



March 28, 2020

Dr. Rick Bright, Ph.D.
Director
Biomedical Advanced Research and Development Authority (BARDA)
Office of Assistant Secretary for Preparedness and Response (ASPR)
U.S. Department of Health and Human Services (HHS)
330 Independence Ave, S.W.
Room 640G
Washington, D.C. 20201

Re: Request for Emergency Use Authorization For Use of Chloroquine Phosphate or Hydroxychloroquine Sulfate Supplied From the Strategic National Stockpile for Treatment of 2019 Coronavirus Disease

Dear Dr. Bright:

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 oral formulations of chloroquine phosphate and hydroxychloroquine sulfate for the treatment of 2019 coronavirus disease (COVID-19) when administered by a healthcare provider (HCP)¹ pursuant to a valid prescription of a licensed practitioner as described in the Scope of Authorization (section II) of this letter. The authorized chloroquine phosphate and hydroxychloroquine sulfate are limited to product supplied from the Strategic National Stockpile (SNS) to public health authorities², 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.^{3,4} Pursuant to Section 564 of the Act, and on the basis of such determination, the Secretary of HHS

¹ For purposes of this EUA, the term “healthcare provider” means licensed healthcare professionals who are acting within their professional scope of practice under the public health authority of official emergency response plans when administering the authorized product.

² “Public health authority” means the public agency or its delegate that has legal responsibility and authority for responding to a public health emergency, based on political or geographical (e.g., city, county, tribal, State, or Federal) or functional (e.g., law enforcement or public health range) or sphere of authority to prescribe, administer, deliver, distribute, or dispense oral chloroquine phosphate and hydroxychloroquine sulfate products during public health emergencies.

³ On February 11, 2020, the virus tentatively named 2019-nCoV was formally designated as Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Also on February 11, 2020, the disease caused by SARS-CoV-2 was

then 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.⁵

Chloroquine phosphate and hydroxychloroquine sulfate are not FDA-approved for treatment of COVID-19. Some versions of chloroquine phosphate are approved by FDA for other indications—for prophylaxis and acute attacks of certain strains of malaria and for the treatment of extraintestinal amebiasis, but the chloroquine phosphate drug product covered by this letter has not been approved. Several versions of hydroxychloroquine sulfate are approved by FDA for prophylaxis of and treatment of malaria, treatment of lupus erythematosus, and treatment of rheumatoid arthritis. The safety profile of these drugs has only been studied for FDA approved indications, not COVID-19.

Based upon limited in-vitro and anecdotal clinical data in case series, chloroquine phosphate and hydroxychloroquine sulfate are currently recommended for treatment of hospitalized COVID-19 patients in several countries, and a number of national guidelines report incorporating recommendations regarding use of chloroquine phosphate or hydroxychloroquine sulfate in the setting of COVID-19. FDA encourages the conduct and participation in randomized controlled clinical trials that may produce evidence concerning the effectiveness of these products in treating COVID-19. FDA is issuing this EUA to facilitate the availability of chloroquine phosphate and hydroxychloroquine sulfate during the COVID-19 pandemic to treat patients for whom a clinical trial is not available, or participation is not feasible.

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 chloroquine phosphate and hydroxychloroquine sulfate, as described in the Scope of Authorization section of this letter (Section II) for treatment of COVID-19 when clinical trials are not available, or participation is not feasible, subject to the terms of this authorization.

Clinical trial data results, and any information derived from clinical trials, as well as clinical trial results from studies of other investigational medical products to treat COVID-19, will continue to inform this risk benefit assessment.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of chloroquine phosphate and hydroxychloroquine sulfate 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:

formally designated as Coronavirus Disease 2019 (COVID-19). This document uses the updated names.

⁴ 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.

⁵ 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. March 27, 2020.

1. The 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 chloroquine phosphate and hydroxychloroquine sulfate may be effective in treating COVID-19, and that, when used under the conditions described in this authorization, the known and potential benefits of chloroquine phosphate and hydroxychloroquine sulfate 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 chloroquine phosphate and hydroxychloroquine sulfate for the treatment of COVID-19.⁶

II. Scope of Authorization

I have concluded, pursuant to Section 564(d)(1) of the Act, that the scope of this authorization is limited to chloroquine phosphate and hydroxychloroquine sulfate for the treatment of COVID-19, as described in this section.

Authorized Chloroquine Phosphate

I am authorizing use of the following chloroquine phosphate product that is distributed from the SNS to public health authorities for response to the COVID-19 pandemic:

- Chloroquine phosphate that is not approved by FDA for any indication.⁷
- The chloroquine phosphate must be administered by a healthcare provider pursuant to a valid prescription of a licensed practitioner.
- The chloroquine phosphate may only be used to treat adult and adolescent patients who weigh 50 kg or more and are hospitalized with COVID-19, for whom a clinical trial is not available, or participation is not feasible.⁸

The product 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:

⁶ No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

⁷ The authorized chloroquine phosphate may be accompanied by a package insert that is not approved labeling in the United States. Instead, refer to the authorized Fact Sheet for Healthcare Providers: Use of Chloroquine Phosphate Supplied from the Strategic National Stockpile for treatment of COVID-19 in Certain Hospitalized Patients. Note that Chloroquine phosphate's U.S. labeling that is FDA-approved for other indications, not COVID-19, does not include information regarding safety or effectiveness for COVID-19, see:

<https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=f398f8a9-92f3-47cb-81c2-6078806a464d>

⁸ For a listing of clinical trials, see: <https://clinicaltrials.gov/>

- Fact Sheet for Healthcare Providers: Emergency Use Authorization (EUA) of Chloroquine Phosphate Supplied from the Strategic National Stockpile for Treatment of COVID-19 in Certain Hospitalized Patients
- Fact Sheet for Patients and Parent/Caregivers: Emergency Use Authorization (EUA) of Chloroquine Phosphate For Treatment of COVID-19 in Certain Hospitalized Patients

The above described products are authorized to be administered under this EUA despite the fact that they do not meet certain requirements otherwise required by applicable federal law.

Authorized Hydroxychloroquine Sulfate

I am authorizing use of the following hydroxychloroquine sulfate product that is distributed from the SNS to public health authorities for response to the COVID-19 pandemic:

- FDA-approved hydroxychloroquine sulfate that is approved by FDA for other uses and accompanied by its FDA-approved labeling and authorized Fact Sheets.
- The hydroxychloroquine sulfate must be administered by a healthcare provider pursuant to a valid valid prescription of a licensed practitioner.
- The hydroxychloroquine sulfate may only be used to treat adult and adolescent patients who weigh 50 kg or more hospitalized with COVID-19 for whom a clinical trial is not available, or participation is not feasible.⁹

The product is authorized to be accompanied by the product information contained in hydroxychloroquine sulfate's approved package insert (for other indications)¹⁰ and together with 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 Healthcare Providers: Emergency Use Authorization (EUA) of Hydroxychloroquine Sulfate Supplied from the Strategic National Stockpile for Treatment of COVID-19 in Certain Hospitalized Patients
- Fact Sheet for Patients and Parent/Caregivers: Emergency Use Authorization (EUA) of Hydroxychloroquine Sulfate For Treatment of COVID-19 in Certain Hospitalized Patients

The above described product, when labeled consistently with the labeling of this product for its approved uses is authorized to be distributed to and administered under this EUA despite the fact that it does not meet certain requirements otherwise required by applicable federal law.

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 chloroquine phosphate and hydroxychloroquine sulfate, when used for the treatment of SARS-CoV-2 and used consistently with the Scope of

⁹ For a listing of clinical trials, see: <https://clinicaltrials.gov/>

¹⁰ For hydroxychloroquine's package insert, see: <https://dailymed.nlm.nih.gov/dailymed/>

Authorization of this letter (Section II), outweigh the known and potential risks of these products.

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 chloroquine phosphate and hydroxychloroquine sulfate may be effective for the treatment of COVID-19, when used consistently with the Scope of Authorization of this letter (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 of this letter, I have concluded that chloroquine phosphate and hydroxychloroquine sulfate (as described in the Scope of Authorization of this letter (Section II)) meets the criteria set forth in Section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of these products 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), these products are authorized for the treatment of 2019 coronavirus disease (COVID-19) when administered by a HCP pursuant to a valid prescription of a licensed practitioner as described in the Scope of Authorization (section II) of this letter.

The EUA will cease to be effective when the HHS declaration that circumstances exist to justify the EUA is terminated under Section 564(b)(2) of the Act or when the EUA is revoked under Section 564(g) of the Act.

III. Waiver of Certain Requirements

Pursuant to Section 564(e)(3) of the Act, with respect to the emergency use of a product for which an authorization under this section is issued, FDA may waive or limit, to the extent appropriate given the circumstances of the emergency, requirements regarding current good manufacturing practice otherwise applicable to the manufacture, processing, packing, or holding of products subject to regulation under this Act, including such requirements established under Section 501. FDA grants that waiver with respect to the products covered by this authorization.

IV. Conditions of Authorization

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

- A. SNS will distribute the authorized chloroquine phosphate and hydroxychloroquine sulfate under its direction to the extent such distributions are consistent with and do not exceed the terms of this letter, including distribution with the authorized labeling.

- B. Through a process of inventory control, SNS will maintain records regarding distribution under its direction of the authorized chloroquine phosphate and hydroxychloroquine sulfate (i.e., lot numbers, quantity, receiving site, receipt date).
- C. HHS will ensure that the terms of this EUA are made available to public health authorities through appropriate means.¹¹ HHS will provide public health authorities a copy of this letter of authorization and communicate to public health authorities any subsequent amendments that might be made to this letter of authorization and its authorized accompanying materials (e.g., Fact Sheets).
- D. BARDA, ASPR, or other organization within HHS may request the authorization of additional chloroquine phosphate and hydroxychloroquine sulfate products under this EUA. Additional such products may be included in this authorization, without amendment of this EUA, upon concurrence of, Office of Infectious Diseases/OND/CDER, CTECS/OCD/CDER, and OCET/OCS/OC.
- E. BARDA may request changes to this authorization, including to the authorized fact sheets for chloroquine phosphate and hydroxychloroquine sulfate products and to require patient outcomes reporting if and when a system is established, without amendment of this EUA, upon concurrence of, Office of Infectious Diseases /OND/CDER, CTECS/OCD/CDER, and OCET/OCS/OC.
- F. HHS will inform public health authorities about the need to have a process in place for performing adverse event monitoring and compliance activities designed to ensure that adverse events and all medication errors associated with the use of the authorized chloroquine phosphate or hydroxychloroquine sulfate are reported to FDA, to the extent practicable given emergency circumstances, as follows: complete the MedWatch FDA Form online at www.fda.gov/medwatch/report.htm, or by using a postage-paid MedWatch Form 3500 (available at <https://www.accessdata.fda.gov/scripts/medwatch/index.cfm?action=reporting.home>), or by calling 1-800-FDA-1088. Submitted reports should state: “use of chloroquine phosphate was under an EUA” or “use of hydroxychloroquine sulfate was under an EUA,” as relevant. If and when HHS establishes a process for collecting outcomes data, HHS will inform public health authorities about such process.
- G. SNS will ensure that the authorized chloroquine phosphate and hydroxychloroquine sulfate is distributed for use under its direction within the expiry dating on the manufacturer’s labeling. If FDA authorizes any expiry dating extensions of the authorized chloroquine phosphate or hydroxychloroquine sulfate under this EUA, SNS will inform emergency response stakeholders receiving the authorized chloroquine phosphate or hydroxychloroquine sulfate of such extensions and any conditions related to such extensions under this EUA. SNS will maintain adequate records regarding the expiry dates by which authorized chloroquine phosphate and hydroxychloroquine sulfate may be used.

¹¹ For example, through hard copy, web posting, and/or mass media.

- H. SNS will make available to FDA upon request any records maintained in connection with this EUA.

Healthcare Systems to Whom the Authorized Chloroquine Phosphate and Hydroxychloroquine Sulfate Is Distributed

- I. Healthcare systems and healthcare providers receiving the chloroquine phosphate and/or hydroxychloroquine sulfate from the SNS will track adverse events and report 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) or FDA Form 3500B (consumer/patient) 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 “chloroquine phosphate treatment under EUA” or “hydroxychloroquine sulfate treatment under EUA.”
- J. Through a process of inventory control, healthcare systems will maintain records regarding the dispensed authorized chloroquine phosphate and hydroxychloroquine sulfate (i.e., lot numbers, quantity, receiving site, receipt date) and maintain patient information and other relevant data as feasible (e.g., patient name, age, disease manifestation, other drugs administered, outcomes).
- K. Healthcare systems will ensure that any records associated with this EUA are maintained until notified by SNS and/or FDA. Such records will be made available to FDA, SNS and BARDA for inspection upon request.

V. 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,

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosures