Coronavirus (COVID-19) Update: FDA Authorizes New Long-Acting Monoclonal Antibodies for Pre-exposure Prevention of COVID-19 in Certain Individuals

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Today, the U.S. Food and Drug Administration issued an emergency use authorization (EUA) for AstraZeneca's Evusheld (tixagevimab co-packaged with cilgavimab and administered together) for the pre-exposure prophylaxis (prevention) of COVID-19 in certain adults and pediatric individuals (12 years of age and older weighing at least 40 kilograms [about 88 pounds]).

The product is only authorized for those individuals who are not currently infected with the SARS-CoV-2 virus and who have not recently been exposed to an individual infected with SARS-CoV-2. The authorization also requires that individuals either have:

- moderate to severely compromised immune systems due to a medical condition or due to taking immunosuppressive medications or treatments and may not mount an adequate immune response to COVID-19 vaccination (examples of such medical conditions or treatments can be found in the fact sheet for health care providers) or;
- a history of severe adverse reactions to a COVID-19 vaccine and/or component(s) of those vaccines, therefore vaccination with an available COVID-19 vaccine, according to the approved or authorized schedule, is not recommended.

"Vaccines have proven to be the best defense available against COVID-19. However, there are certain immune compromised individuals who may not mount an adequate immune response to COVID-19 vaccination, or those who have a history of severe adverse reactions to a COVID-19 vaccine and therefore cannot receive one and need an alternative prevention option," said Patrizia Cavazzoni, M.D., director of the FDA's Center for Drug Evaluation and Research. "Today's action authorizes the use of the combination of two monoclonal antibodies to reduce the risk of developing COVID-19 in these individuals."

One dose of Evusheld, administered as two separate consecutive intramuscular injections (one injection per monoclonal antibody, given in immediate succession), may be effective for pre-exposure prevention for six months. Evusheld is not authorized for individuals for the treatment of COVID-19 or for post-exposure prevention of COVID-19. Patients should talk with their health care provider to determine whether Evusheld is an appropriate pre-exposure prevention option for them.

Pre-exposure prevention with Evusheld is not a substitute for vaccination in individuals for whom COVID-19 vaccination is recommended. The FDA has approved one vaccine and authorized others to prevent COVID-19 and serious clinical outcomes associated with a COVID-19 infection, including hospitalization and death. The FDA urges the public to get vaccinated if eligible. Learn more about FDA-approved or -authorized COVID-19 vaccines.

Monoclonal antibodies are laboratory-made proteins that mimic the immune system's ability to fight off harmful pathogens such as viruses. Tixagevimab and cilgavimab are long-acting monoclonal antibodies that are specifically directed against the spike protein of SARS-CoV-2, designed to block the virus' attachment and entry into human cells. Tixagevimab and cilgavimab bind to different, non-overlapping sites on the spike protein of the virus.

The issuance of an EUA is different than an FDA approval. In determining whether to issue an EUA, the FDA evaluates the totality of available scientific evidence and carefully balances any known or potential risks with any known or potential benefits of the product. Based on the FDA's review of the totality of the scientific evidence available, the agency has determined that it is reasonable to believe that Evusheld may be effective for use as pre-exposure prevention in certain adults and pediatric individuals (12 years of age and older weighing at least 40

kilograms). The agency has also determined that the known and potential benefits of Evusheld, when used consistent with the terms and conditions of the authorization, outweigh the known and potential risks of the product. There are no adequate, approved and available alternatives to Evusheld for the pre-exposure prevention of COVID-19 in the authorized population.

The primary data supporting this EUA for Evusheld are from PROVENT, a randomized, double-blind, placebo-controlled clinical trial in adults greater than age 59 or with a prespecified chronic medical condition or at increased risk of SARS-CoV-2 infection for other reasons who had not received a COVID-19 vaccine and did not have a history of SARS-CoV-2 infection or test positive for SARS-CoV-2 infection at the start of the trial. The main outcome measured in the trial was whether a trial participant had a first case of COVID-19 after receiving Evusheld or placebo and before day 183 of the trial. In this trial, 3,441 people received Evusheld and 1,731 received a placebo. In the primary analysis, Evusheld recipients saw a 77% reduced risk of developing COVID-19 compared to those who received a placebo, a statistically significant difference. In additional analyses, the reduction in risk of developing COVID-19 was maintained for Evusheld recipients through six months. The safety and effectiveness of Evusheld for use in the pre-exposure prevention of COVID-19 continue to be evaluated.

Under the EUA, fact sheets that provide important information about using Evusheld in pre-exposure prevention of COVID-19 as authorized must be made available to health care providers and to patients and caregivers. These fact sheets include dosing instructions, potential side effects and drug interactions.

Possible side effects of Evusheld include: hypersensitivity reactions (including anaphylaxis), bleeding at the injection site, headache, fatigue and cough.

Serious cardiac adverse events were infrequent in PROVENT. However, more trial participants had serious cardiac adverse events (such as myocardial infarction and heart failure) after receiving Evusheld compared to placebo. These participants all had risk factors for cardiac disease or a history of cardiovascular disease before participating in the clinical trial. It is not clear if Evusheld caused these cardiac adverse events.

The FDA is working with sponsors of all currently authorized therapeutics to assess the activity against any global SARS-CoV-2 variant(s) of interest and is committed to communicating with the public as we learn more.

The EUA was issued to AstraZeneca.

Thank you for your continuous support**.**

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