Statement on Use of Monoclonal Antibody for Pre-Exposure Prophylaxis

(Updated September 22, 2022)

Tixagevimab and cilgavimab (Evusheld, AZD7442) received U.S. FDA emergency use authorization (EUA) for COVID-19 pre-exposure prophylaxis in adults and children age 12 and older and who weigh at least 40 kg and who have moderate to severe immunocompromise, including solid organ transplant patients, and those who have medical contraindication to vaccine[1]

The combination of tixagevimab and cilgavimab is the only monoclonal antibody product authorized for use as pre-exposure prophylaxis. The PROVENT trial, conducted among unvaccinated high-risk patients, showed a 77% reduction of infection in the AZD7442 group when compared to placebo up to 183 days. While data suggests that tixagevimab and cilgavimab may be less active against certain circulating SARS-CoV-2 Omicron variants[2], it is still recommended for pre-exposure prophylaxis of immunosuppressed patients, including solid organ transplant recipients.

The recommended dose is 300 mg tixagevimab and 300 mg cilgavimab. With the continued evolution and circulation of newer SARS-CoV-2 variants, the US FDA recommends repeat dosing of tixagevimab (300 mg) and cilgavimab (300 mg) every 6 months. Pharmacokinetic modeling suggests that activity is retained for 6 months at drug concentrations achieved following a dose of 300 mg of tixagevimab and 300 mg of cilgavimab.

Since it was authorized for clinical use, real-world data have emerged on the use of tixagevimab and cilgavimab in solid organ transplant recipients. Among vaccinated solid organ transplant recipients, the rate of breakthrough COVID-19 during the BA.1 and BA.2 wave was lower in the group that received tixagevimab and cilgavimab when compared to those who did not receive pre-exposure prophylaxis[3]. Overall, it was considered safe and the rate of adverse events due to tixagevimab and cilgavimab were uncommon (4%) and mild. One patient (0.5%) developed a mild heart failure exacerbation, and another (0.5%) developed atrial fibrillation requiring cardioversion.

Because breakthrough COVID-19 has been observed among solid organ transplant patients who had received pre-exposure tixagevimab-cilgavimab prophylaxis[4], it is important for patients

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[1] https://www.fda.gov/drugs/drug-safety-and-availability/fda-authorizes-revisions-evusheld-dosing (accessed 9/15/2022)

[2] Takashita et al., NEJM, 2022 Aug 4: https://www.nejm.org/doi/full/10.1056/NEJMc2207519

[3] Al Jurdi A, Morena L, Cote M, Bethea E, Azzi J, Riella LV. Tixagevimab/cilgavimab pre-exposure prophylaxis is associated with lower breakthrough infection risk in vaccinated solid organ transplant recipients during the omicron wave. Am J Transplant. 2022 Jun 21. doi: 10.1111/ajt.17128. Epub ahead of print. PMID: 35727916.

[4] Eloy E Ordaya, Elena Beam, Joseph D Yao, Raymund R Razonable, Paschalis Vergidis, Characterization of Early-Onset Severe Acute Respiratory Syndrome Coronavirus 2 Infection in Immunocompromised Patients Who Received Tixagevimab-Cilgavimab Prophylaxis, *Open Forum Infectious Diseases*, Volume 9, Issue 7, July 2022, ofac283, https://doi.org/10.1093/ofid/ofac283

to continue public health measures to reduce the risk of SARS-CoV-2 exposure, such as masking, social distancing and avoidance of large indoor social gatherings in communities with high level of circulating virus.

Tixagevimab and cilgavimab is NOT authorized for post-exposure prophylaxis and for treatment of COVID-19.

The following provides a framework to help transplant centers plan for the allocation and administration of pre-exposure monoclonal antibody prophylaxis to solid organ transplant patients:

- **Monoclonal antibody for pre-exposure prophylaxis should be offered to solid organ transplant recipients.**
  - The only authorized product, under US FDA EUA, for pre-exposure prophylaxis is tixagevimab and cilgavimab combination.
  - The dose is 300 mg tixagevimab and 300 mg cilgavimab, repeated every 6 months.
  - Patients should be provided education about drug and the potential benefits and adverse effects of this investigational monoclonal antibody. Patients should provide consent prior to the administration of this investigational monoclonal antibody.
  - Patients should not active COVID-19 at the time of administration.
- **Monoclonal antibody prophylaxis should NOT be a substitute for vaccination or for primary prevention strategies, including masking, social distancing, and avoidance of large indoor social gatherings.**
  - Vaccination of close contacts, including household members, continues to be an important
    measure to protect transplant recipients from COVID-19.

The COVID-19 Task Force will continue to monitor the evolution of SARS-CoV-2 and will update this document, as new information is available.