Greetings from Drug Information Bulletin!

It is my proud privilege to pen the editorial at a historical moment – the completion of 15 years of publication of this Drug Information Bulletin. The weekly bulletin started its journey in April 2007, brought out by the Drug Information Centre (DIC), IPA, Bengal Branch and is now a bi-weekly bulletin jointly published by Drug Information Centre, IPA, Bengal Branch & Regulatory Affairs Division, IPA. As far as my knowledge, this is the first of its kind of bulletin serving its readers from all spheres of the society like- Pharmacists, Doctors, Nurses, health workers, NGOs, and general public worldwide. It has received reach accolades and great appreciation from most of the readers due to its content and its regular publication. Initially it was started to serve IPA members then receiving request from other professional stakeholders, as well as request from other countries the bulletin marched ahead. Presently we have readers from different countries all over the world and different strata of the society. Some hospitals and educational institutes are forwarding this bulletin among their faculty members and keeping hard copies in their libraries with our prior permission so that students can read this. A number of Drug Information Centers are reproducing this with our permission both in Govt. and private sector. This is a free service to anybody and everybody, and any person / institute interested in drug information, and we have never accepted any donation or advertisement from anybody for this publication to keep our voice unbiased. This has been possible due to help and co-operation from all of our readers and mentors. Hope this bulletin will continue its service to the society with help from all of you in future too! Greetings to all.

Dr. Subhash C. Mandal  
Editor  
E mail: subhash.mandaldr@gmail.com  
Mob. 9830136291
New Drug: Molnupiravir for COVID-19

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.

References


Source: Australian Prescriber
**Status in India:** Molnupiravir bulk and Molnupiravir capsules 200mg has been approved by CDSCO for treatment of adult patients with COVID-19, with SpO2 >93% and who have high risk of progression of the disease including hospitalization or death, in light of Covid 19 outbreak for restricted emergency use in the country on 28.12.2021. Several manufacturers in India are manufacturing this capsules. It is available in Indian market at a reasonable price.

**INSACOG finds very few recombinant variants of coronavirus in India**

**Global Scenario:**
The number of new COVID-19 cases has decreased for a second consecutive week, with a 16% decline during the week. The number of new deaths also decreased as compared to the previous week. Two recombinant variants XD and XE are being closely monitored worldwide. XD, which has an Omicron S gene incorporated into a Delta genome, is found primarily in France. XE is a BA.1/BA.2 recombinant, with the majority of the genome including the S gene belonging to BA.2. XE shows slightly higher transmission rate. XE also shows a higher growth rate above that of BA.2; however, this finding requires further confirmation.

**Indian Scenario:**
Based on genome sequencing analysis, very few recombinant variants have been discovered in India. So far, none showed either increased transmission (locally or otherwise) or associated with severe disease or hospitalization. Incidences of suspected recombinants and the possible public health relevance are being closely monitored.

Reference: INSACOG Bulletin

**Cefuroxime is associated with ADR of DRESS syndrome**

On the basis of preliminary analysis of the data received from Pharmacovigilance of India (PvPI), the Indian Pharmacopoea Commission (IPC) has reported that Cefuroxime is associated with Drug reaction with eosinophilia and systemic symptoms (DRESS) symptoms.

Reference: PvPI

**Cefuroxime Potential risk of Kounis syndrome**
The SFDA has released a potential safety signal concerning Kounis syndrome associated with the use of cefuroxime. Cefuroxime is cephalosporin antibacterial drug indicated for the treatment of infectious diseases caused by sensitive bacteria. The SFDA reviewed 11 case reports, three of which supported the association, and the literature.


**Empagliflozin Risk of ketoacidosis and Fournier’s gangrene**
The Medsafe has announced that empagliflozin is associated with the risk of ketoacidosis and Fournier’s gangrene (necrotising fasciitis of the perineum). Empagliflozin is a sodium glucose co-transporter 2 (SGLT2) inhibitors and is used for the treatment of type two diabetes mellitus. The CARM received three reports of ketoacidosis and two reports of Fournier’s gangrene following initiation of empagliflozin. For the risk of ketoacidosis, healthcare professionals are advised to consider stopping empagliflozin temporarily during an acute illness, particularly if patients are unwell, febrile or vomiting and not eating. Empagliflozin should also be temporarily stopped before undergoing medical procedures or surgery. For the risk of Fournier’s gangrene, patients should be advised to seek immediate medical attention if they experience pain, tenderness, redness or swelling of the genital or perineal area, particularly with associated fever or malaise.


**DISCLAIMER:**
The Newsletter intends to provide updated and reliable information on medicines and other related issues in an attempt to equip healthcare professionals to take informed decision in recommending medicines to the patients. However, they are encouraged to validate the contents. None of the people associated with the publication of the Newsletter nor the organization shall be responsible for any liability for any damage incurred as a result of use of contents of this publication. The brand names of medicines, if mentioned, are for illustration only and the Newsletter does not endorse them.