January 21, 2022

Madelyn Low, MBS
Manager, Regulatory Affairs
Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404

Dear Ms. Low:

On February 4, 2020, 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 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 COVID-19.[1] 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 Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 360bbb-3), subject to terms of any authorization issued under that section.[2]

On May 1, 2020, the Food and Drug Administration (FDA or Agency) issued an Emergency Use Authorization (EUA) for the emergency use of Veklury® (remdesivir)[3] for treatment of hospitalized patients with severe 2019 coronavirus disease (COVID-19)[4], pursuant to Section 564 of the Act. Veklury is a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleotide analog ribonucleic acid (RNA) polymerase inhibitor. At that time, Veklury was an investigational drug and was not FDA-approved for any indication.

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[1] 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.

[2] 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).

[3] For the purposes of this Letter of Authorization, the use of the tradename, Veklury, is intended to refer to the commercially available Veklury that is in United States distribution under the approved New Drug Application (NDA) 214787, only. As discussed further in Section II of this letter, Veklury that is commercially available under NDA 214787 is authorized for emergency use consistent with the terms and conditions of this letter.

[4] For purposes of the May 1, 2020, EUA, patients with severe disease were defined as patients with oxygen saturation (SpO2) ≤94% on room air or requiring supplemental oxygen or requiring mechanical ventilation or requiring extracorporeal membrane oxygenation (ECMO).

FDA reissued the Letter of Authorization on the following dates: August 28, 2020,[5] October 1, 2020,[6] October 16, 2020,[7] and October 22, 2020.[8]

On October 22, 2020, FDA also approved NDA 214787 for Veklury for the treatment of COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) requiring hospitalization.

On January 21, 2022, FDA approved a supplemental application to NDA 214787 for Veklury expanding the approved uses to include 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. Having concluded that revising this EUA is appropriate to protect the public health or safety under Section 564(g)(2) of the Act, FDA is reissuing the October 22, 2020, letter in its entirety with revisions to the scope of authorization now authorizing Vekury for the treatment of COVID-19 in pediatric patients weighing 3.5 kg to less than 40 kg or pediatric patients less than 12 years of age weighing at least 3.5 kg, with positive results of direct SARS-CoV-2 viral testing, who are hospitalized, or are not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death.

Based on review and extrapolation of the data from the randomized, double-blinded, placebo-controlled trial conducted by NIAID (NCT04280705), from the Gilead-sponsored open-label trial that evaluated different durations of Veklury (NCT04292899), and from the Gilead-sponsored open-label trial that evaluated different durations of Veklury as compared to standard of care (NCT04292730), it is reasonable to believe that Veklury may be effective for the treatment of COVID-19 in hospitalized pediatric patients weighing 3.5 kg to less than 40 kg or hospitalized pediatric patients less than 12 years of age weighing at least 3.5 kg, with positive results of direct SARS-CoV-2 viral testing, and that, when used under such conditions, the known and potential benefits of Veklury outweigh the known and potential risks of such product.

Additionally, based on review and extrapolation of the data from the Gilead-sponsored trial (NCT04501952) evaluating Veklury for the treatment of non-hospitalized patients with mild-to-moderate COVID-19 who are at high risk for progression to severe COVID-19 disease, it is reasonable to believe that Veklury may be effective for the treatment of pediatric patients weighing 3.5 kg to less than 40 kg or pediatric patients less than 12 years of age weighing at least 3.5 kg, with positive results of direct SARS-CoV-2 viral testing, who are not hospitalized, have

[5] In the August 28, 2020 revision, FDA revised the authorized use of Veklury to no longer limit its use for the treatment of patients with severe disease.
[6] In the October 1, 2020 revision, FDA revised the scope of authoirzation and conditions of authorization to designate Gilead Sciences, Inc. and its authorized distributors as the responsible parties for the distribution of Velkury.
[7] In the October 16, 2020 revision, FDA clarified that an alternate care site (ACS) meeting certain criteria was considered an "inpatient hospital setting" for the purposes of the scope of the EUA, and as such, was within the terms and conditions of FDA's authorization.
[8] In the October 22, 2020 revision, FDA revised this EUA to remove uses previously authorized that are now approved uses under NDA 214787 for Veklury. The EUA for Veklury remained authorized for the in treatment of suspected or laboratory-confirmed COVID-19 in hospitalized pediatric patients weighing 3.5 kg to less than 40 kg or hospitalized pediatric patients less than 12 years of age weighing at least 3.5 kg.

mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death, and that, when used under such conditions, the known and potential benefits of Veklury 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 Veklury for treatment of COVID-19, as described in the Scope of Authorization (Section II) and subject to the terms of this authorization.

## I. Criteria for Issuance of Authorization

I have concluded that the emergency use of Veklury for the treatment of 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 Veklury may be effective for the treatment of COVID-19 in pediatric patients weighing 3.5 kg to less than 40 kg *or* pediatric patients less than 12 years of age weighing at least 3.5 kg, with positive results of direct SARS-CoV-2 viral testing, and who -

    - Are hospitalized, or
    - Are not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death.

    And that, when used under the conditions described in the Scope of Authorization (Section II), the known and potential benefits of Veklury outweigh the known and potential risks of such product; and

3. There is no adequate, approved, and available alternative to the emergency use of Veklury for the treatment of COVID-19, as described in the Scope of Authorization (Section II).[9]

## 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:

- Veklury will be used only for the treatment of COVID-19 in pediatric patients weighing 3.5 kg to less than 40 kg *or* pediatric patients less than 12 years of age weighing at least 3.5 kg, with positive results of direct SARS-CoV-2 viral testing, and who -

[9] No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

  - Are hospitalized[10], or
  - Are not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death.

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

**Product Description**

Veklury is a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleotide analog ribonucleic acid (RNA) polymerase inhibitor. The authorized product includes commercially available[11] Veklury for injection (100 mg/vial, NDC 61958-2901-2), which is supplied as a single-dose vial containing a sterile, preservative-free white to off-white to yellow lyophilized powder.[12] It requires reconstitution and further dilution prior to administration by intravenous infusion.

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

Veklury is authorized for emergency use with the following product-specific information required to be made available to healthcare providers, parents, and caregivers, respectively, through Gilead's website at ***www.gilead.com/remdesivir***:

- Fact Sheet for Health Care Providers: Emergency Use Authorization (EUA) of Veklury **(**remdesivir)

- Fact Sheet for Parents and Caregivers: Emergency Use Authorization (EUA) of Veklury **(**remdesivir**)** 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 Veklury, when used for the treatment of COVID-19 as described in this Scope of Authorization (Section II), outweigh its 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 Veklury may be effective for the

[10] Individuals determined as being appropriate for acute inpatient hospitalization and who are admitted or transferred to an alternate care site (ACS) that is capable of providing acute care that is comparable to general inpatient hospital care are within the terms and conditions of this Letter of Authorization. An ACS is intended to provide additional hospital surge capacity and capability for communities overwhelmed by patients with COVID-19.
[11] Supra at Note 3.
[12] Individual vials of remdesivir for injection with a vial label and/or carton labeling that is clearly marked for "emergency use authorization" and Veklury for injection with a vial label and/or carton labeling that is clearly marked for "emergency use authorization" that have been distributed and remain in interstate commerce prior to the reissuance of this letter continue to be authorized for emergency use.

treatment of 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 Veklury (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 Veklury 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), Veklury is authorized for the treatment of COVID-19 as described in the 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:

Gilead Sciences, Inc. (Gilead) and Authorized Distributors

A. Gilead and authorized distributor(s) will ensure that the authorized Veklury is distributed and the authorized labeling (i.e., Fact Sheets) will be made available to healthcare facilities and/or healthcare providers consistent with the terms of this letter.

B. Gilead and authorized distributor(s) will ensure that appropriate storage is maintained until the product is delivered to healthcare facilities and/or healthcare providers.

C. Gilead 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 the authorized Veklury. Gilead 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. Gilead may request changes to this authorization, including to the authorized Fact Sheets for Veklury. 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.[13]

[13] 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

E. Gilead 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 Veklury 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 Veklury are prohibited. Should the Agency become aware of any instructional or educational materials that are inconsistent with the authorized labeling for Veklury, the Agency will require Gilead to cease distribution of such instructional and educational materials.

F. Gilead will report to FDA serious adverse events and all medication errors associated with the use of the authorized Veklury that are reported to Gilead 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: "Veklury (remdesivir) 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 will comply with current good manufacturing practice requirements of Section 501(a)(2)(B) of the Act.

H. Gilead will submit information to the Agency within three working days of receipt of any information concerning significant quality problems with distributed drug product of Veklury 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.

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.

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.

Gilead will include in its notification to the Agency whether the batch, or batches, in question will be recalled.

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

I. Gilead will manufacture Veklury to meet all quality standards and per the manufacturing process and control strategy as detailed in Gilead's EUA request. Gilead 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. Through a process of inventory control, Gilead and authorized distributor(s) will maintain records regarding distribution of the authorized Veklury (i.e., lot numbers, quantity, receiving site, receipt date).

K. Gilead and authorized distributor(s) will make available to FDA upon request any records maintained in connection with this EUA.

Hospitals and Other Healthcare Facilities to Whom the Authorized Veklury Is Distributed and Healthcare Providers Administering the Authorized Veklury

L. Healthcare facilities and healthcare providers will ensure that they are aware of the letter of authorization, and the terms herein, and that the authorized Fact Sheets are made available to healthcare providers and to patients and caregivers, respectively, through appropriate means.

M. Healthcare facilities and healthcare providers receiving Veklury will track serious adverse events that are considered to be potentially attributable to Veklury use under this authorization 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), 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 for questions. Submitted reports must state, "Veklury (remdesivir) use for COVID-19 under Emergency Use Authorization (EUA)" at the beginning of the question "Describe Event" for further analysis. A copy of the completed Form 3500 must also be provided to Gilead per the instructions in the authorized labeling.

N. Healthcare facilities and healthcare providers will ensure that appropriate storage is maintained until the product is administered consistent with the terms of this letter.

O. Through a process of inventory control, healthcare facilities will maintain records regarding the dispensed authorized Veklury (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).

P. Healthcare facilities will ensure that any records associated with this EUA are maintained until notified by Gilead and/or FDA. Such records will be made available to Gilead, HHS, and FDA for inspection upon request.

Conditions Related to Printed Matter, Advertising and Promotion

Q. All descriptive printed matter, advertising, and promotional materials relating to the use of the Veklury 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 and FDA implementing regulations, as applicable. 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 Veklury 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), 21 CFR 200.200 and 21 CFR 201.100(f).
- 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 at the time of initial dissemination or first use.

If the Agency notifies Gilead that any descriptive printed matter, advertising or promotional materials do not meet the terms set forth in conditions Q through S of this EUA, Gilead 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 Gilead to issue corrective communication(s).

R. No descriptive printed matter, advertising, or promotional materials relating to the use of Veklury under this authorization may represent or suggest that Veklury is safe or effective when used for the treatment of COVID-19 as described in the Scope of Authorization (Section II).

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

- Veklury has not been approved, but has been authorized for emergency use by FDA under an EUA, for the treatment COVID-19 in pediatric patients weighing 3.5 kg to less than 40 kg *or* pediatric patients less than 12 years of age weighing at least 3.5 kg, with positive results of direct SARS-CoV-2 viral testing, and who are hospitalized, or are not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death.
- The emergency use of Veklury 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.

## 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,

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Jacqueline A. O'Shaughnessy, Ph.D.
Acting Chief Scientist
Food and Drug Administration