

Guidance on community use of oral COVID-19 antivirals

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1. Background

Nirmatrelvir with ritonavir (Paxlovid), remdesivir (IV treatment) and molnupiravir have been used, in New Zealand, to reduce the risk of severe illness and hospitalisation from COVID-19 infections since April 2022. These medicines are not used for the treatment of long COVID.

The evidence around effectiveness of these medicines is continuously being reviewed and as we learn more, we need to change our approach. Accumulating evidence suggests that at the present time molnupiravir treatment is unlikely to be of benefit and is therefore no longer available in New Zealand. For more information, please refer to the related [Pharmac statement](#).

Paxlovid continues to be the first-line antiviral for the treatment of COVID-19 as supported by clinical guidance from the Ministry of Health COVID-19 Therapeutics TAG.

2. Guidance

Eligibility criteria for COVID-19 antivirals

The access criteria for oral COVID-19 antiviral medicines allows access for people who would be at higher risk of severe health outcomes from COVID-19, particularly hospitalisation and death. Studies have also shown that people with COVID-19 at standard risk, especially when further lowered by vaccination, would have minimal or no benefit from oral antivirals.

The Pharmac access criteria can be found [here](#).

Antiviral options

Paxlovid (oral) and remdesivir (IV) are antivirals which are available to treat COVID-19 in the viral replication phase of the infection.

Evidence suggests that Paxlovid is effective against the Omicron variants in reducing the development of serious illness and hospitalisation in those who are most at risk, in vaccinated populations^{i ii iii iv}. Remdesivir is the recommended 2nd line treatment, in regions where this service is available (for non-hospitalised patients).

Recent evidence suggests that molnupiravir is unlikely to be of benefit^v and is no longer available in New Zealand.

It should be noted that the COVID-19 vaccination booster doses are very effective in reducing the rate of hospitalisation and should be prioritised for all who are eligible and especially for those with higher risk conditions.

Assessing patients

An in-person consultation is not needed in most cases to prescribe or initiate COVID-19 antivirals. When assessing eligibility, shared decision making between the primary care practitioner or pharmacist, the patient, other health providers and whānau is encouraged.

COVID-19 antivirals may be prescribed in advance to patients who meet all the [Pharmac access criteria](#) except for being a confirmed or probable case.

For an advance prescription to be dispensed, the patient must meet ALL the [Pharmac access criteria](#) (including the requirements relating to being a current COVID-19 confirmed or probable case).

See guidance [here](#) for special considerations for advance prescription for these medicines.

Prescriptions for patients who do not meet the [Pharmac access criteria](#) will not be dispensed unless an authorised prescriber has applied for a [Named Patient Pharmaceutical Assessment \(NPPA\)](#) for patients who have exceptional clinical circumstances and do not meet access criteria.

Particular care is needed to manage the clinically important drug interactions with Paxlovid. Pharmacists and prescribers are strongly encouraged to manage drug interactions and dose adjustments collaboratively and keep up to date with training opportunities, and drug information. When drug interactions or the risks of temporary modification of regular medication regimens are assessed to outweigh the benefits of Paxlovid, it will often be the case that no oral antiviral is warranted now that molnupiravir is no longer available. Consideration should be given to the use of remdesivir 2nd line, in regions where this service is available (for non-hospitalised patients).

Private supply of COVID-19 antiviral medicines

Paxlovid

Dosage

Paxlovid is a 5-day course of two medicines:

- a protease inhibitor **nirmatrelvir** (2 pink tablets twice daily) that blocks virus replication
- **ritonavir** (1 white tablet twice daily) which slows the metabolism of nirmatrelvir.

Treatment is recommended to be initiated as soon as possible after a diagnosis of COVID-19 has been made and must be within 5 days of symptom onset.

Precautions and Interactions

Dose adjustment of the nirmatrelvir component is necessary where there is moderate renal impairment, with an eGFR between 30-59 mL/minute.

Some limited early data suggests a reduced Paxlovid dose in renal failure (eGFR < 30) is not associated with significant harm. We recommend consideration of Paxlovid in this population after careful risk-benefit assessment.

Consultation with the patient's renal physician or referring to HealthPathways is recommended. See [Antiviral options for COVID-19 infection in patients with chronic kidney disease](#).

Ritonavir is a potent inhibitor of several important CYP enzymes responsible for drug metabolism. Depending on the severity of the interactions and the relative importance of the other drug, Paxlovid may be contraindicated, or a dose adjustment may be required for some of the patient's usual medicines.

Online interaction checkers that provide guidance on management of interactions are available online. The [University of Liverpool COVID-19 drug interaction checker](#) is one example.

Careful consideration is necessary to weigh the potential benefits versus risks of temporarily halting regular medicines and treating the COVID-19 infection with Paxlovid.

Extra contraception precautions are recommended during and for a week after treatment, particularly when oral contraception is being used.

No dose adjustment is required where there is mild hepatic impairment.

3. Key Resources

- Pharmac [Access Criteria](#)
- Clinical guidance on [HealthPathways](#) Case Management.
- University of Liverpool COVID-19 drug interaction [checker](#)
- The New Zealand Formulary (NZF) drug monograph for [Paxlovid](#).
- He Ako Hiringa has a [clinical resource](#) for Paxlovid.
- Paxlovid [datasheet](#).
- Healthify has created a plain-language consumer information leaflet for Paxlovid as well as a [general overview of COVID-19 antivirals](#)
- List of pharmacies that offer COVID-19 can be found on the Healthpoint website [here](#) (without a prescription) or [here](#) (with a prescription).
- Pharmaceutical Society of New Zealand COVID-19 Antivirals Training Programme available [here](#)

4. Process details

Prescribers

Checks and considerations when prescribing/supplying an oral COVID-19 antiviral therapeutic.

- Check whether the patient meets Pharmac's access criteria.
- Review suitability of the medicine, specifically any contraindications and whether the patient wants an active intervention.
- Consider discussing the management of Paxlovid interactions with medicines initiated in secondary care with the relevant specialist, e.g. Nephrologist, oncologist.
- Consider checking a pregnancy test in people of childbearing potential, and where appropriate, check whether breastfeeding before prescribing.
- If prescribing or supplying Paxlovid:
 - Review renal function and consider dose adjustment if eGFR < 60 mL/minute within the last 3-6 months.
 - Review potential drug interactions.
 - Manage any necessary dose adjustments of medicines. Communicate this clearly to the patient and document details in notes. The community pharmacist

will also be undertaking a medicine review and will need to be able to contact you with any concerns.

How to prescribe an oral COVID-19 antiviral:

- In addition to standard practice, it is important to document key information on the prescription, including
 - endorsing that the person meets the access criteria,
 - date of symptom onset,
 - latest eGFR for Paxlovid (if applicable, noting that the safety of the medicine is now more well-established and not having a current renal function test is not a requirement to initiate treatment),
 - prescriber's contact phone number.

(The contact number is provided to the pharmacist to enable easy access for urgent queries regarding medicines management. Prescribers and practices are asked to prioritise calls from pharmacists due to the tight timelines involved in needing to get the prescription to the patient).

What happens if a patient develops 'COVID-19 rebound' after antiviral treatment?

- Rebound infection is seen in up to 10% of cases within the first 30 days and occurs in both patients who have taken antivirals and those who have not. It usually occurs within 2 weeks of initial COVID-19 onset but can occur up to 4 weeks after initial onset.
- Testing is not required.
- Advise the patient to stay at home if unwell. Isolation is recommended until symptom resolution.
- Further COVID-19 antivirals are not indicated. The patient is unlikely to become severely unwell; review if concerned, especially if the patient is immunocompromised.
- Recommend standard protective measures for household contacts.

What happens if a patient has a re-infection after antiviral treatment?

If a patient tests COVID-19 positive 29 or more days since a previous infection, this is considered a new infection and should be treated as such. Therefore, the prescribing of COVID-19 antivirals should be considered again.

Pharmacists

Pharmacist Only Supply

Pharmacists initiating supply of Paxlovid (as a pharmacist only medicine) should review the relevant prescriber sections:

- Checks and considerations when prescribing/supplying an oral COVID-19 antiviral therapeutic.
- What happens if a patient develops 'COVID-19 rebound' after antiviral treatment?

What do pharmacists need to do when reviewing a prescription for Paxlovid?

Every prescription must be reviewed for completeness and appropriateness.

All prescriptions must be endorsed that the patient meets Pharmac access criteria. The prescriber should also annotate the COVID-19 positive status and date of symptom-onset on every prescription so that the pharmacist can ensure that treatment can be initiated within five days of symptom onset.

Pharmacists must consider the potential for drug interactions with Paxlovid and appropriate management. The participating pharmacy need to access a shared patient information database (e.g., TestSafe), or contact the general practice, patient, or patient's usual pharmacy if an up-to-date list of medicines is not readily available.

Checking the Paxlovid dose is appropriate where renal impairment is present. The prescriber should record the patient's most recent renal function (if required) on the prescription.

Checking that any other contraindications have been identified and appropriately managed.

Pharmacists will need to contact the prescriber if there are any clinical issues with the prescription and resolve these collaboratively. Prescribers are asked to provide their contact phone number on the prescription to facilitate this.

If pharmacists cannot contact the prescriber, then they will need to contact the Whakarongorau Clinical Advice line.

How do pharmacists dispense COVID-19 antivirals?

The dispensing process for these medicines is largely the same as for any medicine. For patients with renal impairment the pharmacist will remove the appropriate number of nirmatrelvir tablets from the original pack of Paxlovid and ensure the instruction label states the reduced dose.

Prescriptions should be processed as not subsidised (NSS).

When counselling a patient:

- Provide them with a copy of the Health Navigator information sheet for Paxlovid.
- Confirm the patient understands how to take the medicine safely and appropriately.
- Confirm pregnancy and breastfeeding status and the potential need to use contraception.
- Discuss management of drug interactions
- Advise them to contact the prescriber or pharmacy if they experience adverse events or worsening symptoms.

Can pharmacists supply Paxlovid on a Practitioner's Supply Order (PSO)?

Only **practices in a rural area**^{vi} can be supplied COVID-19 antivirals on a PSO.

However, prescriptions for these medicines must be retrospectively entered through the pharmacy dispensing system for data capture and reporting purposes.

Are there any other training resources I can access?

The Pharmaceutical Society of New Zealand has created a series of learning modules for COVID-19 Antiviral Training which can be accessed [here](#).

ⁱ Hammond J, Leister-Tebbe H, Gardner A, Abreu P, Bao W, Wisemandle W, et al. Oral Nirmatrelvir for High-Risk, Nonhospitalized Adults with Covid-19. 2022. 1397-408]. Available from: <https://www.nejm.org/doi/full/10.1056/NEJMoa2118542>.

ⁱⁱ Schwartz K, Wang J, Tadrous M, Langford B, Daneman N, Leung V, et al. Real-world effectiveness of nirmatrelvir/ritonavir use for COVID-19: A population-based cohort study in Ontario, Canada. 2022. 2022.11.03.22281881]. Available from: <https://www.medrxiv.org/content/medrxiv/early/2022/11/05/2022.11.03.22281881.full.pdf>.

ⁱⁱⁱ Aggarwal NR, Molina KC, Beaty LE, Bennett TD, Carlson NE, Ginde AA. Real-world Use of Nirmatrelvir-Ritonavir in COVID-19 Outpatients During the Emergence of Omicron Variants BA.2/BA2.12.1. 2022. 2022.09.12.22279866]. Available from:

<https://www.medrxiv.org/content/medrxiv/early/2022/09/15/2022.09.12.22279866.full.pdf>.

^{iv} Shah MM JB, Plumb ID, et al. Paxlovid Associated with Decreased Hospitalization Rate Among Adults with COVID-19 — United States, April–September 2022. MMWR Morb Mortal Wkly Rep 2022;71(14):2597–1. Available from: <https://www.cdc.gov/mmwr/volumes/71/wr/mm7148e2.htm#suggestedcitation>.

^v Molnupiravir plus usual care versus usual care alone as early treatment for adults with COVID-19 at increased risk of adverse outcomes (PANORAMIC): an open-label, platform-adaptive randomised controlled trial The Lancet 2022 [updated 22 December 2022 Available from:

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(22\)02597-1/fulltext#%20](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)02597-1/fulltext#%20).

^{vi} a rural area is defined by the [Pharmaceutical Schedule](#) as an area locally determined as rural by the appropriate DHB.