SA Health

Molnupiravir Drug Monograph

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Version 3.0

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Government of South Australia
SA Health

1. Molnupiravir drug monograph

Molnupiravir (Lagevrio®) [1,7,14,17,20] **ID Approval and patient consent (verbal or written) required** **For more detailed information on the use of Molnupiravir in patients with COVID-19 visit the product information available on the TGA website**	
Drug Class	• Antiviral pro-drug which once metabolised to an active ribonucleoside triphosphate (NHC-TP) is incorporated into SARS-CoV-2 viral RNA resulting in an accumulation of transcribed mutations with each viral replication cycle, thus inhibiting further replication.
Indications	• Second line treatment of mild COVID-19 for non-pregnant adults with symptom onset of no more than 5 days **and** who do not require supplemental oxygen **AND** ○ are not vaccinated or have a not up-to-date vaccine status **with** one or more risk factors for severe or critical illness. **OR** ○ prescribe molnupiravir as per PBS criteria **OR** • are immunosuppressed (and remdesivir is contraindicated or unavailable) • Treatment should not be commenced in hospitalised patients with severe or critical COVID-19 illness, however the course can be completed if commenced prior to initiation of supplemental oxygen or hospitalisation.
Contra-indications	• Hypersensitivity to molnupiravir or any of the excipients in the product. • Children less than 18 years old • **Pregnancy** – the use of molnupiravir in pregnant women is **not recommended** due to potential risk of reduced foetal growth and development • **Breastfeeding** – it is unknown whether molnupiravir is present in human breastmilk, affects breastmilk production, or has an effect on the breastfed infant. Based on the potential for adverse reactions on the infant, breastfeeding is **not recommended** during AND for 4 days after treatment • **Contraception -** Prescribers should consider a pregnancy test prior to commencement of therapy. Advise women of childbearing potential to use effective contraception for the duration of treatment and for 4 days after the last dose of molnupiravir. Advise men who are sexually active with a partner of childbearing potential to use an adequate form of contraception during and 3 months after treatment with molnupiravir.
Precautions	• Exercise caution in patients with a history of anaphylaxis to other medicines. • **Renal Impairment -** Patients with eGFR < 30 and patients on dialysis were excluded from the Phase 3 MOVe-OUT trial. Molnupiravir is a prodrug hydrolysed to NHC. The fraction of dose excreted as NHC was ≤ 3% therefore renal impairment is not expected to have a significant effect on NHC exposure. • **Hepatic impairment -** the pharmacokinetics of molnupiravir and NHC has not been evaluated in patients with hepatic impairment. Hepatic elimination is not expected to be a major route of NHC elimination.

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Drug Interactions	• No formal interaction studies have been conducted with molnupiravir • The metabolite of molnupiravir is not a substrate of major drug metabolising enzymes or transporters. Neither molnupiravir nor its substrate are inhibitors or inducers of major drug metabolising enzymes or transporters. • While the potential for drug interactions with molnupiravir are considered unlikely, as this is a new drug, continue to check the University of Liverpool COVID-19 resource page
Presentation and storage	• Available as 200mg capsules supplied as a bottle of 40 capsules. • Store at room temperature, less than 30^{O}C
Dose	• 800mg (4 x 200mg capsules) orally 12-hourly for 5 days • No dose adjustment is required for renal or hepatic impairment or the elderly (see precautions above) • 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

Administration	• Capsules can be taken with or without food
	• Administration of molnupiravir via an oral solution has not been evaluated in clinical trials however the following advice has been provided for patients with swallowing difficulties and or for administration via an enteric tube.
	• Preparation of the solution:
	  ○ Open FOUR (4) capsules and transfer contents into an oral syringe. Discard empty capsule shells
	  ○ Add approximately 40 mL of water to the oral syringe
	  ○ Mix/stir the capsule contents and water for 3 minutes.
	  ▪ Insoluble capsule contents may not dissolve completely.
	  ▪ Reconstituted solutions prepared according to directions may have visible undissolved particulates and are acceptable for oral administration.
	  ○ Administration should occur as soon as possible after the preparation and no later than 2 hours after the preparation.
	• For administration via enteral tube:
	  ○ Prior to administration redisperse the suspension by mixing or stirring the oral syringe for 1 minute prior to administration
	  ○ Flush enteral tube with 5 mL of water prior to administration.
	  ○ Administer entire volume from the administration syringe.
	  ○ Flush tube with 5 mL of water TWICE (10 mL total) after administration of the suspension.

Handling	• Occupational exposure to non-intact tablets may be harmful. Staff who are actively trying to conceive or who are pregnant or breastfeeding should not prepare or handle a dispersed dose • For all other staff, use standard Personal Protective Equipment (PPE) if preparation or administration of a dispersed tablet is required
Monitoring	• Baseline creatinine, electrolytes and urea, LFTs and complete blood exam • Monitor the patient for adverse effects

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	• If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue and initiate appropriate medications and/or supportive care

Adverse Effects	• It may be difficult to distinguish between adverse effects of molnupiravir and the signs and symptoms of COVID-19.
	• As a new medication, adverse reactions to molnupiravir continue to be investigated. Refer to the product information for a complete list of possible adverse effects. To date reactions include:
	  ○ Common (>1%): diarrhoea, nausea, dizziness, headache
	  ○ Uncommon (0.1-1%): rash, urticaria
	• Suspected or confirmed adverse reactions should be reported via Safety Learning System and also via the Therapeutic Goods Administrations adverse effects online form: TGA adverse event reporting

Patient Information and consent forms	• Molnupiravir patient information leaflets can be found here • Examples of generic patient consent forms can be found here

2. Definitions/Acronyms/ Abbreviations

BMI	Body Mass Index
COPD	Chronic obstructive pulmonary disease
eGFR	estimated Glomerular Filtration Rate
GI	Gastrointestinal
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human Immunodeficiency Virus
ID	Infectious Diseases
IV	Intravenous
LFTs	Liver function Tests
NMS	National Medical Stockpile
NYHA	New York Heart Association

3. Resources

- National COVID-19 Clinical Evidence Taskforce (The Australian Living Guidelines)
- COVID-19 Resources: NSW Therapeutic Advisory Group
- COVID–19 (SARS–COV–2) – Management Guide (CALHN–PRC05409)
- Anaphylaxis: Management Guidelines (CALHN-OWI04038)
- COVID-19: Disease-modifying therapy recommendations for hospitalised adults (CALHN-GDE05778)
- CALHN COVID–19 internet page
- World Health Organisation. Therapeutics and COVID-19: Living Guideline
- Australian Technical Advisory Group on Immunisation (ATAGI)
- Clinical Excellence Commission: Medication Safety Updates

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- COVID-19 Treatment: Nirmatrelvir-Ritonavir (Paxlovid®) (IH-CIS05842)
- COVID-19 Resources: Medicines Use in the treatment of COVID-19 – Consent Forms

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5 Document Ownership

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6 Document History

Version	Date approved	Approved by	Amendment notes
3.0	12/04/22	CALHN Drug and Therapeutics Committee South Australian Medicines Advisory Committee	Updated to align with updated COVID-19: Medication Management of Mild Illness in the Outpatient Setting Clinical Guideline V3.0
2.0	18/02/22	CALHN Drug and Therapeutics Committee COVID-19 Medicines Advisory Group	Add molnupiravir and nirmatrelvir plus ritonavir. Added link on sotrovimab monograph for breastfeeding advice.
1.0	19/01/22	South Australian Medicines Advisory Committee	New guideline to provide a pathway for the medication management of mild COVID-19 illness in the outpatient setting.

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