RACGP

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Oral antiviral treatments for COVID-19 Prescribing information for GPs

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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 was 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 allocated Lagevrio for pre-placement in all RACFs across Australia. States and territories and ACCHOs will be allocated both Paxlovid and Lagevrio.

Both Lagevrio and Paxlovid are now listed on the Pharmaceutical Benefits Scheme (PBS) as Authority Required (Streamlined) items, enabling eligible patients to access these medicines from their local pharmacy where available.

Regardless of how they are accessed, both medicines require a prescription from a GP, physician or nurse practitioner who meets the prescribing requirements before they can be issued.

The National COVID-19 Clinical Evidence Taskforce (https://covid19evidence.net.au/) (the 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. These treatment recommendations are supported by the Taskforce's decision tool for drug treatments and risk classification tool (both available on the Taskforce website (https://covid19evidence.net.au/#clinical-flowcharts)). Please note that the PBS eligibility for both medicines is broader than the Taskforce recommendations.

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 to 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.

A COVID-positive person will not be able to attend in person to collect these medicines. Alternate collection or delivery will need to be arranged.

Confirmation of COVID-positive status

COVID-positive status can be confirmed via a rapid antigen test (RAT) or polymerase chain reaction (PCR) test. When a positive home RAT result is reported and antiviral treatment is being considered, a medically verified confirmatory RAT must be conducted 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. When medicines have been pre-placed in RACFs and ACCHOs, the recommendation for recording and dispensing prescriptions is to follow the same process for other orders when 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 depend 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 in-built 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 (https://www.covid19-druginteractions.org/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 (https://www.health.gov.au/health-alerts/covid-19/treatments/oral) .

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 that you think may be related to the prescribed medicine, you can report this directly to the Therapeutic Goods Administration (https://aems.tga.gov.au/) or via your normal state or territory reporting channels.

Evusheld

Evusheld (tixagevimab and cilgavimab) has been provisionally approved by the TGA for the prevention of COVID-19 in people who are at risk of infection but have not been exposed to the virus (pre-exposure prevention of COVID-19).

Provisional approval has been granted for pre-exposure prophylaxis of COVID-19 in people aged 12 years and older weighing at least 40 kg:

- who have moderate-to-severe immune compromise due to a medical condition or receipt of immunosuppressive medications or treatments that make it likely that they will not mount an adequate immune response to COVID-19 vaccination; or
- for whom vaccination is not recommended due to a history of severe adverse reaction to a COVID-19 vaccine or COVID-19 vaccine component.

Pre-exposure prevention with Evusheld is not a substitute for vaccination in people for whom COVID-19 vaccination is recommended.

Evusheld is distributed via the National Medical Stockpile to state and territory governments. Information on access to this medicine can be found via each state/territory health department website (https://www.health.gov.au/health-alerts/covid-19/treatments/access) .

See the TGA website (https://www.tga.gov.au/tga-provisionally-approves-astrazenecas-combination-therapy-tixagevimab-and-cilgavimab-evusheld-pre-exposure-prevention-prophylaxis-covid-19) for further information on Evusheld.

Lagevrio (molnupiravir)

Lagevrio product information (https://www.tga.gov.au/sites/default/files/lagevrio-pi.pdf) , PBS listing (https://www.pbs.gov.au/info/news/2022/03/lagevrio-molnupiravir-pbs-listing) and consumer medical information (https://www.tga.gov.au/sites/default/files/lagevrio-cmi.pdf)

When to prescribe

Adults who have mild to moderate COVID-19 confirmed by a PCR or medically verified RAT and who can start treatment within five days of symptom onset, can be prescribed PBS-subsidised Lagevrio if:

- they are 65 years of age or older, with two other risk factors for severe disease (as increasing age is a risk factor, patients who are 75 years of age of older only need to have one other risk factor); or
- they identify as Aboriginal or Torres Strait Islander origin, and are 50 years of age or older with two other risk factors for severe disease, or
- they are moderately to severely immunocompromised.

When prescribing Lagevrio via the PBS, ensure the patient meets the eligibility criteria outlined on the PBS listing (https://www.pbs.gov.au/info/news/2022/03/lagevrio-molnupiravir-pbs-listing) . You can review the National COVID-19 Clinical Evidence Taskforce recommendations for the use of Lagevrio here (https://onegp-my.sharepoint.com/personal/pip_walter_racgp_org_au/Documents/Desktop/BIN/v) which includes that Lagevrio should be considered "…where other treatments (such as sotrovimab or nirmatrelvir plus ritonavir [Paxlovid]) are not suitable or available."

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

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.

People 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 (https://www.tga.gov.au/sites/default/files/paxlovid-pi.pdf) , PBS listing (https://www.pbs.gov.au/info/news/2022/04/paxlovid-nirmatrelvir-and-ritonavir-pbs-listing#:~:text=Commencing%201%20May%202022%20Paxlovid,need%20for%20admission%20to%20hospital.) and consumer medical information (https://www.tga.gov.au/sites/default/files/paxlovid-cmi.pdf)

When to prescribe

Adults who have mild to moderate COVID-19 confirmed by a PCR or medically verified RAT and who can start treatment within five days of symptom onset, can be prescribed PBS-subsidised Paxlovid if:

- they are 65 years of age or older, with two other risk factors for severe disease (as increasing age is a risk factor, patients who are 75 years of age of older only need to have one other risk factor); or
- they identify as Aboriginal or Torres Strait Islander origin, and are 50 years of age or older with two other risk factors for severe disease, or
- they are moderately to severely immunocompromised.

When prescribing Paxlovid via the PBS, ensure the patient meets the eligibility criteria outlined on the PBS listing (https://www.pbs.gov.au/info/news/2022/04/paxlovid-nirmatrelvir-and-ritonavir-pbs-listing#:~:text=Commencing%201%20May%202022%20Paxlovid,need%20for%20admission%20to%20hospital.) . You can review the National COVID-19 Clinical Evidence Taskforce recommendations for the use of Paxlovid here (https://app.magicapp.org/#/guideline/L4Q5An/section/LA6kkM) .

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 (https://www.tga.gov.au/sites/default/files/paxlovid-pi.pdf) 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 (https://www.tga.gov.au/sites/default/files/paxlovid-cmi.pdf) , 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	Phenobarbital
Amiodarone	Phenytoin
Apalutamide	Piroxicam
Avanafil	Ranolazine
Carbamazepine	Rifampicin
Clozapine	Sildenafil
Colchicine	Simvastatin
Diazepam	St John’s Wort (hypericum perforatum)
Ergometrine	Tadalafil
Flecainide	Vardenafil

Lurasidone	Venetoclax
Neratinib	
Pethidine	

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 (https://www.tga.gov.au/sites/default/files/paxlovid-pi.pdf) for each of the medicines listed below.

Abemaciclib	Ethinylestradiol	Prednisone
Afatinib	Everolimus	Quetiapine
Alprazolam	Felodipine	Raltegravir
Amitriptyline	Fentanyl	Rifabutin
Amlodipine	Fluoxetine	Riociguat
Atazanavir	Fosamprenavir	Risperidone
Atorvastatin	Glecaprevir	Rivaroxaban
Atovaquone	Haloperidol	Rosuvastatin
Betamethasone	Ibrutinib	Salmeterol
Bictegravir	Imipramine	Saquinavir
Bosentan	Isavuconazonium sulfate	Sertraline
Budesonide	Itraconazole	Sirolimus

Bupropion	Ketoconazole	Sofosbuvir
Ceritinib	Lamotrigine	Tacrolimus
Ciclosporin	Lidocaine	Tenofovir
Clarithromycin	Loratadine	Triamcinolone
Darunavir	Maraviroc	Velpatasvir
Dasatinib	Methadone	Vinblastine
Dexamethasone	Methylprednisolone	Vincristine
Digoxin	Midazolam	Voriconazole
Diltiazem	Nevirapine	Voxilaprevir
Efavirenz	Nifedipine	Warfarin
Emtricitabine	Nilotinib	Zidovudine
Encorafenib	Nortriptyline	Zolpidem
Erythromycin Paroxetine	Pibrentasvir	

Pregnancy, conception and breastfeeding

Paxlovid is not recommended during pregnancy and in people 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, though 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.