State of California—Health and Human Services Agency
California Department of Public Health

TOMÁS J. ARAGÓN, M.D., Dr.P.H.
Director and State Public Health Officer

GAVIN NEWSOM
Governor

Health Alert

Anti-SARS-CoV-2 Monoclonal Antibodies
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Background
Monoclonal antibodies that target the SARS-CoV-2 spike protein have been shown to provide clinical benefit in treating SARS-CoV-2 infected adults and pediatric (12 years of age and older weighing at least 40 kg) outpatients with mild to moderate symptoms who are at risk for disease progression. These treatments reduce the risk of progression to severe disease, hospitalization, and death in high-risk populations[1].

Additionally, some of these anti-SARS-COV-2 monoclonal antibody products can be used as post-exposure prophylaxis (PEP) in high-risk populations and can be dosed monthly when there is ongoing exposures in high risk institutional settings (for example, nursing homes and prisons). The currently available anti-SARS-CoV-2 monoclonal antibodies that have received Emergency Use Authorization (EUA) from the Food and Drug Administration (FDA) and are available for use in California include:

- Bamlanivimab/etesevimab[2] – This product is administered intravenously and approved for use as a treatment or as a post-exposure prophylaxis
- Casirivimab/imdevimab[3] (REGENCOV) – All available forms of casirivimab/imdevimab may be administered **either subcutaneously** or by IV infusion. Instructions for preparation for each route of administration can be found in the Dosage and Administration section of the product EUA. Approved for use as a treatment or as a post-exposure prophylaxis.
- Sotrovimab[4] – This product can be administered intravenously and is approved for use as a treatment.

Providers using these products should carefully review the EUAs[1,2,3] for treatment criteria, dosing, and administration guidance. The approval of a subcutaneous route of administration for casirivimab/imdevimab as of June 2021 provides an alternative to IV administration and should decrease barriers to use.

[1] As listed in product EUAs with additional detail here: https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/underlying-evidence-table.html
[2] https://www.fda.gov/media/145802/download
[3] https://www.fda.gov/media/145611/download
[4] https://www.fda.gov/media/149534/download

These drugs are currently not approved for use as pre-exposure prophylaxis, nor should they be used as replacements for vaccination.

Use Post-Exposure Prophylaxis
Bamlanivimab/etesevimab and casirivimab/imdevimab are approved for use in adult and pediatric individuals (12 years of age and older weighing at least 40 kg) for post-exposure prophylaxis of COVID-19. Use as post-exposure prophylaxis should be considered in individuals who are at high risk of progression to severe COVID-19, including hospitalization or death, and are:

- not fully vaccinated or who are not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination (for example, individuals with immunocompromising conditions) and
    - have been exposed to an individual infected with SARS-CoV-2 consistent with close contact criteria[5] per Centers for Disease Control and Prevention (CDC); or
    - who are at high risk of 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 (for example, nursing homes and prisons).

For individuals in whom repeat dosing is determined to be appropriate for ongoing exposure to SARS-CoV-2, these products can be administered every 4 weeks for the duration of ongoing exposure. Further criteria and instructions for dosing in these scenarios can be found in the product EUAs.

Distribution of Anti-SARS-COV-2 Monoclonal Antibody Products to Facilities
Due to national shortages, the U.S. Department of Health and Human Service (HHS) is allocating courses weekly of all three drugs to U.S. states and territories based on COVID-19 case counts and hospitalizations for the preceding week[6]. The California Department of Public Health (CDPH) allocates product to local jurisdictions based on numbers of new COVID-19 cases and COVID-19 hospital admissions, both expressed as a 7-day average.
Once the number of patient courses has been allocated, local health departments and each jurisdiction's Medical and Health Operational Area Coordinator (MHOAC) will assist in determining which facilities within their jurisdiction receive product. Facilities that would like to obtain product or require more product should contact their MHOAC[7].

Considerations Given Potential Logistical and Supply Constraints
While need for anti-SARS-CoV-2 monoclonal antibodies may increase or decrease depending on COVID-19 prevalence, susceptibility of circulating SARS-CoV-2 variants to specific monoclonal antibody products, patient demand, and other factors, there may be times when logistical or supply constraints exist for anti-SAS-COV-2 monoclonal antibody products.
When supplies are not constrained at facilities, providers should use anti-SARS-COV-2 monoclonal antibody products as both treatment and post-exposure prophylaxis as outlined in the product EUAs.

[5] https://www.cdc.gov/coronavirus/2019-ncov/your-health/quarantine-isolation.html
[6] https://www.phe.gov/emergency/events/COVID19/therapeutics/distribution/Pages/data-tables.aspx
[7] https://emsa.ca.gov/wp-content/uploads/sites/71/2021/09/MHOAC-Contact-List-9.2.2021-Public.pdf

In situations of logistical or supply constraints, priority for providing anti-SARS-COV-2 monoclonal antibody products to patients at high risk for progression to severe COVID-19 should be considered for two uses: 1) treatment over use as post-exposure prophylaxis, and 2) use for patients not fully vaccinated or patients not expected to mount a sufficient immune response according to CDC guidance.

Individual clinical situations vary and use depends on clinical judgment. Useful considerations for prioritizing use of anti-SARS-COV-2 monoclonal antibodies while constraints are present can be found at the National Institutes of Health's COVID-19 Treatment Guidelines website[8].

Activity Against Variants
Casirivimab/imdevimab (REGEN COV), bamlanivimab/etesevimab, and sotrovimab have activity against the variants currently circulating in California, including the current sub-lineages of Delta in circulation.

The Delta sublineages AY.1 and AY.2 (which include the mutation K417N) are resistant to bamlanivimab/etesevimab. Currently these resistant sublineages make up a very small proportion of circulating virus in the United States, data on October 29, 2021, show that AY.1 and AY.2 together make up <1% of circulating variants in California[9].

The FDA does not authorize use of bamlanivimab/etesevimab in any state where resistant variants to this product exceed 5%. The FDA maintains a list of states and territories where resistant strains are circulating, and this page should be reviewed by healthcare providers using this product[10].

As of October 29, 2021, bamlanivimab/etesevimab is approved for use in all U.S. states and territories, and providers should continue to use this therapy at this time.

Additional Resources
For facilities and healthcare providers interested in setting up infusions for high-risk patients with COVID-19, the Assistant Secretary for Preparedness and Response (ASPR) has many resources available[11]. This includes free digital content[12] that your facility can use on social media platforms to help educate providers and patients. HHS has also established the CombatCovid website[13] as a resource for patients and providers.

Reporting of Utilization
All healthcare facilities are required to report utilization of anti-SARS-COV-2 monoclonal antibody products. Utilization does inform distribution, and failure to report use will result in a decrease in the California's allocation from HHS. Full reporting details as well as a link

[8] https://www.covid19treatmentguidelines.nih.gov/therapies/updated-statement-on-the-prioritization-of-anti-sars-cov-2-mabs/
[9] https://covid.cdc.gov/covid-data-tracker/#variant-proportions
[10] https://www.fda.gov/media/151719/download
[11] https://www.phe.gov/emergency/events/COVID19/therapeutics/Pages/default.aspx
[12] https://www.phe.gov/emergency/events/COVID19/therapeutics/toolkit/Pages/default.aspx
[13] https://combatcovid.hhs.gov/

providing detailed instructions on how to access each reporting tool can be found on the Reporting Utilization of COVID-19 Therapeutics website[14].

[14] https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Pages/COVID19-therapeutics-teletracking.aspx