AUSTRALIAN COMMISSION
ON SAFETY AND QUALITY IN HEALTH CARE

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In this issue

This issue of RADAR provides an overview of medicines recently revised on the Pharmaceutical Benefits Scheme (PBS) including:

- Nirmatrelvir and ritonavir (Paxlovid®) and molnupiravir (Lagevrio®) for COVID-19 (amended PBS listing)
- Type 2 diabetes mellitus (T2DM) medicines (amended PBS restrictions).

Nirmatrelvir and ritonavir (Paxlovid®) and molnupiravir (Lagevrio®) for COVID-19 – amended PBS listing

Key Points

- From 1 March 2024, the PBS eligibility criteria changed for COVID-19 oral antiviral medicines – nirmatrelvir and ritonavir (Paxlovid®) and molnupiravir (Lagevrio®).
- Patients aged 50 to 69 years with COVID-19 are required to have two or more risk factors for severe disease to access PBS-subsidised treatment with nirmatrelvir and ritonavir.[1] The change to eligibility for nirmatrelvir and ritonavir was based on advice from the independent and expert Pharmaceutical Benefits Advisory Committee (PBAC)[1] given reduced cost-effectiveness of nirmatrelvir and ritonavir in this lower risk population.
- Molnupiravir can now only be prescribed on the PBS when nirmatrelvir and ritonavir combination is contraindicated. The details/reasons for contraindications to nirmatrelvir and ritonavir must be documented in the patient's medical record.[2] The change to molnupiravir eligibility was based on PBAC advice that the nirmatrelvir and ritonavir combination is a more effective treatment than molnupiravir. However, molnupiravir may be an appropriate treatment for patients for whom nirmatrelvir and ritonavir is contraindicated.
- The nirmatrelvir and ritonavir combination and molnupiravir remain listed on the General Schedule (Schedule 85) of the PBS as Authority Required (Streamlined). The listing is for patient groups with COVID-19 who are at high risk of progressing to severe disease requiring hospitalisation.

What are nirmatrelvir and ritonavir, and molnupiravir?

The nirmatrelvir and ritonavir combination and molnupiravir are oral antiviral medicines 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.[3,4]

Who is eligible for PBS-subsidised nirmatrelvir and ritonavir, and molnupiravir?

Eligible adults with COVID-19, confirmed by a positive polymerase chain reaction (PCR) test or a rapid antigen test (RAT), may be eligible for PBS subsidised COVID-19 antiviral treatments, through a prescription from their doctor or authorised nurse practitioner.[1,2]

Please see **Table 1** for PBS eligibility criteria for the nirmatrelvir and ritonavir combination and molnupiravir, and **Table 2** for the complete list of risk factors.

Complete information on the PBS listings for nirmatrelvir and ritonavir (Paxlovid®) and molnupiravir (Lagevrio®), including eligibility criteria, is available on the PBS website at www.pbs.gov.au by using the search term “Paxlovid” or “Lagevrio” respectively.

Contraindications of nirmatrelvir and ritonavir

The nirmatrelvir and ritonavir combination is contraindicated in patients with severe renal or hepatic impairment.[3] The medicine may also interact with many different medicines, including herbal supplements.[3] Interactions with medicinal products may lead to clinically significant adverse reactions, including severe, life-threatening or fatal events from greater exposures of concomitant medications. In some instances, it may lead to a loss of therapeutic effect of nirmatrelvir and ritonavir.

Although there may be drug interactions between nirmatrelvir and ritonavir and a wide range of medicines, only some of these drug interactions will mean nirmatrelvir and ritonavir is contraindicated.

Prescribers and dispensers should carefully review a patient’s concomitant medications, including over-the-counter medications, herbal supplements, and recreational drug use, before prescribing or dispensing nirmatrelvir and ritonavir to avoid significant adverse reactions.[1] Where it is safe to do so, contraindications to nirmatrelvir and ritonavir can sometimes be managed by withholding the other medication or reducing its dose for the duration of treatment.

Additional tools are available to assist clinicians to identify and manage drug interactions, such as the Liverpool COVID-19 Drug interaction checker.

For complete details on drug interactions, please refer to the Product Information – Paxlovid® approved by the Therapeutic Goods Administration (TGA).

Table 1: PBS eligibility criteria nirmatrelvir and ritonavir, and molnupiravir from 1 March 2024[1,2]

Patient population	PBS eligibility criteria for nirmatrelvir and ritonavir	PBS eligibility criteria for molnupiravir
Adults 70 years or older	Adults with COVID-19 confirmed by a PCR or RAT test can be prescribed PBS-subsidised nirmatrelvir and ritonavir if: • treatment is commenced within 5 days of onset of symptoms, or • treatment is initiated as soon as possible after diagnosis is	Adults with COVID-19 confirmed by a PCR or RAT test can be prescribed PBS-subsidised molnupiravir if: • nirmatrelvir and ritonavir combination is contraindicated, • treatment is commenced within 5 days of onset of symptoms, or

	confirmed when asymptomatic, and • they do not require hospitalisation for COVID-19 infection at the time of prescribing. No further risk factors for progression to severe disease are required for PBS eligibility.	• treatment initiated as soon as possible after diagnosis is confirmed when asymptomatic, and • they do not require hospitalisation for COVID-19 infection at the time of prescribing. No further risk factors for progression to severe disease are required for PBS eligibility.
Adults 50 – 69 years of age	Adults with COVID-19 confirmed by a PCR or RAT test can be prescribed PBS-subsidised nirmatrelvir and ritonavir if: • treatment is commenced within 5 days of onset of symptoms, and • they have at least one sign or symptom attributable to COVID-19, and • they do not require hospitalisation for COVID-19 infection at the time of prescribing, and • they have **two risk factors** for developing severe disease. Please see **Table 2** for a list of risk factors for developing severe disease.	Adults with COVID-19 confirmed by a PCR or RAT test can be prescribed PBS-subsidised molnupiravir if: • nirmatrelvir and ritonavir combination is contraindicated, and • treatment is commenced within 5 days of onset of symptoms, and • they have at least one sign or symptom attributable to COVID-19, and • they do not require hospitalisation for COVID-19 infection at the time of prescribing, and • they have **two risk factors** for developing severe disease. Please see **Table 2** for a list of risk factors for developing severe disease.
Adults 30 years or older identifying as First Nations people	First Nations adults with COVID-19 confirmed by a PCR or RAT test can be prescribed PBS-subsidised nirmatrelvir and ritonavir if: • treatment is commenced within 5 days of onset of symptoms, and • they have at least one sign or symptom attributable to COVID-19, and • they do not require hospitalisation for COVID-19 infection at the time of prescribing, and	First Nations adults with COVID-19 confirmed by a PCR or RAT test can be prescribed PBS-subsidised molnupiravir if: • nirmatrelvir and ritonavir combination is contraindicated, • treatment is commenced within 5 days of onset of symptoms, and • they have at least one sign or symptom attributable to COVID-19, and • they do not require hospitalisation for COVID-19 infection at the time of prescribing, and

	• they have **one risk factor** for developing severe disease. Please see **Table 2** for a list of risk factors for developing severe disease.	• they have **one risk factor** for developing severe disease. Please see **Table 2** for a list of risk factors for developing severe disease.
Adults 18 years or older	Adults with COVID-19 confirmed by a PCR or RAT test can be prescribed PBS-subsidised nirmatrelvir and ritonavir if: • treatment is commenced within 5 days of onset of symptoms, and • they have at least one sign or symptom attributable to COVID-19, and • they do not require hospitalisation for COVID-19 infection at the time of prescribing. AND • they are moderately to severely immunocompromised, or • have been previously hospitalised from COVID-19 disease, and subsequently re-infected. Please see **Table 3** for definition of moderately to severely immunocompromised patients for the purpose of PBS eligibility of nirmatrelvir and ritonavir.	Adults with COVID-19 confirmed by a PCR or RAT test can be prescribed PBS-subsidised molnupiravir if: • nirmatrelvir and ritonavir combination is contraindicated, • treatment is commenced within 5 days of onset of symptoms, and • they have at least one sign or symptom attributable to COVID-19, and • they do not require hospitalisation for COVID-19 infection at the time of prescribing. AND • they are moderately to severely immunocompromised, or • have been previously hospitalised from COVID-19 disease, and subsequently re-infected. Please see **Table 3** for definition of moderately to severely immunocompromised patients for the purpose of PBS eligibility of nirmatrelvir and ritonavir.

For complete information on the PBS listings for nirmatrelvir and ritonavir (Paxlovid®) and molnupiravir (Lagevrio®), including eligibility criteria, please refer to the PBS website at www.pbs.gov.au by using the search term “Paxlovid” or “Lagevrio” respectively.

Table 2: List of risk factors contributing to the PBS definition of high risk for development of severe disease[1,2]

Risk Factors	
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
11.	Past COVID-19 infection episode resulting in hospitalisation

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Table 3: Definition of moderately to severely immunocompromised adults at high risk of severe disease for the purpose of PBS eligibility [1,2]

Moderately to severely immunocompromised includes:	
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.
2. Any significantly immunocompromising condition(s) where, in the last 3 months the patient has received any of these treatments:	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).
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 obituzumab.	
4. Patients with very high-risk conditions including Down Syndrome, cerebral palsy, congenital heart disease, thalassemia, sickle cell disease and other haemoglobinopathies.	
5. People with disability with multiple comorbidities and/or frailty.	

For complete information on the PBS listings for nirmatrelvir and ritonavir (Paxlovid®) and molnupiravir (Lagevrio®), including eligibility criteria, please refer to the PBS website at www.pbs.gov.au by using the search term “Paxlovid” or “Lagevrio” respectively.

References

1. Paxlovid® (nirmatrelvir and ritonavir) Pharmaceutical Benefits Scheme. Canberra: Australian Government Department of Health and Aged Care; 2024 Available from: www.pbs.gov.au/medicine/item/12996B 13147Y (accessed 6 June 2024).
2. Lagevrio® (molnupiravir) Pharmaceutical Benefits Scheme. Canberra: Australian Government Department of Health and Aged Care; 2024. Available from: www.pbs.gov.au/medicine/item/12910L-13144T (accessed 6 June 2024).
3. Therapeutic Goods Administration. Australian Product Information – Paxlovid® (nirmatrelvir/ritonavir tablets) Available from: www.tga.gov.au/resources/artg/377572 (accessed 30 April 2024).
4. Therapeutic Goods Administration. Australian Product Information – Lagevrio® (molnupiravir capsules) Available from: www.tga.gov.au/resources/artg/372650 (accessed 30 April 2024).

Type 2 diabetes mellitus (T2DM) medicines – amended PBS restrictions

Key Points

- On 1 June 2024, PBS restrictions for type 2 diabetes mellitus (T2DM) medicines changed.
- The changes relate to PBS authority level restrictions for glucagon-like peptide 1 receptor agonists (GLP-1 RAs) and PBS restrictions for other T2DM medicines.[1]
- These changes have been made in accordance with PBAC recommendations to:
    - simplify and clarify the PBS restrictions
    - ensure use of these medicines in line with the PBS restrictions
    - align restrictions with current clinical guidelines while considering the cost-effectiveness of comparative treatments.[1]

Changes to PBS authority level and restrictions for GLP-1 RAs

- For patients initiating therapy with GLP-1 RAs, the authority type for all indications was changed from Authority Required (STREAMLINED) to Authority Required (telephone/electronic).[1]
- For patients continuing therapy with GLP-1 RAs, the authority type continues to be Authority Required (STREAMLINED).[1]
- To access PBS-subsidised GLP-1 RA therapy, patients must be contraindicated, intolerant, or must not have achieved a clinically meaningful glycaemic response to a sodium-glucose cotransporter 2 (SGLT2) inhibitor. The definition of a ‘clinically meaningful glycaemic response’ has been left to prescriber discretion in the context of the individual patient.[1]
- The restrictions have been revised to clarify that GLP-1 RAs:
    - are only PBS-subsidised for use in combination with at least one of: metformin, a sulfonylurea, insulin.
    - are not subsidised for use in combination with a dipeptidyl peptidase-4 (DPP4) inhibitor.
    - are not subsidised for use in combination with an SGLT2 inhibitor, except where the SGLT2 inhibitor is prescribed for a different indication (e.g. heart failure or kidney disease) and the patient did not achieve a clinically meaningful glycaemic response to the SGLT2 inhibitor.[1]
    - Patients who have previously received a PBS-subsidised prescription for a GLP-1 RA can access this medicine via the streamlined listing. They do not need to requalify for access under the revised restriction.[1]

Simplification of PBS restrictions for T2DM medicines

- Removal of the requirement for patients to be contraindicated to metformin, to use DPP4 inhibitors, SGLT2 inhibitors, or GLP-1 RAs with insulin.[1]
- Alignment of DPP4 inhibitor restrictions to allow use of all DPP4 inhibitors with insulin or SGLT2 inhibitors.[1]
- Pioglitazone has been changed to a Restricted Benefit listing for T2DM without any clinical criteria. This provides an additional first-line therapy for patients who are contraindicated or intolerant to other first-line therapies.[1]
- DPP4 inhibitors and SGLT2 inhibitors are now subsidised for use in quadruple therapy, in combination with each other, metformin, and insulin.[1]

Please refer to the PBS eligibility requirements for T2DM medicines flow diagram and the Tabular summary of new PBS restrictions for T2DM medicines on the PBS website for further details.

References

1. PBS restriction changes to type 2 diabetes mellitus (T2DM) medicines. Canberra: Australian Government Department of Health and Aged Care; 2024 Available from: www.pbs.gov.au/info/reviews/pbs-restriction-changes-to-type-2-diabetes-mellitus-t2dm-medicines (accessed 6 June 2024).

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