DRUG GUIDELINE
Use of molnupiravir capsule for COVID-19

Introduction[1]

Molnupiravir (Lagevrio®) capsule is provisionally registered by the Therapeutic Goods Administration for use in Australia for the treatment of adults with COVID-19. **Vaccination is the preferred and primary option for the prevention of COVID-19.**

Clinical trials for molnupiravir were conducted when the Delta variant of SARS-CoV-2 was in circulation. Clinical efficacy against the Omicron variant is not yet clear.

This guideline requires endorsement by your local Drug and Therapeutics Committee (DTC) prior to implementation and should be used in conjunction with the molnupiravir resources available here.

Drug class and mechanism of action[1,2,3]

Molnupiravir is a ribonucleoside analog (antiviral) that inhibits the replication of SARS-CoV-2, the causative virus of COVID-19.

Approved indications[2,4]

Use of molnupiravir in NSW must be in accordance with the ACI Model of Care. The information below is derived from the Approved Product Information and the National COVID-19 Clinical Evidence Taskforce recommendations and **may differ from restrictions currently in place in NSW**.

Treatment of COVID-19 in adults (aged 18 years and older) who do not require initiation of supplemental oxygen due to COVID-19 and are at increased risk of progression to hospitalisation or death.

Based on inclusion criteria of the Phase 3 MOVe-OUT trial, the risk factors for disease progression in adults are:

- Age ≥ 60 years
- Obesity (BMI ≥ 30 kg/m^2)
- Type 1 or 2 diabetes mellitus
- Chronic kidney disease (i.e., eGFR < 60 mL/min/1.73m^2), excluding patients on dialysis or with a reduced eGFR of < 30 mL/min/1.73m^2
- Serious heart conditions (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

The efficacy of molnupiravir is unclear in partially or fully vaccinated individuals (individuals who had received one or more doses of SARS-CoV-2 vaccine were excluded from the trial).

See ACI Model of Care for further advice on use in vaccinated patients.

Contraindications[1,3]

- Known allergy to molnupiravir or any of the excipients of this medicine (croscarmellose sodium, hydroxypropyl cellulose, magnesium stearate, microcrystalline cellulose, hypromellose, titanium dioxide, red iron oxide, butyl alcohol, dehydrated alcohol, isopropyl alcohol, potassium hydroxide, propylene glycol, purified water, shellac, strong ammonia solution).
- Safety and efficacy of molnupiravir in children and adolescents aged 18 years and younger has not yet been established, therefore use in these patients is not recommended.
- See below section for information on: men and women of childbearing potential, and women who are pregnant or breastfeeding.

Drug interactions[1,3]

No formal drug interaction studies have been conducted involving molnupiravir. Neither molnupiravir nor it's metabolites are inhibitors or inducers of major drug metabolizing enzymes or transporters. Resources as Liverpool COVID-19 drug interactions tool and Micromedex drug interactions tool do not currently (as of 9 February 2022) identify any drug interactions.

Dose, timing and route of administration[1,2,3]

The recommended dose for adult patients is:

M**olnupiravir 800 mg** (4 x 200 mg capsules) taken orally every 12 hours for five days.

Capsules should be swallowed whole with water and can be taken with or without food. The capsules should not be opened, crushed, or chewed.

Molnupiravir should be started as soon as possible after a diagnosis of symptomatic COVID-19 has been made and within five days of symptom onset.

Missed doses – 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.

No dose adjustments for renal or hepatic function or age are required.

Pregnancy, breastfeeding and contraception[1,3]

Pregnancy

- Molnupiravir is pregnancy category D – it is **not recommended** during pregnancy and in women of childbearing potential not using contraception.
- There are no data from the use of molnupiravir in pregnant women. Studies in animals have shown reproductive toxicity.

Breastfeeding

- Breastfeeding is not recommended during treatment with molnupiravir and for 4 days after the last dose due to the potential for adverse reactions on the infant from molnupiravir.
- Animal lactation studies with molnupiravir have not been conducted.
- It is unknown whether molnupiravir or any of the components of molnupiravir; are present in human milk, affect human milk production, or have an effect on the breastfed infant.

Contraception

Women of childbearing potential should use **effective contraception for the duration of treatment with molnupiravir and for four days after the last dose.**

It is not known if molnupiravir can affect sperm. Men who are sexually active with a partner of childbearing potential should use an **adequate form of contraception during treatment with molnupiravir and for three months after the last dose.**

Presentation[1]

Each hard capsule contains 200 mg of molnupiravir and comes in a bottle of 40 capsules, sufficient for one patient to complete a 5-day course.

Storage and stability[1]

Molnupiravir should be stored in its original packaging; in a cool, dry place (< 30^{o}C).

Monitoring requirements[1]

- Monitor the patient for adverse effects (see *Adverse Effects* section below). If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue, initiate appropriate medications and/or supportive care.

Adverse effects[1]

- As the proposed use is for 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. Refer to the Product Information for a complete list of possible adverse effects.
- The most reported adverse reactions during treatment with molnupiravir were dizziness, diarrhoea and nausea.

Reporting[1]

- Molnupiravir is subject to additional monitoring in Australia – this will allow rapid identification of new safety information. Healthcare professionals are asked to report any suspected adverse events to the TGA, MSD (drug sponsor) and via their facility's incident management system.
- For hospital-initiated treatment, Drug and Therapeutics Committee oversight in the access process will enable appropriate medicines governance and ensure the collection and analysis of patient outcomes and systematic monitoring of medicine use. Molnupiravir use and outcome reporting should occur as per local clinical governance processes.

References

1. Australian Product information https://www.tga.gov.au/sites/default/files/lagevrio-pi.pdf
2. Jayk Bernal A, Gomes da Silva MM, Musungaie DB, *et al*. Molnupiravir for oral treatment of Covid-19 in nonhospitalized patients. N Engl J Med. DOI: 10.1056/NEJMoa2116044.
3. Fact sheet for Healthcare Providers: Emergency use authorization for molnupiravir https://www.merck.com/eua/molnupiravir-hcp-fact-sheet.pdf
4. Australian National COVID-19 Clinical Evidence Taskforce. (2022). *Australian guidelines for clinical care of people with COVID-19.* https://app.magicapp.org/#/guideline/L4Q5An/rec/jzoKoa