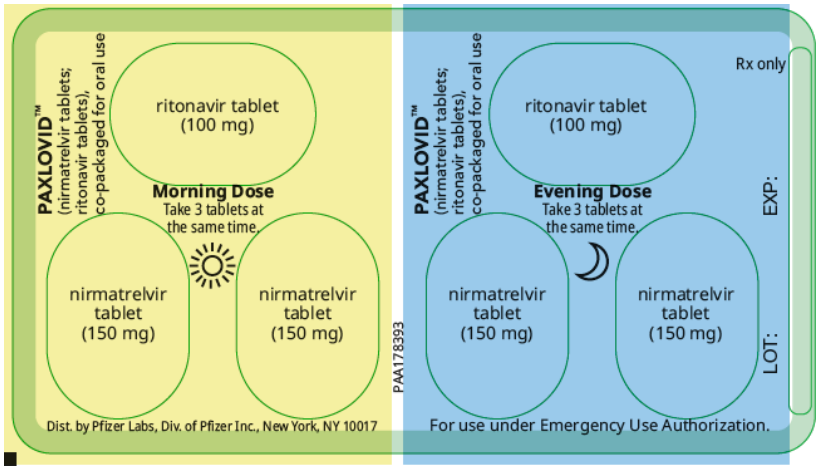
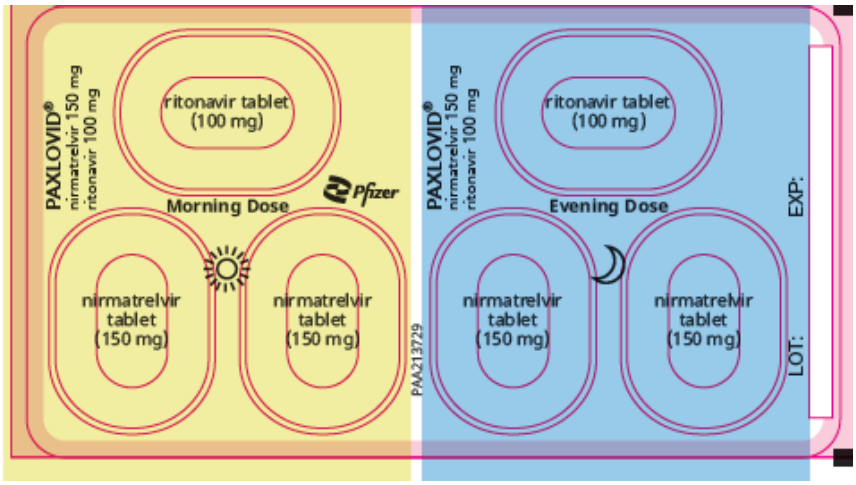


Figure 4: Blister card in the New Zealand pack containing morning and evening dose (new)



Updated contraindications

Updated contraindications have been highlighted in Tables 2 and 3.

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

In tables 2 and 3 below are the updated list of contraindications for PAXLOVID. Those highlighted in grey are new contraindications.

Table 2: Medicinal products that are contraindicated for concomitant use with PAXLOVID and are associated with serious and/or life-threatening reactions

Medicinal product class	Medicinal products within class
Interactions that result in an increase or decrease in concentrations of concomitant medicine	
Antianginal	ranolazine
Antiarrhythmics	amiodarone, flecainide, propafenone
Antibiotic	fusidic acid
Anticancer	neratinib, venetoclax
Anti-gout	colchicine
Antipsychotics	clozapine
Cardiovascular agents	**eplerenone**
Ergot derivatives	ergometrine
Lipid-modifying agents HMG-CoA reductase inhibitors	simvastatin
Migraine medications	**eletriptan**
Opioid antagonists	**naloxegol**
PDE5 inhibitor when used for pulmonary arterial hypertension (PAH)	sildenafil
Sedative/hypnotics	triazolam
Vasopressin receptor antagonists	**tolvaptan**

Table 3: Medicinal products that are contraindicated for concomitant use with PAXLOVID and associated potential loss of virologic response and possible resistance

Interactions that result in decrease in nirmatrelvir/ritonavir concentrations	
Anticancer	apalutamide
Anticonvulsant	carbamazepine, phenobarbital, phenytoin, **primidone**
Antimycobacterials	rifampicin
Herbal products	St. John's Wort (*hypericum perforatum*)

Patients with renal impairment

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). This is the dose for patients with normal renal function or with mild renal impairment (see table below).

For patients with moderate renal impairment, each daily blister card contains more nirmatrelvir tablets than is needed (see table below). **Therefore, it is critical that all prescriptions specify the numeric dose for each active ingredient within PAXLOVID. Any tablets that are not required must be discarded prior to dispensing and that this is discussed with the patient.**

Table 4: Dosage for PAXLOVID in patients with renal impairment

Renal Function (eGFR*)	PAXLOVID Dose
Normal renal function or mild renal impairment (≥60 mL/min/1.73m^2)	300 mg nirmatrelvir with 100 mg ritonavir, taken every 12 hours for 5 days
Moderate renal impairment (≥30 to <60 mL/min/1.73m^2)	150 mg nirmatrelvir with 100 mg ritonavir, taken every 12 hours for 5 days
Severe renal impairment (<30 mL/min/1.73m^2)	PAXLOVID is contraindicated.

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

For your patients with moderate renal impairment, stickers with dosing information are available upon request and should be affixed to the pack as per the instructions provided as an appendix to this letter (*Appendix - Re-packing Instructions for Patients with Moderate Renal Impairment*). To order the stickers, contact the local Pfizer representative or send a request email to paxlovidnz@pfizer.com.

PLEASE REVIEW THE CURRENT NEW ZEALAND DATA SHEET BEFORE PRESCRIBING OR DISPENSING.

The New Zealand Data Sheet and Consumer Medicine Information can be found at https://www.medsafe.govt.nz.

Adverse Event Reporting

Healthcare professionals are asked to report any suspected adverse events at https://pophealth.my.site.com/carmreportsnz/s/. Alternatively, any adverse events which are experienced with PAXLOVID can be reported to Pfizer on 0800 736 363 or by email to AUS.AEReporting@pfizer.com

Medical Enquiries

Please direct any medical enquiries to Pfizer Medical Information via: www.pfizermedicalinformation.co.nz or 0800 736 363.

Yours sincerely,

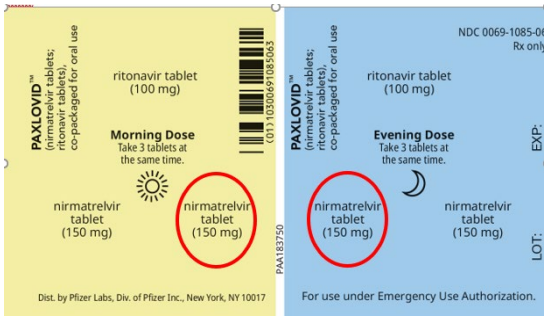
Kenneth Hargreaves
Senior Medical Manager
Pfizer New Zealand Limited

Appendix - Re-packing Instructions for Patients with Moderate Renal Impairment

To dispense PAXLOVID dose (150 mg nirmatrelvir with 100 mg ritonavir) for patients with moderate renal impairment, the pharmacist or dispensary technician should:

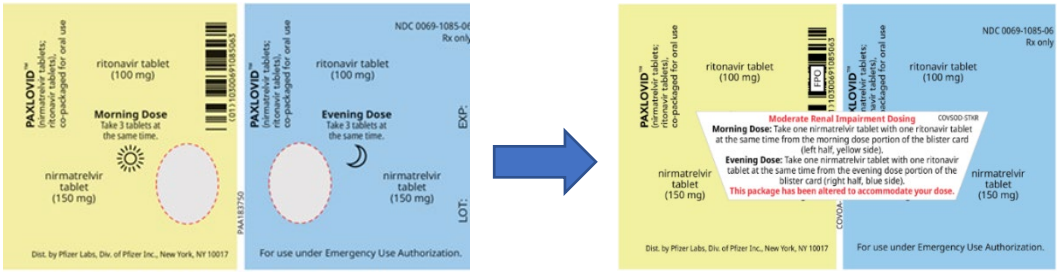
STEP ONE: Remove one of the 150 mg nirmatrelvir tablets from the morning dose and remove one of the 150 mg nirmatrelvir tablets from the evening dose of the blister card (see Figure 1 below). The nirmatrelvir tablets that are removed should be the ones closest to the middle of the blister card.

Figure 1: Remove the nirmatrelvir tablets circled in red from the blister card



STEP TWO: Affix to the blister card one of the stickers provided to cover the empty blister cavities as shown in Figure 2 below. The exact placement of this sticker is important to cover the empty blister cavities from the tablets. Ensure the sticker also covers the pre-printed dosing instruction that is on the blister card.

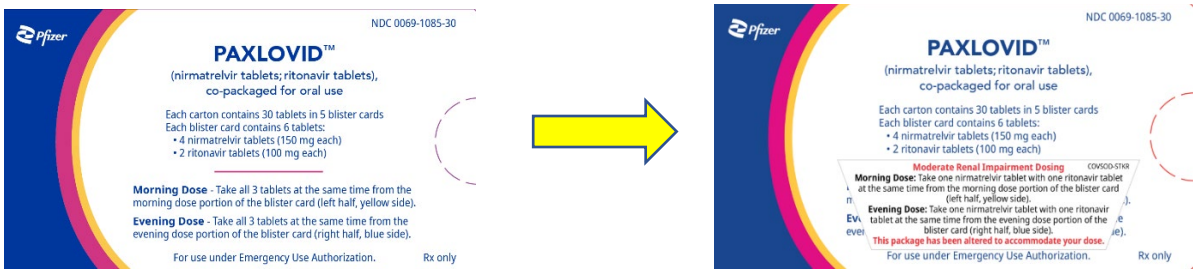
Figure 2: Placement of sticker over empty blister cavities and pre-printed dosing instruction after removal of nirmatrelvir tablets



STEP THREE: Repeat steps one and two for every blister card in the carton (each carton contains five blister cards for a full 5-day dosing regimen).

STEP FOUR: Affix one of the stickers provided to cover over the pre-printed dosing regimen on the carton as shown in Figure 3 below:

Figure 3: Placement of sticker over pre-printed dosing regimen on carton



Note: Images of the international pack have been used above for illustrative purposes.