Molnupiravir Prescribing Guideline

Last updated 28/11/2022

Background

Molnupiravir has been granted provisional approval by the Therapeutic Goods Administration (TGA) for treatment of COVID-19 in Australia.

For public hospitals, Molnupiravir has a restricted listing on the Queensland Health Medicines Formulary. Please refer to the List of Approved Medicines (LAM) and the Pharmaceutical Benefits Scheme (PBS) for details.

It is recommended this guideline is endorsed by local Medicines Management or Drug and Therapeutics Committees prior to use at your facility.

Mechanism of action

Molnupiravir is an oral pro-drug that is hydrolysed to the ribonucleoside analogue, beta-D-N4-hydroxycytidine (NHC), prior to reaching the systemic circulation. NHC distributes into cells where it is phosphorylated and incorporated into the viral RNA by viral RNA-polymerases. It subsequently misdirects the viral polymerase to incorporate either guanosine or adenosine during viral replications, leading to an accumulation of deleterious errors resulting in viral mutations and lethal mutagenesis. This mechanism of action is known as viral error catastrophe.[1,2]

Indications

- Refer to Decision Pathway for drug treatment of mild to moderate COVID 19 and Guidance on the use of COVID-19 therapeutics for treatment or prophylaxis of SARS-CoV-2. For detailed information on rationale for use please refer to the National Clinical Evidence Taskforce (NCET) and the Pharmaceutical Benefits Scheme (PBS)
- Molnupiravir is NOT recommended for use in those less than 18 years of age as safety and efficacy has not been stablished and it may affect bone and cartilage growth
- For information on use in pregnancy and breastfeeding please refer to advice in the NCET Guidelines and the Product Information for the individual COVID therapeutics as well as the Guideline for Treatment of mild to moderate COVID-19.

Contraindications and precautions

Use is contraindicated in patients with hypersensitivity to the active substance or to any of the excipients.

Please also refer to the Product Information for further considerations and precautions.

Drug interactions

No formal drug-drug interaction studies have been undertaken with molnupiravir. Based on in-vitro studies, neither molnupiravir nor its active metabolite NHC are substrates of major drug metabolising enzymes or transporters. Therefore, the potential for molnupiravir or NHC to interact with concomitant medications is considered unlikely.[1]

Refer to the Liverpool COVID-19 Drug Interactions Checker for advice on specific drugs.

Dosing and duration (adults)

800 mg (4 x 200 mg capsules) orally TWICE daily for FIVE days.

Molnupiravir can be taken with or without food.

There are no dose adjustments required in elderly patients or those with renal or hepatic impairment.

Adverse effects and reporting

Molnupiravir is a provisionally approved product, all possible and confirmed adverse events must be reported. These should be notified to the TGA Reporting adverse events | Therapeutic Goods Administration (TGA) and reported via local adverse event processes (e.g. Riskman). In clinical trials, the most common adverse reactions reported in the molnupiravir treatment group were:

- diarrhoea
- nausea
- dizziness

Please refer to the Product Information for further advice.

Storage and Stability

Please refer to the Product Information for advice on storage and stability.

Preparation and administration

There are limited data on the pharmacokinetics of molnupiravir following administration via enteral feeding tubes. Five participants enrolled in the phase 2 clinical study received at least one dose via nasogastric (NG) or orogastric (OG) tube. Concentrations from samples taken following oral administration were observed to fall within the same range as concentrations following administration via NG/OG tube, suggesting no difference in pharmacokinetics.[3]

Dose preparation:[4]

NB. The risk of exposure to molnupiravir powder was assessed by sponsor (MSK); although the risk is negligible, it is recommended to wear gloves and a mask, and follow local safety standards.

1. Open FOUR capsules and disperse contents in 40 mL of sterile water, mix or stir for 3 minutes.
2. Transfer the mixture to an enteral syringe.
3. Flush the tube with 5 mL of water. Shake the enteral syringe for one minute then give via the tube. Flush the tube twice with 5 mL of water.
4. Dose should be given within 2 hours of preparing the dispersion.

Further information on preparation of an oral solution can be found at Oral antiviral treatment for COVID-19 (nps.org.au) In patients unable to tolerate thin fluids, the capsule may be opened and mixed with a spoonful of yoghurt or apple puree.[4] Absorption is not expected to be impacted by mixing the contents of the capsules with soft food.[4]

References

1. Merck Sharp & Dohme (Australia) Pty Ltd. Australian product information – Lagevrio® (molnupiravir) capsules. 2021. Published 2022 January 20.
2. Kabinger F, Stiller C, Schmitzova J et al. Mechanism of molnupiravir-induced SARS-CoV-2 mutagenesis. Nat Struct Mol Biol. 2021; 28:740-746.
3. Medical information. Information request AU22-00197 [email]. Macquarie Park, NSW: Merck Sharp & Dohme; 11/02/2022.
4. Symons K, Ermer J (editors) Don't rush to crush 4th edition [Internet]. Melbourne (VIC). Society of Hospital Pharmacists of Australia: MIMS Australia; 2022. Molnupiravir; [updated 2022 Mar 01; cited 2022 Mar 17]. Available from: https://www.mimsonline.com.au/Search/DNC.aspx?ModuleName=Product%20Info&searchKeyword=molnupiravir&PreviousPage=~/Search/QuickSearch.aspx&SearchType=&ID=140040001_2

Version	Amendments	Author/s	Approved for Publication
1.0	New document	Ashlea McCarron Panteha Voussoughi Dr Andrew Henderson	Approved by: Prof. Keith McNeil, Chief Medical Officer, Queensland Health 27/10/22
1.1	Minor update - Name change from NCCET to NCET - Update NCET link	Panteha Voussoughi	CTWG Chair 28/11/22