Molnupiravir (Lagevrio™) Safety Reference Sheet

Purpose of This Document

The purpose of this Safety Reference Sheet is to provide information to clinicians regarding warnings and potential risks associated with use of molnupiravir such as contraindications, precautions, adverse effects (ADRs), and significant drug-drug interactions (DDIs).

Important Note

The content referenced in this Safety Reference Sheet is based on information available at the time of publishing (12/23/2021). For most recent guidance and updates regarding molnupiravir, please refer to the US Food and Drug Administration (FDA) at https://www.fda.gov/drugs, and/or Merck at https://www.merck.com/media/news/.

Introduction

Molnupiravir (Lagevrio) was approved by the FDA under emergency use authorization on 12/23/2021. It is a nucleoside analog and oral prodrug that inhibits severe acute respiratory syndrome coronavirus-2 (SARS-Co-V-2) replication by viral mutagenesis. Below is a summary of important points from the molnupiravir EUA.

Indication of Molnupiravir:

- Treatment of mild-to-moderate COVID-19 in non-hospitalized adults:
    - with positive results of direct SARS-CoV-2 viral testing, and who are at high-risk for progression to severe COVID-19, including hospitalization or death
    - having one or more pre-defined risk factors for disease progression
        - over 60 years of age, diabetes, obesity (BMI ≥30), chronic kidney disease, serious heart conditions, chronic obstructive pulmonary disease, or active cancer
    - for whom alternative COVID-19 treatment options authorized by FDA are not accessible or clinically appropriate
    - with symptom onset ≤5 days

Limitations of Authorized Use:

- Not authorized for treatment in patients requiring hospitalization due to severe or critical COVID-19
- Not authorized for use in pediatric patients younger than 18 years of age
- Not authorized for pre-exposure or post-exposure prophylaxis for prevention of COVID-19
- Not authorized for use for longer than 5 consecutive days

Dosage, Administration, and Other Important Points:

- Dose in adults 18 years old and older: 800 mg (four 200 mg capsules) taken orally every 12 hours for 5 days, with or without food, initiated within 5 days of symptom onset
- If a dose is missed 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 dose is missed by more than 10 hours, the patient should not take the missed dose and instead take the next dose at the regularly scheduled time
- No dosage adjustment is recommended in renal or hepatic impairment, or in geriatric patients
- Not recommended for use in pregnant and lactating individuals

Contraindications

- No contraindications have been identified

Warnings and Precautions

A) Embryo-Fetal Toxicity
    a. Molnupiravir is not recommended for use during pregnancy based on findings from animal reproduction studies
    b. Assess the pregnancy status of an individual of childbearing potential prior to initiating molnupiravir
    c. Molnupiravir can be prescribed to a pregnant individual if:
        i. The prescriber has determined that the benefits of treatment outweigh the risks for that individual AND
        ii. The prescriber must document that the patient has been informed of the known and potential risks of molnupiravir use during pregnancy, and that the individual was made aware of Merck Sharp & Dohme's pregnancy surveillance program
    d. Females of childbearing potential should use a reliable method of contraception for the duration of treatment and for 4 days after the last dose of molnupiravir
    e. Males of reproductive potential who are sexually active with females of reproductive potential should use a reliable method of contraception correctly and consistently during treatment and for at least 3 months after the last dose of molnupiravir
B) Bone and Cartilage Toxicity
    a. Molnupiravir is not authorized for use in patients younger than 18 years of age because it may interfere with bone and cartilage growth

Adverse Reactions

Per the MOVe-OUT trial, most common adverse events (all were either grade 1 (mild), or grade 2 (moderate) reported in patients receiving molnupiravir versus placebo:

	Molnupiravir, N= 710	Placebo, N = 701
Diarrhea	2%	2%
Nausea	1%	1%
Dizziness	1%	1%

Drug-Drug Interactions

No drug interactions have been identified based on the current data.

Use in Specific Populations

A) Pregnancy
    a. Please refer to the "Warnings and Precautions, part A" section above
B) Lactation
    a. Breastfeeding is not recommended during treatment with molnupiravir and for 4 days after the final dose
C) Contraception
    a. Please refer to the "Warnings and Precautions, part A" section above
D) Renal and Hepatic Impairment: please refer to the "Introduction" section under "Dosage and Administration."

Reporting

Report adverse events to FDA MedWatch

https://www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program

References

1) Fact Sheet for Healthcare Providers: Emergency Use Authorization for Molnupiravir. 12/23/2021. https://www.fda.gov/media/155054/download