



November 19, 2020

Eli Lilly and Company
Attention: Jillian Venci Fuhs, JD, PharmD
Advisor, Global Regulatory Affairs – North America
Lilly Corporate Center
Drop Code 2543
Indianapolis, IN 46285

Dear Dr. Fuhs:

This letter is in response to Eli Lilly and Company's ("Lilly") request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of baricitinib (Olumiant), in combination with remdesivir (Veklury), for the treatment of suspected or laboratory confirmed coronavirus disease 2019 (COVID-19) in certain hospitalized patients requiring supplemental oxygen, invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO), 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 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

Baricitinib is a Janus kinase (JAK) inhibitor. JAKs are intracellular enzymes which transmit signals arising from cytokine or growth factor-receptor interactions on the cellular membrane to influence cellular processes of hematopoiesis and immune cell function. Baricitinib (Olumiant) is approved by FDA for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more tumor necrosis factor antagonist therapies. Baricitinib has not been approved by FDA for the treatment of COVID-19.

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).

Based on review of the data from the randomized, double-blind, placebo-controlled trial conducted by the National Institute of Allergy and Infectious Diseases (NIAID) comparing baricitinib in combination with remdesivir to remdesivir alone, also called ACTT-2 (NCT04401579), data for baricitinib that FDA reviewed for the FDA-approved indication of rheumatoid arthritis (NDA 207924), and data from populations studied for other indications, including pediatric patients, it is reasonable to believe that baricitinib may be effective, in combination with remdesivir, for the treatment of suspected or laboratory confirmed COVID-19 in hospitalized adults and pediatric patients 2 years of age or older requiring supplemental oxygen, invasive mechanical ventilation, or ECMO, and that, when used under the conditions described in this authorization, the known and potential benefits of baricitinib when used to treat COVID-19 in such patients 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 baricitinib for treatment of COVID-19, 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 baricitinib 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 baricitinib, in combination with remdesivir, may be effective in treating suspected or laboratory confirmed COVID-19 in hospitalized adults and pediatric patients 2 years of age or older requiring supplemental oxygen, invasive mechanical ventilation, or ECMO, and that, when used under the conditions described in this authorization, the known and potential benefits of baricitinib when used in combination with remdesivir to treat COVID-19 in such patients outweigh the known and potential risks of such product; and
3. There is no adequate, approved, and available alternative to the emergency use of baricitinib, in combination with remdesivir, for treatment of suspected or laboratory confirmed COVID-19 in hospitalized adults and pediatric patients 2 years of age or older requiring supplemental oxygen, invasive mechanical ventilation, or ECMO.^{3, 4}

³ No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

⁴ On October 22, 2020, remdesivir was approved to treat COVID-19 in adults and pediatric patients (12 years of age and older and weighing at least 40 kg) requiring hospitalization. Remdesivir is a nucleoside ribonucleic acid polymerase inhibitor that has demonstrated antiviral activity against SARS-COV-2. Baricitinib is a Janus kinase (JAK) inhibitor, a class of drugs that block extracellular signals from multiple cytokines that are involved in inflammatory diseases and thought to contribute to inflammation and worsening of COVID-19. The Adaptive COVID-19 Treatment Trial 2 (ACTT-2) trial provided scientific evidence that the combination of baricitinib plus

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:

- The baricitinib covered by this authorization will be used only by healthcare providers, in combination with remdesivir, to treat suspected or laboratory confirmed COVID-19 in hospitalized⁵ adults and pediatric patients 2 years of age or older requiring supplemental oxygen, invasive mechanical ventilation, or ECMO; and
- The use of baricitinib covered by this authorization must be in accordance with the dosing regimens as detailed in the authorized Fact Sheets.

Product Description

Baricitinib is a Janus kinase (JAK) inhibitor. Baricitinib is available as debossed, film-coated, immediate-release tablets. Each tablet contains a recessed area on each face of the tablet surface. Baricitinib tablets are to be taken orally or can be crushed, dispersed in water, and given via a gastrostomy tube. The authorized baricitinib includes commercially available⁶ Olumiant (baricitinib) supplied in 30 count bottles as follows:

- OLUMIANT (baricitinib) 1 mg (NDC 0002-4732-30)
- OLUMIANT (baricitinib) 2 mg (NDC 0002-4182-30)

Baricitinib should be stored at 20° to 25°C (68° to 77°F) with excursions permitted to 15° to 30°C (59° to 86°F).

Baricitinib is authorized for emergency use with the FDA-approved package insert and the following product-specific information required to be made available to healthcare providers and patients/caregivers, respectively, through Lilly's website at www.baricitinibemergencyuse.com:

- Fact Sheet for Health Care Providers: Emergency Use Authorization (EUA) of Baricitinib
- Fact Sheet for Patients, Parents and Caregivers: Emergency Use Authorization (EUA) of Baricitinib

remdesivir provided a potential clinically meaningful benefit as compared to remdesivir alone in time to recovery, NIAID Ordinal Scale outcome at Day 15, and progression to ventilation or death at Day 29. Veklury's FDA-approved indication is for a narrower population than the use authorized for baricitinib under this EUA.

⁵ 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.

⁶ For the purposes of this Letter of Authorization, commercially available Olumiant (baricitinib) tablets refers to product in United States distribution under the approved New Drug Application 207924.

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 baricitinib, 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 baricitinib 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 baricitinib (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 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 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), baricitinib is authorized, in combination with remdesivir, to treat suspected or laboratory confirmed COVID-19 in hospitalized adults and pediatric patients 2 years of age or older requiring supplemental oxygen, invasive mechanical ventilation, or ECMO 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:

Eli Lilly and Company (Lilly) and Authorized Distributors⁷

- A. Lilly and authorized distributor(s) will ensure that the authorized baricitinib is distributed and the FDA-approved package insert and 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. Lilly and authorized distributor(s) will ensure that appropriate storage is maintained until the authorized product is delivered to healthcare facilities and/or healthcare providers.
- C. Lilly 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 authorized baricitinib. Lilly will provide to all relevant

⁷ “Authorized Distributor(s)” are identified by Lilly as an entity or entities allowed to distribute authorized baricitinib.

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. Lilly may request changes to this authorization, including to the authorized Fact Sheets for baricitinib, that do not alter the analysis of benefits and risks that underlies this authorization and FDA may determine that such changes may be permitted without amendment of this EUA. That determination must be made by joint decision 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 the Center Director/CDER, and Office of Counterterrorism and Emerging Threats/Office of the Chief Scientist/Office of the Commissioner.

E. Lilly will report to FDA serious adverse events and all medication errors associated with the use of the authorized baricitinib that are reported to Lilly 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: “Baricitinib treatment 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.

F. All manufacturing facilities will comply with Current Good Manufacturing Practice requirements.

G. Lilly will submit information to the Agency within three working days of receipt of any information concerning any batch of authorized baricitinib (whether the batch is distributed or not), as follows: (1) information concerning any incident that causes the drug product or its labeling to be mistaken for, or applied to, another article; and (2) information concerning any bacteriological or microscopic contamination, or any significant chemical, physical, or other change in deterioration in the drug product, or any failure of one or more batches of the drug product to meet the established specifications. Lilly will include in its notification to the Agency whether the batch, or batches, in question will be recalled.

H. Lilly will not implement any changes to the description of the authorized 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.

- I. Lilly will manufacture and test authorized baricitinib per the process and methods, including in-process sampling and testing and finishing product testing (release and stability) to meet all specifications as detailed in Lilly’s EUA request.
- J. Through a process of inventory control, Lilly and authorized distributor(s) will maintain records regarding distribution of the authorized baricitinib (i.e., lot numbers, quantity, receiving site, receipt date).
- K. Lilly and authorized distributor(s) will make available to FDA upon request any records maintained in connection with this EUA.

Healthcare Facilities to Whom the Authorized Baricitinib Is Distributed and Healthcare Providers Administering the Authorized Baricitinib

- 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, prior to administration of baricitinib for the authorized use.
- M. Healthcare facilities and healthcare providers will track serious adverse events that are considered to be potentially attributable to the authorized baricitinib 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](tel:1-800-FDA-1088) for questions. Submitted reports should state, “Baricitinib treatment under Emergency Use Authorization (EUA)” at the beginning of the question “Describe Event” for further analysis.
- N. Healthcare facilities and healthcare providers will ensure that appropriate storage is maintained until the authorized 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 baricitinib (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 Lilly and/or FDA. Such records will be made available to Lilly, HHS, and FDA for inspection upon request.

Conditions Related to Printed Matter, Advertising and Promotion

- Q. All descriptive printed matter, advertising, and promotional material, relating to the use of the baricitinib under this authorization 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.

- R. No descriptive printed matter, advertising, or promotional material, relating to the use of baricitinib under this authorization may represent or suggest that such products are safe or effective when used, in combination with remdesivir, for the treatment of suspected or laboratory confirmed COVID-19 in hospitalized adults and pediatric patients 2 years of age or older requiring supplemental oxygen, invasive mechanical ventilation, or ECMO.
- S. All descriptive printed matter, advertising, and promotional material, relating to the use of the baricitinib under this authorization clearly and conspicuously shall state that:
- the baricitinib has not been approved, but has been authorized for emergency use by FDA, in combination with remdesivir, for the treatment of suspected or laboratory confirmed COVID-19 in hospitalized adults and pediatric patients 2 years of age or older requiring supplemental oxygen, invasive mechanical ventilation, or ECMO.
 - the baricitinib is authorized, in combination with remdesivir, for the treatment of suspected or laboratory confirmed COVID-19 in hospitalized adults and pediatric patients 2 years of age or older requiring supplemental oxygen, invasive mechanical ventilation, or ECMO only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of the baricitinib 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 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,

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration