UCSF Bamlanivimab Use Process

Background

On November 10, 2020, the Federal Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for the use of Bamlanivimab for the treatment of outpatients with mild to moderate COVID-19. Bamlanivimab is a neutralizing monoclonal antibody that binds the receptor-binding domain of the SARS-CoV-2 spike protein. Recently, preliminary analysis of the BLAZE-1 phase 2 double-blind, randomized, controlled trial studying this agent in symptomatic outpatients within 3 days of first positive COVID-19 test demonstrated an accelerated decrease in viral loads at day 11 after treatment with a 4.7% absolute decrease in ED visits and hospitalizations with an even larger difference noted in a post-hoc analysis of the highest-risk population (11% absolute risk reduction).

The EUA allows for the treatment of COVID-19 in ambulatory adults and children ≥ 12 years-old with mild to moderate disease.

The data on monoclonal antibodies remains new and evolving, and these agents should not be considered standard of care. Therapies through controlled trials should be considered as well as usual supportive care.

References:

Eligibility for Bamlanivimab via EUA

<table>
<thead>
<tr>
<th>Inclusion criteria: Meets all of these and no Exclusions</th>
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</thead>
<tbody>
<tr>
<td>COVID-19 infection confirmed by PCR, NAAT, or Antigen testing</td>
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<tr>
<td>Symptomatic with time from symptom onset &lt; 10 days</td>
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<td>Mild-moderate disease*</td>
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<tr>
<td>Meets at least one of^:</td>
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<tr>
<td>• Have a body mass index (BMI) ≥ 35</td>
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<tr>
<td>• Have ≥ stage 3b chronic kidney disease (eGFR &lt; 45 mL/min per 1.73 m²)</td>
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<td>• Have diabetes that is poorly controlled or requires medical treatment</td>
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<tr>
<td>• Have immunocompromised condition*</td>
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<tr>
<td>• Are currently receiving immunosuppressive treatment (see Appendix A)</td>
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<tr>
<td>• Are ≥65 years of age</td>
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V.2
12/13/20
Owner: Sarah Doernberg
UCSF Bamlanivimab Use Process

- Are ≥55 years of age AND have cardiovascular disease (e.g. coronary artery disease, congestive heart failure, cerebrovascular accident), OR hypertension (poorly controlled or requiring medical treatment), OR chronic obstructive pulmonary disease/other chronic respiratory disease.
- Are 12 – 17 years of age AND have one of the following:
  - BMI ≥99th percentile for their age and gender based on CDC growth charts, [https://www.cdc.gov/growthcharts/clinical_charts.htm](https://www.cdc.gov/growthcharts/clinical_charts.htm), OR
  - sickle cell disease, OR
  - congenital or acquired heart disease, OR
  - neurodevelopmental disorders, for example, cerebral palsy, OR
  - a medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19), OR
  - asthma, reactive airway or other chronic respiratory disease that requires daily medication for control.

*Mild Illness:* Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain) without shortness of breath, dyspnea, or abnormal chest imaging and who do not meet criteria for moderate, severe, or critical illness. **Moderate Illness:** Individuals who have evidence of lower respiratory disease by clinical assessment or imaging, and a saturation of oxygen (SpO2) ≥94% on room air at sea level.

*Pregnancy itself is not a criterion, but any pregnant woman meeting another criterion listed above will be eligible for administration of the drug. Any administration in pregnant patients must be discussed with Maternal Fetal Medicine

#The degree of immunocompromise for the patient is ultimately determined by the treating provider. Conditions include but are not limited to: (adapted from [https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-hospitalized-patients.html#definitions](https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-hospitalized-patients.html#definitions))

1. Receiving current chemotherapy for malignancy
2. Having a hematologic malignancy that may be suppressing the immune system
3. HIV infection with CD4 T lymphocyte count < 200
4. Primary severe immunodeficiency disorder
5. Solid organ or hematopoietic stem cell (bone marrow) transplant recipient
6. Receipt of prednisone 20 mg/day or the equivalent for more than 14 days, or treatment with other high-risk immunosuppressive medications (see Appendix A for examples)

### Exclusion criteria

<table>
<thead>
<tr>
<th>Hospitalized</th>
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<tbody>
<tr>
<td>New O2 requirement</td>
</tr>
<tr>
<td>Worsening O2 requirement in those on supplemental O2</td>
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<tr>
<td>Pregnancy*</td>
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*In the future, pregnancy may be allowed but requires further discussion with Maternal Fetal Medicine*

**Pediatrics:** While Bamlanivimab treatment is an option for adolescents meeting the EUA criteria, the Pediatric COVID-19 Clinical Working Group and the Bamlanivimab Task Force do not recommend routine use of this therapy for our pediatric patients with risk factors as defined per the EUA but it is available on a case-by-case basis for patients evaluated and judged to be at exceptionally high risk for severe COVID-19. At BCHSF, individual patients should be discussed with the MB RSC Medical Director, Manisha Israni-Jiang, (Voalte or email) and with a Pediatric Infectious Diseases physician. At BCHO, individual patients should be discussed with a Pediatric Infectious Diseases physician.

V.2  
12/13/20  
Owner: Sarah Doernberg  2
Breastfeeding mothers: Given limited data, the manufacturer recommends that bamlanivimab be used with caution in breastfeeding patients. However, because of the antibody molecule's large size, it is unlikely to be present in large quantity in breast milk and unlikely to be absorbed from the infant gut. Additionally the anticipated effect on infant health from possible absorption is minimal.

High Risk Immunosuppressive Medications (Examples, not all-inclusive)

<table>
<thead>
<tr>
<th>High Risk Immunosuppression</th>
<th>Class</th>
<th>Generic</th>
<th>Trade</th>
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<tbody>
<tr>
<td>Steroids</td>
<td>Prednisone &gt; 20 mg/day (adults) or &gt; 1mg/kg/day (children) for &gt;14 days or the equivalent for other steroid agents</td>
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<tr>
<td>Purine analog</td>
<td>Azathioprine &gt; 3mg/kg/day 6-Mercaptopurine &gt; 1.5 mg/kg/day</td>
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<tr>
<td>Steroids</td>
<td>Methotrexate &gt; 0.4 mg/kg/week</td>
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<td>Alkylating agents</td>
<td>Cyclophosphamide Chlorambucil</td>
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<tr>
<td>TNF inhibitor</td>
<td>Etanercept Infliximab Adalimumab Certolizumab pegol Golimumab</td>
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<tr>
<td>CTLA-4 Ig</td>
<td>Abatacept</td>
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<tr>
<td>B-cell inhibitor</td>
<td>Rituximab Belimumab Ocrelizumab</td>
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<tr>
<td>Anti-IL 12/23</td>
<td>Ustekinumab</td>
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<tr>
<td>Anti-IL 17/23</td>
<td>Secukinumab Ixekizumab Brodalumab</td>
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<tr>
<td>Anti-IL-1</td>
<td>Anakinra Rilonacept Canakinumab</td>
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<tr>
<td>Phosphodiesterase 4</td>
<td>Apremilast</td>
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<tr>
<td>Jak/Stat inhibitors</td>
<td>Tofacitinib Baricitinib Ocalacitinib</td>
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<tr>
<td>Anti-IL-5</td>
<td>Tocilizumab Resilizumab Benralizumab</td>
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V.2
12/13/20
Owner: Sarah Doernberg
UCSF Bamlanivimab Use Process

Distribution plan:

Guiding principles

- No patient should be denied access to Bamlanivimab on the basis of 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 Bamlanivimab 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 Bamlanivimab via the EUA if eligible.

Responsibilities

- RSC, ED:
  - Reviews eligible patients in each location for Bamlanivimab eligibility
  - RSC may receive referrals from subspecialty groups who become aware of patients tested elsewhere
  - Contacts the patient/caregiver and educates on Bamlanivimab EUA and alternative options
  - Provides EUA fact sheet when patient arrives in clinic
  - Orders drug via orderset
  - Picks up drug from pharmacy
  - Administers drug
  - Monitors for adverse events
- RSC Schedulers:
  - Place the patient on the schedule
- COVID-ID attending
  - Available as a resource if questions arise
  - Approves drug given outside of adult RSCs and ED
  - Reviews administrations weekly
- Study teams
  - Review patient eligibility for clinical trials
  - Inform patients of alternatives to trials
- Pharmacy
  - Prepares the drug
  - Medication Safety: reports to FDA Medwatch as needed
  - Notifies RSC or ED RN when drug is available for pick-up
- ID Pharmacist
  - Maintains list of Bamlanivimab supply
UCSF Bamlanivimab Use Process

RSC workflow:

Patient Referral
- RSC provider reviews RSC, VACC and Mobile Unit positive results daily
- Occupational Health assesses eligibility of employees and refers to RSC/outside PCP
- APeX report from UCSF COVID Registry coming soon
- Refer UCSF patients tested elsewhere via secure email to COVIDOutpatientTreatment@ucsf.edu

Eligibility Assessment
- RSC provider reviews patient chart to confirm
  - Direct SARS-CoV-2 (+) test + within 10 days of symptom onset
  - Patient fulfills “high risk” inclusion & exclusion criteria of EUA

Informed Consent
- RSC Provider performs video visit to
  - Assess eligibility and severity of illness
  - Discuss potential risks, benefits, and alternatives
  - Provide patient/caregiver with EUA fact sheet

Scheduling
- RSC schedules patient for 3 hr infusion visit in Mission Bay RSC
  - 2 infusions available (9AM and 1.30PM) every weekday (10/week)
  - Medication compounded after RN respiratory assessment, 1 hour infusion followed by 1 hr monitoring

Reviewed by representation from:
- Respiratory Screening Clinic
- Emergency Department
- Infectious Diseases
- Care Delivery
- Nursing
- Pharmacy
- Ethics
- Occupational Health