PEMGARDA (Pemivibart) injection (VYD222)
VA Frequently Asked Questions (FAQ)
UPDATED June 2025

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

Background

The COVID-19 pandemic caused by the SARS-CoV-2 virus has resulted in significant morbidity and mortality, and no therapies are currently FDA approved to prevent infections due the virus. Pemivibart (PEM) is a monoclonal antibody developed by Invivyd, Inc., developed as a COVID-19 pre-exposure prophylaxis (PrEP) option, and was granted an FDA Emergency Use Authorization (EUA) on 3/22/24 for use as PrEP in those unlikely to mount an adequate response to COVID-19 vaccine due to moderate to severe immunocompromise. This FAQ is designed to serve as a resource for VHA healthcare personnel on the use of PEM.

What's new in the June 2025 update? Updated information on the activity of PEM against recently circulating COVID-19 variants, showing relative activity compared with against the JN.1 variant, exploratory clinical data from the CANOPY trial, and updated information regarding the immunobridging analysis used to determine potential effectiveness. Links to most up-to-date PEM activity and circulating strains of SARS-CoV-2 are also included for providers to reference.

PEMGARDA EUA SUMMARY

- PEM is authorized for PrEP against COVID-19 in persons with moderate-to-severe immune compromise who may not mount an adequate response to vaccine as an intravenous infusion and may be repeated every 3 months. The FDA determined PEM "may be effective" through an immunobridging analysis using titers from an older mAbs compared to titers of PEM in CANOPY. Evaluating the risk vs. benefit requires an understanding of this analysis and its limitations.

- **Regarding risk**:
  - PEM has a **black box warning** for anaphylaxis, reported in 0.6% of subjects in CANOPY and was life-threatening in 2 of the 4 cases (1.3% of Cohort A, which were immunocompromised).
  - Systemic infusion-reactions/hypersensitivity reactions occurred in 9% of Cohort A and led to discontinuation in 2%.
  - Local infusion site reactions occurred in 2% and infiltration, extravasation, or vein rupture in 5% of Cohort A.
  - Other common adverse events in at least 2% included upper respiratory tract infection, viral infection, influenza-like illness, fatigue, headache, and nausea, although causality was not assessed.

- **Regarding efficacy:**
  - **The primary endpoint in the CANOPY trial was immunobridging by comparing the ratio of geometric mean titers (GMTs) of PEM (day 28 concentration divided by the EC_{50} of JN.1) to geometric mean titers of another mAb, adintrevimab (ADI) against the Delta variant of COVID-19.).**
  - Immunobridging has been used for new vaccines if there is a known antibody titer associated with clinical protection but has not previously been used for COVID-19 mAbs and the FDA acknowledged many limitations to this approach. FDA stated Immunobridging to support PEM EUA would be met if in the ratio of geometric mean titers, the lower limit of the 90% confidence interval (CI) was greater than 0.8 compared with ADI.
  - In EVADE, ADI decreased symptomatic COVID-19 in high-risk, non-immunocompromised, unvaccinated persons during the Delta wave but was underpowered to show a difference in hospitalization or death as the Omicron variant was no longer susceptible to ADI.
  - Using pseudotyped lentivirus GMTs, the ratio for PEM vs. ADI was 0.7, which did not meet the endpoint assigned by the FDA, however, the FDA also looked at GMTs for PEM against a range of GMTs from other Mabs for COVID-19 and concluded that PEM ***may be effective*** despite not meeting the primary efficacy endpoint.
  - Of note, updated in vitro information of PEM against newer variants was included in the EUA HCP fact sheet, as well as a new way of displaying relative activity as a fold-change from the JN.1 variant.
  - Exploratory clinical data from the CANOPY trial is available and provides some support that PEM may reduce the incidence of symptomatic COVID-19 in patients exposed to variants that have similar susceptibility to JN.1
    - However, PEM is unlikely to be effective in variants with EC_{50} values many-fold greater than the JN.1 lineage variant. Providers can refer to TABLE 2 in PEMGARDA - Fact Sheet for Healthcare Providers for information on EC_{50} values for different SARS-CoV-2 variants
    - Providers may refer to https://covid.cdc.gov/covid-data-tracker/#variant-proportions for up-to-date information on circulating SARS-CoV-2 variants in the United States

- **SUMMARY: The FDA stated that based on the totality of available scientific evidence it is reasonable to believe the product MAY be effective s and it is reasonable to believe that known and potential benefits of the product outweigh the known and potential risks until such time as when 90% of circulating strains have reduced susceptibility to PEM.**

PEMGARDA EUA Indication and Requirements

- **<u>The FDA EUA has authorized PEM ONLY if specific criteria are met</u>**. VHA Providers MUST follow the FDA's EUA when prescribing PEM and patient requests must be added to the EUA COVID-19 SharePoint
- The FDA EUA for PEM authorizes it for pre-exposure prophylaxis of 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 **<u>AND</u>**
        - 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, including, but not limited to:
            - Active treatment for solid tumor and hematologic malignancy
            - 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 (withing 2 years of transplant or taking current immunosuppressive therapy)
            - Moderate to severe primary immunodeficiency (e.g., common variable immunodeficiency disease, severe combined immunodeficiency, DiGeorge syndrome, Wiskott-Aldrich syndrome)
            - Advanced or untreated HIV (those with CD4+ cell < 200/mm^3, history of AIDS-defining illness without immune reconstitution or clinical manifestations of symptomatic HIV)
            - Active treatment with high-dose corticosteroids (i.e., ≥ 20mg/day prednisone or equivalent 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.)

- **Limitations of use**
    - PEMGARDA is **<u>NOT</u>** FDA approved for any use and is not authorized for use:
        - For treatment of COVID-19 **<u>OR</u>**
        - For post-exposure prophylaxis of COVID-19 in individuals 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 with moderate to severe immune compromise who may derive benefit from vaccination, should receive COVID-19 vaccine as recommended.
    - PEMGARDA should not be for at least two weeks after COVID-19 vaccination.
    - PEM is authorized for use only when the combined national frequency of variants with substantially reduced susceptibility to PEM is ≤ 90% based on available information including variant susceptibility to PEM and national variant frequencies. PBM will provide updates when this threshold is reached.
    - PEM must be administered in setting where healthcare providers have immediate access to medications to treat anaphylaxis and the ability to activate the emergency medical system, as necessary.
    - **Use of PEM covered by this EUA must be consistent with and may not exceed, the terms of the Authorization, including the scope and conditions.**

PEMGARDA: Detailed Safety and Adverse Events

- Safety of PEM is based on data from the ongoing Phase 3 trial, CANOPY, of PEM as PrEP in adults as well as Phase 1 data. In CANOPY 623 individuals received an intravenous infusion of PEM 4500 mg, repeated 90 days later. Patients with a history of COVID-19 or vaccine within 120 days before randomization or with a positive SARS-CoV-2 antigen or PCR at time of screening are excluded. Two cohorts of patients are enrolled:
    - **Cohort A is a single-arm, open-label group of patients with moderate to severe immune compromise** (n=306)
        - 296 participants received a second dose of PEM 3 months after the initial dose.
        - **This is the population authorized under the EUA.**
    - Cohort B is a randomized, placebo-controlled trial in adults who do NOT have moderate to severe immune compromise (PEM n=317 and placebo n=162)
        - 450 participants received a second dose of PEM or placebo 3 months after the initial dose.

Second dose safety is only based on Cohort A as the second dose of Cohort B was not unblinded at the time of authorization

CONTRAINDICATIONS

- PEM is contraindicated **in individuals with previous severe hypersensitivity reactions, including anaphylaxis to any component.**
- There is also a black box warning for anaphylaxis.

WARNINGS and PRECAUTIONS

- **Anaphylaxis**
  - **Anaphylaxis occurred in 4 of 623 (0.6%) participants who received PEM in CANOPY, all in cohort A. In all 4 PEM was permanently discontinued**
    - **Infusion-related reactions and hypersensitivity reactions were observed in 9% (27/306) of participants in Cohort A (moderate-to-severe immune compromise)**
  - When prescribing PEM, consider the risk of anaphylaxis against the potential benefit of PEM in preventing COVID-19.
    - Clinically monitor individuals during the 60-minute infusion and for at least 2 hours after completion.
    - If signs and symptoms of a severe allergic reaction occur, immediately discontinue administration, and initiate appropriate supportive care. **Discontinue PEM permanently in those with signs or symptoms of anaphylaxis.**
  - Administration of PEM should be in a location with immediate access to medications to treat anaphylaxis.

- **Hypersensitivity and infusion-related reactions**
  - Hypersensitivity and infusion-related reaction occurred during and up to 24 hours after PEM administration. These reactions may be severe or life-threatening.
    - If signs and symptoms of a severe allergic reaction occur, immediately discontinue administration, and initiate appropriate supportive care. Signs and symptoms of infusion-related or hypersensitivity reactions may include
      - Fever, chills, or diaphoresis
      - Fatigue, myalgia, nausea, or weakness,
      - Headache, dizziness or altered mental status
      - Difficulty breathing, reduced oxygen saturation or bronchospasm
      - Arrhythmia (atrial fibrillation, sinus tachycardia and bradycardia), chest pain/discomfort, hypotension, hypertension or vasovagal reactions
      - Rash including urticaria, angioedema, throat irritation or pruritis
    - For mild infusion-related reactions, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care and monitoring patient for 2 hours after discontinuation or completion.
    - Reactions more than 24 hours after infusion have been reported with other SARS-CoV-2 monoclonal antibodies.

- **Risk of cross-hypersensitivity with COVID-19 vaccines**
  - PEM contains polysorbate 80, which is in some COVID-19 vaccines and is similar to polyethylene glycol (PEG) and ingredient in other COVID-19 vaccines.
  - **For individuals with a history of severe hypersensitivity to a COVID-19 vaccine, consider consultation with an allergist-immunologist prior to PEM.**

- **Risk for COVID-19 due to variants with substantially reduced susceptibility to PEM**
  - Certain viral variants may have substantially reduced susceptibility to PEM. Patients should be informed that PEM may not be effective against those viral variants that exhibit reduced susceptibility, and that they should seek medical attention if signs or symptoms of COVID-19 occur.
  - PEM is authorized for use only when the combined national frequency of variants with substantially reduced susceptibility is ≤ 90% based on available information including variant susceptibility to PEM and national variant frequencies.
  - **Antiviral Resistance**
    - There is a potential risk of treatment failure due to viral variants that are resistant to PEM.
    - Recently, activity of PEM against KP.3 demonstrated a 3-fold increase in EC_{50} versus JN.1
    - Preliminary, non-peer reviewed data indicated KP.3.1.1 had a 33 fold increase in EC_{50} and PEM is unlikely to be effective against this variant, which is rapidly expanding as of late August 2024.

ADVERSE REACTIONS

- **Anaphylaxis was observed in 4 of 623 participants (0.6%), all in Cohort A of CANOPY (immune compromised).**
    - PEM was permanently discontinued, and the reaction completely resolved in 3 subjects. One person had acute resolution with sequelae related to a flare of an underlying condition.
    - **In 2 subjects, anaphylaxis occurred with the first infusion. Both subjects received diphenhydramine as treatment.**
        - Symptoms in one of these subjects included dyspnea, diaphoresis, facial erythema, chest discomfort and tachycardia
        - In the other, flushing, dizziness, tinnitus and wheezing occurred
    - **Two subjects developed anaphylaxis during and after the second infusion and both were reported as life-threatening.**
        - Both subjects experienced pruritis, urticaria, angioedema, dyspnea and erythema or flushing. One also experienced headache, dizziness, and chest pain
        - Pruritis, erythema and urticaria reoccurred within 24 hours of initial onset in one subject
        - Both were treated with diphenhydramine and epinephrine, and one received oral prednisone and metoprolol for a flare of an underlying condition.

- **Systemic infusion-related reactions and hypersensitivity reactions**
    - **First dose reactions:**
        - Systemic infusion-reactions and hypersensitivity reactions occurred in 7% of Cohort A (n=306) and 1% of Cohort B.
        - First dose: Reactions occurring within 24 hours of the first dose were all mild to moderate (with 2 anaphylaxis cases):
            - Hypersensitivity / infusion-reaction
            - Brain fog, fatigue, myalgia, headache, paresthesia
            - Tachycardia, presyncope
            - Nausea, diarrhea
            - Dermatitis
        - Cumulative data from cohort A for first and second dose
            - Cumulatively, 9% of participants (27/306) from cohort A had infusion-related or hypersensitivity reactions.
                - **Severity was mild in 63% (17/27), moderate in 30% (8/27) and life-threatening in 7% (2/27).**
                - Infusion-related / hypersensitivity reactions led to discontinuation of the first or 2nd infusion in 2% (7/306) of cohort A
                - In addition, 2% (5/306) overall from Cohort A had an infusion-related or hypersensitivity reaction WITH BOTH DOSES

    - **Local infusion-site reactions:**
        - Cumulatively, 6/306 subjects in cohort A (2%) had local infusion site reactions. No local reactions were observed in cohort B.
        - Local reactions included bruising, erythema, rash or reaction at the infusion site.
        - In addition, 5% of Cohort A had infusion site infiltration, extravasation, or vein rupture.

- **Other common adverse events in Cohort A:** Treatment-emergent adverse events occurring in ≥ 2% of subjects in Cohort A included upper respiratory tract infection (6%), viral infection (4%), influenza-like illness (3%), fatigue (3%), headache (2%) and nausea (2%).

- **Pregnancy and Lactation:** there are insufficient data to evaluate a drug-related risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. PEM should only be used in pregnancy if the potential benefit outweighs the potential risk to mother and fetus. Human antibodies are known to cross the placental barrier; therefore, PEM has the potential to be transferred to the developing fetus. Similarly, maternal IgG is found in breast milk, but there are no available data with PEM.

- **Healthcare providers and/or the provider's designee are required to report all medication errors and all serious adverse events potentially related to treatment within 7 days of healthcare provider awareness – see FDA fact sheet for more information on what to include**

PEMGARDA in vitro antiviral activity, pharmacokinetics and pharmacodynamics

- **PEM Antiviral activity**
  - In the original authorization the FDA noted that limitations to the analysis, including variability in EC_{50} values with different assays used to calculate neutralization titers, the analysis was only applicable to JN.1 or variants with very similar EC_{50} values determined in the same or similar assays.
  - In the updated EUA Fact Sheet for health care providers, the table of in vitro activity was changed to show fold-changes in mean EC_{50} values from JN.1 in order to more clearly identify variants where activity may be substantially reduced, and unlikely to show clinical effectiveness.
    - Some historical variants have significant increases in fold-change, including BA.2.75 (18 fold) and BN.1 (28 fold)
    - More recent variants (JN.1.11.1, JN.1.13.1, KQ.1, KP.1.1, KP.2 and KP.3) showed 2-4 fold increases in EC_{50}
    - While not available in the Fact Sheet, early pre-print data found that EC_{50} for KP.3.1.1 (the most predominant variant as of August 2024) had a 23 fold increase in EC_{50} compared to JN.1.
  - Continuous evaluation is ongoing on PEM neutralization of variants that emerge and the variant proportions identified through global surveillance.

- **PEM Pharmacokinetics / Pharmacodynamics**:
  - PEMGARDA is a human IgG1 mAb which generates serum neutralizing antibody titers that target the SARS-CoV-2 spike protein receptor binding domain (RBD), inhibiting attachment to human ACE2 on the host cell. Data from other mAbs supports a relationship between neutralizing titers and COVID-19 prophylactic efficacy.
  - A 4500 mg IV dose results in calculated geometric mean titer values against the JN.1 strain ranging from 19,227 on day 1, to 2942 on day 90 (**PEM concentration divided by JN.1 EC_{50})**
  - PEM has a half-life of 45 days and is catabolized in the same method as endogenous IgG.
  - Neither renal nor hepatic impairment is likely to impact pharmacokinetics of PEM.

PEMGARDA DETAILED EFFICACY DATA: FDA concludes it "may be effective"

What efficacy data currently exist for prevention of COVID-19 with PEM?

- **The FDA used an immunobridging approach to support the "may be effective" standard. While they note that actionable clinical data from the CANOPY trial to support authorization would be preferred, there was a need to expedite development of new mAbs for PrEP of immunocompromised patients and allowed an estimate of possible effectiveness based on comparison of PEM to other monoclonal antibodies against prior SARS-CoV-2 variants.**
  - Immunobridging has been used for new vaccines when a known antibody titer is associated with clinical protection but not for other monoclonal antibodies against the SARS-CoV-2 virus
  - The immunobridging primary efficacy endpoint for Cohort A from the CANOPY trial was to estimate protection against symptomatic COVID-19 based on comparison to historical data from a trial of adintrevimab (ADI),
    - EVADE was a Phase 2/3 blinded trial of COVID-19 pre-exposure prophylaxis of ADI vs. placebo in patients at high risk of severe outcomes from COVID-19, but very few were moderately to severely immunocompromised and patients who had received COVID-19 vaccine were excluded.
    - ADI had activity against early variants (including Delta) but reduced activity against Omicron variants and subvariants and was never authorized for use by the FDA.
    - In EVADE, ADI reduced the incidence of symptomatic COVID-19 through 3 months, but hospitalizations and death were rare, so evaluating efficacy against those endpoints was not possible.
    - FDA set an endpoint to accept immunobridging if the ratio of titers of PEM against JN.1 (calculated as day 28 concentration divided by the EC_{50} of the dominant variant JN.1) versus ADI against Delta was ≥ 0.8 based on the lower bounds of the 95% CI. *Of note, day 28 concentrations of ADI were extrapolated from day 90 concentration as 28 day concentrations were not available.*
    - As a supplemental analysis, the FDA also looked at previous studies of 3 prior COVID-19 monoclonal antibodies and compared the relationship between titers and clinical efficacy.
  - Updated in vitro information of PEM against newer variants was included in the EUA HCP fact sheet, as well as a new way of displaying relative activity as a fold-change from the JN.1 variant. Based on that information, KP.3 activity is 3.0 (a 3-fold increase from JN.1) and data from a preprint suggests activity against KP.3.1.1 was markedly reduced. This was the predominant variant forecasted to be circulating as of 8/31/24.

- **Exploratory clinical outcomes from CANOPY for PEM in non-immunocompromised patients:**
  - As described above, **CANOPY** is an ongoing clinical trial of PEM as PrEP in adults. CANOPY has two cohorts. Cohort A is a single-arm, open-label evaluation of PEM in adults or adolescents with significant immune compromise. Cohort B is a double-blind, placebo-controlled evaluation of PEM in non-immunocompromised persons who are at risk for COVID-19 due to regular unmasked face-to-face interactions in indoor settings. For both cohorts, a 4500 mg infusion was given on day 1 and repeated approximately 90 days later.
    - Patients with known or suspected history of COVID-19 or vaccine within 120 days before randomization or with a positive SARS-CoV-2 antigen or PCR at time of screening were excluded. Most of the evaluation focuses on cohort A, given this is the authorized population for PEM.
    - Demographic information from cohort A: 61% were female, 86% White and 12% Black / African American, with a median age of 59 years (31% were ≥ 65 years old).
      - All patients had underlying moderate-to-severe immune compromise
        - 65% were on high-dose steroids or other immunosuppressive medications
        - 13% acute leukemia, chronic lymphocytic leukemia, non-Hodgkin lymphoma or multiple myeloma
        - 12% primary immunodeficiency
        - 11% solid organ transplant recipient
        - 9% advanced HIV infection
        - 7% actively on treatment for solid tumor / hematologic malignancies
    - **Exploratory clinical data from the CANOPY trial provides some support that PEM may reduce the incidence of symptomatic COVID-19 in patients where variants have similar susceptibility to PEM as JN.1.**
      - In Cohort B (non- immunocompromised, PEM vs. placebo) PCR-confirmed, symptomatic COVID-19 through month 3 occurred in 0.3% of patients with PEM (1/317) versus 5% of patients with placebo (8/160)
      - Through month 6 (including redosing), symptomatic COVID-19 occurred in 1.9% of PEM (6/317) vs. 12% of placebo (19/160) patients
      - NO COVID-19 related hospitalizations or deaths occurred in either treatment arm by month 6.
      - **In Cohort A (immunocompromised), 1% had symptomatic COVID-19, COVID-19 hospitalization or all-cause death through month 3, and 4% through month 6 (with redosing).**
        - **No hospitalizations were reported in Cohort A**
        - **Two deaths (one suicide and one unknown)**
        - **No comparator is available in Cohort A**
  - **Based on the totality of available scientific evidence the FDA stated it is <u>reasonable to believe</u> that the product <u>MAY be effective</u> for pre-exposure prophylaxis of COVID-19 caused by SUSCEPTIBLE SARS-Cov-2 VARIANTS. The exploratory clinical results from Cohort B also support the possible effectiveness. There are limitations of the immunobridging data. Evidence of efficacy for other monoclonal antibodies against SARS-CoV-2 was based on different populations and variants that are no longer circulating. Additionally, the variability associated with cell-based EC_{50} value determinations and limitations to pharmacokinetic data estimates for products in prior clinical trials impact the ability to precisely estimate protective titer ranges. The potential benefits of PEM as pre-exposure for COVID-19 caused by variants other than JN.1 may vary based on variant susceptibility and national variant frequencies.**

PEMGARDA Dosing, Administration and Storage

How is PEM supplied, prepared, dosed and administered?

- **PEM is given as a single intravenous (IV) infusion of 4500 mg with repeat doses every 3 months in adults and adolescents (12 years of age or older and weighing at least 40 kg) infused over a minimum of 60 minutes.**
  - **No adjustment is recommended for hepatic or renal dysfunction, in geriatrics, or in pregnant or lactating persons.**
- **Preparation**
  - PEM is supplied as a single dose vial preservative-free vials of 500 mg (4 mL) each.
  - Unopened vials should be stored refrigerated (36 to 46° F) in the original carton and should be allowed to equilibrate for 10 minutes prior to preparation.

- PEM should be prepared and administered by a qualified healthcare worker using aseptic technique. To prepare, 36 mL should be withdrawn from pre-filled bag of normal saline, and 9 vials of PEM (**36 mL**) total added to the remaining 14 mL of 0.9% sodium chloride. Once diluted, it may be stored at room temperature for up to 4 hours.

- **Administration**
  - **PEM should ONLY be administered in settings in which healthcare providers have immediate access to medications to treat a severe hypersensitivity reaction such as anaphylaxis, and the ability to activate the emergency medical system, as necessary.**
  - An inline 0.2-micron filter should be used, and the entire dose administered over a minimum of 60 minutes. The entire contents of the bag should be administered, and the line flushed with 0.9% sodium chloride after complete.
  - Patients should be clinically monitored during and for at least 2 hours after completion of infusion.

Other issues

How do I obtain PEM for a patient at my facility?

- PEM will be commercially distributed through Mckesson (see Pemivibart product page PBM EUA Orders SharePoint for additional details).
- The provider **must document on the PBM SharePoint** when a McKesson order is received, that the patient meets all criteria for PEM, and that the patient or caregiver has been provided the FDA fact sheet for patients, parents and caregivers
- The provider is responsible for reporting all medication errors and all serious adverse events potentially related to treatment within 7 calendar days and respond to FDA request for information about adverse events.

Will the VA be monitoring for adverse events associated with PEM?

- YES – given the limited safety data, vigilance in monitoring for adverse events is critical. Physicians, nurses, pharmacists, and other healthcare providers should be monitoring patients closely for unusual clinical or laboratory events, record them as per local policy and report them to VA ADERS.
  - Note: the provider (or designee) is responsible for reporting all medication errors and all serious adverse events potentially related to treatment within 7 calendar days of the healthcare provider's awareness of the event and respond to FDA request for information about adverse events.
    - ***Healthcare providers must report ALL medication errors and ALL serious adverse events potentially related to PEM through VA ADERS and per local policy*** **Serious adverse events include:**
      - □ **Death**
      - □ **A life-threatening adverse event**
      - □ **Inpatient hospitalization or prolongation of hospitalization**
      - □ **Persistent or significant incapacity or disruption of ability to conduct normal life functions**
      - □ **Congenital abnormality / birth defect**
      - □ **Medical or surgical intervention was required to prevent death, a life-threatening adverse event, hospitalization, disability, or congenital abnormality**
- **All serious events and all medication errors are to be reported to VA ADERS as a MedWatch report (a separate FDA MedWatch report is not required when submitted in VA ADERS)**
- The VHA Center for Medication Safety will also be conducting prospective pharmacovigilance to identify potential adverse events.

References:

1. FDA Fact Sheet for Healthcare Providers for PEMGARDA, updated 8/26/24., Accessed 9/10/24.
2. FDA Fact Sheet for Patients, Parents and Caregivers for PEMGARDA, 8/26/24. Accessed 9/10/24.
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4. Ison M, Weinstein D, Dobryanska M 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 Inf Dis* 2024; https://doi.org/10.1093/ofid/ofad314
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6. Stadler E, Burgess M, Schlub T, et al. Monoclonal antibody levels and protection from COVID-19. *Nature Communications* 2023;14:4545. https://doi.org/10.1038/s41467-023-40204-1

7. Wang Q, Gua Y, Ho J, et al. Pemivibart is less activity against recent SARS-CoV-2 JN.1 sublineages. bioRxiv preprint. Aug 19, 2024. https://doi.org/10.1101/2024.08.12.607496