Background: On December 8, 2021, the U.S. Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for tixagevimab and cilgavimab (Evusheld, AztraZeneca) for use as pre-exposure prophylaxis (prevention) of COVID-19 in certain eligible patients who are not currently infected nor exposed to COVID-19. This drug is not a substitute for vaccination, and all patients who can receive vaccination should do so. This document contains information about how the drug will be allocated to adults at UCSF Health.

For treatment of COVID-19 infection with monoclonal antibodies, refer to the UCSF Adult Monoclonal Antibody Use Process for Treatment here.

Table of changes:

| 1/7/22 | Updated booster timing consistent with CDC guidelines |
|        | Added definition of maximally vaccinated for newly immunosuppressed patients |
|        | Clarified that patients with very recent transplants can receive Evusheld regardless of whether maximally vaccinated and regardless of spike positivity pre-transplant |
|        | Added information about timing of vaccine post-tixagevimab/cilgavimab infusion |

Definitions:
Eligibility for Monoclonal Antibodies for Pre-Exposure Prophylaxis (PrEP) of COVID-19 via EUA for immunocompromised hosts:

1. Adult patient ≥ 18 years old
2. Weight ≥ 40 kg
3. Meets definition of Immunocompromised host/Not expected to mount an adequate immune response to complete vaccination (see Definitions)
4. Maximally vaccinated (see Definitions)^
5. SARS-CoV-2 Spike antibody (IgG or total) test considered negative (qualitative or quantitative) via one of the accepted labs (see Definitions section), checked 2 or more weeks after receipt of most recent eligible vaccine dose*,#
6. Not currently symptomatic or known to be infected with COVID-19
8. Not allergic to any component of tixagevimab/cilgavimab (Evusheld) injection
9. Has not received COVID-directed mAb therapy within prior 90 days that has predicted activity against current circulating strains

^For patients within 30 days of transplant (SOT or HSCT) or CAR-T cell therapy, tixagevimab/cilgavimab may be administered even if does not yet meet maximal vaccination criteria
*Individuals with detectable but low-level titers may become eligible for future administration if supplies improve
# Eligibility for Monoclonal Antibodies for Pre-Exposure Prophylaxis (PrEP) of COVID-19 via EUA for patients with medical vaccine contraindication:

1. Adult patient ≥ 18 years old
2. Weight ≥ 40 kg
3. Maximal vaccination is medically contraindicated due to history of severe adverse reaction to vaccines
4. Not currently symptomatic or known to be infected with COVID-19
6. Not allergic to any component of tixagevimab/cilgavimab (Evusheld) injection
7. Has not received COVID-directed mAb therapy within prior 90 days that has predicted activity against current circulating strains

## Dosing:

-150 mg tixagevimab and 150 mg cilgavimib administered as two separate IM injections (gluteal)
-May be redosed every 6 months if patient still meets the criteria above

## General guidance for those at risk of bleeding:

**Proceed with caution in these populations**

| Thrombocytopenia with platelets < 30 (Patient to receive platelets the morning of each dose of injection and apply manual pressure to injection site for 10 minutes following injection) |
| Severe bleeding diathesis (Must not have supratherapeutic INR if on warfarin; discuss as needed with patient’s Hematologist or Hematology e-consultant) |

- All lab orders will be placed by the referring clinician.
- If an intervention is recommended, please discuss directly with your patient, and include information in the or “OK to treat” section of the PrEP Therapy Plan
- All: Hold pressure x10 min (sit) post injection and monitor for hematoma formation
- **IM Vaccination in Adults with Therapeutic Anticoagulation Article**

### Platelets

- If no concern for thrombocytopenia, ok to inject drug
- If patient is at risk for thrombocytopenia
  - OK to inject mAb if platelet count >30k checked in the past 30 days

*For patients on chronic immunoglobulin replacement (SCIg or IVIg) for immunodeficiency or those who recently received casirivimab/imdevimab for post-exposure prophylaxis, the spike Ab does not need to be checked since there is a risk of false positive results. For those immediately post-transplant (solid organ or HSCT), spike Ab does not need to be checked.*
Concern that platelet count may be <30K; check CBC the same day pre-IM injection; If plt <30K, transfuse 1 unit of platelets in the Parnassus infusion center (PIC) and inject during or after; confirmatory count not needed. Contact Shagun Arora if this is needed.

**On vitamin K antagonist/coumadin**

- Platelet as above and
- If well controlled INR and no concern for supratherapeutic INR, ok to inject mAb without checking INR.
- If concern for uncontrolled INR, check INR same day as injection
  - If INR <4 ok to inject
  - If INR ≥4, injection will be rescheduled and referred back to referring clinician.

**On direct-acting anticoagulant (DOAC) /low molecular weight heparin (LMWH)**

- Platelet as above and
- If no concern for bleeding, ok to inject mAb OR
  - Advise patient to hold DOAC or LMWH dose for 24 hours before IM injection (ie last dose morning prior to the IM Injection) and resume the same day evening or next day morning.

**Severe hemophilia – most patients are on prophylactic factor replacement**

- Platelet as above and
- Advise patient to self-administer factor replacement on the morning scheduled for IM mAb injection
- Hold pressure x10min post injection and monitor for hematoma formation

**Timing of tixagevimab/cilgavimab (Evusheld) and COVID-19 vaccination**

It is not known whether monoclonal antibodies for COVID-19 prevention interfere with vaccine response, though the theoretical concern has been raised. When possible, patients should receive COVID-19 vaccination at least 2 weeks prior to tixagevimab/cilgavimab administration. The CDC recommends deferring vaccine for 90 days after monoclonal antibody administration for COVID-19 infection and 30 days after administration for post-exposure prophylaxis but has not provided recommendation for pre-exposure prophylaxis. One case report looking at antibody response after bamlanivimab treatment for COVID-19 infection demonstrated serological response comparable to that of patients who did not receive antibody treatment when vaccine was started 20 days after antibody receipt. Tixagevimab/cilgavimab (Evusheld) has a longer half-life than all other monoclonal antibodies and the optimal timing between tixagevimab/cilgavimab and subsequent vaccination is unknown.

Balancing the theoretical risk for interference with vaccine response and importance of continuing with recommended schedules of booster doses, vaccine can be administered starting 30 days after tixagevimab/cilgavimab (Evusheld).

**Allocation:**
Guiding principles

- No patient should be denied access to pre-exposure prophylaxis based on age, disability, religion, race, ethnicity, national origin, immigration status, gender/gender identity, perceived quality of life, or sexual orientation
- To maximize distribution of drug, the medication should not be stockpiled for future use
- Patients eligible for pre-exposure prophylaxis via clinical trials should be offered participation in the trials but should not be compelled to participate in trials for the sole purpose of accessing the drug. Patients who opt not to participate in trials shall be offered pre-exposure prophylaxis via the EUA if eligible.

Process

Among individuals eligible for receipt of the agent by the guidelines above, allocation will occur as outlined in the detailed Tixagevimab/cilgavimab (Evusheld) Allocation Guidance document when drug supply is limited. Patients referred for treatment may not receive treatment right away in the setting of demand outstripping supply.

PrEP Workflow (see screenshots below)
EUVSHELD – how to REFER and ORDER therapy plan

REFERRAL REF802:

1. Open an encounter where orders can be placed.
2. Enter REF802 in the Order Search Bar at the bottom of your screen
3. Review Scheduling instructions
4. Enter comments if needed
5. Sign order.
THERAPY PLAN

1. Open an Orders Only Encounter

2. Click on the DropDown Arrow at the TOP RIGHT of you screen (just to the left of the wrench)

3. Select Therapy Plans
4. Select **Monoclonal Antibodies** on the Left.

5. Select **AMB EVUSHELD** (or enter EVUSHELD into the search field)

6. Complete and Sign therapy plan, Sign encounter.