Sutter Health Guidance for COVID-19 Antibody Therapy

Version: 1.27.2022

The neutralizing activity of several monoclonal antibody therapy are diminished when used against the Omicron variant. Sotrovimab is the only EUA authorized monoclonal antibody that retains sufficient activity against Omicron. Based on CDPH recommendations, when the prevalence of Omicron is above 80%, only sotrovimab will be used for treatment of mild to moderate disease in patients 12 years and older. Sotrovimab is available IV only and is not authorized for post exposure prophylaxis or for patients less than 12 years of age.

Emergency use of tixagevimab/cilgavimab (Evusheld®) is authorized by the FDA for pre-exposure prophylaxis of COVID-19 in adults and pediatric individuals (12 years of age and older weighing at least 40 kg). Supply and distribution of Evusheld® is limited and may not yet be available at your affiliate.

Given COVID-19 antibody therapy is scare, Sutter Health aim to assure the products are administered in a fair and equitable manner in the most safe and efficient way possible.

The high-risk patient criteria are defined in the healthcare provider EUA fact sheet.

Sotrovimab Fact Sheet for Health Care Providers

Tixagevimab/cilgavimab (Evusheld®) Fact Sheet for Health Care Providers

Sutter Health Guidance (Based on NIH Guidance 12/23/2021):

**Sotrovimab**

- When the Omicron variant represents the majority (e.g., >80%) of infections in a region, it is expected that bamlanivimab plus etesevimab and casirivimab plus imdevimab will not be active for treatment or post-exposure prophylaxis (PEP) of COVID-19.
- In this setting, the only antibody therapy available to treat outpatients with mild to moderate COVID-19 (per CDPH) who are at high risk of clinical progression is sotrovimab given as a single infusion.
- Prioritization recommendations when there is logistical or supply constraints:
  - Prioritize therapy for unvaccinated or incompletely vaccinated individuals and vaccinated individuals who are not expected to mount an adequate immune response
  - Prioritize use in patients with highest risk for clinical progression
    - Medical conditions or other factors that are considered high risk with A level evidence include: age ≥ 65 (AIIa), BMI > 30 (AIIa), diabetes (AIIa), CV disease (including congenital heart disease) or hypertension (AIIa), chronic lung disease (AIIa), immunocompromising condition or on immunosuppressive treatment (AIII), or pregnancy (any gestation age) if approved by OB.

**Tixagevimab/cilgavimab (Evusheld®)**

- Pre-exposure prophylaxis (PREP) can be considered for patients 12 years and older and weighing ≥ 40 kg who do not have COVID-19 infection, who have not been recently exposed to an individual with COVID-19 and meet the following criteria:
  - Moderately to severely compromised and may have an inadequate response to vaccination OR
  - Are not able to be fully vaccinated with available COVID-19 vaccines due to a documented history of severe adverse reactions to a COVID-19 vaccine or any of its components
- **As with any other intramuscular injection, tixagevimab/cilgavimab should be given with caution to individuals with thrombocytopenia or any coagulation disorder.**
  - Proceed with caution in patients with thrombocytopenia with platelets less than 30
  - Severe bleeding diathesis or taking oral anticoagulants (Discuss as needed with patients’ hematologist)
• In the PROVENT trial, there was a higher rate of cardiovascular serious adverse events including myocardial infarction (one fatal SAE) and cardiac failure. A causal relationship has not been established. Risks and benefits should be weighed prior to use in patients at high risk for cardiovascular events.

**Sutter Health Patient Selection Criteria**

Sutter Health has developed guidelines for the use of COVID-19 antibody therapy. A tier system has been created to allow affiliates to provide therapy to patients based on capacity, logistical constraints, and/or the availability of the antibodies. The determination of the tier status is an individual affiliate-based decision.

**Sotrovimab** *(Note: Sotrovimab is not authorized for post-exposure prophylaxis)*

A. Tier 1: Full Emergency Use Authorization Criteria
B. Tier 2 (shown below): Sutter Criteria based on literature review that identified patients who are most likely to benefit from COVID-19 antibody therapy
   o Adult patients with at least one of the following risk factors: BMI ≥ 30, age ≥ 65, CV disease (including hypertension), diabetes, chronic lung disease, immunocompromising condition or active immunosuppressive therapy, or pregnancy (any gestation age) if approved by OB
      i. Treatment of mild to moderate COVID-19 (prioritized based on available resources if necessary)
         • Symptom onset needs to be ≤ 5 days
         • Restricted to outpatient use (including ED and patients under observation status where admission for COVID-19 is not anticipated), L&D triage, hospitalized patients who are not admitted for COVID-19, and approved infusion centers
   o Use is further restricted by the FDA EUA limitations of authorized use
   o **Additional exclusion criteria:** Patients who are hospitalized for COVID-19

*Following administration of COVID-19 antibody therapy for treatment, defer COVID-19 vaccination for 90 days*

**Tixagevimab/cilgavimab (Evusheld®)** *(Note: tixagevimab/cilgavimab is not authorized in unvaccinated individuals for whom COVID-19 vaccination is recommended)*

A. Tier 1: Full Emergency Use Authorization Criteria
B. Tier 2 (shown below): Sutter Criteria based on NIH Guidance that identified patients who are at the highest risk for severe outcomes.
   o Pre-exposure prophylaxis of coronavirus disease 2019 (COVID-19) in adults and pediatric patients with at least one of the following risk factors:
      • Patients who are within 1 year of receiving B-cell depleting therapies (e.g., rituximab, ocrelizumab, ofatumumab, alemtuzumab)
      • Patients receiving Bruton tyrosine kinase inhibitors
      • Chimeric antigen receptor T cell recipients
      • Post-hematopoietic cell transplant recipients who have chronic graft versus host disease or who are taking immunosuppressive medications for another indication
      • Patients with hematologic malignancies who are on active therapy
      • Lung transplant recipients
      • Patients who are within 1 year of receiving a solid-organ transplant (other than lung transplant)
      • Solid-organ transplant recipients with recent treatment for acute rejection with T or B cell depleting agents
      • Patients with severe combined immunodeficiencies
      • Patients with untreated HIV who have a CD4 T lymphocyte cell count <50 cells/mm3
      • Use is further restricted by the FDA EUA limitations of authorized use

C. Tier 3 (For extremely limited resources)
   o Tier 2 and who have at least one additional risk factor for disease including but not limited to BMI ≥ 30, age ≥ 65, CV disease (including hypertension), diabetes, chronic kidney disease, chronic lung disease, sickle cell disease, or pregnancy (any gestation age) if approved by OB.

*For patients who have received a COVID-19 vaccine, Evusheld® should be administered at least 2 weeks after vaccination.*
**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.

**Prescriber Ordering**

**Ordering:**

**Sotrovimab**

- An order panel "COVID-19 SOTROVIMAB ANTIBODY EUA ORDER PANEL" has been developed to aid with accurate ordering and documenting the requirements for use in the inpatient setting.
  - Answer the required order-specific questions before signing the order. Each panel also includes contingent orders for the management of infusion reaction that are selected by default.
- In order to assist with compliance to FDA EUA requirements, providers will be asked to attest that the following tasks were completed and documented in the patient’s medical record:
  - Discussion regarding the EUA status and investigational nature of sotrovimab with patient/caregiver including the risks and benefits of sotrovimab and alternatives if available.
  - Provision of the required FDA Patient Fact Sheet, available via direct hyperlink within the order.
  - A SmartLinks "COVID19SOTROVIMABEU" has been created to support proper documentation in the medical record.

**Tixagevimab/cilgavimab (Evusheld®)**

- An Order Panel "COVID-19 TIXAGEVIMAB/CILGAVIMAB (EVUSHELD) ANTIBODY FOR PREP EUA ORDER PANEL" and Smart Set "COVID-19 MONOCLONAL ANTIBODY SH AMB" have been developed to aid with ordering and documentation requirements for use in the inpatient and ambulatory setting, respectively.
  - Answer the required order-specific questions before signing the order. Each panel also includes contingent orders for the management of infusion reaction.
- In order to assist with compliance to FDA EUA requirements, providers will be asked to attest that the following tasks were completed and documented in the patient’s medical record:
  - Discussion regarding the EUA status and investigational nature of tixagevimab/cilgavimab with patient/caregiver including the risks and benefits of tixagevimab/cilgavimab.
  - Provision of the required FDA Patient Fact Sheet, available via direct hyperlink within the order.
  - A SmartLinks "COVID19TIXAGEVIMABCILGAVIMAB" has been created to support proper documentation in the medical record.
**COVID-19 Monoclonal Antibody and Antiviral Management SH AMB®**

### Documentation
- Consent for Treatment
  - COVID-19 Eucalyptus Antibody ELISA
  - COVID-19 Sarscovis Antibody ELISA
- COVID-19 Monoclonal Antibody & Antiviral Orders

### Orders
A three-tier system has been created to allow affiliates to provide therapy to patients based on capacity, logistical restraints, and the availability of the antibiotics. The determination of the tier status is an individual affiliate-based decision.

Please refer to the Sutter Health Medication Algorithm for ED/Ambulatory care available on the SHEMS and Pharmacy COVID-19 Resources pages for the most up-to-date information on clinical criteria and appropriate use of this agent:
- Pre-Exposure Prophylaxis
- Treatment
- COVID-19 Antibody hypersensitivity Reaction Treatment

### Diagnosis
- At increased risk of exposure to COVID-19 virus (291.88)
- Infection due to 2019-NCov (U07.1)
- Hypersensitivity reaction, initial encounter (784.804)

### Patient Instructions
- Patient Instructions
  - Putting in English version will be automatically translated into Spanish, Traditional Chinese or Russian, if listed as Patient’s Language

- COVID-19 Complete Patient Instructions
Management of infusion reaction orders

**Management of Covid-19 Antibody Infusion Reaction**

**Rescue**

1. **Measure** the patient’s vital signs (heart rate, blood pressure, respiratory rate, oxygen saturation) before and during the infusion.
2. **Administer** acetaminophen 1600 mg (8 tablets) or ibuprofen 400 mg (2 tablets) orally, if needed.
3. **Monitor** the patient for any signs of allergic reaction, such as wheezing, rash, or difficulty breathing.
4. **Notify** the healthcare provider immediately if any of the following occur:
   - Severe allergic reaction (anaphylaxis): Swelling of the face, tongue, or throat; difficulty breathing; hives; or anaphylactic shock.
   - Severe infusion reaction: Severe asthma, difficulty breathing, wheezing, or chest tightness.
   - Mild infusion reaction: Mild discomfort, redness, or itching at the infusion site.

**Pre-Infusion Prophylaxis**

- **Brushfield PEP (200mg l)
  - Dose:** 150 mg/0.5 mL - 150 mg/0.5 mL.
  - **Route:** Intramuscular.
  - **Frequency:** 1-27-2022

**Sotrovimab Fact Sheet for Patients, Parents, and Caregivers**

**Tixagevimab/cilgavimab (Evusheld®) Fact Sheet for Patients, Parents, and Caregivers**

- **Preparation:** 3 vials of tixagevimab/cilgavimab (Evusheld®) must be mixed and administered simultaneously.
- **Dosage:** 800 mg (400 mg tixagevimab and 400 mg cilgavimab) intramuscularly every 90 days.

**Evaluation Prophylaxis**

- **Dose:** 150 mg/0.5 mL - 150 mg/0.5 mL.
- **Route:** Intramuscular.
- **Frequency:** 1-27-2022

**Doxorubicin**

- **Dose:** 40 mg/m².
- **Route:** Intravenous.
- **Frequency:** Every 21 days.

**Patient Education**

- **Identification:** Patients receiving chemotherapy should be identified with a chemotherapy wristband or ID bracelet.
- **Communication:** Patients should be informed about the potential side effects of chemotherapy, such as hair loss, fatigue, and nausea.

**Monitoring**

- **Vital Signs:** Monitor vital signs (heart rate, blood pressure, respiratory rate, oxygen saturation) before and during chemotherapy.
- **Symptoms:** Monitor for signs of infection, such as fever, chills, and increased white blood cell count.

**Documentation**

- **Records:** Document all chemotherapy doses and patient responses to chemotherapy in the medical record.
- **Follow-Up:** Schedule follow-up appointments to assess for any complications or side effects.
Adverse Events and Monitoring

- Injection site reactions
- Serious hypersensitivity reactions including anaphylaxis and infusion related reactions have been reported.
- Clinical worsening of COVID-19 has been observed after administration of COVID-19 monoclonal antibody therapy. It is currently not known if these events were the result of using sotrovimab.

Monitoring

- Patient should be monitored for at least 1 hour after drug administration.
- Signs and symptoms of infusion related reactions include: fever, difficulty breathing, reduced oxygen saturation, chills, fatigue, arrhythmia (e.g., atrial fibrillation, tachycardia, bradycardia), chest pain or discomfort, weakness, altered mental status, nausea, headache, bronchospasm, hypotension, hypertension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, dizziness, and diaphoresis.
- If hypersensitivity or infusion related reactions occur, immediately stop administration, and notify the provider. The provider should immediately assess the patient and consider providing medications and supportive care as necessary.

Error and Adverse Event Reporting

As part of the EUA, health care providers will be required to report all medication errors and serious adverse events potentially associated with casirivimab/imdevimab or sotrovimab within 7 calendar days from event onset. Reports can be submitted online via [http://www.fda.gov/medwatch/report.htm](http://www.fda.gov/medwatch/report.htm)

Sotrovimab

The report needs to include in the field name, “Describe Event, Problem, or Product Use/Medication Error” and the statement “Sotrovimab use for COVID-19 under Emergency Use Authorization (EUA).” A copy of the submitted FDA MedWatch forms should also be sent to [WW.GSKAREportingUS@gsk.com](mailto:WW.GSKAREportingUS@gsk.com)

Tixagevimab/cilgavimab (Evusheld®)

The report needs to include in the field name, “Describe Event or Problem, Relative Tests/Laboratory Data, Concomitant Medical Products and Therapy Dates, and Other Relevant History” and the statement “Tixagevimab/cilgavimab use for COVID-19 under Emergency Use Authorization (EUA).” A copy of the submitted FDA MedWatch forms should also be sent to Astra Zeneca at [https://contactazmedical.astrazeneca.com/content/astrazeneca-champion/us/en/amp-form.html](https://contactazmedical.astrazeneca.com/content/astrazeneca-champion/us/en/amp-form.html).

For Pharmacists:

Order Verification

Prior to verifying a COVID-19 antibody therapy order, confirm that the ordering provider has completed the appropriate documentation described above.

Product Availability and Preparation

Sotrovimab

- Available as 500 mg (62.5 mg/mL) single-dose vials
- Remove vial from refrigerated storage and allow the vial to equilibrate to room temperature while protected from light (wait appropriately 15 minutes). Inspect the vial visually for particulate matter and discoloration
- Swirl the vial gently several times without creating bubbles. Do not shake.
- Withdraw 8 mL of sotrovimab and inject into a 100 mL 0.9% sodium chloride infusion bag (final volume 108 mL). Discard remaining products in the vial.
- Gently rock the infusion bag back and forth 3-5 times before infusion. Do not invert the bag and avoid forming air bubbles.

Tixagevimab/cilgavimab (Evusheld®)

- Each co-packaged carto contains 1 tixagevimab 150 mg/1.5 ml single dose vial (dark grey cap) and 1 single dose vial of cilgavimab 150 mg/1.5 ml single dose vial (white cap)
- Visually inspect the vials for particulate matter and discoloration. DO NOT SHAKE. Tixagevimab and cilgavimab are clear to opalescent, colorless to slightly yellow solutions. Discard the vials if the solution is
cloudy, discolored or visible particles are observed.

- Withdraw 1.5 mL of tixagevimab solution and 1.5 mL of cilgavimab solution into TWO separate syringes. Discard unused portion in vials.
- This product is preservative-free and therefore, the prepared syringes should be administered immediately.

**Product Storage and Documentation**

**Sotrovimab**
- Store unopened vials in the original carton to protect the vials from light and at a temperature of 2°C to 8°C (36°F to 46°F). Do not freeze or shake the vials.
- The admixed infusion bag can be stored between 2°C to 8°C (36°F to 46°F) for up to 24 hours or at room temperature for up to 6 hours, including transportation and infusion time. If refrigerated, let the solution equilibrate to room temperature for approximately 15 minutes prior to infusion.

**Tixagevimab/cilgavimab (Evusheld®)**
- Store unopened vials in a refrigerator at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. Discard any unused portion. DO NOT FREEZE. DO NOT SHAKE.
- Prepared syringes should be administered immediately. If immediate administration is not possible, and the prepared tixagevimab and cilgavimab syringes need to be stored, the total time from vial puncture to administration should not exceed 4 hours in a refrigerator at 2°C to 8°C (36°F to 46°F) or at room temperature up to 25°C (77°F).

Individual pharmacies may require staff to confirm completion of all required steps prior to dispensing COVID-19 antibody therapy, either via electronic I-Vent or paper documentation.

**TABLE 1: Antibody Therapy At A Glance**

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<th><strong>Sotrovimab</strong></th>
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<td><strong>ANTIBODY</strong></td>
<td>Monoclonal</td>
<td>Long-acting antibody combination</td>
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| **DOSE**                | **Treatment Only** Sotrovimab – 500 mg (8 mL)                                                   | **PREP Only**
|                         |                                                                                                 | **Tixagevimab 150 mg/1.5 ml and cilgavimab 150 mg/1.5 ml prepared into TWO separate syringes** |
| **VOLUME/ INJECTION**   | Treatment  
|                         | • Final volume of 108 mL infused over 30 minutes                                                  | **PREP**  
|                         |                                                                                                 | • Administer the IM injections consecutively at different injection sites, preferably one in each of the gluteal muscles |
| **POTENTIAL BENEFIT**   | • Data show, in high risk patients, the risk of hospitalization or death is reduced (1% vs. 7% in the placebo group) | • Results of the PROVENT trial demonstrated a 77% reduction in the incidence of symptomatic COVID-19 infection among high risk patients. |
| **STABILITY OF PREPARED PRODUCTS** | Admixed infusion bag: 24 hours refrigerated or 6 hours at room temperature, including transportation and infusion time. | Prepared syringes: 4 hours from vial puncture to administration refrigerated or at room temperature |
| **ADVERSE EVENTS**      | • Infusion related events and hypersensitivity reactions.                                         | • Hypersensitivity reactions, including anaphylaxis                                              |
|                         | • Observe patient for 1-hour post administration                                                  | • Observe patient for 1-hour post administration                                                  |
| **SMARTLINKS**          | .COVID19SOTROVIMABEUA                                                                           | .COVID19TIXAGEVIMABABCILGAVIMAB                                                                |