Background

The Federal Drug Administration (FDA) has now issued an Emergency Use Authorization (EUA) for the use of several neutralizing monoclonal antibodies (mAbs) that bind the receptor-binding domain of the SARS-CoV-2 spike protein both for the treatment of outpatients with mild to moderate COVID-19 and for post-exposure prophylaxis to those exposed to COVID-19. Published and unpublished data suggest that antibodies may help to augment decline in viral load and prevent a proportion of ED visits and hospitalizations.

The data on monoclonal antibodies remains new and evolving. Therapies through controlled trials should be considered as well as usual supportive care.

Eligibility for Monoclonal Antibodies for Post-Exposure Prophylaxis (PEP) of COVID-19 exposure via EUA

<table>
<thead>
<tr>
<th>Inclusion criteria: Meets all of these and no Exclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 18 years</td>
</tr>
<tr>
<td>Weight ≥ 40 kg</td>
</tr>
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</table>

Meets one of the following:
1. Not fully vaccinated (see Definitions)
2. Not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination (see Definitions)

Meets one of the following:
1. Exposed to an individual infected with SARS-CoV-2 consistent with close contact criteria per CDC (see Definitions)
2. At high-risk for exposure to an individual infected with SARS-CoV-2 because of occurrence of SARS-CoV-2 infection in other individuals in the same institutional setting, including:
   a. Living in a congregate setting, such as a skilled nursing facility or prison
   b. Working in direct patient-facing care in a congregate setting, which may include working directly with patients in the acute care or outpatient clinical setting

Meets at least one of high-risk for progression to severe COVID-19 criteria (see Definitions)

Eligibility for Monoclonal Antibodies for Treatment of COVID-19 Infection via EUA

<table>
<thead>
<tr>
<th>Inclusion criteria: Meets all of these and no Exclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>COVID-19 infection confirmed by PCR, NAAT, or Antigen testing</td>
</tr>
<tr>
<td>Symptomatic with time from symptom onset &lt; 10 days</td>
</tr>
<tr>
<td>Mild-moderate disease (see Definitions)</td>
</tr>
<tr>
<td>Meets at least one of high-risk for progression to severe COVID-19 criteria (see Definitions)</td>
</tr>
</tbody>
</table>

Exclusion criteria

<table>
<thead>
<tr>
<th>Hospitalized for COVID-19</th>
</tr>
</thead>
<tbody>
<tr>
<td>New O2 requirement</td>
</tr>
<tr>
<td>Worsening O2 requirement in those on supplemental O2</td>
</tr>
</tbody>
</table>
Definitions

High-risk for progression to severe COVID-19

- Age ≥65 years of age
- Body mass index (BMI) ≥ 25
- Pregnancy
- ≥ stage 3b chronic kidney disease (eGFR < 45 mL/min per 1.73 m^2)
- Diabetes that is poorly controlled or requires medical treatment
- Have immunocompromising condition or currently receiving immunosuppressive treatment (see Appendix A)
- Cardiovascular disease or hypertension
- Chronic lung diseases
- Sickle cell disease
- Neurodevelopmental disorders or other disorders that confer medical complexity
- Medical-related technological dependence
- Clinician-determined medical condition or demographic factor presumed to place the patient at high risk for disease progression

Immunocompromised host/Not expected to mount an adequate immune response to complete vaccination

- Active treatment for solid tumor and hematologic malignancies
- Receipt of solid-organ transplant and taking immunosuppressive therapy
- Receipt of CAR-T-cell or hematopoietic stem cell transplant (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 (i.e., ≥20mg prednisone or equivalent per day), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, TNF blockers, and other biologic agents that are immunosuppressive or immunomodulatory
- Chronic conditions associated with varying degrees of immune deficit, such as asplenia, sickle cell and chronic renal disease
- Other diagnosed chronic condition with equivalent moderate to severe level of immunocompromise.

Fully vaccinated

- Individuals are fully vaccinated 2 weeks after their second vaccine dose in a 2-dose series (such as the Pfizer or Moderna vaccines), or 2 weeks after a single-dose vaccine (such as Johnson & Johnson’s Janssen vaccine)

Close contact

- Close contact with an infected individual is defined as: being within 6 feet for a total of 15 minutes or more, providing care at home to someone who is sick, having direct physical contact with the person (hugging or kissing, for example), sharing eating or drinking utensils, or being exposed to respiratory droplets from an infected person (sneezing or coughing, for example). See this website for additional details: https://www.cdc.gov/coronavirus/2019-ncov/if-you-are-sick/quarantine.html

Illness severity

- Mild: 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: 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: Monoclonal antibodies can be considered on a case-by-case basis in consultation with Maternal Fetal Medicine for pregnant patients.

Breastfeeding mothers: Given limited data, the manufacturer recommends that monoclonal antibodies 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.

Vaccine: Due to limited data on the safety and efficacy of mRNA COVID-19 vaccines in persons receiving mAb therapy, the CDC recommends deferring vaccination (either first or second dose) for 90 days after the treatment, in order to avoid interference with vaccine immune response.

Distribution plan:

Guiding principles

V.8
8.25.2021
Owner: Sarah Doernberg on behalf of Monoclonal Antibody Working Group
UCSF COVID-19 Monoclonal Antibody Use Process

- No patient should be denied access to mAbs 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 mAbs 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 mAb via the EUA if eligible.

Responsibilities

- Primary care provider/specialty care provider
  - Reviews eligible patients for mAb eligibility
  - Refers eligible patients for mAb treatment as per below
  - Refers eligible patients for mAb PEP as per below
    - Provides the EUA fact sheet to the patient
    - Orders the medication
- RSC, ED:
  - Reviews eligible patients in each location for mAb treatment eligibility
  - RSC may receive referrals from subspecialty groups who become aware of patients tested elsewhere
  - Contacts the patient/caregiver and educates on mAb EUA and alternative options for treatment indication
  - Provides EUA fact sheet when patient arrives in clinic for mAb EUA treatment indication (all available in English, Spanish, Russian, Traditional and Simplified Chinese: casirivimab-imdevimab)
  - Orders drug via orderset for mAb treatment indication
  - Picks up drug from pharmacy
  - Administers drug
  - Monitors for adverse events
- Population Health 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 mAb supply
MAB SINGLE POST-EXPOSURE PROPHYLAXIS WORKFLOW:

Eligibility

Primary provider/specialty clinic reviews criteria 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

Patient Referral

• Refer with the Apex "Referral to COVID Testing/RSC" REF778 --> Select "Post-exposure prophylaxis" --> "Monoclonal Antibody Treatment"
• Order for COVID-19 PCR recommended but not required
• Under Smart Sets, order "casirivimab-imdevimab post-exposure prophylaxis (PEP) and treatment-EUA use" along with rescue medications (pre-checked)

Scheduling

• Population Health schedules patient for nursing only infusion visit within 7 days of exposure
MAB ONGOING POST-EXPOSURE PROPHYLAXIS FOR ONGOING INSTITUTIONAL EXPOSURES WORKFLOW

Eligibility
Primary provider/specialty clinic reviews criteria 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
  - Review ongoing ~q28 day SQ treatment

Patient Referral
- **Refer** to Parnassus Infusion Center [PIC] via APeX REF800 order
- **Order** Therapy Plan > Monoclonal Antibody > AMB Casirivimab-Imdevimab PEP
- **Sends secure email** to Shagun Arora and Tricia Estacio (ucsf) to confirm patient eligibility / obtain pharmacy code

Scheduling
- PIC will schedule patient
MAB TREATMENT WORKFLOW:

**Patient Referral**
- Patients tested at UCSF are automatically included on an Apex report for review by CRISM Team
- Refer UCSF patients tested elsewhere by using Apex "Referral to COVID Testing/RSC” REF778 --> Select ”Provider appt” --> “Monoclonal Antibody Treatment”
- Occupational Health assesses eligibility of employees and refers to RSC/outside PCP
- Referrals for non-UCSF patients should be sent via Fax using [this form](https://infectioncontrol.ucsfmedicalcenter.org/sites/g/files/tkssra4681/f/Monoclonal_Antibody_Outpatient_Treatment.pdf) to 415-353-4785

**Eligibility Assessment**
- CRISM RN assesses for symptoms, eligibility window and co-morbidites during initial intake.
- Patients identified by CRISM and the ambulatory referral order are scheduled for a video visit with a VACC provider
- Central Scheduling will process referral, register them as UCSF patient and schedule video visit

**Informed Consent**
- VACC Provider performs video visit to
  - Assess eligibility and severity of illness and discuss potential risks, benefits, and alternatives
  - Provide patient/caregiver with EUA fact sheet
  - Order the monoclonal antibody treatment and route to MZ RSC pool for scheduling

**Scheduling**
- RSC schedules patient for infusion visit. Most infusions will be via IV, though SQ option available if venous access is an issue

*https://infectioncontrol.ucsfmedicalcenter.org/sites/g/files/tkssra4681/f/Monoclonal_Antibody_Outpatient_Treatment.pdf*
UCSF COVID-19 Monoclonal Antibody Use Process

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

References: