U.S. FOOD & DRUG ADMINISTRATION

Frequently Asked Questions on the Emergency Use Authorization for Lagevrio (molnupiravir) for Treatment of COVID-19

Q: What is an emergency use authorization (EUA)?
A: Under section 564 of the Federal Food, Drug & Cosmetic Act, after a declaration by the HHS Secretary based on one of four types of determinations, FDA may authorize an unapproved product or unapproved uses of an approved product for emergency use. In issuing an EUA, FDA must determine, among other things, that based on the totality of scientific evidence available to the agency, including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing a serious or life-threatening disease or condition caused by a chemical, biological, radiological, or nuclear agent; that the known and potential benefits of the product, when used to treat, diagnose or prevent such disease or condition, outweigh the known and potential risks for the product; and that there are no adequate, approved, and available alternatives. Emergency use authorization is NOT the same as FDA approval or licensure.

Q: What does this EUA authorize? What are the limitations of authorized use?
A: FDA has issued an EUA for the emergency use of the unapproved product Lagevrio (molnupiravir) for the treatment of adults with a current diagnosis of mild-to-moderate coronavirus disease 2019 (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 approved or authorized by FDA are not accessible or clinically appropriate. Lagevrio is not FDA-approved for any use including for the treatment of COVID-19. Prior to initiating treatment with Lagevrio, carefully consider the known and potential risks and benefits.

Lagevrio is not authorized:

- for use in patients less than 18 years of age.
- for initiation of treatment in patients requiring hospitalization due to COVID-19. Benefit of treatment with Lagevrio has not been observed in subjects when treatment was initiated after hospitalization due to COVID-19.
- for use for longer than five consecutive days.
- for pre-exposure or post-exposure prophylaxis for prevention of COVID-19.

Q: How is high risk defined under the EUA?
A: Information about conditions that place a patient with mild-to-moderate COVID-19 at increased risk for disease progression or death can be found at the Centers for Disease Control and Prevention's People with Certain Medical Conditions website. Health care providers should consider the benefit-risk for an individual patient.

Q: Does the EUA require a positive result from a direct SARS-CoV-2 viral test prior to prescribing Lagevrio to a patient who is at high risk for severe COVID-19?"
A: No. The Agency removed the requirement for positive test results effective February 1, 2023. FDA recognizes that, in rare instances, individuals with a recent known exposure (e.g., a household contact) who develop signs and symptoms consistent with COVID-19 may be diagnosed by their health care provider as having COVID-19 even if they have a negative direct SARS-CoV-2 viral test result. In such instances, their health care provider may determine that treatment with Lagevrio for COVID-19 is appropriate if the patient reports mild-to-moderate symptoms of COVID-19 and is at high-risk for

progression to severe COVID-19, including hospitalization or death, and the terms and conditions of the authorization are met, as detailed in the Fact Sheet for Healthcare Providers.

The Agency continues to recommend that providers use direct SARS-CoV-2 viral testing to help diagnose COVID-19.

Q: What does direct SARS-CoV-2 viral testing mean?
A: Direct SARS-CoV-2 viral tests diagnose current COVID-19 infection. Direct SARS-CoV-2 viral tests include two types of diagnostic tests for COVID-19:

- Molecular tests, such as reverse transcription polymerase chain reaction (RT-PCR) tests, that detect the virus's genetic material.
- Antigen tests that detect specific proteins from the virus.

Antibody tests should not be used to diagnose COVID-19 and are not direct SARS-CoV-2 viral tests. Antibody tests look for antibodies that the immune system makes in response to the SARS-CoV-2 virus.

Q: Are there any warnings or precautions that should be taken when administering Lagevrio?
A: Yes, health care providers and patients must be aware of the following warnings and precautions:

- Pregnancy
  Lagevrio may cause fetal harm when administered to pregnant individuals. Therefore, **Lagevrio is not recommended for use during pregnancy.** Prior to initiating treatment with Lagevrio, health care providers should assess whether an individual of childbearing potential is pregnant or not, if clinically indicated. Lagevrio is authorized to be prescribed to a pregnant individual only after the health care provider has determined that the benefits would outweigh the risks for that individual patient and the known and potential benefits and potential risks of using Lagevrio during pregnancy are communicated to the pregnant individual.

- Lactation
  Breastfeeding is not recommended during treatment with Lagevrio and for four days after the final dose. A lactating individual may consider interrupting breastfeeding and may consider pumping and discarding breast milk during treatment and for 4 days after the last dose of Lagevrio.

- Females of Reproductive Potential
  Females of childbearing potential are advised to use a reliable method of contraception correctly and consistently, as applicable, for the duration of treatment and for four days after the last dose of Lagevrio.

- Males of Reproductive Potential
  While the risk is regarded as low, studies to fully assess the potential for Lagevrio to affect offspring of treated males have not been completed. Sexually active individuals with partners of childbearing potential are advised to use a reliable method of contraception correctly and consistently during treatment and for at least three months after the last dose of Lagevrio. The risk beyond three months after the last dose of Lagevrio is unknown. Studies to understand the risk beyond three months are ongoing.

- Hypersensitivity Including Anaphylaxis
  Hypersensitivity reactions, including anaphylaxis, have been reported with Lagevrio. If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue Lagevrio and initiate appropriate medications and/or supportive care.

Q: Are there potential side effects of Lagevrio?
A: Possible side effects of Lagevrio include diarrhea, nausea, and dizziness. Lagevrio is not recommended for use during pregnancy because findings from animal reproduction studies showed that Lagevrio may cause fetal harm when administered to pregnant individuals.

Hypersensitivity, anaphylaxis, angioedema, erythema, rash, and urticaria adverse reactions have been identified during post-authorization use of Lagevrio.

Q: Why is Lagevrio only authorized in adults?
A: Lagevrio is not authorized for use in patients less than 18 years of age because it may affect bone and cartilage growth.

Q: Is Lagevrio approved by the FDA to prevent or treat COVID-19?
A: No. Lagevrio is not FDA-approved to prevent or treat any diseases or conditions, including COVID-19. Lagevrio is an investigational drug.

Q: How can Lagevrio be obtained for use under the EUA?
A: For questions on how to obtain Lagevrio, please contact COVID19therapeutics@hhs.gov.

Q. Who may prescribe Lagevrio under the EUA?
A. Under the authorization, 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).

Q: When should Lagevrio be administered to a patient?
A: Patients should talk to their healthcare provider to determine whether, based on their individual circumstances and whether alternative COVID-19 treatment options approved or authorized by FDA are accessible or clinically appropriate, they are eligible to receive Lagevrio. Patients should take Lagevrio as soon as possible after a diagnosis of COVID-19 has been made, and within five days of symptom onset.

More information about administration is available in the Fact Sheet for Health Care Providers.

Q: Does the EUA permit the use of Lagevrio as authorized in patients hospitalized *for reasons other* than COVID-19?
A: If a patient is hospitalized *for reasons other* than COVID-19, such as for an elective orthopedic procedure, and the patient has a current diagnosis of mild-to-moderate COVID-19, then treatment with Lagevrio is authorized if the patient is also at high risk for progression to severe COVID-19, including hospitalization or death, and the terms and conditions of the authorization are met as detailed in the Fact Sheet for Health Care Providers.

Lagevrio is also authorized for patients who require hospitalization after starting treatment with Lagevrio. These patients may complete the full five-day treatment course per the health care provider's discretion.

Q: Are there data showing treatment with Lagevrio may benefit adults with mild-to-moderate COVID-19 who are at high risk for progressing to severe COVID-19 and/or hospitalization?
A: Yes. The most important scientific evidence supporting the authorization of Lagevrio is from MOVe-OUT, a randomized, placebo-controlled, double-blind clinical trial studying Lagevrio for the treatment of non-hospitalized patients with mild-to-moderate COVID-19 who are at risk for progressing to severe COVID-19 and/or hospitalization. Eligible subjects were 18 years of age and older and had 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. The study included symptomatic subjects not vaccinated against SARS CoV-2 and who had laboratory confirmed SARS-CoV-2 infection and symptom onset within five days of randomization.

The main outcome measured in the trial was the percentage of people who were hospitalized or died due to any cause during 29 days of follow-up. Of the 709 people who received Lagevrio, 6.8% were hospitalized or died within this time period compared to 9.7% of the 699 people who received a placebo. This represented an adjusted relative risk reduction of Lagevrio compared to placebo of approximately 30% for all those randomized. Of the people who received Lagevrio, one died within this time period compared to nine people who received a placebo. The safety and effectiveness of Lagevrio for the treatment of COVID-10 continue to be evaluated.

Q: Are there requirements for health care facilities and prescribing health care providers as part of the EUA?
A: Yes.

- As part of the EUA, FDA requires health care providers who prescribe Lagevrio to report all medication errors and serious adverse events considered to be potentially related to Lagevrio through FDA's MedWatch Adverse Event Reporting program. Providers can complete and submit the report online; or download and complete the form, then submit it via fax at 1-800-FDA-0178. This requirement is outlined in the EUA's Fact Sheet for Health Care Providers. FDA MedWatch forms should also be provided to Merck Sharp & Dohme Corp.
- Health care facilities and providers must report therapeutics information and utilization data as directed by the U.S. Department of Health and Human Services.
- Healthcare providers must provide an electronic or hard copy of the "Fact Sheet for Patients, and Caregivers" prior to the patient receiving Lagevrio and must document that the patient has been given an electronic or hard copy of the "Fact Sheet for Patients and Caregivers".
- Healthcare providers must inform the patient or caregiver that:
    - Lagevrio is an unapproved drug that is authorized for use under this Emergency Use Authorization.
    - Other therapeutics are currently approved or authorized for the same use as Lagevrio [see Emergency Use Authorization (1) - Information Regarding Available Alternatives for the EUA Authorized Use].
    - There are benefits and risks of taking Lagevrio as outlined in the "Fact Sheet for Patients and Caregivers."

  - There is a pregnancy registry for patients exposed to Lagevrio.
  - Females of childbearing potential should use a reliable method of contraception correctly and consistently, as applicable, for the duration of treatment and for four days after the last dose of Lagevrio.
  - Males of reproductive potential who are sexually active with females of childbearing potential should use a reliable method of contraception correctly and consistently during treatment and for at least three months after the last dose.
- The prescribing health care provider must assess whether an individual of childbearing potential is pregnant or not, if clinically indicated.
- Based on findings from animal reproduction studies, Lagevrio may cause fetal harm when administered to pregnant individuals. If Lagevrio is used during pregnancy, prescribing healthcare providers must communicate to the patient the known and potential benefits and the potential risks of Lagevrio use during pregnancy, as outlined in the "Fact Sheet for Patients and Caregivers".
- If the decision is made to use Lagevrio during pregnancy, the prescriber must document that the known and potential benefits and the potential risks of Lagevrio use during pregnancy, as outlined in the "Fact Sheet for Patients and Caregivers," were discussed with the patient.
- 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.

Q: Do patient outcomes need to be reported under the EUA?
A: No, reporting of patient outcomes is not required under the EUA. However, reporting of all medication errors and serious adverse events considered to be potentially related to Lagevrio occurring during treatment is required.

Q: FDA has issued a number of EUAs, including for therapeutics. If state laws impose different or additional requirements on the medical product covered by an EUA, are those state laws preempted?
A: As stated in FDA's Emergency Use Authorization of Medical Products and Related Authorities; Guidance for Industry and Other Stakeholders, "FDA believes that the terms and conditions of an EUA issued under section 564 preempt state or local law, both legislative requirements and common-law duties, that impose different or additional requirements on the medical product for which the EUA was issued in the context of the emergency declared under section 564." The guidance explains the basis for FDA's views on this subject.

Q: Can health care providers share the patient/caregiver fact sheet electronically?
A: Yes. The letter of authorization for Lagevrio authorizes healthcare providers to share the patient/caregiver fact sheet electronically.