May 1, 2020

Ashley Rhoades, MBS, RAC
Senior Associate, Regulatory Affairs
Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404

Dear Ms. Rhoades:

This letter is in response to your request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of remdesivir for the treatment of hospitalized 2019 coronavirus disease (COVID-19) patients, as described in the Scope of Authorization (section II) of this letter, pursuant to Section 564 of the Federal Food, Drug and Cosmetic Act (the Act) (21 U.S.C. 360bbb-3).

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 biologics during the COVID-19 outbreak, pursuant to section 564 of the Act, subject to terms of any authorization issued under that section.[2]

Remdesivir is a direct acting antiviral drug that inhibits viral RNA synthesis. It is an investigational drug and is not currently approved for any indication. Remdesivir has activity in cell culture and animal models against SARS-CoV, MERS-CoV, and SARS-CoV-2.

Based on review of the topline data from the randomized, double-blinded, placebo-controlled trial conducted by NIAID (NCT04280705) and from the Gilead-sponsored open-label trial that evaluated different durations of remdesivir (NCT04292899), it is reasonable to believe that the known and potential benefits of RDV outweigh the known and potential risks of the drug for the treatment of patients hospitalized with severe COVID-19.

Having concluded that the criteria for issuance of this authorization under 564(c) of the Act are met, I am authorizing the emergency use of remdesivir for treatment of COVID-19, as described

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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).

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 remdesivir for the treatment of COVID-19 when administered as described in the Scope of Authorization (section II) meet 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 remdesivir may be effective in treating COVID-19, and that, when used under the conditions described in this authorization, the known and potential benefits of remdesivir when used to treat COVID-19 outweigh the known and potential risks of such products; and
3. There is no adequate, approved, and available alternative to the emergency use of remdesivir for the treatment of COVID-19.[3]

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:

- Distribution of the authorized remdesivir will be controlled by the United States (U.S.) Government for use consistent with the terms and conditions of this EUA. Gilead will supply remdesivir to authorized distributors[4], or directly to a U.S. government agency, who will distribute to hospitals and other healthcare facilities as directed by the U.S. Government, in collaboration with state and local government authorities, as needed;

- The remdesivir covered by this authorization will be used only to treat adults and children with suspected or laboratory confirmed COVID-19 and severe disease defined as SpO2 ≤ 94% on room air, requiring supplemental oxygen, mechanical ventilation, or extracorporeal membrane oxygenation (ECMO);

- Remdesivir is administered in an in-patient hospital setting via intravenous (IV) infusion by a healthcare provider; and

[3] No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.
[4] "Authorized Distributor(s)" are identified by Gilead as an entity or entities allowed to distribute authorized remdesivr.

- The use of remdesivir covered by this authorization should be in accordance with the dosing regimens as detailed in the authorized Facts Sheets.

Product Description

Remdesivir is a nucleoside ribonucleic acid (RNA) polymerase inhibitor. Remdesivir for injection, 100 mg, is a sterile, preservative-free lyophilized solid that is to be reconstituted with 19mL of sterile water for injection and diluted into 0.9% saline prior to intravenous (IV) administration. Following reconstitution, each single-dose, clear glass vial contains a 5 mg/mL remdesivir concentrated solution with sufficient volume to allow withdrawal of 20 mL. Remdesivir Injection, 5 mg/mL, is a sterile, preservative- free, clear, solution that is to diluted into 0.9% saline prior to intravenous (IV) administration. The authorized remdesivir vial label and/or the carton labeling is clearly marked for "emergency use authorization" or for "investigational use."[5]

Remdesivir for injection, 100 mg, vials should be stored below 30 °C until time of use. Remdesivir injection, 5 mg/mL vials should be stored at refrigerated temperatures (2 °C to 8 °C) until time of use. Following dilution with 0.9% saline, the solution can be stored for up to 4 hours at room temperature (20 °C to 25 °C) or 24 hours at refrigerated temperatures (2 °C to 8 °C).

Remdesivir is authorized to be accompanied by the following product-specific information pertaining to emergency use, which is required to be made available to healthcare providers and patients respectively:

- Fact Sheet for Health Care Providers: Emergency Use Authorization (EUA) of Remdesivir (GS-5734)
- Fact Sheet for Patients and Parent/Caregivers: Emergency Use Authorization (EUA) of 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 remdesivir when used for the treatment of COVID-19 and used in accordance with 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 remdesivir may be effective for the 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 remdesivir (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.

[5] The product labeled "investigational use" is authorized for use under this EUA; FDA is not requiring it to be relabeled given the immediate need for the product.

The emergency use of your product under an 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 IV). 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), remdesivir is authorized for the treatment of suspected or laboratory confirmed COVID-19 in adults and children who are hospitalized with severe disease 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)

A. Gilead will ensure that the authorized remdesivir, accompanied with the authorized labeling (i.e., Fact Sheets), is distributed to hospitals and healthcare facilities as directed by the U.S. Government, consistent with the terms of this letter.

B. Gilead will ensure that appropriate storage and cold chain is maintained.

C. Gilead 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 authorized remdesivir. 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 remdesivir, and such changes may be permitted without amendment of this EUA, upon concurrence of the Office of Infectious Diseases/Office of New Drugs/Center for Drug Evaluation and Research (CDER), the Counter-Terrorism and Emergency Coordination Staff/Office of Center Director/CDER, and Office of Counterterrorism Emerging Threats/Office Chief Scientist/Office of Commissioner.

E. Gilead will report to FDA serious adverse events and all medication errors associated with the use of the authorized remdesivir that are reported to Gilead during the pandemic 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 should state: "use of remdesivir was under an 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.

F. Through a process of inventory control, Gilead will maintain records regarding distribution of the authorized remdesivir (i.e., lot numbers, quantity, receiving site, receipt date).

G. Gilead will make available to FDA upon request any records maintained in connection with this EUA.

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

H. 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.

I. Healthcare facilities and healthcare providers receiving remdesivir will track serious adverse events that are considered to be potentially attributable to remdesivir 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), 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 should state, "use of remdesivir was under an EUA" at the beginning of the question "Describe Event" for further analysis.

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

K. 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

L. All descriptive printed matter, including advertising and promotional material, relating to the use of the remdesivir shall be consistent with the authorized labeling, as well as the terms set forth in this EUA and the applicable requirements set forth in the Act and FDA regulations.

M. No descriptive printed matter, including advertising or promotional material, relating to the use of the remdesivir may represent or suggest that such products are safe or effective.

N. All descriptive printed matter, including advertising and promotional material, relating to the use of the remdesivir clearly and conspicuously shall state that:

- the remdesivir have not been approved;
- the remdesivir have been authorized by FDA under an EUA;
- the remdesivir is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of the remdesivir under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or 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 biologics for prevention and treatment of COVID-19 is terminated under Section 564(b)(2) of the Act or the EUA is revoked under Section 564(g) of the Act.

Sincerely,

--/s/--

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosures