EUA 000104

GRANTING LETTER-
REVISED FACT SHEET

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

Dear Dr. Cromer Berman:

Please refer to your Emergency Use Authorization (EUA) authorizing EVUSHELD™ (tixagevimab co-packaged with cilgavimab) under section 564 of the Federal Food, Drug, and Cosmetic Act (FDCA) (21 U.S.C. 360bbb-3) for emergency use as pre-exposure prophylaxis of coronavirus disease 2019 (COVID-19) 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 or

- 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).

We refer to your submissions dated June 2 and June 23, 2022 to EUA 000104 wherein you submitted revisions to the authorized Fact Sheet for Healthcare Providers to support recommendations for 6-month repeat dosing of 600 mg IM EVUSHELD (300 mg tixagevimab and 300 mg of cilgavimab). We also refer to supporting data you included in your April 22 and June 8, 2022, submissions.

We have completed our review and concur with the revisions to the Fact Sheet for Healthcare Providers which consist of the following:

Full Fact Sheet for Healthcare Providers

- Dosage for Emergency Use of EVUSHELD (Section 2.1): This section was revised to add the repeat dosing recommendations.
- Pharmacokinetics (Section 12.3): This section was updated to include pharmacokinetic data from the PROVENT repeat dose sub-study and align language in the paragraph on pharmacokinetic and pharmacodynamic modeling to describe

the current dosing recommendations for the currently circulating SARS-CoV-2 variants.

- Microbiology (Section 12.4): This section was updated to add neutralization data of cilgavimab, tixagevimab, and tixagevimab and cilgavimab in combination against more recent variants including BA.2.12.1, BA.3, and BA.4/5.

- Immunogenicity (Section 12.6): This is a new section which was added to provide available data on the development of anti-EVUSHELD antibodies (ADA) in the parent PROVENT study and the PROVENT repeat dose sub-study, as well the impact of ADA on the serum concentrations of EVUSHELD.

In addition, edits were made to the Fact Sheet for Patients, Parents and Caregivers to be consistent with these changes. These documents must be made available consistent with the terms and conditions of this authorization.

By submitting this amendment for review by the Food and Drug Administration (FDA), you have complied with the Conditions of Authorization stated in the Letter of Authorization for EUA 000104, dated May 17, 2022[1], authorizing the emergency use of EVUSHELD 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).

Sincerely,

--/S/--

Debra Birnkrant, MD
Director
Division of Antivirals
Office of Infectious Diseases
Center for Drug Evaluation and Research

ENCLOSURE(S):
- Fact Sheet for Healthcare Providers
- Fact Sheet for Patients, Parents and Caregivers

[1] FDA's Letter of Authorization for EVUSHELD was initially issued on December 8, 2021. The letter was subsequently re-issued on December 10, 2021, December 20, 2021, February 24, 2022, and May 17, 2022.