ORAL ANTIVIRALS FAQS

NATIONAL COVID-19 CLINICAL EVIDENCE TASKFORCE

To view the list of recommended treatments please refer to www.covid19evidence.net.au

AS AT 21 JULY 2022

What are antivirals?

Paxlovid (nirmatrelvir and ritonavir) and Lagevrio (molnupiravir) are oral medications which reduce the ability of SARS-CoV-2, the virus that causes COVID-19, to multiply in your body. The aim of using these medications is to reduce the chance of developing severe illness as a result of COVID-19.

Do they work?

Paxlovid

Evidence for the effectiveness of Paxlovid comes from a study that compared it with a placebo (an inactive treatment) in 2,246 unvaccinated adults who had mild to moderate COVID-19 within 5 days of onset of symptoms. They had risk factors for severe disease but didn't need admission to hospital. Nearly all patients in the study had the delta variant of COVID-19, associated with more severe disease than the current Omicron variants.

The group that took Paxlovid had a reduced chance of being admitted to hospital, with a rate of eight per 1,000 people. This compares with 63 per 1,000 in the group that didn't receive Paxlovid: **a big reduction**.

Paxlovid may also prevent people dying of COVID-19, though this is less clear, as there were only small numbers of deaths in the study.

Lagevrio

Evidence for the effectiveness of Lagevrio comes from a study that compared it with a placebo in 1,433 unvaccinated adults who had mild to moderate COVID-19 within 5 days of onset of symptoms. They had risk factors for severe disease but didn't need admission to hospital.

In the first half of the study, patients who received Lagevrio had a lower chance of being admitted to hospital or dying, but in the second half of the study there wasn't a meaningful difference between the groups, so it's slightly tricky to interpret the results. Overall, Lagevrio may reduce hospitalisation or death in unvaccinated individuals with mild COVID-19, however the evidence is limited, the magnitude of effect is small and there is not a lot of safety data. Given this, the Taskforce recommends that, until further evidence is available, use of Lagevrio should only be considered where other treatments such as Paxlovid or remdesivir (another antiviral that is administered intravenously) are not suitable or available.

Who is eligible to be prescribed Paxlovid or Lagevrio?

Under Pharmaceutical Benefits Scheme (PBS) Eligibility criteria, people with mild to moderate COVID-19 confirmed by a PCR or medically verified RAT, can be prescribed PBS-subsidised Paxlovid and Lagevrio by their doctor or authorised nurse practitioner if they are:

- 70 years of age or older
- 50 years of age or older with two additional risk factors for developing severe disease;
- 30 years of age or older, identifying as Aboriginal or Torres Strait Islander, with two additional risk factors for developing severe disease; or
- 18 years of age or older, with moderate to severe immunocompromise.

PBS outlines the risk factors as:

1. The patient is in residential aged care,
2. The patient has disability with multiple comorbidities and/or frailty
3. Neurological conditions, including stroke and dementia and demyelinating conditions,
4. Respiratory compromise, including COPD, moderate or severe asthma (required inhaled steroids), and bronchiectasis, or caused by neurological or musculoskeletal disease,
5. Heart failure, coronary artery disease, cardiomyopathies
6. Obesity (BMI greater than 30 kg/m^2),
7. Diabetes type I or II, requiring medication for glycaemic control,
8. Renal impairment (eGFR less than 60mL/min),
9. Cirrhosis, or
10. The patient has reduced, or lack of, access to higher level healthcare and lives in an area of geographic remoteness classified by the Modified Monash Model as Category 5 or above.

As well as these criteria, Paxlovid can have serious interactions with several other medications, so it's important that your doctor checks any medications (including herbal supplements) against the Liverpool interaction checker and TGA PI before prescribing Paxlovid.

Lagevrio is not recommended during pregnancy and breastfeeding. Contraception is recommended until 4 days after the final dose of Lagevrio in sexually active women of childbearing potential, and for 3 months in men who are sexually active with a partner of childbearing potential (TGA PI).

What does the Taskforce recommend?

Paxlovid (nirmatrelvir plus ritonavir) for adults

The Taskforce recommends that Paxlovid be considered for unvaccinated adults with COVID-19 who:

- are within 5 days of symptom onset
- do not require oxygen; AND
- have one or more risk factors for disease progression.

In addition to at-risk unvaccinated adults, also consider using Paxlovid within 5 days of symptom onset in adults with COVID-19 who do not require oxygen and:

- are immunocompromised; or
- are at particularly high risk of severe disease on the basis of advanced age and multiple risk factors.

To view the full recommendation for Paxlovid, click here.

Lagevrio (molnupiravir) for adults

The Taskforce recommends that Lagevrio be considered for unvaccinated adults with COVID-19 who:

- are within 5 days of symptom onset
- do not require oxygen
- have one or more risk factors for disease progression;

AND where other treatments (such as remdesivir or Paxlovid) are not suitable or available.

In addition to at-risk unvaccinated adults, also consider using Lagevrio within 5 days of symptom onset in adults with COVID-19 who do not require oxygen and:

- are immunocompromised; or
- are at particularly high risk of severe disease on the basis of advanced age and multiple risk factors

AND where other treatments (such as remdesivir or Paxlovid) are not suitable or available.

To view the full recommendation for Molnupiravir, click here.

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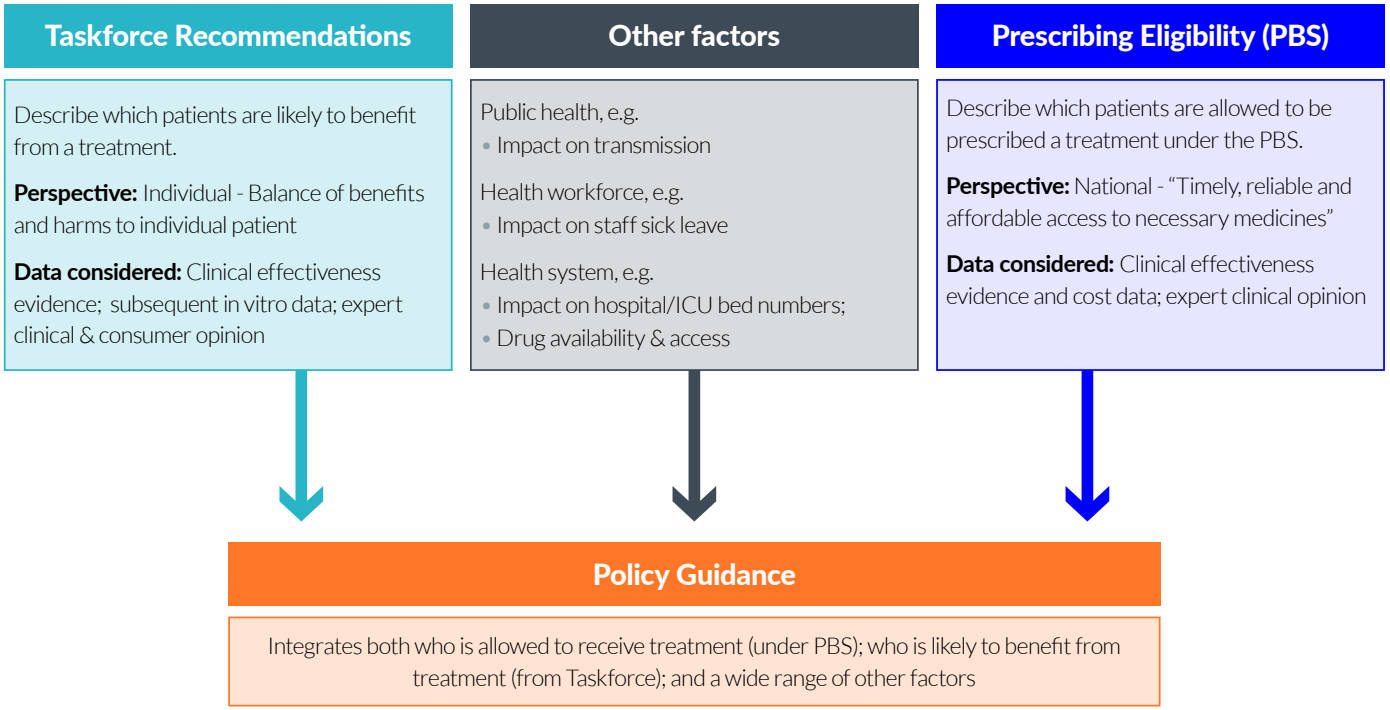
Why are the Taskforce recommendations different from PBS and other policy guidance?

The PBS listing provides an outline of the population of patients for whom Paxlovid and Lagevrio prescription can be considered.

The Taskforce guidance aims to help clinicians identify which patients are most likely to benefit from Paxlovid or Lagevrio, and to assist clinicians and patients to decide whether these medications are appropriate for them, given their specific situation, including other health conditions, current medications and other factors.

The figure below demonstrates how the Taskforce guidance fits within the broader Australian COVID-19 treatments ecosystem.

AUSTRALIAN COVID-19 TREATMENT GUIDANCE ECO-SYSTEM



Who is most likely to benefit from antivirals?

These drugs are most likely to help people who are at highest risk of developing severe illness as a result of COVID-19. This includes people with mild COVID-19 in the first 5 days of symptoms who:

- are immunocompromised or;
- are unvaccinated or;
- have multiple risk factors for severe disease, such as
  - No vaccination or infection in the last ~3-6 months
  - Older age, over 50 years for Aboriginal and Torres Strait Islander people*, or otherwise over 65 years
  - Lung disease, including chronic obstructive pulmonary disease (COPD), asthma or bronchiectasis
  - Cardiovascular disease, including hypertension
  - Obesity (BMI > 30 kg/m^2)
  - Diabetes
  - Renal failure
  - Limitations on access to higher level care due to geographical remoteness or other factors

*The risk of developing severe illness is considered to be higher in Aboriginal and Torres Strait Islander people as a result of inequity arising from social determinants of health

Refer to the Taskforce Risk Classification Tool and Decision Tool for further guidance.

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How do I access Paxlovid and Lagevrio?

The PBS listings for Paxlovid and Lagevrio means eligible Australians can access these medicines from their local community pharmacy with a prescription from their doctor or nurse practitioner.

How should consumers find a GP if they don't have a regular doctor or can't get an appointment quickly?

HealthDirect has a free helpline 1800 022 222 or you can use the Service Finder to search for one near you.
The Find a Pharmacy website may also be helpful to consumers trying to fill prescriptions.

What else should I know about Paxlovid and Lagevrio?

All medications come with some risks and side-effects. Diarrhoea and nausea/vomiting were reported side effects in the trials for both Paxlovid and Lagevrio. People receiving Paxlovid also reported high blood pressure, muscle pain, dysgeusia (weird taste in the mouth) and headache. People receiving Lagevrio also reported dizziness.

One of the components on Paxlovid may reduce the efficacy of combined hormonal contraceptives. Patients using combined hormonal contraceptives should use an effective alternative method of contraception during treatment with Paxlovid, and the menstrual cycle after stopping Paxlovid.

As a result of studies in animals, concerns have been raised about the potential impact of Lagevrio on reproduction. Women, children & adolescents were not included in the trial and its safety in these groups is not clear. Reflecting this, Lagevrio is not recommended during pregnancy and breastfeeding. Contraception is recommended until 4 days after the final dose of Lagevrio in sexually active women of childbearing potential, and for 3 months in men who are sexually active with a partner of childbearing potential (TGA PI).

Do we still need vaccines?

Yes! Vaccination is still the best form of defence against serious disease and death for COVID-19.

It's great that new treatments for COVID-19 are becoming available, especially for those who can't be vaccinated or for whom vaccination is unlikely to be effective but continue to follow advice from ATAGI regarding recommended vaccine doses.

Further resources:

- NPS MedicineWise Factsheet:Oral COVID-19 medicines
- Australian Government Department of Health and Aged Care website
- Consumer Medicine Information leaflet for molnupiravir (Lagevrio)
- Consumer Medicine Information leaflet for nirmaltrevir plus ritonavir (Paxlovid)