Community-based access to oral antiviral treatments for COVID-19 in Australia

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Background
The availability of oral antivirals for SARS-CoV-2 infection reduces the risk of severe, acute illness in people at higher risk for death and hospitalisation.

Objective
The process for antiviral prescription and dispensing in Australia is outlined using nationwide data.

Discussion
Australia has focused on providing rapid access to antivirals to high-risk people in the community via general practices and community pharmacies. Although the introduction of oral antiviral treatments is an important part of the response to the COVID-19 pandemic, vaccination remains the most effective way of mitigating the risk of developing severe complications of COVID-19, including hospitalisation and death.

AUSTRALIA has prioritised the prescription of oral antivirals for COVID-19 infection for people who were most likely to die or be hospitalised with infection. Current evidence shows that advancing age is the highest risk for a poor acute outcome from infection, followed closely by vaccination status.[1] Planning for prescribing and dispensing antivirals began in 2021 and focused on enabling rapid access to treatments in the community close to where people live. Primary care, including general practice and community pharmacy, is central to the provision of oral antivirals to higher risk populations in Australia. This paper outlines how oral antivirals have been used in the Australian COVID-19 pandemic, as guided by emerging evidence and aims to document a contemporary history of the pandemic response.

Two oral antivirals have been available since early 2022 in Australia. Pfizer's oral COVID-19 treatment, nirmatrelvir + ritonavir (trade name of PAXLOVID), and Merck Sharp & Dohme's oral COVID-19 treatment, molnupiravir (trade name of LAGEVRIO). These oral antiviral treatments, taken as tablets or capsules, both work by blocking the ability of the SARS-CoV-2 virus to replicate in the human body. Antivirals have been shown in registration studies to reduce severe acute outcomes including hospitalisation and mortality, and they may also reduce the length of symptomatic illness and infectivity.[2] Recent evidence from Hong Kong also confirmed benefit for hospitalised patients with mild to moderate COVID-19 and recommended early initiation of these treatments during hospitalisation.[3] It should be remembered, however, that vaccination remains the best protection from poor COVID-19 outcomes.[4]

The Platform Adaptive trial of Novel antiviRals for eArly treatment of COVID-19 in the Community (PANORAMIC) open-label study of molnupiravir used in non-hospitalised, vaccinated people in the United Kingdom found a decrease in symptomatic days and viral load, but no difference (compared to the low rate observed in the usual care arm) in the rate of hospitalisation or death.[5] However, the PANORAMIC study population was younger than those who are receiving treatment under Australia's Pharmaceutical Benefits Scheme (PBS) and was also not at high risk for severe outcomes from SARS-CoV-2 infection.[6] Following the publication of PANORAMIC, Australia's National Clinical Evidence Taskforce recommended against the routine use of molnupiravir while recognising that it may still be appropriate for the highest risk patients when all other treatment options are contraindicated.[7] The November 2022 meeting of Australia's Pharmaceutical Benefits Advisory Committee (PBAC) contrasted the PANORAMIC results to observational data showing benefit in older patients and added an Administrative Note to the PBS listing of molnupiravir, for it to only be considered if nirmatrelvir + ritonavir are unsuitable.[8] The nirmatrelvir + ritonavir arm of the PANORAMIC trial is still in progress and not yet reported.

Observational Australian data for the use of oral antivirals in patients aged >70 years found a reduction in hospitalisation, but only for people treated within 48 hours of diagnosis (32% for nirmatrelvir + ritonavir and 26% for molnupiravir).[9] Similarly, risk of death was reduced if treatment was commenced within four days of diagnosis (72% for nirmatrelvir + ritonavir and 54% for molnupiravir).[9] A recent observational study from the US found reduced 28-day all-cause hospitalisation, all-cause mortality, and emergency department presentations during an Omicron surge after treatment with nirmatrelvir + ritonavir only.[10]

There is early evidence that antivirals may decrease the incidence of long COVID and further trials are awaited.[11] An advantage of these oral medications is that many people can receive treatment for COVID-19 in their own homes or in residential aged care facilities, without the need to travel to hospital as was necessary with intravenous treatments. Both oral medications are also less vulnerable than monoclonal antibodies (eg sotrovimab) to loss of efficacy against emerging variants due to their different mechanism of action that is less susceptible to mutations.[12,13]

The first supplies of oral antivirals arrived into Australia's National Medical Stockpile (NMS) in January 2022. The NMS is a strategic reserve of supplies for national health emergencies. Supplies of the oral antivirals were rapidly deployed to aged care facilities, Aboriginal Community Controlled Health Organisations (ACCHOs), the Royal Flying Doctor Service, and state and territory health departments. Aged care facilities were only supplied with molnupiravir whereas both antivirals were supplied to other sites. This supply from the NMS allowed antivirals to be immediately available to those most at risk of poor acute outcomes, while the process for formal listing of the medicines on Australia's PBS could take place.

The PBS in Australia allows for subsidised dispensing of medications recommended for listing by the PBAC after consideration of clinical effectiveness, cost-effectiveness and safety. Only six weeks after approval of molnupiravir by the Australian Therapeutic Goods Administration (TGA) on 18 January 2022, and after consideration by the PBAC in February, the medicine was listed on the PBS on 1 March 2022. The process for approving molnupiravir for PBS listing was the fastest ever to occur in Australia. Nirmatrelvir + ritonavir was subsequently listed in May 2022, both as streamlined authorities. Although some PBS-listed medications require specified approval prior to prescribing for individual patients, streamlined approval allows the prescribing clinician to write a code on the prescription (rather than seeking phone or online approval) for patients who meet the eligibility criteria (Box 1).[14]

Throughout 2022, national advisory committees for high-risk groups, including for people receiving aged care services, people with disability, Aboriginal and Torres Strait Islander people, and people from culturally and linguistically diverse backgrounds, have provided input on who should be targeted for antiviral use. After consultation with key aged care experts, antivirals were made available on the PBS on 22 June 2022 for any person aged ≥70 years who was diagnosed with COVID-19 infection regardless of other risk factors or whether they had developed symptoms from COVID-19 infection.

Both medical practitioners and eligible nurse practitioners can prescribe these medications and most antivirals are dispensed through community pharmacies. This focus on community prescribing and dispensing was deliberate to increase ease of access for patients. Aged care facilities were provided molnupiravir from the NMS to store in the facility to ensure 24-hour access to antivirals for this highly vulnerable group of people.

National data on how many prescriptions were dispensed via the PBS for molnupiravir and nirmatrelvir + ritonavir is shown in Figure 1. The antivirals are most commonly used in those aged >70 years, which follows the PBS criteria. Molnupiravir has been dispensed more than threefold as often as nirmatrelvir + ritonavir, possibly due to its earlier introduction on the PBS and the higher number of drug–drug interactions with nirmatrelvir + ritonavir. The trend in the number of prescriptions dispensed aligns with the trend in the

Box 1. Pharmaceutical Benefits Scheme listing eligibility for Lagevrio® (molnupiravir) and Paxlovid® (nirmatrelvir + ritonavir) (April 2023)

Treatment to be commenced within five days of symptom onset or as soon as possible in the case of asymptomatic infection. The use of COVID-19 antivirals is not recommended during pregnancy and breastfeeding.

Eligibility criteria:

- People who are aged ≥70 years, regardless of symptoms;
- People aged 60–69 years with one additional risk factor for developing severe disease;
- People aged ≥50 years, with two additional risk factors for developing severe disease;
- People aged ≥30 years, identifying as Aboriginal or Torres Strait Islander, with one risk factor for developing severe disease;
- People aged ≥18 years, with moderate to severe immunocompromise;
- People aged >18 years who have been previously hospitalised with COVID-19 infection; and
- People aged ≥18 years who have been previously hospitalised because of COVID-19 disease, if subsequently re-infected.

Risk factors for development of severe, acute disease:

- The patient is in residential aged care;
- The patient has disability with multiple comorbidities and/or frailty;
- Neurological conditions, including stroke and dementia and demyelinating conditions;
- Respiratory compromise, including chronic obstructive pulmonary disease, moderate or severe asthma (required inhaled steroids), and bronchiectasis, or caused by neurological or musculoskeletal disease;
- Heart failure, coronary artery disease, cardiomyopathies;
- Obesity (body mass index >30 kg/m^2);
- Type 1 or 2 diabetes requiring medication for glycaemic control;
- Renal impairment (estimated glomerular filtration rate <60 mL/min/1.73 m^2);
- Cirrhosis; or
- 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.
- Past COVID-19 infection resulting in hospitalisation.

number of COVID-19 cases over time, peaking in July 2022. In July 2022, Australia's Chief Medical Officer made a strong statement of support for targeted use of these oral antivirals, declaring that rapid availability of these medications for anyone who tests positive for COVID-19 should be the expected standard of care in residential aged care facilities.[15] It is notable that the data in Figure 1 do not include medications provided through the NMS, which could narrow the gap between the number of prescriptions dispensed and the number of COVID-19 cases.

Conclusion

Although the introduction of these oral antiviral treatments represented an important new landmark in the Australian response to the COVID-19 pandemic, vaccination remains the most effective way of protecting all people from the risks of developing moderate to severe symptoms of COVID-19, and from the development of long COVID. Although questions remain about the relative effectiveness of oral antivirals in a highly vaccinated population during a predominately Omicron outbreak of COVID-19, equitable and efficient access to treatments for those most at risk continues to be the central principle for provision of oral antiviral medicines for the treatment of COVID-19 in Australia.

Key points

- Oral antivirals reduce severe, acute illness in people at higher risk from SARS-CoV-2 infection.
- Oral antivirals have been available in Australia since early 2022.
- Two antivirals are available: nirmatrelvir + ritonavir and molnupiravir.
- Access to antivirals in Australia has mainly been via prescribing from general practices and dispensing from community pharmacies.
- Vaccination remains the most effective way to reduce the risk of severe disease.

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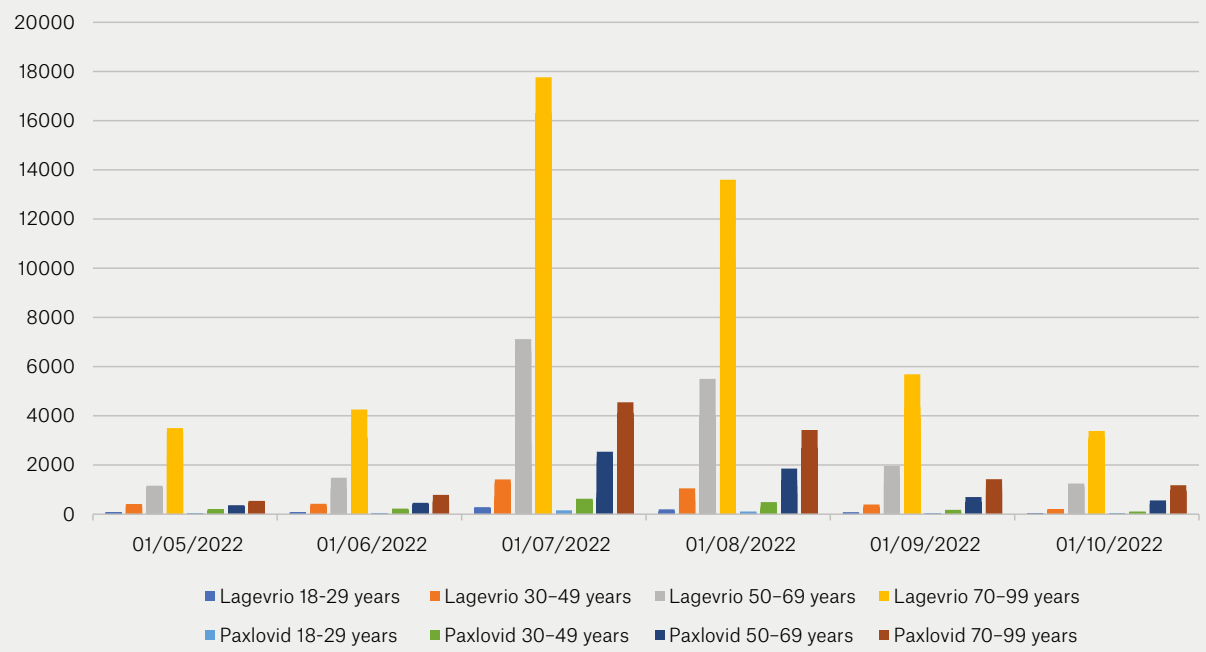

Figure 1. Pharmaceutical Benefits Scheme prescriptions dispensed for molnupiravir and nirmatrelvir + ritonavir by age cohort from 1 May to 1 October 2022.

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