NEW DRUGS

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Molnupiravir

Approved indication: COVID-19

Lagevrio (Merck Sharp & Dohme)
200 mg capsules

With the continuing healthcare burden of COVID-19, molnupiravir is another antiviral drug to be approved for use in Australia. Molnupiravir is a prodrug of N-hydroxycytidine, a ribonucleoside analogue that is incorporated into viral RNA, resulting in the inhibition of SARS-CoV-2 replication. The provisional approval is for the treatment of COVID-19 in adults who do not require oxygen and who are at risk of progressing to severe COVID-19.

Molnupiravir should be started as soon as possible after a diagnosis of COVID-19 and within five days of symptom onset. Four 200 mg capsules are taken every 12 hours, with or without food, for five days. The peak plasma concentration of N-hydroxycytidine is reached 1.5 hours after an oral dose of molnupiravir. N-hydroxycytidine has a half-life of about 3.3 hours and is metabolised via the same pathways as those involved in endogenous pyrimidine metabolism. Molnupiravir and N-hydroxycytidine do not induce or inhibit the major drug-metabolising enzymes or transporters, so drug interactions are unlikely. Doses do not need to be adjusted in patients with renal or hepatic impairment, although there are limited clinical trial data for patients with severe renal impairment or any degree of hepatic impairment.

A phase III trial randomised 1433 non-hospitalised, unvaccinated adults with confirmed mild-to-moderate COVID-19 who had developed symptoms no more than five days previously and who had at least one risk factor for progressing to severe COVID-19. At the time the trial was published, the Delta variant was the most common, being isolated in 58% of the participants with sequence data available. The primary efficacy end point was the incidence of hospitalisation or death from any cause at day 29. Of 709 participants who received 800 mg molnupiravir twice daily for 5 days, 48 (6.8%) were hospitalised or died, compared with 68 of 699 (9.7%) in the placebo group. One patient taking molnupiravir died, compared to nine in the placebo group. Although the confidence intervals overlapped, the efficacy outcomes were generally consistent across pre-specified subgroups including sex, time from symptom onset (0–3 vs more than 3 days), baseline COVID-19 severity (mild vs moderate) and risk factors for severe illness (age >60 years, obesity, cardiovascular disease).[1]

The most common adverse effects of molnupiravir include diarrhoea, nausea and dizziness, but these are typically mild or moderate. In the phase III trial, adverse events were reported in 216 of 710 participants (30.4%) in the molnupiravir group compared with 231 of 701 (33%) in the placebo group. Serious adverse events, such as pneumonia, were mostly related to COVID-19 rather than the drug or placebo.[1]

The safety and efficacy of molnupiravir administration for more than five days are unknown. Women are advised to use contraception during and for four days after treatment. Molnupiravir was found to be harmful in studies of pregnant animals so it is not recommended for pregnant or breastfeeding women. The medicine is not recommended in patients younger than 18 years of age due to a lack of safety and efficacy data.

Molnupiravir reduces the risk of hospitalisation or death in unvaccinated adults with COVID-19 who have a risk of progressing to severe COVID-19 when started within five days after symptom onset. However, the difference in the primary outcome from placebo is moderate, and approximately 15 patients must be treated for one to benefit.[2] In some subgroups, such as patients with diabetes, there was no benefit.[1] The potential benefit of molnupiravir for the treatment of vaccine breakthrough infections is currently unknown.

T manufacturer responded to request for availability

REFERENCES

1. Bernal AJ, da Silva MMG, Musungaie DB, Kovalchuk E, Gonzalez A, Reyes VD, et al. Molnupiravir for oral treatment of Covid-19 in nonhospitalized patients. N Engl J Med 2022;386:509-20. https://doi.org/10.1056/NEJMoa2116044
2. Sidebottom DB, Smith DD, Gill D. Safety and efficacy of antivirals against SARS-CoV-2. BMJ 2021;375:n2611. https://doi.org/10.1136/bmj.n2611

The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.

At the time the comment was prepared, information about this drug was available on the websites of the European Medicines Agency and the Therapeutic Goods Administration.