



December 9, 2021

****Emergency Use Authorization****

Tixagevimab and Cilgavimab (Evusheld®) for COVID-19 Pre-Exposure Prophylaxis

Mechanism of action¹:

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.

Current Status & Indications^{1,2}:

On December 9, 2021, the U.S. Food and Drug Administration issued an [emergency use authorization](#) (EUA) for Evusheld® (tixagevimab co-packaged with cilgavimab and administered together) for the pre-exposure prophylaxis of COVID-19 in certain adults and pediatric individuals (12 years of age and older weighing at least 40 kg).

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** (see examples immediately below) and may not mount an adequate immune response to COVID-19 vaccination or;
- a history of severe adverse reactions to a COVID-19 vaccine and/or vaccine component(s), therefore vaccination with an available COVID-19 vaccine, according to the approved or authorized schedule, is not recommended.

**Medical conditions or treatments that may result in moderate to severe immune compromise and an inadequate immune response to COVID-19 vaccination include but are not limited to:*

- Active treatment for solid tumor and hematologic malignancies
- Receipt of solid-organ transplant and taking immunosuppressive therapy
- Receipt of chimeric antigen receptor (CAR)-T-cell or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy)
- Moderate or severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome)
- Advanced or untreated HIV infection (people with HIV and CD4 cell counts <200/mm³ history of an AIDS-defining illness without immune reconstitution, or clinical manifestations of symptomatic HIV)
- Active treatment with high-dose corticosteroids (i.e., ≥20 mg prednisone or equivalent per day when administered for ≥2 weeks), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, tumor-necrosis (TNF) blockers, and other biologic agents that are immunosuppressive or immunomodulatory (e.g., B-cell depleting agents)

Availability¹:

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), 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. The IHS National Supply Service Center anticipates that ordering will be available for IHS facilities in a limited capacity during the month of December 2021.

Limitations of Authorized Use³:

1. Evusheld® is not authorized for use in individuals:
 - For treatment of COVID-19, or
 - For post-exposure prophylaxis of COVID-19 in individuals exposed to someone infected with SARS-CoV-2.
2. *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.*
3. In individuals who received a COVID-19 vaccine, Evusheld® should be administered at least 2 weeks after vaccination.

Efficacy and Safety:

The primary data supporting this EUA are from the PROVENT trial, a randomized, double-blind, placebo-controlled clinical trial in adults aged >59 years or with a pre-specified 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 with placebo, a statistically significant difference. In additional analyses, the reduction in risk of developing COVID-19 was maintained for Evusheld® recipients through 6 months. The safety and effectiveness of Evusheld® for use in the pre-exposure prevention of COVID-19 continue to be evaluated.

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

Dosage and Administration^{2,3:}

The dosage of Evusheld® for authorized emergency use is 150 mg of tixagevimab and 150 mg of cilgavimab administered as two separate consecutive IM injections (one injection per monoclonal antibody, given in immediate succession) and may be effective for pre-exposure prevention for 6 months.

Warnings and Precautions^{3:}

- Hypersensitivity Including Anaphylaxis: Serious hypersensitivity reactions, including anaphylaxis, have been observed with IgG1 monoclonal antibodies like Evusheld®. If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive therapy. Clinically monitor individuals after injections and observe for at least 1 hour.
- Clinically Significant Bleeding Disorders: As with any other intramuscular injection, Evusheld® should be given with caution to individuals with thrombocytopenia or any coagulation disorder.
- Cardiovascular Events: A higher proportion of subjects who received Evusheld® versus placebo reported myocardial infarction and cardiac failure serious adverse events. All subjects with events had cardiac risk factors and/or a prior history of CVD, and there was no clear temporal pattern. A causal relationship between Evusheld® and these events has not been established. Consider the risks and benefits prior to initiating Evusheld® in individuals at high risk for cardiovascular events, and advise individuals to seek immediate medical attention if they experience any signs or symptoms suggestive of a cardiovascular event.

Current EUA Fact Sheets for Evusheld®^{3,4:}

- ❖ (1) [Healthcare Providers](#) -AND- (2) [Patients, Parents and Caregivers](#)

Required Reporting for Serious Adverse Events and Medication Errors under the EUA^{3:}

The prescribing healthcare provider and/or the provider's designee is/are responsible for mandatory reporting of all serious adverse events and medication errors potentially related to Evusheld® within 7 calendar days from the healthcare provider's awareness of the event. The FDA recommends that reports, using FDA Form 3500, include:

- Patient demographics and baseline characteristics (patient identifier, age or DOB, gender, weight, ethnicity, and race)
- A statement "Evusheld® use for COVID-19 under Emergency Use Authorization (EUA)" under the "Describe Event, Problem, or Product Use/Medication Error" heading
- Information about the serious adverse event or medication error (e.g., signs and symptoms, test/laboratory data, complications, timing of drug initiation in relation to the occurrence of the event, duration of the event, treatments required to mitigate the event, evidence of event improvement/disappearance after stopping or reducing the dosage, evidence of event reappearance after reintroduction, clinical outcomes)
- Patient's preexisting medical conditions and use of concomitant products
- Information about the product (e.g., dosage, route of administration, NDC #)

Submit adverse event reports to **FDA MedWatch** using one of the following methods:

1. Complete and submit the report online: www.fda.gov/medwatch/report.htm or
2. Complete and submit a postage-paid FDA Form 3500: www.fda.gov/media/76299/download

***Please put "IHS" or "Indian Health Service" in the reporter section of the form (section G)*

References:

1. Food and Drug Administration. AstraZeneca Evusheld® [Letter of Authorization](#). Published December 8, 2021.
2. Food and Drug Administration. FDA News Release. [Coronavirus \(COVID-19\) Update: FDA Authorizes New Long-Acting Monoclonal Antibodies for Pre-Exposure Prevention of COVID-19 in Certain Individuals](#). Published online December 8, 2021.
3. Food and Drug Administration. Tixagevimab and cilgavimab: [FACT SHEET FOR HEALTHCARE PROVIDERS](#). December 8, 2021.
4. Food and Drug Administration. Tixagevimab and cilgavimab: [FACT SHEET FOR PATIENTS, PARENTS AND CAREGIVERS](#). December 8, 2021.