Lagevrio® (molnupiravir)

Pharmaceutical Benefits Scheme Factsheet – December 2024

Lagevrio® (molnupiravir) PBS listing

Lagevrio is listed on the Pharmaceutical Benefits Scheme (PBS) as a treatment for COVID-19. The recommendation to add Lagevrio to the PBS was made by the independent, expert Pharmaceutical Benefits Advisory Committee (PBAC). A PBS listing for Lagevrio means eligible patients can access this medicine from their local community pharmacy on a prescription from their doctor or authorised nurse practitioner. Medical practitioners and nurse practitioners are able to add Lagevrio to their Prescriber's Bag supplies.

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. Risk factors include older age, certain medical conditions and being moderately or severely immunocompromised.

Lagevrio is a prescription only, oral antiviral medicine which can be used by patients with COVID-19 who have a high risk for developing severe disease, reducing the need for admission to hospital. A course of Lagevrio must be started within the first 5 days from the onset of COVID-19 symptoms (more detail is provided below).

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

Changes to access to PBS subsidised treatment with Lagevrio

People at high risk of progression to severe disease where Paxlovid is contraindicated remain the population eligible for access to Lagevrio on the PBS.

At its May 2024 meeting, the PBAC recommended amending the PBS criteria for Lagevrio and Paxlovid to be method-agnostic with regards to nucleic acid testing for respiratory pathogen detection.

From 1 December 2024, the PBS eligibility criteria for Lagrevrio have been updated to remove the need for a positive polymerase chain reaction (PCR) test result. All other eligibility criteria remain unchanged.

PBS eligibility criteria

Adults 70 years of age or older, with COVID-19 confirmed by a nucleic acid test or a Rapid Antigen Test (RAT), can be prescribed PBS-subsidised Lagevrio by their doctor or authorised nurse practitioner where:

- Paxlovid is contraindicated,
- treatment is commenced within 5 days of the onset of symptoms, or treatment is initiated as soon as possible after diagnosis is confirmed where asymptomatic, and
- patients do not require hospitalisation for COVID-19 infection at the time of prescribing.

For adults 70 years of age or older, no further risk factors for progression to severe disease are required for PBS eligibility.

Adults with COVID-19 confirmed by a nucleic acid test or a RAT can be prescribed PBS-subsidised Lagevrio by their doctor or authorised nurse practitioner where Paxlovid is contraindicated and the patient is:

- 50 years of age or older, with two additional risk factors for developing severe disease;
- 30 years of age or older, identifying as First Nations people, with one risk factor for developing severe disease;
- 18 years of age or older, with moderate to severe immunocompromise; OR
- 18 years of age or older who have been previously hospitalised from COVID-19 disease, if are subsequently re-infected.

Patients are also required to have at least one sign or symptom attributable to COVID-19, not require hospitalisation for COVID-19 at the time of prescribing and commence treatment within 5 days of the onset of symptoms.

First Nations adults under age 30 and other adults under age 50 are not eligible for PBS subsidised treatment, unless they have a moderate to severe immunocompromising condition or have been previously hospitalised with COVID-19 disease.

The PBS restrictions for COVID-19 antiviral treatments do not restrict the number of courses of treatment a person can have in a lifetime. Provided patients meet the eligibility criteria for the treatment, they may access second or subsequent courses of antiviral treatment for second or subsequent COVID-19 infections.

The following is a list of risk factors (conditions) contributing to the PBS definition of high risk for development of severe disease:

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/m2),
7. Diabetes type I or II, requiring medication for glycaemic control,
8. Renal impairment (eGFR less than 60mL/min),
9. Cirrhosis,
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.

For the purpose of PBS eligibility, “moderately to severely immunocompromised” patients are those with:

1. any primary or acquired immunodeficiency including:
    a. Haematologic neoplasms: leukaemias, lymphomas, myelodysplastic syndromes, multiple myeloma and other plasma cell disorders
    b. Post-transplant: solid organ (on immunosuppressive therapy), haematopoietic stem cell transplant (within 24 months),
    c. Immunocompromised due to primary or acquired (HIV/AIDS) immunodeficiency OR
2. any significantly immunocompromising condition(s) where, in the last 3 months the patient has received:
    a. Chemotherapy or whole body radiotherapy,
    b. High-dose corticosteroids (≥20 mg of prednisone per day, or equivalent) for at least 14 days in a month, or pulse corticosteroid therapy,

c. Biological agents and other treatments that deplete or inhibit B cell or T cell function (abatacept, anti-CD20 antibodies, BTK inhibitors, JAK inhibitors, sphingosine 1-phosphate receptor modulators, anti-CD52 antibodies, anti-complement antibodies, anti-thymocyte globulin),
d. Selected conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) including mycophenolate, methotrexate, leflunomide, azathioprine, 6-mercaptopurine (at least 1.5mg/kg/day), alkylating agents (e.g. cyclophosphamide, chlorambucil), and systemic calcineurin inhibitors (e.g. cyclosporin, tacrolimus) OR

3. any significantly immunocompromising condition(s) where, in the last 12 months the patient has received anti-CD20 monoclonal antibody treatment, including rituximab, ocrelizumab, ofatumumab and obinutuzumab.
4. others with very high-risk conditions including Down Syndrome, cerebral palsy, congenital heart disease, thalassemia, sickle cell disease and other haemoglobinopathies OR
5. people with disability with multiple comorbidities and/or frailty.

Patients who are hospitalised for another condition, and test positive to COVID-19 while in hospital, are permitted to access Lagevrio through the PBS provided they meet the remaining eligibility criteria. The PBS criteria note:

- *Patient must not require hospitalisation **for COVID-19 infection** at the time of prescribing*

If a patient is prescribed a COVID-19 oral antiviral while in hospital the patient should be discharged with any remaining treatment, as part of usual discharge planning, to allow the patient to finish the full course at home.

Additional information regarding dispensing and claiming for hospitals can be found on the Services Australia website or by contacting Services Australia on 132 290 24.

Patients not eligible for Paxlovid access through the PBS

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 the updated eligibility criteria for PBS access to Lagevrio strike an appropriate balance, given what is known about COVID-19, recent PBS utilisation patterns, and what is known about the mechanism of action of Lagevrio.

The PBAC will continue to monitor the conditions for PBS access to Lagevrio 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.

Importance of Vaccination

- Lagevrio 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.

Therapeutic Goods Administration Provisional Approval

- Lagevrio 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 Lagevrio 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 and Aged Care's response to the pandemic, the TGA has agreed to accept rolling data for COVID-19 vaccines and treatments, 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 test for COVD-19 is valid and to record that in the patient records. See below extract from the PBS eligibility criteria.

PBS Indication	SARS-CoV-2 infection
Clinical criteria	Patient must have received a positive nucleic acid test result; or Patient must have received a positive rapid antigen test (RAT) result
Prescriber Instructions	Where nucleic acid testing is used to confirm diagnosis, the result, testing date, location and test provider must be recorded on the patient record. Where a RAT is used to confirm diagnosis, available information about the test result, testing date, location and test provider (where relevant) must be recorded on the patient record.

Contraindications to Paxlovid

- The prescriber should consider if risk of drug-drug interactions can be managed safely with additional monitoring and/or by temporarily withholding or adjusting the dose of the patient's interacting medications.
- As Paxlovid is more effective than Lagevrio, the use of Lagevrio should be limited to situations where in the opinion of the prescriber, Paxlovid cannot be used due to contraindications.

The onus is on the prescriber to be satisfied that Paxlovid is contraindicated and details/reasons for contraindication to Paxlovid must be documented in the patient's medical record.

Clinical criteria	The treatment must be for use when Paxlovid is contraindicated.
Prescriber Instructions	The contraindications to Paxlovid can be found using the Liverpool COVID-19 Drug interaction checker or the TGA-approved Product Information for Paxlovid. Details/reasons of contraindications to Paxlovid must be documented in the patient's medical records.

Treatment Administration

- Treatment with Lagevrio should be commenced as soon as possible after a diagnosis of COVID-19 and within 5 days of symptom onset (or, for asymptomatic adults 70 years of age or older, as soon as possible after diagnosis is confirmed). It is taken as 4 capsules 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 Lagevrio is limited to results from a single Phase 3 clinical trial. In this trial, the most frequently reported side effects occurring in ≥1% of subjects receiving were diarrhoea (2% of participants); nausea (1%); and dizziness (1%). All these reactions were classified as either mild or moderate in severity. Older people receiving Lagevrio should be closely monitored for side effects.
- Based on the limited available data, there have been no drug interactions identified.

Pregnancy, breastfeeding and contraception

- The use of Lagevrio is not recommended during pregnancy and breastfeeding. It is recommended that sexually active women of childbearing potential use contraception during and for 4 days after treatment with molnupiravir. There is no data available in relation to whether molnupiravir affects sperm. It is recommended that men who are sexually active with a partner of childbearing potential use an adequate form of contraception during and 3 months after treatment with molnupiravir.

Paediatric use

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

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 Government and the Minister for Health and Aged Care 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 PBAC's consideration is generally initiated by the pharmaceutical company responsible for a medicine applying for the medicine to be considered for PBS listing. The pharmaceutical company usually holds the scientific data and other information necessary to inform the PBAC's consideration. Pharmaceutical companies are private entities that make their own decisions on the availability of their medicines.
- 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 at:

- PBS website: Complete information on the PBS listings for Lagevrio can be found on the PBS website at www.pbs.gov.au by using the search term "Molnupiravir".

- The Department of Health and Aged Care website: Oral treatments for COVID-19 | Australian Government Department of Health and Aged Care
- The TGA website: COVID-19 treatments: Provisional registrations | Therapeutic Goods Administration (TGA)
- Liverpool COVID-19 Drug interaction checker: www.covid19-druginteractions.org/checker