Therapeutics Technical Advisory Group | Te Rōpū Haumanu Kowheori-19
Update for health professionals: molnuparivir is no longer recommended by Therapeutics TAG due to lack of clinical benefit

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The Therapeutics Technical Advisory Group (Therapeutics TAG) was established by the Ministry of Health in August 2021 to provide expert advice on existing and emerging medicines for use in the management of COVID-19.

Clincal evidence suggesting lack of effectiveness

The initial evidence used to support the approval and recommendation to use molnuparivir (Lagevrio®) was completed in an early period of the pandemic. This was before to the emergence of Omicon and its sublineages and prior to the development of and widespread uptake of vaccines. The clinical trial, MOVe-OUT, reported that molnupiravir treatment had a 30% reduction of hospitalisations and deaths compared to placebo in unvaccinated adults during the Delta period. [1]

The clinical evidence supporting the use of alternative oral antiviral Paxlovid (nirmatrelvir-ritonavir) reported a considerably greater effectiveness then evidence for molnupiravir. Paxlovid has always been the first-line antiviral for the treatment of COVID-19, with molnupiravir an alternative option for patients that cannot take Paxlovid due to contraindications. Remdesivir also showed greater effectiveness than molnupiravir, however has challenges with administration as it is an IV antiviral. As such, molnuparivir has been previously recommended as a second-line or third-line option for the treatment of COVID-19.

More recently, a large scale, open-label trial (PANORAMIC), did not report a reduction in hospitalisation or mortality from molnuparivir and provided evidence that suggests a lack of clinical effectiveness in a more highly vaccinated population and against Omicron variants. [2] The PANORAMIC study provides evidence that most closely aligns with the current situation in Aotearoa New Zealand, with a highly vaccinated population and transmission of Omicron variants. **Therefore Paxlovid remains the first line treatment for COVID-19, with remdesivir a second-line option. However, molnupiravir is no longer recommended.**

Evidence of mutations from molnuparivir treatment

Global sequencing data of patients following molnupiravir treatment has suggested that a specific class of variants contained molnupiravir mutational profiles. These mutational profiles appeared almost exclusively after 2022, when molnupiravir usage became common, and were more widespread in countries that used it more often (including Australia and the United States). [3] The development of mutational signatures due to molnupiravir use is being monitored closely internationally, though it remains unknown if this could lead to new variants of concern.

Updates to the COVID-19 clinical guidelines

The COVID-19 Therapeutics Technical Advisory group has clinical guidelines (link) that are updated at regular intervals and when new evidence emerges. An update was made on 25 November 2022 to indicate that accumulating evidence suggests that molnupiravir may not be associated with any meaningful clinical benefit in vaccinated adults. **These guidelines were updated again on 24 February 2023 to reflect that Therapeutics TAG no longer recommends the use of molnupiravir.**

References

1. Jayk Bernal A, Gomes da Silva MM, Musungaie DB, Kovalchuk E, Gonzalez A, Delos Reyes V, et al. Molnupiravir for Oral Treatment of Covid-19 in Nonhospitalized Patients 2022 [509-20]. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa2116044.
2. Molnupiravir plus usual care versus usual care alone as early treatment for adults with COVID-19 at increased risk of adverse outcomes (PANORAMIC): an open-label, platform-adaptive randomised controlled trial The Lancet2022 [updated 22 December 2022 Available from: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)02597-1/fulltext#%20.
3. Sanderson T, Hisner R, Donovan-Banfield Ia, Peacock T, Ruis C. Identification of a molnupiravir-associated mutational signature in SARS-CoV-2 sequencing databases 2023 [2023.01.26.23284998]. Available from: https://www.medrxiv.org/content/medrxiv/early/2023/01/27/2023.01.26.23284998.full.pdf.