Frequently Asked Questions on the Emergency Use Authorization for Pemgarda (pemivibart) for Pre-exposure Prophylaxis (PrEP) of COVID-19

Q. What is an Emergency Use Authorization (EUA)?
A. Under section 564 of the Federal Food, Drug & Cosmetic Act, after a declaration by the HHS Secretary based on one of four types of determinations, FDA may authorize an unapproved product or unapproved uses of an approved product for emergency use. In issuing an EUA, FDA must determine, among other things, that based on the totality of scientific evidence available to the Agency, including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing a serious or life-threatening disease or condition caused by a chemical, biological, radiological, or nuclear agent; that the known and potential benefits of the product, when used to treat, diagnose or prevent such disease or condition, outweigh the known and potential risks for the product; and that there are no adequate, approved, and available alternatives. Emergency use authorization is NOT the same as FDA approval or licensure.

Q. What does this EUA authorize? What are the limitations of authorized use?
A. The EUA authorizes Invivyd's Pemgarda (pemivibart) for the pre-exposure prophylaxis of COVID-19 in adults and adolescents (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** are unlikely to mount an adequate immune response to COVID-19 vaccination

Limitations of Authorized Use

- Pemgarda is not authorized for use:
  - 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 Pemgarda 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 recently received a COVID-19 vaccine, Pemgarda should be administered at least two weeks after vaccination.

Q. What is the initial dose of Pemgarda (pemivibart)?
A. The authorized Pemgarda initial dose is 4500 mg administered as a single intravenous infusion over a minimum of 60 minutes.

Q. Is repeat dosing of Pemgarda needed after the initial dose for ongoing protection?
A. Yes. If ongoing protection is needed, a repeat dose of 4500 mg of Pemgarda should be administered every 3 months when consistent with the terms and conditions of the authorization.

Q. Is Pemgarda a monoclonal antibody? What is a monoclonal antibody?
A. Yes, Pemgarda is a monoclonal antibody. Monoclonal antibodies are laboratory-produced molecules engineered to serve as substitute antibodies that can restore, enhance, or mimic the immune system's attack on pathogens. Pemgarda is designed to block viral attachment and entry into human cells, thus neutralizing the virus.

Q. What are some medical conditions or treatments that may lead to an inadequate immune response to the COVID-19 vaccination?
A. Medical conditions or treatments that may result in moderate to severe immunocompromise and an inadequate immune response to COVID-19 vaccination include:

- Active treatment for solid tumor and hematologic malignancies
- Hematologic malignancies associated with poor responses to COVID-19 vaccines regardless of current treatment status (e.g., chronic lymphocytic leukemia, non-Hodgkin lymphoma, multiple myeloma, acute leukemia)
- Receipt of solid-organ transplant or an islet 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., common variable immunodeficiency disease, severe combined immunodeficiency, DiGeorge syndrome, Wiskott-Aldrich syndrome)
- Advanced or untreated HIV infection (people with HIV and CD4 cell counts <200/mm^3, 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, and biologic agents that are immunosuppressive or immunomodulatory (e.g., B-cell depleting agents)

Q. Are people who have received Pemgarda eligible to receive COVID-19 treatments if they develop COVID-19?
A. Yes. There are several treatments – including Paxlovid, Veklury (remdesivir), and Lagevrio (molnupiravir) – that are expected to retain activity against currently circulating variants, and that are authorized or approved to treat certain patients with mild-to-moderate COVID-19 who are at high risk for progression to severe disease, including hospitalization or death. Health care providers should assess whether these treatments are right for their patients in the event the patient develops COVID-19.

FDA is closely monitoring the variants circulating in the United States that may impact the use of the available COVID-19 therapeutics, including Pemgarda. The Agency will provide further updates as new information becomes available.

Q. Can people who have had a severe allergic reaction to a COVID-19 vaccine receive Pemgarda?
A. If the individual being considered for Pemgarda meets the terms and conditions of the authorization, the individual can receive the drug; however, clinicians should consider consulting an allergist-immunologist prior to administering Pemgarda to individuals with a history of a severe allergic reaction (e.g., anaphylaxis) to a COVID-19 vaccine. Pemgarda contains polysorbate 80, which is in some COVID-19 vaccines and is structurally similar to polyethylene glycol (PEG), an ingredient in other COVID-19 vaccines.

Administration of Pemgarda should be done under the supervision of a healthcare provider with appropriate medical support to manage severe hypersensitivity reactions. Everyone who receives Pemgarda should be clinically monitored during the infusion and for at least two hours after completion of the infusion to monitor for hypersensitivity reactions. If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur during administration of Pemgarda, the healthcare provider should immediately discontinue administration and initiate appropriate medications and/or supportive care.

Q. Is Pemgarda approved by the FDA to prevent or treat COVID-19?
A. No. Pemgarda is not FDA-approved to prevent or treat any diseases or conditions, including COVID-19. Pemgarda is an investigational drug.

Q. How can Pemgarda be obtained for use under the EUA?
A. For questions on how to obtain Pemgarda, please go to Invivyd's website, www.PEMGARDA.com.

Q. Who may prescribe Pemgarda under the EUA?
A. Pemgarda may only be prescribed for an individual patient by physicians, advanced practice registered nurses, and physician assistants that are licensed or authorized under State law to prescribe drugs.

Q. When should Pemgarda be administered to a patient?
A. Patients should talk to their health care provider to determine whether, based on their individual circumstances, they are eligible to receive Pemgarda, and when it should be administered.

More information about administration is available in the Fact Sheet for Health Care Providers.

Q. Are there potential side effects of Pemgarda?
A. Possible side effects of Pemgarda include hypersensitivity reactions (including anaphylaxis), infusion-related reactions, fatigue, nausea, and headache.

Anaphylaxis, which can be life-threatening, was reported with Pemgarda in 4 of 623 (0.6%) of participants in a clinical trial. Other hypersensitivity reactions and infusion-related reactions were also reported. Pemgarda should only be administered in settings in which healthcare providers have immediate access to medications to treat anaphylaxis and the ability to activate the emergency medical system (EMS), as necessary. Individuals receiving Pemgarda should be clinically monitored during the 60-minute infusion and for at least two hours after completion of the infusion. The use of Pemgarda should be permanently discontinued in individuals who experience signs or symptoms of anaphylaxis or any severe systemic reaction. Clinicians should consider consulting an allergist-immunologist prior to administering Pemgarda to individuals with a history of a severe allergic reaction to a COVID-19 vaccine.

These are not all the possible side effects of Pemgarda. Not a lot of people have been given Pemgarda. Serious and unexpected side effects may happen. Pemgarda is still being studied so it is possible that all of the risks are not known at this time.

Q. Are there reporting requirements for health care facilities and providers as part of the EUA?
A. Yes. As part of the EUA, FDA requires health care providers who prescribe Pemgarda to report all serious adverse events and medication errors considered to be potentially related to Pemgarda through FDA's MedWatch Adverse Event Reporting program. Providers can complete and submit the report online; or download and complete the form, then submit it via fax at 1-800-FDA-0178. This requirement is outlined in the EUA's health care provider Fact Sheet. FDA MedWatch forms should also be provided to Invivyd.

Q. Do patient outcomes need to be reported under the EUA?
A. No, reporting of patient outcomes is not required under the EUA. However, reporting of all medication errors and serious adverse events considered to be potentially related to Pemgarda occurring during treatment is required.

Q. FDA has issued a number of EUAs including for therapeutics. If state laws impose different or additional requirements on the medical product covered by an EUA, are those state laws preempted?
A. As stated in FDA's Emergency Use Authorization of Medical Products and Related Authorities Guidance, "FDA believes that the terms and conditions of an EUA issued under section 564 preempt state or local law, both legislative requirements and common-law duties, that impose different or additional requirements on the medical product for which the EUA was issued in the context of the emergency declared under section 564." The guidance explains the basis for FDA's views on this subject.

Q. Can health care providers share the patient/caregiver Fact Sheet electronically?
A. The letter of authorization for Pemgarda, requires that Fact Sheets be made available to health care providers and to patients/caregivers "through appropriate means." Electronic delivery of the patient/caregiver Fact Sheet is an appropriate means. For example, when the patient requests the Fact Sheet electronically, it can be delivered as a PDF prior to medication administration. Health care providers should confirm receipt of the Fact Sheet with the patient.

Q. Can I receive a COVID-19 vaccine if I received Pemgarda?
A. Receiving Pemgarda does not prevent you from being able to receive a COVID-19 vaccine. Patients and health care providers should refer to recommendations of the Advisory Committee on Immunization Practices regarding vaccination.

Q. Can I receive Pemgarda if I recently received a COVID-19 vaccine?
A. Pemgarda may reduce your body's immune response to a COVID-19 vaccine. If you receive a COVID-19 vaccine, you should wait to receive Pemgarda until at least two weeks after your COVID-19 vaccination.

Q. What were the data that support authorization of Pemgarda?
A. The primary data supporting this EUA for Pemgarda are from CANOPY, an ongoing clinical trial evaluating PEMGARDA for the pre-exposure prophylaxis of COVID-19 in adults ≥18 years of age in two cohorts:

- Cohort A: a single-arm, open-label trial in adults who have moderate-to-severe immune compromise.
- Cohort B: a placebo-controlled, randomized trial in adults who do not have moderate-to-severe immune compromise.

A total of 623 participants, 306 in Cohort A and 317 in Cohort B, received at least one dose of Pemgarda 4500 mg in the trial. In Cohort B, 162 participants received at least one dose of placebo. In Cohort A, 296 participants received a second dose of Pemgarda 4500 mg at Month 3. In Cohort B, a total of 450 blinded participants received a second dose of either Pemgarda 4500 mg or placebo at Month 3.

To support this EUA, an immunobridging approach was used to determine if Pemgarda may be effective for pre-exposure prophylaxis of COVID-19. Immunobridging is based on the serum neutralization titer-efficacy relationships identified with other neutralizing human monoclonal antibodies against SARS-CoV-2. This includes adintrevimab, the parent mAb of Pemgarda, and certain other mAbs that were previously authorized for the prevention of COVID-19. To support immunobridging, serum neutralization titer was utilized to compare Pemgarda to these mAbs. The Pemgarda data used to support immunobridging came from Cohort A of the CANOPY trial.

Based on the totality of scientific evidence available, it is reasonable to believe that Pemgarda may be effective for pre-exposure prophylaxis of COVID-19 in the authorized population. The calculated pemivibart serum neutralizing antibody titers were consistent with the titer levels associated with efficacy in prior clinical trials of adintrevimab and certain other monoclonal antibody products.

There are limitations of the data supporting the benefits of Pemgarda. Evidence of clinical efficacy with other neutralizing human monoclonal antibodies against SARS-CoV-2 was based on different populations and SARS-CoV-2 variants that are no longer circulating. Additionally, the variability associated with cell culture-based EC_{50} value determinations, along with limitations related to pharmacokinetic data and efficacy estimates for the mAbs in prior clinical trials, impact the ability to precisely estimate protective titer ranges.

Details on the clinical trial results can be found in Section 14 of the authorized Fact Sheet for Health Care Providers.