Yale NewHaven Health

Tixagevimab/Cilgavimab (Evusheld™)

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Tixagevimab/Cilgavimab (Evusheld™)

- Combination of 2 monoclonal antibodies which bind to different parts of the RBD of the SARS CoV-2 spike protein
- Granted an EUA by the FDA on 12/8/2021 for:
  - **PRE-EXPOSURE** prophylaxis for COVID-19 in adults and children ≥ 12 years & weighing at least 40kg)

    AND
  - Who have moderate to severe immune compromise and may not mount an adequate immune response to COVID-19 vaccination

    OR
  - For whom COVID-19 vaccination is not recommended due to a history of severe adverse reactions (e.g., severe allergic reaction) to a COVID-19 vaccine and/or vaccine components

(Anonymous. Fact Sheet for Healthcare Providers: EUA for Evusheld™ . 12/2021. Available at: https://www.fda.gov/media/154701/download)

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- Evusheld is not authorized for use in the following individuals:
  - For the treatment of COVID-19
  - 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.
  - In individuals who have received a COVID-19 vaccine, Evusheld should be administered at least two weeks after vaccination.

(Anonymous. Fact Sheet for Healthcare Providers: EUA for EvusheldTM . 12/2021. Available at: https://www.fda.gov/media/154701/download)

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- Administered as 2 separate IM injections of each drug (1.5ml for each injection)
  - Gluteal site preferred, one injection in each gluteus
  - Observation for 60 minutes following the injections
- Expected to provide sufficient antibody levels for possibly up to 6 months
- Given at an outpatient visit

Clinical Efficacy
PROVENT

- PROVENT enrolled adults ≥18 years of age who were either ≥60 years of age, had pre-specified co-morbidities or were at increased risk of SARS-CoV-2 infection due to their living situation or occupation. Subjects could not have previously received a COVID-19 vaccine or have known prior or current SARS-CoV-2 infection.
- Results

Table 6 Incidence of Symptomatic COVID-19 in Adults (PROVENT)

	N*	Number of events, n (%)	Relative Risk Reduction, % (95% CI)
EVUSHELD†	3,441	8 (0.2%)	77% (46, 90)
Placebo	1,731	17 (1.0%)	

N = number of subjects in analysis; CI = Confidence Interval
* subjects were censored after receiving the vaccine or being unblinded to consider the vaccine, whichever occurred earlier
† EVUSHELD dose (150 mg tixagevimab and 150 mg cilgavimab)

- Among subjects who received EVUSHELD, there were no severe/critical COVID-19 events (defined as SARS-CoV-2 RT-PCR-positive symptomatic illness characterized by a minimum of either pneumonia [fever, cough, tachypnea or dyspnea, and lung infiltrates] or hypoxemia [SpO^2 <90% in room air and/or severe respiratory distress] and a WHO Clinical Progression Scale score of 5 or higher) compared to one event (0.1%) among subjects who received placebo.

(Anonymous. Fact Sheet for Healthcare Providers: EUA for Evusheld™ . 12/2021. Available at: https://www.fda.gov/media/154701/download)

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Adverse Effects

- Most common adverse events (> 3%) were
  - Headache
  - Fatigue
  - Cough
- Although Evusheld is a monoclonal antibody therapy, hypersensitivity reactions requiring treatment following COVID-19 monoclonal administration have been uncommon.

(Anonymous. Fact Sheet for Healthcare Providers: EUA for EvusheldTM . 12/2021. Available at: https://www.fda.gov/media/154701/download)

Tixagevimab/Cilgavimab (Evusheld™) Additional Considerations

- Evusheld has only been studied in clinical trials as a 1-time combination therapy; therefore, no safety or efficacy data exist for repeat dosing.
- The median follow-up time during the PROVENT trial was 83 days; therefore, the long-term duration of protection is not well defined.
- Evusheld is authorized for use as pre-exposure prophylaxis for a population that was not well represented in the PROVENT trial (i.e., a very small proportion of the participants in the trial were immunocompromised).
- There are no data on the effectiveness of Evusheld preventing infection from the Omicron variant.

(NIH. Statement on Evusheld for PReP. January 5, 2022
Available at: http://dept.ynhh.org/pharmacy/_layouts/15/start.aspx#/default.aspx

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