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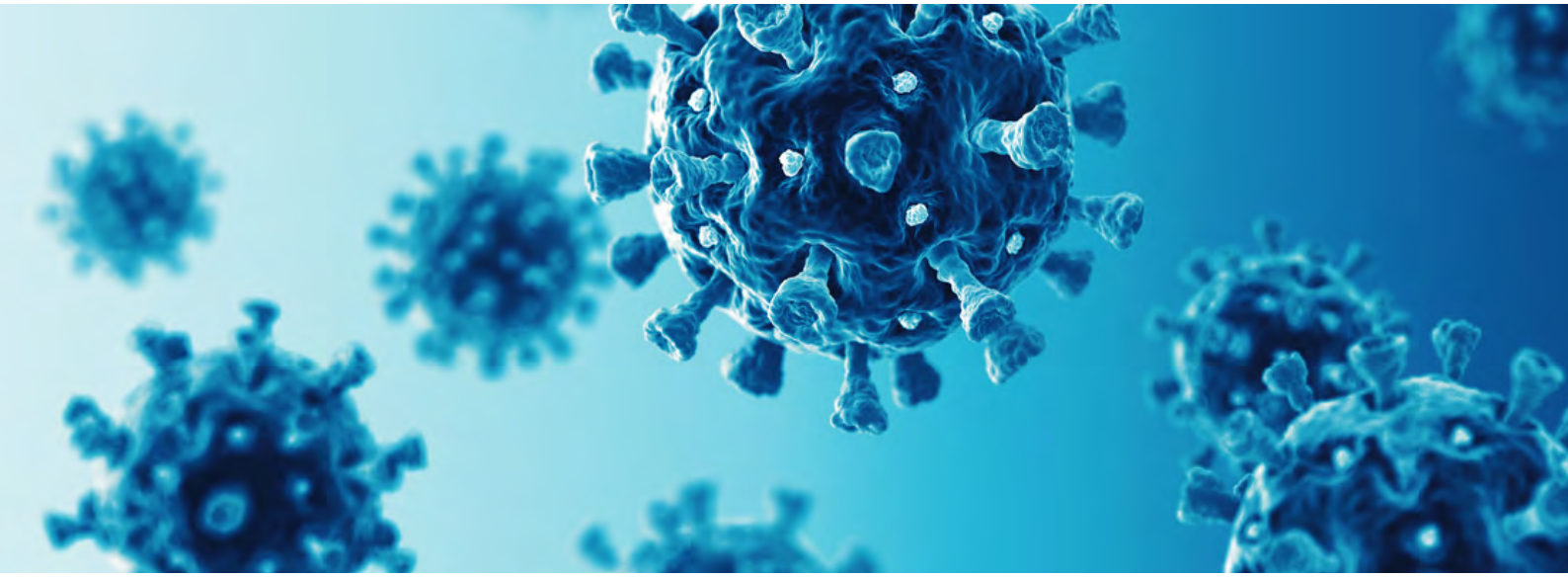
Oral antiviral treatments for COVID-19

Information for GPs



Introduction

Two antiviral medicines, Lagevrio (molnupiravir) and Paxlovid (nirmatrelvir plus ritonavir) were provisionally approved for use in Australia for the treatment of COVID-19 in January 2022, with supply of the medicines commencing in February 2022.

Initially, supply is limited to state and territory health departments, residential aged care facilities (RACFs), and Aboriginal and Torres Strait Islander communities via Aboriginal Controlled Community Health Organisations (ACCHOs). The Federal Government has allocated Lagevrio for pre-placement in all RACFs across Australia. States and territories and ACCHOs will be allocated both Paxlovid and Lagevrio.

Both medicines require a prescription from a GP, physician or a nurse practitioner who meet the prescribing requirements before they can be issued.

The National COVID-19 Clinical Evidence Taskforce has released treatment recommendations for the use of both medicines for people aged 18 years or older with confirmed COVID-19 who do not require oxygen and who have one or more risk factors for disease progression.

Both medicines can decrease the risk of hospitalisation if taken within five days of symptom onset.

Not everyone who tests positive for COVID-19 will require these medicines and they will both be of most benefit for people at risk of severe disease. GPs are well placed to make decisions with their patients on the appropriateness of these medicines to treat COVID-19 based on the person's individual risk for disease progression, medical history, current medicines, age, and COVID-19 vaccination status – including time since vaccination.

Any future Pharmaceutical Benefits Scheme (PBS) listing of these medicines will be dependent on application to and approval from the Pharmaceutical Benefits Advisory Committee.

If recommended, it may be that in time GPs will be able to prescribe one or both of these antiviral medicines as part of the PBS, and patients may be able to have them dispensed from their local pharmacy, noting the COVID-positive person will not be able to attend in person. Alternate collection or delivery will need to be arranged.

Confirmation of COVID-positive status

Confirmation of positive status can be via a rapid antigen test (RAT) or polymerase chain reaction (PCR) test. It is recommended where a positive home RAT result is reported and antiviral treatment is being considered, a confirmatory RAT (home or point-of-care) should be conducted by a qualified health professional before commencement of treatment.

Prescribing

Telehealth consultations will be sufficient in many cases to determine if treatment is appropriate, including via normal after-hours medical deputising services. It is recommended medical deputising GPs and nurse practitioners work in partnership with the usual treating GP or physician to determine if treatment is appropriate.

A prescription needs to be issued for the medicine to be administered. The recommendation for the recording and dispensing of prescriptions is to follow the same process for other orders where medicines that are held in stock are issued (for example, antibiotics). Some RACFs and ACCHOs will do this differently and how prescriptions are handled, and the medicines allocated, will be dependent on the local processes in place, and local state or territory requirements.

While clinical information systems (CIS) are being updated to include these medicines, they may not initially appear for prescribing purposes. In the interim you can still prescribe the medicines in your CIS by creating a custom medicine entry. It is important to note that the inbuilt medicine interaction and medical condition checker will not work, and you will need to be aware of the risks and contraindications as outlined in the product information for each medicine, and as per the University of Liverpool's COVID-19 drug interactions checker.

The two treatments should not be prescribed for the same person at the same time.

Please refer to the prescribing requirements in your state or territory.

Consent

As with all medicines, patients or carers will need to provide informed consent for these medicines to be prescribed. GPs working with patients in RACFs may find it helpful to pre-emptively discuss these medicines with their patients, even if they do not have COVID-19, to determine eligibility criteria and obtain pre-consent for these medicines to be prescribed in the event they test positive for COVID-19.

A subsequent discussion is advised at the point at which the patient requires the medicine to confirm the pre-consent is still applicable.

Adverse event reporting

If a patient experiences an adverse event which you think may be related to the prescribed medicine you can report this directly to the Therapeutic Goods Administration or via your normal state or territory reporting channels.

Lagevrio (molnupiravir)

Lagevrio product information and consumer medical information

When to prescribe

The National COVID-19 Clinical Evidence Taskforce recommends Lagevrio be considered for use:

- within five days of symptom onset in adults with COVID-19 who do not require oxygen; and
- who are unvaccinated and have one or more risk factors for disease progression;* or
- who are immunosuppressed or not immunocompetent regardless of vaccination status; or
- who have received one or two doses of vaccine and are at high risk of severe disease on the basis of age and multiple risk factors; and
- where other treatments (such as intravenous infusion of sotrovimab or oral nirmatrelvir plus ritonavir) are not suitable or available.

* Based on the inclusion criteria for the medicine's trial, risk factors for disease progression include:

- age ≥ 60 years
- BMI ≥ 30 kg/m^2
- chronic kidney disease (eGFR 30–60 mL/min/1.73m^2 by MDRD), excluding patients on dialysis
- serious heart conditions such as heart failure, coronary artery disease or cardiomyopathies
- chronic obstructive pulmonary disease
- active cancer (excluding minor cancers not associated with immunosuppression, eg basal cell carcinomas)
- immunocompromised state following solid organ transplant
- sickle cell disease
- diabetes.

Dosage

The standard dose of Lagevrio is 800 mg (administered as four 200 mg capsules), taken every 12 hours for five days, with or without food.

Lagevrio should be taken regularly at the same time each day. If a dose is missed and it has been less than 10 hours since the last dose the patient can take it as soon as it is remembered. If it has been more than 10 hours since the missed dose this should be skipped, and the next dose taken at the scheduled time. A double dose should not be taken to make up for a missed dose. Patients should not stop taking Lagevrio without speaking to their GP or physician.

The capsules should not be opened, broken or crushed, and must be swallowed whole.

Contraindications

A person should not take Lagevrio if they are allergic to molnupiravir or any of the other ingredients listed in the product information, listed below.

- Croscarmellose sodium
- Ethanol absolute
- Hyprolose
- Hypromellose
- Iron oxide red
- Isopropyl alcohol
- Magnesium stearate
- Microcrystalline cellulose
- Potassium hydroxide
- Propylene glycol
- Purified water
- Shellac
- Strong ammonia solution
- Tert-butyl alcohol
- Titanium dioxide

To date, there have been no medicine interactions identified with Lagevrio based on the limited data currently available.

Pregnancy, conception and breastfeeding

Lagevrio is not recommended during pregnancy.

Women of childbearing potential should use effective contraception for the duration of treatment and for four days after the last dose of Lagevrio. Men who are sexually active with a person of childbearing potential should use an effective contraception during treatment and for three months after treatment with Lagevrio.

Breastfeeding is not recommended during treatment and for four days after the last dose of Lagevrio.

Side effects

The most common side effects of Lagevrio are diarrhoea, nausea and dizziness. These side effects can lead to significant morbidity in frail and elderly patients, including dehydration, delirium and increased falls risk. It is important older people who are administered Lagevrio are closely monitored. Patients should be advised to speak with their GP or prescribing physician if they are concerned about any side effects while taking the medication.

Paxlovid (nirmatrelvir plus ritonavir)

Paxlovid product information and consumer medical information

When to prescribe

The National COVID-19 Clinical Evidence Taskforce recommends Paxlovid be considered for use:

- within five days of symptom onset in adults with COVID-19 who do not require oxygen; and
- who are unvaccinated and have one or more risk factors for disease progression;** or
- who are immunosuppressed or not immunocompetent regardless of vaccination status; or
- who have received one or two doses of vaccine and are at high risk of severe disease on the basis of age and multiple risk factors.

** Based on the population included within the medicine's trial, risk factors for disease progression include:

- age ≥ 60 years
- diabetes (requiring medication)
- BMI ≥ 25 kg/m2
- cardiovascular disease
- hypertension
- chronic lung disease.

Dosage

The standard dose of Paxlovid is 300 mg of nirmatrelvir (two 150 mg tablets) together with 100 mg of ritonavir (one tablet). All tablets must be taken together, with or without food. The tablets should be swallowed whole and not chewed, broken, or crushed.

The tablets are dispensed in pre-dosed blistered cards.

Paxlovid is taken every 12 hours for five days. If patients miss a dose, they should not take a double dose to make up for the missed dose and should take their next dose as scheduled. Patients should not stop taking Paxlovid or change their dosage without speaking to their GP or physician.

Dosage adjustment for patients with renal impairment

Patients with moderate renal impairment (eGFR ≥30 to <60 mL/min) can be prescribed a lower dose of 150 mg nirmatrelvir (one tablet) with one 100 mg tablet of ritonavir. Paxlovid is contraindicated in patients with severe renal impairment (eGFR <30 mL/min). Refer to the product information for further details on dose adjustment.

Patients receiving an adjusted dose must be made aware that as the tablets are dispensed in pre-dosed blistered cards, **only one tablet of nirmatrelvir** with the tablet of ritonavir should be taken every 12 hours.

Contraindications

Paxlovid is contraindicated for patients with severe renal (eGFR <30 mL/min) or severe hepatic impairment (Child-Pugh Class C), and those who are allergic to nirmatrelvir or ritonavir or any of the ingredients listed in the product information, including:

- microcrystalline cellulose
- lactose monohydrate
- croscarmellose sodium
- colloidal silicon dioxide
- sodium stearyl fumarate.

The following medicines are contraindications to Paxlovid. **People taking these medicines should not be prescribed Paxlovid.**

- Alfuzosin
- Amiodarone
- Apalutamide
- Avanafil
- Carbamazepine
- Clozapine
- Colchicine
- Diazepam
- Ergometrine
- Flecainide
- Lurasidone
- Neratinib
- Pethidine
- Phenobarbital
- Phenytoin
- Piroxicam
- Ranolazine
- Rifampicin
- Sildenafil
- Simvastatin
- St John's Wort (hypericum perforatum)
- Tadalafil
- Vardenafil
- Venetoclax

Medicines with established and potentially significant interactions with Paxlovid

The following medicines have established and potentially significant interactions with Paxlovid and may cause serious or life-threatening side effects or affect how the medicine works. Refer to the clinical comments in the Paxlovid product information for each of the medicines listed below.

- Abemaciclib
- Afatinib
- Alprazolam
- Amitriptyline
- Amlodipine
- Atazanavir
- Atorvastatin
- Atovaquone
- Betamethasone
- Bictegravir
- Bosentan
- Budesonide
- Bupropion
- Ceritinib
- Ciclosporin
- Clarithromycin
- Darunavir
- Dasatinib
- Dexamethasone
- Digoxin
- Diltiazem
- Efavirenz
- Emtricitabine
- Encorafenib
- Erythromycin
- Ethinylestradiol
- Everolimus
- Felodipine
- Fentanyl
- Fluoxetine
- Fosamprenavir
- Glecaprevir
- Haloperidol
- Ibrutinib
- Imipramine
- Isavuconazonium sulfate
- Itraconazole
- Ketoconazole
- Lamotrigine
- Lidocaine
- Loratadine
- Maraviroc
- Methadone
- Methylprednisolone
- Midazolam
- Nevirapine
- Nifedipine
- Nilotinib
- Nortriptyline
- Pibrentasvir
- Paroxetine
- Prednisone
- Quetiapine
- Raltegravir
- Rifabutin
- Riociguat
- Risperidone
- Rivaroxaban
- Rosuvastatin
- Salmeterol
- Saquinavir
- Sertraline
- Sirolimus
- Sofosbuvir
- Tacrolimus
- Tenofovir
- Triamcinolone
- Velpatasvir
- Vinblastine
- Vincristine
- Voriconazole
- Voxilaprevir
- Warfarin
- Zidovudine
- Zolpidem

Pregnancy, conception and breastfeeding

Paxlovid is not recommended during pregnancy and in women of childbearing potential not using contraception. Breastfeeding should be discontinued during treatment with Paxlovid and for seven days after the last dose.

Side effects

As with most medicines, Paxlovid can cause side effects and, while most of these will be minor and temporary, more severe side effects may need medical treatment. The most common side effects of Paxlovid include vomiting, diarrhoea, headache, high blood pressure, aching muscle, muscle tenderness or weakness not due to exercise and changes in taste or a metallic taste in the mouth. Patients should be advised to speak with their GP or prescribing physician if they are concerned about any side effects while taking Paxlovid.

Disclaimer

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