Evusheld™ (tixagevimab/cilgavimab) – Emergency use authorization

- On December 8, 2021, the FDA announced the emergency use authorization (EUA) approval of AstraZeneca's Evusheld (tixagevimab/cilgavimab), for the 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 (eg, severe allergic reaction) to a COVID-19 vaccine(s) and/or COVID-19 vaccine component(s).

- Evusheld is not authorized for use 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.

- 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.

- Evusheld is a combination of two long-acting monoclonal antibodies and is the only antibody therapy authorized in the U.S. for COVID-19 pre-exposure prophylaxis and the only COVID-19 antibody delivered as an intramuscular (IM) dose.
    - Evusheld neutralizes all previous SARs-CoV-2 variants to date. Testing is being conducted to establish its efficacy against the new Omicron variant.

- The EUA was approved based on data from PROVENT, a double-blind, placebo-controlled study for the pre-exposure prophylaxis of COVID-19 in adults ≥18 years of age. A total of 5,172 subjects who were SARS-CoV-2 negative and unvaccinated were randomized to Edusheld or placebo as a one-time dose.
    - There were 0.2% (8/3,441) of Evusheld-treated patients who experienced symptomatic COVID-19 vs. 1.0% (17/1,731) of placebo-treated patients (Relative risk reduction: 77%; 95% CI: 46, 90; $p < 0.001$). At the time of analysis, the median follow-up time post-administration was 83 days (range 3 to 166 days). There were no cases of severe/critical COVID-19 in the Edusheld arm vs. one case in the placebo arm.
    - In a post-hoc updated efficacy and safety analysis, the median follow-up was 6.5 months. The relative risk reduction of SARS-CoV-2 positive symptomatic illness was 83% (95% CI: 66, 91) with 11/3,441 (0.3%) events in the Evusheld arm vs. 31/1,731 (1.8%) events in the placebo arm. There were no cases of severe/critical COVID-19 in the Edusheld arm vs. 5 cases in the placebo arm.

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- Warnings and precautions for Edusheld include hypersensitivity including anaphylaxis, clinically significant bleeding disorders, and cardiovascular events.

- The most common adverse reactions (all grades, incidence ≥ 3%) with Edusheld use were headache, fatigue, and cough.

- The recommended dose of Edusheld in adults and pediatric patients (12 years of age and older weighing at least 40 kg) is 150 mg of tixagevimab and 150 mg of cilgavimab administered as two separate consecutive IM injections.

    — In individuals who have received a COVID-19 vaccine, Evusheld should be administered at least two weeks after vaccination.
    — While SARS-CoV-2 remains in circulation, individuals who qualify for Evusheld, per the conditions of the EUA, can be redosed every 6 months.

- AstraZeneca plans to launch Edusheld in the coming weeks. Edusheld will be available as separate single-dose vials containing tixagevimab 150 mg/1.5 mL (100 mg/mL) and cilgavimab 150 mg/1.5 mL (100 mg/mL).

- AstraZeneca plans to supply 700,000 doses to the U.S. government. The U.S. government plans to distribute these doses to states and territories at no cost.