Paxlovid® (nirmatrelvir and ritonavir)
Pharmaceutical Benefits Scheme Factsheet

Paxlovid® (nirmatrelvir and ritonavir) Pharmaceutical Benefits Scheme listing

Paxlovid is being added to the Pharmaceutical Benefits Scheme (PBS) from 1 May 2022 as a treatment for COVID-19.

Vaccines are proven to provide the best protection against COVID-19, however there are some individuals who are at higher risk for severe disease if they become infected with COVID-19.

Factors that put people at high risk include age and other medical conditions or being moderately or severely immunocompromised.

Paxlovid is an oral anti-viral medicine which can be used by patients with mild-moderate COVID-19 who have a high risk for developing severe disease, reducing the need for admission to hospital.

Paxlovid is a prescription only medicine which must be started as soon as possible after a diagnosis of COVID-19 and within 5 days of developing symptoms. The two active substances of the medicine, nirmatrelvir and ritonavir, which are given as separate tablets, must be taken together twice a day for 5 days.

A PBS listing for Paxlovid means eligible patients can access this medicine from their local community pharmacy on a prescription from their doctor or nurse practitioner.

It is important that patients continue to follow local health guidance to isolate if they test positive for COVID-19, including using Telehealth to see their doctor and asking their pharmacy to arrange for Paxlovid to be delivered at home, if necessary.

The recommendation to add Paxlovid to the PBS was made by the independent, expert Pharmaceutical Benefits Advisory Committee (PBAC).

Access to PBS subsidised treatment with Paxlovid

Adults who have mild to moderate COVID-19 confirmed by a PCR or medically verified RAT and who can start treatment within 5 days of symptom onset, can be prescribed PBS-subsidised Paxlovid by their doctor or nurse practitioner 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.

The criteria for accessing PBS-subsidised treatment with Paxlovid are well aligned with the National COVID-19 Clinical Evidence Taskforce recommendations for treatment with a disease modifying medicine:

- the age threshold is the same (50 years of age and older for Aboriginal or Torres Strait Islander people and 65 years of age and older for all others);

- both require older patients to have other risk factors. The list of risk factors in the PBS eligibility criteria has been expanded to include cirrhosis; neurological conditions, including stroke and dementia; and the patient is in residential aged care or residential disability care.
- both include adult patients who are moderately to severely immunocompromised regardless of immunisation status. The list of eligible immunocompromising conditions in the PBS eligibility criteria has been expanded to include rituximab in past 12 months; very high-risk conditions including cerebral palsy, congenital heart disease, thalassemia, sickle cell disease and other haemoglobinopathies and severe physical or intellectual disabilities requiring residential care.

The PBS eligibility criteria also allow vaccinated older patients access to treatment if they have multiple other risk factors for developing severe COVID-19.

Unvaccinated Aboriginal or Torres Strait Islander adults under age 50 and other unvaccinated adults under age 65 are not eligible for PBS subsidised treatment, unless they have a moderate to severe immunocompromising condition.

The independent, expert PBAC takes account of a range of factors including the effectiveness and cost of a medicine when considering it for PBS subsidy. The PBAC considered that the eligibility criteria for PBS access to Paxlovid strike an appropriate balance, given what is known about COVID-19, and what is known about the mechanism of action of Paxlovid.

The PBAC will continue to monitor the conditions for PBS access to Paxlovid by considering new evidence for its effectiveness and safety and the epidemiology of COVID-19.

The PBS is an appropriate mechanism to provide timely and equitable access to oral COVID-19 treatments. The Department has been working closely with the PBAC to make this available on the PBS in recognition of the urgent public health need related to the prevention, management, and treatment of SARS-CoV-2 infections.

The Department is working with distributors and peak medical and pharmacy organisations to prioritise Paxlovid for those patients at highest risk of developing severe COVID-19 as reflected in the PBS eligibility criteria, and to discourage private prescriptions.

State and territory hospital systems provide complementary mechanisms for access where the prescriber considers treatment is clinically indicated but the patient is not eligible under the PBS. The Government has provided Paxlovid and a range of other COVID-19 treatments to state and territory health departments via the National Medical Stockpile for use in people at risk. The Government has also provided Paxlovid to Aboriginal Controlled Community Health Organisations and the Royal Flying Doctor Service for use in people at risk.

Importance of Vaccination

- Paxlovid is not intended to be used as a substitute for vaccination against COVID-19.
- Vaccinations are the best way to protect individuals and the wider community from COVID-19.

TGA Provisional Approval

- Paxlovid was provisionally approved by the Therapeutic Goods Administration (TGA) on 18 January 2022, for the treatment of adults with COVID-19 who do not require initiation of oxygen and who are at increased risk of progression to hospitalisation or death.

- Australians can be confident that the TGA's review process of Paxlovid was rigorous. The decision to provisionally approve the medicine was informed by expert advice from the Advisory Committee on Medicines, an independent committee with expertise in scientific, medical and clinical fields including consumer representation.
- Data was provided as a rolling submission. Under normal circumstances, the TGA's assessment (for both provisional and general registration) begins once all information to support registration is available. As part of the Department of Health's response to the pandemic, the TGA has agreed to accept rolling data for COVID-19 vaccines and medicines, to enable early evaluation of data as it comes to hand.
- Pharmaceutical companies are required to continue providing information to the TGA on longer-term efficacy and safety from ongoing clinical trials and post-market assessment, both in Australia and around the world.

Diagnosis for PBS eligibility

- The onus is on the prescriber to be satisfied that the COVID-19 test is valid and to record that in the patient records.

Condition: SARS-CoV-2 infection
Indication: SARS-CoV-2 infection
Clinical criteria:
Patient must have received a positive polymerase chain reaction (PCR) test result **OR**
Patient must have received a positive rapid antigen test (RAT) result verified by a medical practitioner or nurse practitioner
Prescriber instructions:
Where PCR is used to confirm diagnosis, the result, testing date, location and test provider must be recorded on the patient record
Prescriber instructions:
Where a RAT is used to confirm diagnosis, the test must be verified by a medical practitioner or nurse practitioner. The test result, testing date, location and test provider (where relevant) must be recorded on the patient record

Treatment Administration

- Treatment with Paxlovid should be commenced as soon as possible after a diagnosis of COVID-19 and within 5 days of symptom onset. The standard dosage for most people is 300 mg nirmatrelvir (two 150 mg tablets) with 100 mg ritonavir (one 100 mg tablet) taken together orally every 12 hours for 5 days. Patients with moderately reduced kidney function may be prescribed a dose of 150 mg of nirmatrelvir (one 150mg tablet) with 100 mg of ritonavir (one 100mg tablet), every 12 hours for 5 days.
- A benefit of this treatment is that it can be taken orally, rather than as an injection or infusion in hospital. This makes the treatment easier to administer in the community, particularly for patients in rural and remote areas and in residential aged care and disability services.
- Pivotal safety data for Paxlovid is limited to results from a Phase 2/3 clinical trial. In this trial, the most frequently reported side effects occurring in subjects receiving Paxlovid were dysgeusia (5.6 % of participants), diarrhoea (3.1%); headache (1.4%); and vomiting (1.1%). Older people receiving Paxlovid should be closely monitored for side effects.

- Safety and efficacy of Paxlovid have not been established in patients less than 18 years of age, therefore use in paediatric patients is not recommended.

Interactions with other medicines

- Paxlovid interacts with many different medicines, including herbal supplements. These may lead to clinically significant adverse reactions, potentially leading to severe, life-threatening or fatal events from greater exposures of concomitant medications. They may also lead to a loss of therapeutic effect of Paxlovid (due to reduced exposure to Paxlovid).
- Paxlovid is contraindicated with drugs that are highly dependent on CYP3A for clearance and for which elevated concentrations are associated with serious and/or life-threatening reactions.
- Paxlovid is also contraindicated with drugs that are potent CYP3A inducers where significantly reduced nirmatrelvir or ritonavir plasma concentrations may be associated with the potential for loss of virologic response and possible resistance. Paxlovid cannot be started immediately after discontinuation of a potent CYP3A inducer, due to the delayed offset of the recently discontinued CYP3A inducer.
- In addition to the above contraindications, careful monitoring is recommended when Paxlovid is used with a wide range of other medicines.
- For complete details of drug interactions, including medicines for which concomitant use of Paxlovid is contraindicated, please refer to the Paxlovid Product Information approved by the TGA.
- Prescribers and dispensers should carefully review a patient's concomitant medications including over-the-counter medications, herbal supplements, and recreational drug before prescribing or dispensing Paxlovid.

Contraindications

- The use of Paxlovid is contraindicated with drugs that are highly dependent on CYP3A for clearance, or potent inducers of CYP3A. Please refer to 'Interactions with other medicines' above for more information.
- Paxlovid is contraindicated in patients with severe renal or hepatic impairment.

Listing of medicines on the PBS

- The PBS is the main mechanism through which the Government subsidises the cost of medicines for the treatment of Australian patients.
- The PBAC is an independent, expert, statutory body established under the *National Health Act 1953* to make recommendations and give advice to the Australian Government and the Minister for Health about which drugs and medicinal preparations should be subsidised on the PBS.
- Under legislation, a new medicine cannot be listed by the Government on the PBS unless the PBAC makes a recommendation in favour of listing. The Government does not interfere with the PBAC's considerations or process to develop recommendations to Government.
- When the PBAC evaluates applications for PBS subsidy, it is legally required to take into account the clinical effectiveness (how well it works) and cost effectiveness (value for money) of the medicine compared to other available therapies. The PBAC also takes into account the approval of a product granted by the TGA.
- While assessing applications, the PBAC uses a rigorous health technology assessment methodology to evaluate a range of factors including the comparative effectiveness and cost of alternative treatments.

Further information

Further information is available from

The NPS MedicineWise website:

Nirmatrelvir and ritonavir for COVID-19

Oral antivirals and sotrovimab for adults with mild-to-moderate COVID-19 who do not require oxygen - NPS MedicineWise

The Department of Health website:

Oral treatments for COVID-19 | Australian Government Department of Health

The TGA website:

COVID-19 treatments: Provisional registrations | Therapeutic Goods Administration (TGA)

The National COVID-19 Clinical Evidence Taskforce website:

FLOWCHART-2-MANAGEMENT-OF-MILD.pdf (covid19evidence.net.au)

FLOWCHART-2-MANAGEMENT-OF-MOD-SEVERE.pdf (covid19evidence.net.au)

FLOWCHART-Drug Treatment for Adults with COVID-19 (covid19evidence.net.au) and

FLOWCHART - Risk Classification Tool for Adults with mild COVID-19 (covid19evidence.net.au)