



November 15, 2023

Merck Sharp & Dohme LLC  
Attention: Sushma Kumar, PhD, PMP  
Senior Director, Global Regulatory Affairs and Clinical Safety  
1 Merck Drive  
PO Box 100  
Whitehouse Station, NJ 08889-0100

RE: Emergency Use Authorization 108

Dear Dr. Kumar:

This letter is in response to Merck Sharp & Dohme LLC's (Merck) request that the Food and Drug Administration (FDA or Agency) issue an Emergency Use Authorization (EUA) for the emergency use of LAGEVRIO (molnupiravir)<sup>1</sup> for the treatment of mild-to-moderate coronavirus disease 2019 (COVID-19) in certain adults who are at high risk for progression to severe COVID-19, including hospitalization or death, pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3).

On February 4, 2020, as amended on March 15, 2023, pursuant to Section 564(b)(1)(C) of the Act, the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency, or a significant potential for a public health emergency, that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes coronavirus disease 2019 (COVID-19).<sup>2</sup> On the basis of such determination, the Secretary of HHS on March 27, 2020, declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic, pursuant to Section 564 of the Act (21 U.S.C. 360bbb-3), subject to terms of any authorization issued under that section.<sup>3</sup>

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<sup>1</sup> The December 23, 2021, and February 11, 2022 Letters of Authorization (LOA) referred to the authorized drug as "molnupiravir,"; however, Merck subsequently requested, and FDA concurred, that the Fact Sheets be revised to add references to molnupiravir's trade name, "LAGEVRIO." "LAGEVRIO" has been used since the March 23, 2022 reissuance of this letter.

<sup>2</sup> U.S. Department of Health and Human Services, *Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3*. February 4, 2020; U.S. Department of Health and Human Services, *Amended Determination of a Public Health Emergency or Significant Potential for a Public Health Emergency Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)*. March 15, 2023. 88 FR 16644 (March 20, 2023) ("Amended Determination").

<sup>3</sup> U.S. Department of Health and Human Services, *Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3*, 85 FR 18250 (April 1, 2020). See Amended Determination ("The declarations issued pursuant to section 564(b)(1) of the FD&C Act that circumstances exist justifying the authorization of emergency use of certain in vitro diagnostics, personal respiratory protective devices, other medical devices and drugs and biological products, as set forth in those

On December 23, 2021, FDA issued an EUA for emergency use of LAGEVRIO as treatment of mild-to-moderate COVID-19 in adults with positive results of direct SARS-CoV-2 viral testing, 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.

LAGEVRIO capsules contain molnupiravir; a nucleoside analogue that inhibits SARS-CoV-2 replication by viral mutagenesis. LAGEVRIO is not FDA-approved for any uses, including use as treatment for COVID-19.

FDA subsequently reissued the LOA on February 11, 2022<sup>4</sup>, March 23, 2022<sup>5</sup>, August 5, 2022<sup>6</sup>, October 27, 2022<sup>7</sup>, February 1, 2023<sup>8</sup>, and October 3, 2023<sup>9</sup>.

On November 15, 2023, again having concluded that revising this EUA is appropriate to protect

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declarations, and that are based on the February 4, 2020 determination, remain in effect until those declarations are terminated in accordance with section 564 of the FD&C Act.”).

<sup>4</sup> In its February 11, 2022 revision, FDA revised the scope of this LOA to account for the FDA approval of Veklury (remdesivir) for the treatment of COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, who are not hospitalized and have mild-to-moderate COVID-19, and who are at high risk for progression to severe COVID-19, including hospitalization or death. The letter of authorization was also revised to include a new condition regarding registration and listing. The authorized Fact Sheets were also revised to reflect the revision to the scope of authorization for LAGEVRIO as described above and include information on post-authorization reports of hypersensitivity reactions and rashes.

<sup>5</sup> In its March 23, 2022 revision, FDA revised this LOA to add references to molnupiravir’s trade name, “LAGEVRIO”. Corresponding revisions were also made to the authorized Fact Sheets. The Fact Sheet for Healthcare Providers was also revised to include updated antiviral activity and resistance information.

<sup>6</sup> In its August 5, 2022 revision, FDA revised this LOA to update certain post-authorization requirements as detailed in Condition O of this letter. The Fact Sheet for Healthcare Providers was also revised to include additional virology information and to identify Veklury (remdesivir) as an approved alternative to Lagevrio.

<sup>7</sup> In its October 27, 2022 revision, FDA incorporated clarifying revisions to Condition BB of this letter. Condition AA was also revised to require that all printed matter, advertising and promotional materials relating to the use of LAGEVRIO under this authorization be submitted to FDA for consideration at least 14 calendar days prior to initial dissemination or first use.

<sup>8</sup> In its February 1, 2023 revision, FDA revised the scope of authorization to no longer require positive results of direct SARS-CoV-2 viral testing. As revised, the scope of authorization required, in addition to other requirements, that adults have a current diagnosis of mild-to-moderate COVID-19. Corresponding changes were also made to the authorized Fact Sheets. Conditions P and U in this letter and the Fact Sheets were also revised to include updated information on the collection of pregnancy exposure and outcomes data through a pregnancy registry. The Fact Sheets were also revised to include information on administering LAGEVRIO via nasogastric and orogastric tubes. The Fact Sheet for Healthcare Providers was also revised to reflect the current indication for Veklury, an approved alternative to Lagevrio, and to include additional carcinogenicity and virology information.

<sup>9</sup> In its October 3, 2023 revision, FDA revised the scope of authorization to no longer require the distribution of LAGEVRIO under this EUA to be directed by the United States Government. Accordingly, the LOA and authorized Fact Sheet for Health Care Providers no longer required healthcare facilities and providers to report therapeutics information and utilization data to HHS. The LOA, the authorized Fact Sheet for Health Care Providers and the authorized Fact Sheet for Patients and Caregivers were revised to incorporate clarifying revisions to the authorized use of LAGEVRIO under this EUA. The LOA and authorized Fact Sheets were also revised to explain that while Paxlovid is now an approved alternative to the authorized use of LAGEVRIO, the criteria for issuance of this EUA continue to be met. Clarifying revisions to Condition K of this letter were incorporated. Lastly, the Conditions Related to Printed Matter, Advertising, and Promotion of this letter were revised to clarify that reminder advertisements and reminder labeling intended only to provide price information to consumers are permissible, so long as the conditions in 21 CFR 200.200 are met.

the public health or safety under section 564(g)(2) of the Act, FDA is reissuing the October 3, 2023 letter in its entirety, to remove Condition O from this LOA as the post-authorization requirements previously detailed have been fully satisfied based on Merck's submission of data or information to the Agency. Condition L relating to the monitoring and assessment of global viral variants of SARS-CoV-2 has also been revised to facilitate more efficient reporting and review of the data submitted to the Agency.

Based on the review of the data from the MOVE-OUT clinical trial (NCT04575597), a Phase III randomized, double-blind, placebo-controlled clinical trial studying LAGEVRIO for the treatment of non-hospitalized patients with mild-to-moderate COVID-19 who are at high risk for progression to severe COVID-19, including hospitalization or death, it is reasonable to believe that LAGEVRIO may be effective for the treatment of adults with 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 approved or authorized by FDA are not accessible or clinically appropriate, as described in the Scope of Authorization (Section II), and when used under the conditions described in this authorization, the known and potential benefits of LAGEVRIO outweigh the known and potential risks of such product.

Having concluded that the criteria for issuance of this authorization under Section 564(c) of the Act are met, I am authorizing the emergency use of LAGEVRIO for the treatment of adults with mild-to-moderate COVID-19 who are at high risk for progression to severe COVID-19, including hospitalization or death, as described in the Scope of Authorization section of this letter (Section II) and subject to the terms of this authorization.

## **I. Criteria for Issuance of Authorization**

I have concluded that the emergency use of LAGEVRIO for treatment of mild-to-moderate COVID-19, when administered as described in the Scope of Authorization (Section II), meets the criteria for issuance of an authorization under Section 564(c) of the Act, because:

1. SARS-CoV-2 can cause a serious or life-threatening disease or condition, including severe respiratory illness, to humans infected by this virus;
2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that LAGEVRIO may be effective for the treatment of adults with mild-to-moderate COVID-19 who are at high risk for progression to severe COVID-19, including hospitalization or death, as described in the Scope of Authorization (section II), and that, when used under the conditions described in this authorization, the known and potential benefits of LAGEVRIO outweigh the known and potential risks of such product; and

3. There is no adequate, approved, and available alternative<sup>10</sup> to the emergency use of LAGEVRIO for the treatment of adults with mild-to-moderate COVID-19 as further described in the Scope of Authorization (section II).<sup>11</sup>

## II. Scope of Authorization

I have concluded, pursuant to Section 564(d)(1) of the Act, that the scope of this authorization is limited as follows:

- LAGEVRIO may only be used for the treatment of adults with mild-to-moderate COVID-19:
  - Who are at high risk<sup>12</sup> for progression to severe COVID, including hospitalization or death, and for
  - Whom alternative COVID-19 treatment options approved or authorized by FDA are not accessible or clinically appropriate.

### Limitations on Authorized Use

- 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 requiring hospitalization due to COVID-19.<sup>13</sup> Benefit of treatment with LAGEVRIO has not been observed in subjects when treatment was initiated after hospitalization due to COVID-19.
  - LAGEVRIO is not authorized for use for longer than 5 consecutive days.
  - LAGEVRIO is not authorized for use as pre-exposure or as 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<sup>14</sup> law to prescribe drugs in the therapeutic class to which LAGEVRIO belongs (i.e., anti-infectives).

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<sup>10</sup> Although Veklury (remdesivir) is an approved alternative to treat COVID-19 in adults within the scope of this authorization, FDA does not consider it to be an adequate alternative for certain patients for whom it may not be feasible or practical (e.g., it requires a 3-day treatment duration). Although Paxlovid (nirmatrelvir/ritonavir) is also an approved alternative to treat COVID-19 in adults within the scope of this authorization, FDA does not consider Paxlovid to be an adequate alternative because it may not be clinically appropriate for patients on medications that are primarily metabolized by CYP3A and/or that are strong CYP3A inducers.

<sup>11</sup> No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

<sup>12</sup> For information on medical conditions and factors associated with increased risk for progression to severe COVID-19, see the Centers for Disease Control and Prevention (CDC) website: <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html>.

<sup>13</sup> Patients requiring hospitalization after starting treatment with molnupiravir may complete the full 5-day treatment course per the healthcare provider's discretion.

<sup>14</sup> The term "State" includes any State or Territory of the United States, the District of Columbia, and the Commonwealth of Puerto Rico. See section 201(a)(1) of the Act.

- The use of LAGEVRIO covered by this authorization must be in accordance with the authorized Fact Sheets.

### **Product Description**

The authorized LAGEVRIO is supplied as a bottle (NDC-0006-5055-06, NDC-0006-5055-07, NDC-0006-5055-09) containing a sufficient quantity of LAGEVRIO 200 mg capsules to complete a full treatment course (i.e., 40 capsules). LAGEVRIO is manufactured as a Swedish Orange, opaque capsule containing the Merck corporate logo and “82” printed in white ink.

The authorized storage and handling information is included in the authorized Fact Sheet for Healthcare Providers.

LAGEVRIO is authorized for emergency use with the following product-specific information required to be made available to healthcare providers and to patients and caregivers, respectively, through Merck’s website [www.molnupiravir.com](http://www.molnupiravir.com) (referred to as the “authorized labeling”):

- Fact Sheet for Healthcare Providers: Emergency Use Authorization (EUA) for LAGEVRIO
- Fact Sheet for Patients and Caregivers: Emergency Use Authorization (EUA) of LAGEVRIO for Coronavirus Disease 2019 (COVID-19)

I have concluded, pursuant to Section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of LAGEVRIO, when used for the treatment of adults with mild-to-moderate COVID-19 and used in accordance with this Scope of Authorization (Section II), outweigh the known and potential risks.

I have concluded, pursuant to Section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that LAGEVRIO may be effective for the treatment of adults with mild-to-moderate COVID-19 when used in accordance with this Scope of Authorization (Section II), pursuant to Section 564(c)(2)(A) of the Act.

Having reviewed the scientific information available to FDA, including the information supporting the conclusions described in Section I above, I have concluded that LAGEVRIO (as described in this Scope of Authorization (Section II)) meets the criteria set forth in Section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of LAGEVRIO product under this EUA must be consistent with, and may not exceed, the terms of the Authorization, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section III). Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS's determination under Section 564(b)(1)(C) described above and the Secretary of HHS’s corresponding declaration under Section 564(b)(1), LAGEVRIO is authorized for the treatment of adults with mild-to-moderate COVID-19 as described in this Scope of Authorization (Section II) under this EUA, despite the fact that it does not meet certain requirements otherwise required by applicable federal law.

### III. Conditions of Authorization

Pursuant to Section 564 of the Act, I am establishing the following conditions on this authorization:

#### Merck and Authorized Distributors<sup>15</sup>

- A. Merck and authorized distributor(s) will ensure that LAGEVRIO is distributed and the authorized labeling (i.e., Fact Sheets) will be made available to healthcare facilities and/or healthcare providers as described in Section II of this Letter of Authorization.
- B. Merck and authorized distributor(s) will ensure that appropriate storage is maintained until the product is delivered to healthcare facilities and/or healthcare providers.
- C. Merck and authorized distributor(s) will ensure that the terms of this EUA are made available to all relevant stakeholders (e.g., U.S. government agencies, state and local government authorities, authorized distributors, healthcare facilities, healthcare providers) involved in distributing or receiving LAGEVRIO. Merck will provide to all relevant stakeholders a copy of this Letter of Authorization and communicate any subsequent amendments that might be made to this Letter of Authorization and its authorized accompanying materials (i.e., Fact Sheets).
- D. Merck may request changes to this authorization, including to the authorized Fact Sheets for LAGEVRIO. Any request for changes to this EUA must be submitted to the Office of Infectious Diseases/Office of New Drugs/Center for Drug Evaluation and Research. Such changes require appropriate authorization prior to implementation.<sup>16</sup>
- E. Merck may develop and disseminate instructional and educational materials (e.g., materials providing information on product administration and/or patient monitoring) that are consistent with the authorized emergency use of LAGEVRIO as described in this Letter of Authorization and authorized labeling, without FDA's review and concurrence, when necessary to meet public health needs. Any instructional and educational materials that are inconsistent with the authorized labeling for LAGEVRIO are prohibited. If the Agency notifies Merck that any instructional and educational materials are inconsistent with the authorized labeling, Merck must cease distribution of such instructional and educational materials. Furthermore, as part of its notification, the Agency may also require Merck to issue corrective communication(s).

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<sup>15</sup> "Authorized Distributor(s)" are identified by Merck as an entity or entities allowed to distribute the authorized LAGEVRIO.

<sup>16</sup> The following types of revisions may be authorized without reissuing this letter: (1) changes to the authorized labeling; (2) non-substantive editorial corrections to this letter; (3) new types of authorized labeling, including new fact sheets; (4) new carton/container labels; (5) expiration dating extensions; (6) changes to manufacturing processes, including tests or other authorized components of manufacturing; (7) new conditions of authorization to require data collection or study; (8) new strengths of the authorized product, new product sources (e.g., of active pharmaceutical ingredient) or of product components. For changes to the authorization, including the authorized labeling, of the type listed in (3), (6), (7), or (8), review and concurrence is required from the Counter-Terrorism and Emergency Coordination Staff/Office of the Center Director/CDER and the Office of Counterterrorism and Emerging Threats/Office of the Chief Scientist.

- F. Merck will report to FDA all serious adverse events and medication errors potentially related to LAGEVRIO use that are reported to Merck using either of the following options.

Option 1: Submit reports through the Safety Reporting Portal (SRP) as described on the [FDA SRP](#) web page.

Option 2: Submit reports directly through the Electronic Submissions Gateway (ESG) as described on the [FAERS electronic submissions](#) web page.

Submitted reports under both options must state: “LAGEVRIO use for COVID-19 under Emergency Use Authorization (EUA).” For reports submitted under Option 1, include this language at the beginning of the question “Describe Event” for further analysis. For reports submitted under Option 2, include this language at the beginning of the “Case Narrative” field.

- G. All manufacturing, packaging, and testing sites for both drug substance and drug product used for EUA supply will comply with current good manufacturing practice requirements of Section 501(a)(2)(B) of the Act.

- H. Merck will submit information to the Agency within three working days of receipt of any information concerning significant quality problems with distributed drug product of LAGEVRIO that includes the following:

- Information concerning any incident that causes the drug product or its labeling to be mistaken for, or applied to, another article; or
- Information concerning any microbiological contamination, or any significant chemical, physical, or other change or deterioration in the distributed drug product, or any failure of one or more distributed batches of the product to meet the established specifications.

If a significant quality problem affects unreleased product and may also impact product(s) previously released and distributed, then information must be submitted for all potentially impacted lots.

Merck will include in its notification to the Agency whether the batch, or batches, in question will be recalled. If FDA requests that these, or any other batches, at any time, be recalled, Merck must recall them.

If not included in its initial notification, Merck must submit information confirming that Merck has identified the root cause of the significant quality problems, taken corrective action, and provide a justification confirming that the corrective action is appropriate and effective. Merck must submit this information as soon as possible but no later than 45 calendar days from the initial notification.

- I. Merck will manufacture LAGEVRIO to meet all quality standards and per the manufacturing process and control strategy as detailed in Merck’s EUA request. Merck

will also test the active pharmaceutical ingredient (API) starting material for additional quality attributes agreed upon by Merck and the Agency. Merck will not implement any changes to the description of the product, manufacturing process, facilities and equipment, and elements of the associated control strategy that assure process performance and quality of the authorized product, without notification to and concurrence by the Agency as described under condition D.

- J. Merck will list LAGEVRIO with a unique product NDC under the marketing category of Emergency Use Authorization. Further, the listing will include each establishment where manufacturing is performed for the drug and the type of operation performed at each such establishment.
- K. Through a process of inventory control, Merck and authorized distributor(s) will maintain records regarding distribution of LAGEVRIO.
- L. Merck will establish a process for monitoring genomic database(s) for the emergence of global viral variants of SARS-CoV-2 and will submit the following to the agency:
  - a. On a monthly basis, Merck will provide reports to the Agency summarizing any SARS-CoV-2 variants or sub-lineages carrying previously uncharacterized nsp7, nsp8, nsp12, or nsp14 amino acid polymorphism(s) that are rapidly spreading in the U.S. or worldwide.
  - b. On a quarterly basis (every 3 months), Merck will provide detailed reports describing key findings from analyses of nsp7, nsp8, nsp12, and nsp14 polymorphism frequencies over the most recent ~3-month period. These quarterly reports should highlight novel variant data, predominant polymorphisms within specific variants, and any specific amino acid positions where polymorphisms have been detected in independent variants/lineages. In addition, the reports should include cumulative summaries of NHC and molnupiravir antiviral activity data against different SARS-CoV-2 variants and plans for additional assessments based on the findings of the viral genomic monitoring. The quarterly report submissions should include an accompanying table(s) of polymorphism frequency data in an analyzable format for the most recent ~3-month period.
- M. FDA may require Merck to assess the activity of the authorized LAGEVRIO against any global SARS-CoV-2 variant(s) of interest (e.g., variants that are prevalent or becoming prevalent that harbor substitutions in the target protein or in protein(s) that interact with the target protein). Merck will perform the required assessment in a manner and timeframe agreed upon by Merck and the Agency. Merck will submit to FDA a preliminary summary report immediately upon completion of its assessment followed by a detailed study report within 30 calendar days of study completion. Merck will submit any relevant proposal(s) to revise the authorized labeling based on the results of its assessment, as may be necessary or appropriate based on the foregoing assessment.

- N. Merck shall provide samples as requested of LAGEVRIO to the U.S. Department of Health and Human Services (HHS) for evaluation of activity against emerging global viral variants of SARS-CoV-2, including specific amino acid substitution(s) of interest (e.g., variants that are highly prevalent or that harbor substitutions in the target protein) within 5 business days of any request made by HHS. Analyses performed with the supplied quantity of LAGEVRIO may include, but are not limited to, cell culture potency assays, biochemical assays, and in vivo efficacy assays.
- O. Merck must participate in a pregnancy registry to collect information through telephone and online reporting of pregnancies and collect outcomes for individuals who are exposed to LAGEVRIO during pregnancy. Merck must submit to the Agency reports detailing any available exposure information and outcome(s) data on a monthly basis unless otherwise notified by FDA.
- P. Merck and authorized distributor(s) will make available to FDA upon request any records maintained in connection with this EUA.

Healthcare Facilities to Whom LAGEVRIO Is Distributed and Healthcare Providers Administering LAGEVRIO

- Q. Healthcare facilities and healthcare providers will ensure that they are aware of the Letter of Authorization, and the terms herein. Healthcare providers must provide and document that a copy of the authorized Fact Sheet for Patients and Caregivers has been provided, either through electronic means or hardcopy, to the patient or caregiver prior to prescribing LAGEVRIO.
- R. Healthcare providers must inform patients or caregivers of the information detailed in the section *Mandatory Requirements for Administration of LAGEVRIO Under Emergency Use Authorization* in the Fact Sheet for Healthcare Providers.
- S. LAGEVRIO may only be prescribed to a pregnant individual after the prescribing healthcare provider has completed the mandatory requirements on patient assessment, patient counseling, and documentation as described in the Fact Sheet for Healthcare Providers. See *Mandatory Requirements for Administration of LAGEVRIO Under Emergency Use Authorization* in the Fact Sheet for Healthcare Providers.
- T. Healthcare providers must inform and document that pregnant individuals who are prescribed LAGEVRIO have been made aware of the pregnancy registry at <https://covid-pr.pregistry.com> or 1-800-616-3791.
- U. Healthcare facilities and healthcare providers receiving LAGEVRIO will track all serious adverse events and medication errors that are considered to be potentially related to LAGEVRIO use and must report these to FDA in accordance with the Fact Sheet for Healthcare Providers. Complete and submit a MedWatch form ([www.fda.gov/medwatch/report.htm](http://www.fda.gov/medwatch/report.htm)), or complete and submit FDA Form 3500 (health professional) by fax (1-800-FDA-0178) (these forms can be found via link above). Call [1-800-FDA-1088](tel:1-800-FDA-1088) for questions. Submitted reports must state, “LAGEVRIO use for COVID-

19 under Emergency Use Authorization” at the beginning of the question “Describe Event” for further analysis.

- V. Healthcare facilities and healthcare providers will ensure that appropriate storage is maintained until the product is administered consistent with the terms of this letter and the authorized labeling.
- W. Through a process of inventory control, healthcare facilities will maintain records regarding the dispensing and administration of LAGEVRIO for the use authorized in this letter (i.e., lot numbers, quantity, receiving site, receipt date), product storage, and maintain patient information (e.g., patient name, age, disease manifestation, number of doses administered per patient, other drugs administered).
- X. Healthcare facilities will ensure that any records associated with this EUA are maintained until notified by Merck and/or FDA. Such records will be made available to Merck, HHS, and FDA for inspection upon request.

Conditions Related to Printed Matter, Advertising, and Promotion

- Y. All descriptive printed matter, advertising, and promotional materials relating to the use of LAGEVRIO under this authorization shall be consistent with the authorized labeling, as well as the terms set forth in this EUA, and meet the requirements set forth in Section 502(a) and (n) of the Act, as applicable, and FDA implementing regulations. References to “approved labeling”, “permitted labeling” or similar terms in these requirements shall be understood to refer to the authorized labeling for the use of LAGEVRIO under this authorization. In addition, such materials shall:
  - Be tailored to the intended audience.
  - Not take the form of reminder advertisements, as that term is described in 21 CFR 202.1(e)(2)(i) and 21 CFR 201.100(f), except that reminder advertisements and reminder labeling intended only to provide price information to consumers, as described in 21 CFR 200.200, are permissible so long as such materials meet all conditions described in 21 CFR 200.200(a)(1)-(4).
  - Present the same risk information relating to the major side effects and contraindications concurrently in the audio and visual parts of the presentation for advertising and promotional materials in audio-visual format.
  - Be accompanied by the authorized labeling, if the promotional materials are not subject to Section 502(n) of the Act.
  - Be submitted to FDA accompanied by Form FDA-2253 for consideration at least 14 calendar days prior to initial dissemination or first use.
- Z. Merck may disseminate descriptive printed matter, advertising, and promotional materials relating to the emergency use of LAGEVRIO that provide accurate descriptions of safety results and efficacy results on a clinical endpoint(s) from the

clinical trial(s) summarized in the authorized labeling. Such materials must include any limitations of the clinical trial data as described in the authorized labeling. Merck may not imply that LAGEVRIO is FDA-approved for its authorized use by making statements such as “LAGEVRIO is safe and effective for the treatment of COVID-19.”

AA. All descriptive printed matter, advertising, and promotional material, relating to the use of LAGEVRIO under this authorization clearly and conspicuously shall state that:

- LAGEVRIO has not been approved, but has been authorized for emergency use by FDA under an EUA, for the treatment of adults with 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 approved or authorized by FDA are not accessible or clinically appropriate; and
- The emergency use of LAGEVRIO is only authorized for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products during the COVID-19 pandemic under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization revoked sooner.

If the Agency notifies Merck that any descriptive printed matter, advertising or promotional materials do not meet the terms set forth in conditions Y through AA of this EUA, Merck must cease distribution of such descriptive printed matter, advertising, or promotional materials in accordance with the Agency’s notification. Furthermore, as part of its notification, the Agency may also require Merck to issue corrective communication(s).

#### **IV. Duration of Authorization**

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products during the COVID-19 pandemic is terminated under Section 564(b)(2) of the Act or the EUA is revoked under Section 564(g) of the Act.

Sincerely,

**Patrizia A. Cavazzoni -S** Digitally signed by  
Patrizia A. Cavazzoni -S  
Date: 2023.11.15  
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Patrizia Cavazzoni, M.D.  
Director  
Center for Drug Evaluation and Research  
U.S. Food and Drug Administration