Molnupiravir (Lagevrio®)
What Prescribers and Pharmacists Need to Know

Why is molnupiravir used to treat COVID-19?
Molnupiravir is an antiviral medication that works via a mechanism of action known as viral error catastrophe. It is a prodrug that is metabolised to the ribonucleoside analogue n-hydroxycytidine (NHC). NHC distributes into cells where it is phosphorylated to form the pharmacologically active ribonucleoside triphosphate (NHC-TP). NHC-TP incorporation into viral RNA by the viral RNA polymerase results in an accumulation of errors in the viral genome leading to inhibition of replication.

What is the benefit of molnupiravir for COVID-19?
Available research does not currently provide enough evidence to determine the benefits of molnupiravir in specific subgroups of patients. In the absence of definitive evidence, the National COVID-19 Clinical Evidence Taskforce has arrived at a consensus recommendation based on their clinical expertise to guide clinical decisions about which patients are most likely to benefit from molnupiravir.
There is no evidence evaluating the effectiveness of molnupiravir in partially or fully vaccinated patients. Given this, and the lower risk of deterioration in these patients, it is unlikely that molnupiravir will have a significant treatment benefit in patients who have received three doses of vaccine, unless the patient is immunosuppressed. There is limited evidence on the effectiveness of molnupiravir in immunosuppressed patients. However, given the likely higher risk of deterioration in these patients, and the absence of reasons to believe otherwise, it is likely that molnupiravir will be beneficial for immunosuppressed patients.

Who should receive molnupiravir?
Within the patient population for which molnupiravir is recommended for use, decisions about the appropriateness of treatment with molnupiravir should be based on the patient’s individual risk of severe disease, on the basis of age and multiple risk factors, COVID-19 vaccination status and time since vaccination.
Provide a molnupiravir patient information leaflet and obtain patient consent prior to commencing therapy.

As per the National COVID-19 Clinical Evidence Taskforce Guidelines, adults are eligible for treatment with molnupiravir if:
- they are unvaccinated against COVID-19; AND
- they are within five (5) days of symptom onset; AND
- they have mild to moderate COVID-19 disease (i.e. do not require oxygen); AND
- they have one or more of the risk factors for disease progression (below); AND
- other treatments (such as sotrovimab or nirmatrelvir plus ritonavir) are not suitable or available.

Risk factors:
Based on the inclusion criteria for the MOVe-OUT trial, risk factors for disease progression include the following:
- Age ≥ 60 years
- Obesity (BMI ≥ 30kg/m²)
- Chronic kidney disease (i.e. eGFR <60 mL/min/1.73m² by MDRD), excluding patients on dialysis
- Serious heart conditions such as heart failure, coronary artery disease or cardiomyopathies
- Chronic obstructive pulmonary disease
- Active cancer (excluding minor cancers not associated with immunosuppression, e.g. basal cell carcinomas)
- Immunocompromised state following solid organ transplant
- Sickle cell disease
- Diabetes mellitus
Who should receive molnupiravir continued …

In addition to at-risk unvaccinated adults, molnupiravir may also be considered for use within 5 days of symptom onset in adults with COVID-19 who do not require oxygen and:

- are immunosuppressed or not immunocompetent regardless of vaccination status; OR
- have received one or two doses of vaccine and who are at high risk of severe disease on the basis of age and multiple risk factors (see above);

AND where other treatments (such as sotrovimab or nirmatrelvir plus ritonavir) are not suitable or available.

Molnupiravir dosing requirements for treatment of COVID-19

The recommended dose of molnupiravir is:

800 mg (4 x 200mg capsules) taken orally every 12 hours for 5 days.

Mulnupiravir capsules may be taken with or without food and should be swallowed whole (i.e. not opened, broken or crushed).

The safety and efficacy of molnupiravir when administered for more than 5 days has not been established.

In women of childbearing potential, healthcare providers should discuss the chance that they may be pregnant and consider the need for a pregnancy test before commencing treatment.

No dosage adjustment is required in patients with renal or hepatic impairment.

It is important for health professionals to minimise handling of the molnupiravir capsules, especially if pregnant. Use personal protective gloves when handling.

For patients with swallowing difficulties, consult ‘Don’t Rush to Crush’ or a Hospital Medicines Information Pharmacist for further information.

What if a patient misses a dose?

If the patient misses a dose of molnupiravir within 10 hours of the time it is usually taken, the patient should take it as soon as possible and resume the normal dosing schedule.

If a patient misses a dose by more than 10 hours, the patient should not take the missed dose and instead take the next dose at the regularly scheduled time. The patient should not double the dose to make up for a missed dose.

What side effects should I be aware of?

The most common adverse reactions in the molnupiravir treatment group in the MOVe-OUT trial were diarrhoea (2%), nausea (1%) and dizziness (1%), all of which were Grade 1 (mild) or Grade 2 (moderate).

While serious adverse events occurred in 7% of patients receiving molnupiravir, none were considered drug-related by the investigator and most were COVID-19 related. Refer to the product information for a complete list of possible adverse effects.

As molnupiravir is a provisionally approved medicine which has no relevant post-marketing data, it is important to document and report all (from possible to confirmed) adverse effects experienced by the patient during treatment to inform its safety profile and future use.

Lagevrio® is subject to additional monitoring in Australia to allow quick identification of new safety information. Healthcare professionals should report any suspected adverse events to the TGA at http://www.tga.gov.au/reporting-problems.

Presentation and Storage:

Lagevrio® is available as a ‘Swedish Orange’ opaque capsule with “82” printed with white ink. Each capsule contains 200mg of molnupiravir.

Lagevrio® should be stored below 30°C in the original bottle, away from heat, light and moisture.

For further information:

Visit:
- Lagevrio Product Information (tga.gov.au)
- WA COVID-19 Information for health professionals - under Clinical Guidelines
Special Warnings and Precautions for Use:

**Paediatric patients:**
The safety and efficacy of molnupiravir has not been established in patients less than 18 years of age, therefore use in paediatric patients is not recommended. Molnupiravir may affect bone and cartilage, consisting of an increase in the thickness of physeal and epiphyseal growth cartilage with decreases in trabecular bone.

**Use in the elderly:**
In the MOVe-OUT trial, there was no difference in safety and tolerability between patients >65 years of age and younger patients who were treated with molnupiravir. No dose adjustment is recommended based on age.

**Use in pregnancy (Category D):**
The use of molnupiravir is not recommended during pregnancy.

Women of childbearing potential should be advised to use effective contraception for the duration of treatment and for at least four (4) days after the last dose of molnupiravir.

Based on animal data, molnupiravir may cause fetal harm, and there are no available data on the use of molnupiravir in pregnant women to evaluate the risk of major birth defects, miscarriage or adverse maternal or fetal outcomes.

**Fertility**
There is no data available on whether molnupiravir affects sperm.

It is recommended that men who are sexually active with a partner of childbearing potential use an effective form of contraception during treatment and three (3) months after treatment with molnupiravir.

**Use in lactation:**
It is unknown whether molnupiravir or any of the components of molnupiravir are present in human milk, affect human milk production, or have effect on the breastfed infant.

Breastfeeding is not recommended during treatment and for four (4) days after the last dose of molnupiravir.

Access to National Medical Stockpile Medicines
This medication is regulated by the National Medical Stockpile (NMS). Access to stock requires completion of a WA Emergency COVID-19 Treatment Approval for Molnupiravir (Lagevrio®) Form and confirmation by the prescriber that the patient fulfils required criteria. The request is then reviewed by an Infectious Disease Physician for eligibility and approval. The Commonwealth Department of Health are working to target access to those most vulnerable including the elderly and those in aged care with the view to transition to the Pharmaceutical Benefits Scheme (PBS) arrangements as supply continues to grow. By law medicines can only be listed on the PBS following a positive recommendation from the Pharmaceutical Benefits Advisory Committee (PBAC)." This does not apply to Residential Aged Care Facilities and Aboriginal Community Controlled Health Organisations (ACCHOs) that have received stock directly from the Commonwealth. It is expected that stock management under these circumstances will be managed as per the Authorisation to supply or administer a poison COVID-19 Treatment – National Medical Stockpile

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