

## **PBAC - OUTCOME STATEMENT**

### **ITEM 14.04 - COVID-19 ANTIVIRAL RESTRICTIONS**

**MOLNUIRAVIR, Capsule 200 mg, Lagevrio<sup>®</sup>, Merck Sharp & Dohme Australia Pty Ltd**

**NIRMATRELVIR AND RITONAVIR, Pack containing 4 tablets nirmatrelvir 150 mg and 2 tablets ritonavir 100 mg, Paxlovid<sup>®</sup>, Pfizer Australia Pty Ltd**

At its November 2022 meeting, the Pharmaceutical Benefits Advisory Committee (PBAC) considered several aspects of the Pharmaceutical Benefits Scheme (PBS) listings of the COVID-19 oral antivirals, molnupiravir (Lagevrio<sup>®</sup>) and nirmatrelvir and ritonavir (Paxlovid<sup>®</sup>).

The PBAC noted correspondence from Queensland Health, drawing attention to PBS molnupiravir and nirmatrelvir and ritonavir eligibility criteria relevant for patients taking anti-CD20 monoclonal antibodies.

The PBAC agreed that anti-CD20 monoclonal antibodies including rituximab, ocrelizumab, ofatumumab and obinutuzumab have similar activity and duration of B cell suppression.

**The PBAC recommended that listings for molnupiravir and nirmatrelvir and ritonavir be amended to allow PBS access for patients with any significantly immunocompromising condition where in the last 12 months, the patient has received anti-CD20 monoclonal antibody treatment.**

The PBAC noted correspondence suggesting that restrictions should be amended to allow PBS access to molnupiravir and nirmatrelvir and ritonavir, in patients (not meeting the current PBS definition of high risk) who have previously been hospitalised with severe COVID-19 disease.

**The PBAC recommended that the listings for molnupiravir and nirmatrelvir and ritonavir be amended to allow PBS access for patients who have been previously hospitalised with COVID-19 disease if subsequently re-infected.**

The PBAC noted correspondence from the Chief Health Officer of the Victorian Department of Health, concerning current PBS requirements for verification of a positive COVID-19 rapid antigen test. Correspondence suggested that practitioners taking a strict interpretation of what is meant by verification of RAT results might cause delay in prescription and / or additional burden on Emergency Departments.

**The PBAC recommended that the listings for molnupiravir and nirmatrelvir and ritonavir be amended so that clinical criteria around COVID-19 testing are:**

- Patient must have received a positive polymerase chain reaction (PCR) test result;  
OR
- Patient must have received a positive rapid antigen test (RAT) result

**The note concerning use of a RAT to confirm diagnosis should be updated to state: “Where a RAT is used to confirm diagnosis, available information about the test result, testing date, location and test provider (where relevant) should be recorded on the patient record”.**

The PBAC noted the posting in October 2022 of a pre-print describing preliminary analysis of the UK’s PANORAMIC trial of molnupiravir plus usual care versus usual care, for community treatment of adults with COVID-19 at increased risk of adverse outcomes.

The PBAC noted that there have been two routes to access treatments for COVID-19 in non-hospitalised patients in the UK, namely targeted deployment for those at highest risk of progression to severe disease, and for others, enrolment in the PANORAMIC study. N=25,783 patients ( $\geq 50$  years of age, or  $\geq 18$  years with comorbidities) were randomised between December 2021 and April 2022, but patients at highest risk of progression were not the target population. Patients in PANORAMIC were highly vaccinated, and the mean age was 56.6 years with only 6% being  $>75$  years of age. The PBAC noted a modest imbalance in the number of patients excluded from the primary analysis across arms (97.7% of randomised patients were included in the primary analysis in the molnupiravir arm, and 96.3% in the usual care arm).

The primary endpoint was the composite of all-cause hospitalisation and death within 28 days of randomisation, and this endpoint was observed in only 0.8% of patients in both arms, indicating that in the studied group, addition of molnupiravir to usual care did not reduce the risk of the composite outcome of hospitalisation or death.

A secondary endpoint was time to first recovery, and after adjustment for age and comorbidity, time to first recovery was 4.2 days faster in the molnupiravir arm (95% Bayesian credible interval, 3.8-4.6 days). This improvement met the pre-specified superiority threshold.

In a small subset of patients in whom virological outcomes were assessed, at day 7, SARS-CoV-2 virus was not detected in 21% of molnupiravir patients and 4% of usual care patients.

The study did not uncover any new safety concerns about use of molnupiravir.

The PBAC observed that subjects in PANORAMIC were, as a whole, younger than subjects receiving molnupiravir in Australia. Two-thirds of PBS utilisation of molnupiravir has been in patients  $\geq 70$  years of age, whereas  $<15\%$  of PANORAMIC subjects were  $\geq 70$  years of age. Also, patients at highest risk of progression to severe disease in the UK were not the target population in PANORAMIC.

The PBAC noted several journal publications or pre-print articles describing observational studies of the use of molnupiravir in Israel and Hong Kong, as well as initial information from a Victorian Department of Health data linkage project in patients  $\geq 70$  years of age, taken together suggesting benefit of molnupiravir over no treatment in patients at high risk of progression to severe disease.

The PBAC concluded that while nirmatrelvir and ritonavir may be preferred for many patients with mild to moderate COVID-19 at high risk of progression to severe disease, in many common clinical circumstances nirmatrelvir and ritonavir will be contraindicated or unsuitable for use, and molnupiravir remains a suitable option in such patients.

**The PBAC recommended that an Administrative Note be added to the molnupiravir listing stating that molnupiravir should be considered for use only if nirmatrelvir and ritonavir is contraindicated or otherwise unsuitable.**

The PBAC noted the importance of ensuring that clinicians and the community were informed about appropriate use of COVID-19 oral antivirals.