



February 01, 2023

IMPORTANT DRUG WARNING

Subject: Important Safety Information Regarding Use of LAGEVRIO™ (molnupiravir) in Pregnancy and Individuals of Childbearing Potential

Dear Healthcare Provider:

This letter was previously issued on December 23, 2021, revised on June 1, 2022 to reflect the addition of the trade name LAGEVRIO and updated on February 01, 2023 to remove positive SARS-CoV-2 viral testing result from the indication text and to add a change in the process of reporting pregnancy exposures. There are no other changes to the information or instructions contained in this letter.

The purpose of this letter is to inform you of important safety information regarding the use of LAGEVRIO (molnupiravir) in pregnancy and in individuals of childbearing potential. Molnupiravir is an investigational nucleoside analogue that inhibits severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) replication.

LAGEVRIO is an unapproved product that was authorized by the FDA on December 23, 2021 under an Emergency Use Authorization (EUA) for the treatment of adults with a current diagnosis of mild-to-moderate COVID-19 who are at high risk for progression to severe COVID-19, including hospitalization or death, and for whom alternative COVID-19 treatment options authorized by FDA are not accessible or clinically appropriate.

This letter will provide information regarding the potential risks of LAGEVRIO use during pregnancy, requirements for healthcare providers prior to initiating treatment with LAGEVRIO during pregnancy, and how to report pregnancy exposures and outcomes.

Use of LAGEVRIO in Pregnancy and in Individuals of Childbearing Potential

LAGEVRIO is not recommended for use during pregnancy.

Based on findings from animal reproduction studies, LAGEVRIO may cause fetal harm when administered to pregnant individuals. There are no available human data on the use of LAGEVRIO in pregnant individuals to evaluate the risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Please refer to the Animal Data section below for more details.

Healthcare Provider Action

Prior to initiating treatment with LAGEVRIO:

- Assess whether an individual of childbearing potential is pregnant or not, if clinically indicated. Refer to Warnings and Precautions (5.1) and Use in Specific Populations (8.3) of the **[“Fact Sheet for Healthcare Providers.”](#)**
- If LAGEVRIO is used during pregnancy, the prescribing healthcare provider must communicate to the patient the known and potential benefits and the potential risks of using LAGEVRIO during



pregnancy, as outlined in the [“Fact Sheet for Patients and Caregivers.”](#) Also see Warnings and Precautions (5.1, 5.3), Use in Specific Populations (8.1, 8.3) and Nonclinical Toxicology (13.1) of the [“Fact Sheet for Healthcare Providers.”](#)

- If the decision is made to use LAGEVRIO during pregnancy, the prescribing healthcare provider must document that the known and potential benefits and potential risks of using LAGEVRIO during pregnancy were communicated to the pregnant individual as outlined in the [“Fact Sheet for Patients and Caregivers.”](#)
- The prescribing healthcare provider must document that a pregnant individual was made aware of the pregnancy registry at <https://covid-pr.pregistry.com> or 1-800-616-3791.
- Advise individuals of childbearing potential of the potential risk to a fetus and to use an effective method of contraception, correctly and consistently, during treatment with LAGEVRIO and for 4 days after the final dose of LAGEVRIO.
- Advise individuals of childbearing potential to inform their healthcare provider of a known or suspected pregnancy.

Reporting LAGEVRIO™ (molnupiravir) Pregnancy Exposures and Pregnancy Outcomes

There is a pregnancy registry that monitors pregnancy outcomes in individuals exposed to LAGEVRIO during pregnancy. The prescribing healthcare provider must document that a pregnant individual was made aware of the pregnancy registry at <https://covid-pr.pregistry.com> or 1-800-616-3791. Pregnant individuals exposed to LAGEVRIO or their healthcare providers can also report the exposure by contacting Merck Sharp & Dohme LLC, Rahway, NJ USA at 1-877-888-4231.

Animal Data

Molnupiravir is the prodrug of the nucleoside analogue N-hydroxycytidine (NHC). In an embryofetal development (EFD) study in rats administered LAGEVRIO during the organogenesis period (gestation days 6 through 17), developmental toxicities including post-implantation losses, malformation of the eye, kidney and axial skeleton, and rib variations were observed at 8-times the human NHC exposure at the recommended human dose (RHD). At this exposure, rat maternal toxicities included decreased food consumption and body weight losses, resulting in the early sacrifice of two of sixteen animals. Decreased fetal weight and delayed fetal ossification as well as maternal decreased body weight gain were observed at 3-times the human NHC exposure at the RHD.

In an EFD study in rabbits administered molnupiravir during the organogenesis period (gestation days 7 through 19), developmental toxicity was limited to reduced fetal body weight at 18-times the human NHC exposure at the RHD. There was no developmental toxicity at 7 times the human NHC exposure at the RHD.

In a pre- and post-natal developmental study, molnupiravir was administered orally to female rats at exposures (similar to the human NHC exposure at the RHD) from GD6 through lactation day 20. No effects were observed in offspring.



Important Prescribing Information

LAGEVRIO™ (molnupiravir) is authorized for treatment of adults with a current diagnosis of mild to moderate COVID-19

- who are at high risk for progression to severe COVID-19, including hospitalization or death. Refer to CDC website¹ for additional details, and
- for whom alternative COVID-19 treatment options approved or authorized by FDA are not accessible or clinically appropriate.

LAGEVRIO is not authorized for use in patients who are less than 18 years of age.

LAGEVRIO is not authorized for initiation of treatment in patients hospitalized due to COVID-19.

LAGEVRIO is not authorized for use for longer than 5 consecutive days.

LAGEVRIO is not authorized for pre-exposure or post-exposure prophylaxis for prevention of COVID-19.

LAGEVRIO may only be prescribed for an individual patient by physicians, advanced practice registered nurses, and physician assistants that are licensed or authorized under state law to prescribe drugs in the therapeutic class to which LAGEVRIO belongs (i.e., anti-infectives).

The LAGEVRIO dosage regimen is 800 mg (four 200 mg capsules) taken orally every 12 hours for 5 days, with or without food.

Reporting Adverse Events and Medication Errors

Under the EUA, all serious adverse events and medication errors potentially related to LAGEVRIO use must be reported within 7 calendar days from the Healthcare Provider's awareness of the event.

Serious adverse event reports and medication error reports should be submitted to FDA's MedWatch program using one of the following methods:

- Complete and submit the report online: www.fda.gov/medwatch/report.htm, or
- Complete and submit a postage-paid Form FDA 3500 (<https://www.fda.gov/media/76299/download>) and return by mail (MedWatch, 5600 Fishers Lane, Rockville, MD 208529787, or by fax (1-800-FDA0178), or
- Call 1-800-FDA-1088 to request a reporting form.

In addition, please provide a copy of all FDA MedWatch forms to:
Merck Sharp & Dohme LLC, Rahway, NJ USA Fax: 215-616-5677
E-mail: d poc.usa@msd.com

If you require further information about the information contained in this letter, please contact the Merck National Service Center at 1-800-672-6372.

¹ <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html>.



This letter is not intended as a complete description of the benefits and risks related to the use of LAGEVRIO™ (molnupiravir). Please refer to the full prescribing information in the [“Fact Sheet for Healthcare Providers.”](#)

The [“EUA Letter of Authorization”](#), the [“Fact Sheet for Healthcare Providers”](#), and the [“Fact Sheet for Patients and Caregivers”](#) are also available at [“lagevrio.com”](#)

Sincerely,

A handwritten signature in blue ink, appearing to read "Haupt", with a long horizontal line extending to the right.

Richard M. Haupt, MD, MPH

Vice President and Head, Vaccines & Infectious Diseases Global Medical & Scientific Affairs

Merck Research Labs

Merck Sharp & Dohme LLC