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COVID-19 UPDATE

An EUA for Pemivibart *(Pemgarda)* for Pre-Exposure Prophylaxis

The FDA has issued an Emergency Use Authorization (EUA) for the long-acting investigational IV monoclonal antibody pemivibart (*Pemgarda* – Invivyd) for pre-exposure prophylaxis of COVID-19 in persons ≥12 years old (weight ≥40 kg) who have moderate to severe immune compromise and are unlikely to respond adequately to COVID-19 vaccination (see Table 1).[1] *Pemgarda* is the only drug that is currently authorized in the US for pre-exposure prophylaxis of COVID-19. Tixagevimab/cilgavimab *(Evusheld)* was previously available under an EUA for this indication, but it lacks activity against currently circulating SARS-CoV-2 variants.[2]

THE NEW PRODUCT — Pemivibart is a human IgG1 monoclonal antibody derived from adintrevimab, an investigational antibody that was effective against the Delta variant of SARS-CoV-2, but not against circulating Omicron variants.[3] Unlike adintrevimab, pemivibart has activity against the currently dominant JN.1 Omicron lineage of SARS-CoV-2.[4] Pemivibart is catabolized slowly (median half-life 44.8 days).[5]

CLINICAL STUDIES — No clinical efficacy data were required for authorization of pemivibart. Issuance of the EUA was based on the results of an unpublished immunobridging trial (CANOPY Cohort A; summarized in the FDA Fact Sheet) in 306 adults with moderate to severe immune compromise. Titer levels of anti-SARS-CoV-2 JN.1 neutralizing antibodies 28 days after administration of one dose of pemivibart were compared to extrapolated titer levels of anti-SARS-CoV-2 B.1.617.2 (Delta) neutralizing antibodies 28 days after administration of a single adintrevimab dose in historical controls.

Results from the trial were mixed; antibody levels with pemivibart met the prespecified criteria for immunobridging when an authentic virus neutralization assay was used, but not when a pseudotyped virus-like particle neutralization assay was used. A supplementary analysis found the immunogenicity of pemivibart against the JN.1 variant to be consistent with the immunogenicity of other antibodies against SARS-CoV-2 variants that they successfully targeted.[5]

Table 1. Some Immunocompromising Conditions[1]

- Moderate or severe primary immunodeficiency
- Advanced or untreated HIV infection
- Active treatment for a solid-tumor or hematologic malignancy
- Hematologic malignancy associated with poor vaccine response (e.g., acute leukemia, chronic lymphocytic leukemia, non-Hodgkin lymphoma, multiple myeloma)
- Use of immunosuppressive therapy after a solid-organ or islet transplant
- Receipt of CAR T-cell therapy or hematopoietic stem cell transplant within previous 2 years
- Active treatment with other immunosuppressive or immunomodulatory drugs, such as high-dose corticosteroids (≥20 mg/day of prednisone or equivalent for ≥2 weeks) and tumor necrosis factor (TNF) inhibitors

1. FDA. Fact sheet for healthcare providers: Emergency Use Authorization for Pemgarda (pemivibart). March 2024. Available at: https://bit.ly/3Q3K5AL. Accessed April 25, 2024.

ADVERSE EFFECTS — A hypersensitivity or infusion-related reaction occurred in 9% of patients in CANOPY Cohort A. Anaphylaxis occurred in 0.6% of 623 patients who received pemivibart in clinical trials. Pemivibart contains polysorbate 80, which is similar in structure to polyethylene glycol and has been associated with hypersensitivity reactions to COVID-19 vaccines; an immunology consult should be considered before use in patients who had a severe hypersensitivity reaction to a COVID-19 vaccine.

Influenza-like illness, fatigue, headache, and nausea have also occurred with use of pemivibart.[5]

DOSAGE AND ADMINISTRATION — The recommended dosage of *Pemgarda* is 4500 mg infused intravenously over at least 60 minutes. Patients should be monitored during and for at least 2 hours after the infusion. Additional doses can be given every 3 months. Pemivibart should not be used for post-exposure prophylaxis or treatment of COVID-19, within 2 weeks after administration of a COVID-19 vaccine, or as a substitute for vaccination.[5] ■

1. FDA News Release. FDA roundup: March 22, 2024. Available at: https://bit.ly/3xEwjhA. Accessed April 25, 2024.
2. COVID-19 update: Evusheld unlikely to neutralize XBB.1.5 omicron variant. Med Lett Drugs Ther 2023; 65:e25.
3. MG Ison et al. Prevention of COVID-19 following a single intramuscular administration of adintrevimab: results from a phase 2/3 randomized, double-blind, placebo-controlled trial (EVADE). Open Forum Infect Dis 2023; 10:ofad314.
4. CDC. COVID data tracker. Variant proportions. April 13, 2024. Available at: https://bit.ly/3Ka3HhH. Accessed April 25, 2024.
5. FDA. Fact sheet for healthcare providers: Emergency Use Authorization of Pemgarda (pemivibart). March 2024. Available at: https://bit.ly/3Q3K5AL. Accessed April 25, 2024.