U.S. FOOD & DRUG ADMINISTRATION

January 26, 2023

AstraZeneca Pharmaceuticals LP
Attention: Stacey Cromer Berman, PhD
Senior Regulatory Affairs Director and Team Lead
One MedImmune Way
Gaithersburg, MD 20878

RE: Emergency Use Authorization 104

Dear Dr. Cromer Berman:

This letter is in response to AstraZeneca Pharmaceuticals LP's (AstraZeneca) request that the Food and Drug Administration (FDA or Agency) issue an Emergency Use Authorization (EUA) for the emergency use of EVUSHELD™ (tixagevimab co-packaged with cilgavimab) for the pre-exposure prophylaxis of coronavirus disease 2019 (COVID-19) in certain adults and pediatric individuals (12 years of age and older weighing at least 40 kg), 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 coronavirus disease 2019 (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 Act (21 U.S.C. 360bbb-3), subject to terms of any authorization issued under that section.[2]

On December 8, 2021, the Food and Drug Administration (FDA) issued an EUA for emergency use of EVUSHELD for use as pre-exposure prophylaxis of COVID-19 in certain adults and pediatric individuals (12 years of age and older weighing at least 40 kg), as described in the Scope of Authorization (Section II) of the letter. Tixagevimab and cilgavimab, the active components of EVUSHELD, are neutralizing IgG1 monoclonal antibodies that bind to distinct, non-overlapping epitopes within the receptor binding domain of the spike protein of SARS-CoV-2. EVUSHELD is an investigational drug and is not approved for any uses, including use as pre-exposure prophylaxis of COVID-19.

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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).

FDA subsequently reissued the Letter of Authorization (LOA) on December 10, 2021[3], December 20, 2021[4], February 24, 2022[5], May 17, 2022[6], October 27, 2022[7], and December 8, 2022.[8]

On January 26, 2023, having concluded that revising this EUA is appropriate to protect the public health or safety under section 564(g)(2)(C) of the Act, FDA is reissuing the December 8, 2022 letter in its entirety, to revise the scope of authorization to limit the use of EVUSHELD for pre-exposure prophylaxis of COVID-19 in the United States only when, based on available information including variant susceptibility to EVUSHELD and national variant frequencies, the combined frequency of non-susceptible variants nationally is less than or equal to 90%. Condition O in this letter has also been revised to modify the timing for submitting aggregate reports detailing serious adverse events in the Cardiac Disorder System Order Class (SOC) and other non-cardiac thrombotic serious adverse events.

Based on the review of the data from the PROVENT clinical trial (NCT04625725), a Phase III randomized, double-blind, placebo-controlled clinical trial, it is reasonable to believe that EVUSHELD may be effective for use as pre-exposure prophylaxis of COVID-19 in certain adults and pediatric individuals (12 years of age and older weighing at least 40 kg), 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 EVUSHELD 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 EVUSHELD for use as pre-exposure prophylaxis of COVID-19, as described in the Scope of Authorization section of this letter (Section II) and subject to the terms of this authorization.

[3] In its December 10, 2021 revision, FDA revised the LOA to add a new limitation in the Scope of Authorization (section II) detailing the scope of healthcare providers who are authorized to prescribe EVUSHELD for use under this EUA.
[4] In its December 20, 2021 revision, FDA revised the limitation in the Scope of Authorization (section II) in the LOA detailing the scope of healthcare providers who are authorized to prescribe EVUSHELD for use under this EUA. The Fact Sheet for Healthcare Providers was also revised to reflect this limitation.
[5] In its February 24, 2022 revision, FDA revised the LOA to include a new condition of authorization on registration and listing. The authorized Fact Sheet for Healthcare Providers and authorized Fact Sheet for Patients, Parents and Caregivers were also revised to include updated dosing information for EVUSHELD.
[6] In its May 17, 2022 revision, FDA revised the scope of authorization in the LOA to refer to section 5.2 (Warnings and Precautions) of the authorized Fact Sheet for Healthcare Providers, which as of the reissuance, included new information on hypersensitivity reactions and the risk of cross-hypersensitivity with COVID-19 vaccines and related clinical recommendations. Corresponding information was also incorporated into the authorized Fact Sheet for Patients, Parents and Caregivers.
[7] In its October 27, 2022 revision, FDA revised the LOA to incorporate clarifying revisions to Condition X of this letter. Condition W was also revised to require that all printed matter, advertising and promotional materials relating to the use of EVUSHELD under this authorization be submitted to FDA for consideration at least 14 calendar days prior to initial dissemination or first use.
[8] In its December 8, 2022 revision, FDA revised the LOA to update certain post-authorization requirements as detailed in Condition O.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of EVUSHELD for pre-exposure prophylaxis 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 EVUSHELD may be effective for use as pre-exposure prophylaxis of COVID-19 in certain adults and pediatric individuals (12 years of age and older weighing at least 40 kg), 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 EVUSHELD outweigh the known and potential risks of such product; and

3. There is no adequate, approved, and available alternative to the emergency use of EVUSHELD as pre-exposure prophylaxis of COVID-19 as further 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:

- Distribution of the authorized EVUSHELD will be controlled by the United States (U.S.) Government for use consistent with the terms and conditions of this EUA. AstraZeneca will supply EVUSHELD to authorized distributor(s)[10], who will distribute to healthcare facilities or healthcare providers as directed by the U.S. Government, in collaboration with state and local government authorities as needed;

- EVUSHELD may only be used in adults and pediatric individuals (12 years of age and older weighing at least 40 kg):

    - Who are not currently infected with SARS-CoV-2 and who have not had a known recent exposure to an individual infected with SARS-CoV-2 **and**
        - Who have moderate to severe immune compromise due to a medical condition or receipt of immunosuppressive medications or treatments **and** may not mount an adequate immune response to COVID-19 vaccination[11] **or**

[9] No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.
[10] "Authorized Distributor(s)" are identified by AstraZeneca as an entity or entities allowed to distribute authorized EVUSHELD.
[11] For additional information please see https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html. Healthcare providers should consider the benefit-risk for an individual patient.

- For whom vaccination with any available COVID-19 vaccine, according to the approved or authorized schedule, is not recommended due to a history of severe adverse reaction to a COVID-19 vaccine(s) and/or COVID-19 vaccine component(s).[12]

Limitations on Authorized Use

- EVUSHELD is authorized for use only when the combined frequency of non-susceptible variants nationally is less than or equal to 90%, based on available information including variant susceptibility to EVUSHELD and national variant frequencies[13].

- Evusheld is **not** authorized for the following uses in individuals:

  - For treatment of COVID-19, or
  - For post-exposure prophylaxis of COVID-19 in individuals who have been exposed to someone infected with SARS-CoV-2.

- EVUSHELD may only be prescribed for an individual patient by physicians, advanced practice registered nurses, and physician assistants that are licensed or authorized under State law to prescribe drugs in the therapeutic class to which EVUSHELD belongs (i.e., anti-infectives).[14]

- Pre-exposure prophylaxis with EVUSHELD is not a substitute for vaccination in individuals for whom COVID-19 vaccination is recommended. Individuals for whom COVID-19 vaccination is recommended, including individuals with moderate to severe immune compromise who may derive benefit from COVID-19 vaccination, should receive COVID-19 vaccination.

- For individuals who have received a COVID-19 vaccine, EVUSHELD should be administered at least two weeks after vaccination.

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

[12] See section 5.2, *Warnings and Precautions*, of the authorized Fact Sheet for Healthcare Providers for additional information.

[13] FDA will monitor conditions to determine whether use is consistent with the scope of authorization, referring to available information, including information on variant susceptibility (e.g., Section 12.4 of the authorized Fact Sheet for Healthcare Providers) and CDC variant frequency data available at: https://covid.cdc.gov/covid-data-tracker/#variant-proportions. FDA's determination and any updates will be available at: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs.

[14] Under section 201(a)(1) of the Act, the term "State" is defined to mean "any State or Territory of the United States, the District of Columbia, and the Commonwealth of Puerto Rico."

Product Description

EVUSHELD is supplied as a single carton (NDC 0310-7442-02) containing 1 single-dose vial of tixagevimab injection and 1 single-dose vial of cilgavimab injection.

Tixagevimab injection (NDC 0310-8895-01) is a sterile, preservative-free, clear to opalescent and colorless to slightly yellow solution supplied in a single-dose vial for intramuscular use. The vial stoppers are not made with natural rubber latex. Each 1.5 mL contains 150 mg tixagevimab, L- histidine (2.4 mg), L- histidine hydrochloride monohydrate (3.0 mg), polysorbate 80 (0.6 mg), sucrose (123.2 mg), and Water for Injection, USP.

Cilgavimab injection (NDC 0310-1061-01) is a sterile, preservative-free, clear to opalescent and colorless to slightly yellow solution supplied in a single-dose vial for intramuscular use. The vial stoppers are not made with natural rubber latex. Each 1.5 mL contains 150 mg cilgavimab, L-histidine (2.4 mg), L- histidine hydrochloride monohydrate (3.0 mg), polysorbate 80 (0.6 mg), sucrose (123.2 mg), and Water for Injection, USP.

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

EVUSHELD is authorized for emergency use with the following product-specific information required to be made available to healthcare providers and to patients, parents, and caregivers, respectively, through AstraZeneca's website www.EVUSHELD.com (referred to as the "authorized labeling"):

- Fact Sheet for Healthcare Providers: Emergency Use Authorization (EUA) for EVUSHELD
- Fact Sheet for Patients, Parents and Caregivers: Emergency Use Authorization (EUA) of EVUSHELD 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 EVUSHELD, when used for pre-exposure prophylaxis of COVID-19 in certain adults and pediatric individuals (12 years of age and older weighing at least 40 kg) 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 EVUSHELD may be effective for pre-exposure prophylaxis of COVID-19 in certain adults and pediatric individuals (12 years of age and older weighing at least 40 kg) 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 EVUSHELD (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), EVUSHELD is authorized for use as pre-exposure prophylaxis of 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:

AstraZeneca and Authorized Distributors[15]

A. AstraZeneca and authorized distributor(s) will ensure that EVUSHELD is distributed with 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. AstraZeneca and authorized distributor(s) will ensure that appropriate storage and cold chain is maintained until the product is delivered to healthcare facilities and/or healthcare providers.

C. AstraZeneca 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 EVUSHELD. AstraZeneca 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. AstraZeneca may request changes to this authorization, including to the authorized Fact Sheets for EVUSHELD. 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.[16]

[15] "Authorized Distributor(s)" are identified by AstraZeneca as an entity or entities allowed to distribute EVUSHELD for the use authorized in this letter.

[16] 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.

E. AstraZeneca 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 EVUSHELD 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 EVUSHELD are prohibited. If the Agency notifies AstraZeneca that any instructional and educational materials are inconsistent with the authorized labeling, AstraZeneca must cease distribution of such instructional and educational materials. Furthermore, as part of its notification, the Agency may also require AstraZeneca to issue corrective communication(s).

F. AstraZeneca will report to FDA all serious adverse events and medication errors potentially related to EVUSHELD use that are reported to AstraZeneca 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: "EVUSHELD 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. AstraZeneca will submit information to the Agency within three working days of receipt of any information concerning significant quality problems with drug product distributed under this emergency use authorization for EVUSHELD 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 should be submitted for all potentially impacted lots.

AstraZeneca 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, AstraZeneca must submit information confirming that AstraZeneca 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. AstraZeneca must submit this information as soon as possible but no later than 45 calendar days from the initial notification.

I. AstraZeneca will manufacture EVUSHELD to meet all quality standards and per the manufacturing process and control strategy as detailed in AstraZeneca's EUA request. AstraZeneca 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. AstraZeneca will list EVUSHELD with a unique 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 such establishment.

K. Through a process of inventory control, AstraZeneca and authorized distributor(s) will maintain records regarding distribution of EVUSHELD (i.e., lot numbers, quantity, receiving site, receipt date).

L. AstraZeneca will establish a process for monitoring genomic database(s) for the emergence of global viral variants of SARS-CoV-2. A summary of AstraZeneca's process should be submitted to the Agency as soon as practicable, but no later than 30 calendar days of the issuance of this letter, and within 30 calendar days of any material changes to such process. AstraZeneca will provide reports to the Agency on a monthly basis summarizing any findings as a result of its monitoring activities and, as needed, any follow-up assessments planned or conducted.

M. FDA may require AstraZeneca to assess the activity of the authorized EVUSHELD 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). AstraZeneca will perform the required assessment in a manner and timeframe agreed upon by AstraZeneca and the Agency. AstraZeneca 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. AstraZeneca 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. AstraZeneca shall provide samples as requested of tixagevimab and of cilgavimab 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 the individual drug substances for tixagevimab and cilgavimab may include, but are not limited to, cell culture potency assays, protein binding assays, cell culture variant assays (pseudotyped virus-like particles and/or authentic virus), and *in vivo* efficacy assays.

O. AstraZeneca must provide the following information to the Agency:

- All anti-drug antibody (ADA) assessments that have not been completed at the time of this authorization for subjects from the PROVENT clinical trial for days 1, 29, 58, and 183 by April 22, 2022.
- Interim analysis results through Day 28 for the first 50 subjects to receive a second dose from the PROVENT repeat-dose sub-study by April 22, 2022.
- AstraZeneca must conduct an additional study attempting to select for SARS-CoV-2 with reduced susceptibility to tixagevimab in culture. Such study must employ alternative strategies as agreed upon between AstraZeneca and the Agency. AstraZeneca must provide the Agency with a proposed protocol by January 7, 2022. AstraZeneca must submit a report of summary findings as soon as available but no later than June 30, 2022.
- Report from AstraZeneca's study evaluating the potential for tixagevimab and cilgavimab to mediate antibody-dependent enhancement of infection using sub-saturating concentrations of each monoclonal antibody by June 30, 2022.
- The final Clinical Study Report for the clinical trial STORM CHASER by December 30, 2022.
- The final Clinical Study Report for the clinical trial PROVENT by March 31, 2023.
- Topline data, to include safety, pharmacokinetic, ADA, and biomarkers for thrombotic events (d-dimer, P-selectin, thrombin, and Factor VIII), for all subjects in the PROVENT repeat-dose sub-study up to the 9-month study visit by March 31, 2023.
- Biannual (every 6 months) aggregate reports for serious adverse events in the Cardiac Disorder System Order Class (SOC) and other non-cardiac thrombotic serious adverse events.
- Assessments from AstraZeneca's ongoing analyses to genotype and phenotype virus isolated from prophylaxis failures to identify pre-existing polymorphisms or emergent substitutions that reduce susceptibility to neutralization by tixagevimab and/or cilgavimab.
- AstraZeneca will conduct an additional randomized, dose-ranging clinical trial in individuals with moderate to severe immunocompromise who may not mount an adequate immune response to COVID-19 vaccination evaluating the following dosing regimens for COVID-19 pre-exposure prophylaxis:

- EVUSHELD (300 mg tixagevimab and 300 mg cilgavimab) administered as two consecutive IM injections followed 3 months later by EVUSHELD (150 mg tixagevimab and 150 mg cilgavimab) administered as two consecutive IM injections with subsequent redosing every 3 months.
- EVUSHELD (600 mg tixagevimab and 600 mg cilgavimab) administered as an intravenous infusion followed 6 months later by EVUSHELD (300 mg tixagevimab and 300 mg cilgavimab) administered as two consecutive IM injections with subsequent redosing every 6 months

At least 100 subjects should be randomized to each dosing regimen. The primary objectives of the trial would be to evaluate safety and immunogenicity, but pharmacokinetic, pharmacodynamic, and efficacy data should also be collected. AstraZeneca must provide the Agency with a final protocol for this trial no later than March 11, 2022.

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

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

Q. 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, parents, and caregivers, respectively, through appropriate means, prior to administration of EVUSHELD.

R. Healthcare facilities and healthcare providers receiving EVUSHELD will track all serious adverse events and medication errors that are considered to be potentially attributable to EVUSHELD 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, "EVUSHELD use for COVID-19 under Emergency Use Authorization" at the beginning of the question "Describe Event" for further analysis. A copy of the completed FDA Form 3500 should also be provided to AstraZeneca per the instructions in the authorized labeling.

S. Healthcare facilities and healthcare providers will ensure that appropriate storage and cold chain is maintained until the product is administered consistent with the terms of this letter and the authorized labeling.

T. Through a process of inventory control, healthcare facilities will maintain records regarding the dispensing and administration of EVUSHELD 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).

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

V. Healthcare facilities and providers will report therapeutics information and utilization data as directed by the U.S. Department of Health and Human Services.

Conditions Related to Printed Matter, Advertising, and Promotion

W. All descriptive printed matter, advertising, and promotional materials relating to the use of EVUSHELD 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 EVUSHELD 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 for consideration at least 14 calendar days prior to initial dissemination or first use.

X. AstraZeneca may disseminate descriptive printed matter, advertising, and promotional materials relating to the emergency use of EVUSHELD 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. AstraZeneca may not imply that EVUSHELD is FDA-approved for its authorized use by making statements such as "EVUSHELD is safe and effective for the pre-exposure prophylaxis of COVID-19."

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

- EVUSHELD has not been approved, but has been authorized for emergency use by FDA under an EUA, for pre-exposure prophylaxis of COVID-19 in

certain adults and pediatric individuals (12 years of age and older weighing at least 40 kg); and

- The emergency use of EVUSHELD 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 AstraZeneca that any descriptive printed matter, advertising or promotional materials do not meet the terms set forth in conditions W-Y of this EUA, AstraZeneca 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 AstraZeneca 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,

--/S/--

Patrizia Cavazzoni, M.D.
Director
Center for Drug Evaluation and Research
U.S. Food and Drug Administration