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:

<table>
<thead>
<tr>
<th>Date</th>
<th>Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/7/22</td>
<td>Updated booster timing consistent with CDC guidelines</td>
</tr>
<tr>
<td></td>
<td>Added definition of maximally vaccinated for newly immunosuppressed patients</td>
</tr>
<tr>
<td></td>
<td>Clarified that patients with very recent transplants can receive Evusheld regardless of whether maximally vaccinated and regardless of spike positivity pre-transplant</td>
</tr>
<tr>
<td></td>
<td>Added information about timing of vaccine post-tixagevimab/cilgavimab infusion</td>
</tr>
<tr>
<td>1/12/22</td>
<td>Removed requirement for spike Ab to be checked before referral</td>
</tr>
<tr>
<td></td>
<td>Added factors to consider when determining which patients to refer for treatment</td>
</tr>
<tr>
<td></td>
<td>Updated plan for inpatient administration</td>
</tr>
<tr>
<td>1/25/22</td>
<td>Updated EUA fact sheet link and added Spanish EUA link</td>
</tr>
<tr>
<td></td>
<td>Clarified that outpatients will be scheduled for visits with authorization pending</td>
</tr>
<tr>
<td></td>
<td>Added Appendix “Clinical considerations for pre-exposure prophylaxis referral prioritization”</td>
</tr>
<tr>
<td>2/22/22</td>
<td>Removed requirement for weight &gt;40 kg for adults (this limit only applies to pediatrics)</td>
</tr>
<tr>
<td></td>
<td>Updated definitions of maximal vaccination to reflect updated CDC guidance</td>
</tr>
<tr>
<td></td>
<td>Updated recommendations about timing of vaccine after mAb administration</td>
</tr>
<tr>
<td>3/16/22</td>
<td>Updated dosing to reflect latest FDA guidance</td>
</tr>
<tr>
<td></td>
<td>Added section on how to order catch-up dosing</td>
</tr>
<tr>
<td>4/3/22</td>
<td>Removed requirement for maximal vaccination; unless there is a medical contraindication, must be seeking to complete vaccination series</td>
</tr>
<tr>
<td></td>
<td>Updated guidance on catch-up dosing to reflect new FDA guidance based on time since prior dose</td>
</tr>
<tr>
<td>4/19/22</td>
<td>Updated CPT code</td>
</tr>
<tr>
<td>6/29/22</td>
<td>Updated language around vaccination recommendation for immunocompromised hosts</td>
</tr>
<tr>
<td></td>
<td>Added section on re-dosing</td>
</tr>
<tr>
<td>8/23/22</td>
<td>Updated information surrounding re-dosing</td>
</tr>
<tr>
<td></td>
<td>Updated information re: therapy plan and REF802</td>
</tr>
<tr>
<td></td>
<td>Removed information re: catch-up dosing</td>
</tr>
<tr>
<td></td>
<td>Removed “Clinical considerations for pre-exposure prophylaxis referral prioritization” appendix</td>
</tr>
</tbody>
</table>
Definitions:

- Active treatment for solid tumor and hematologic malignancies
- Receipt of solid-organ transplant and taking immunosuppressive therapy
- Receipt of CAR T-cell or HSCT (within 2 years of transplantation or taking immunosuppressive therapy)
- Moderate or severe primary immunodeficiency (e.g., DiGeorge, Wiskott-Aldrich syndromes)
- Advanced or untreated HIV infection
- Active treatment with high-dose corticosteroids or other drugs that may suppress your immune response
- Other diagnosed chronic condition with severe level of immunocompromise.

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

1. Adult patient ≥ 18 years old
2. Meets definition of Immunocompromised host/Not expected to mount an adequate immune response to complete vaccination (see Definitions)
3. Strongly recommend that patient be in the process of becoming up-to-date with COVID-19 vaccination, including primary series plus booster shots, as outlined by the CDC
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 (e.g., bebtelovimab) within prior 90 days.

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. Up-to-date vaccination is medically contraindicated due to history of severe adverse reaction to vaccines
3. Not currently symptomatic or known to be infected with COVID-19
5. Not allergic to any component of tixagevimab/cilgavimab (Evusheld) injection
6. Has not received COVID-directed mAb therapy (e.g., bebtelovimab) within prior 90 days.

Dosing:

- 300 mg tixagevimab and 300 mg cilgavimib administered as two separate IM injections (gluteal)
- For patients who received the prior 150 mg dosing of tixagevimab/cilgavimab, a catch-up dose may be administered:
If the patient received their initial dose ≤ 3 months ago, the patient should receive a dose of 150 mg of tixagevimab and 150 mg of cilgavimab.

If the patient received their initial dose > 3 months ago, the patient should receive a dose of 300 mg of tixagevimab and 300 mg of cilgavimab.

**Redosing**

- On 6/29/22 the FDA updated guidance to recommend repeat dosing every 6 months of 300 mg tixagevimab and 300 mg of cilgavimab if ongoing protection is needed.
  - Repeat dosing should be timed from the most recent tixagevimab/cilgavimab dose.
- Recommendations for how to find patients who previously received Evusheld via workbench, and order and schedule repeat dosing at UCSF can be found at this link: https://ucsf.box.com/v/CovidEvusheldReDoseAug2022

**General guidance for those at risk of bleeding:**

<table>
<thead>
<tr>
<th>Proceed with caution in these populations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia with platelets &lt; 30 (Patient to receive platelets the morning of each dose of injection and apply manual pressure to injection site for 10 minutes following injection)</td>
</tr>
<tr>
<td>Severe bleeding diathesis (Must not have supratherapeutic INR if on warfarin; discuss as needed with patient’s Hematologist or Hematology e-consultant)</td>
</tr>
</tbody>
</table>

- 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 OR
  - 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**

Tixagevimab/cilgavimab should be delayed two weeks after latest vaccine dose. However, according to the CDC, COVID-19 vaccination does not need to be delayed after mAb administration.

**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.

**Inpatient PrEP Workflow**

Starting 1/18/22, PrEP may be administered to eligible inpatients meeting criteria.

Primary provider should:
1. Discuss potential risks, benefits, and alternatives with the patient
2. Provide patient/caregiver with EUA fact sheet (English or Spanish)

Outpatient PrEP Workflow for New Starts (see screenshots below)

- **Eligibility**
  - Primary provider/specialty clinic reviews inclusion/exclusion criteria, considers bleeding risk, and determines eligibility

- **Informed Consent**
  - Primary provider/specialty clinic
  - Discuss potential risks, benefits, and alternatives with the patient
  - Provide patient/caregiver with EUA fact sheet (English: https://www.fda.gov/media/154702/download and Spanish: https://www.fda.gov/media/155196/download)

- **Patient Referral**
  - Order and Sign Therapy Plan > Monoclonal Antibody > Evusheld (sign therapy plan first)
  - Order and sign Referral via APeX REF802 order
  - Referring team must obtain auth for CPT code: CPT-M0220 (however pts will be scheduled even with auth pending).
  - If both are not signed, patients cannot be scheduled.
  - Please do not use REF800 order.

- **Scheduling**
  - Injection clinic (mainly at Laurel Heights) will schedule patients in order of receipt of BOTH orders and pending eligibility (ie 6 months from last dose)
  - See Allocation Guidance document
  - Contact Shagun Arora MD for questions
**EUVSHELD – how to ORDER therapy plan and REFER patients for scheduling**

**THERAPY PLAN**

1. Open an encounter where orders can be placed.
2. Click on the Dropdown Arrow at the TOP RIGHT of your screen (just to the left of the wrench).
3. Select Therapy Plans

![Therapy Plans dropdown](image)

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.

**REFERRAL REF802 to refer a patient for scheduling:**

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.
   a. *If the pt previously received Evusheld at UCSF, the date of this last administration will appear in the COMMENTS box.*
5. Sign order.
   a. *Please sign therapy plan before ordering REF802.
   b. REF800 cannot be used for Evusheld.*