SANTÉ PHYSICIANS

MEMORANDUM

DATE: **October 22, 2021**

TO: **Santé Physicians**

FROM: **Michael Synn, M.D. Chief Medical Officer**

RE: **UPDATE #3 - Monoclonal Antibody Treatments for COVID-19**

Santé continues to be grateful to all our providers for their dedication and service during this pandemic crisis. As promised per our previous communications, we wanted to provide an update regarding the Monoclonal Antibody Treatments (MABs).

The Fresno County Department of Public Health continues to recommend monoclonal antibody infusions (bamlanivimab / etesevimab and Regeneron- casirivimab / imdevimab) as COVID-19 treatment options available to healthcare providers. Monoclonal antibodies (MABs) are indicated for confirmed COVID-19 patients in the first 10 days of symptoms with mild to moderate symptoms that are high risk for progressing to severe COVID-19 or hospitalization. It has been shown to (1) decrease hospitalizations and deaths by up to 80% and (2) be effective against current variants including the contagious Delta variant. In addition, MABs have been approved for post-exposure prophylaxis in high-risk individuals with close contact who are not fully vaccinated or are immunocompromised. *See updated Health Advisory attachment for details.*

As you saw in our previous communication, Santé successful media / print public awareness campaign to inform our patients of this potentially life-saving opportunity has raised the level of awareness for both patients and providers. MABs treatment has expanded to multiple locations in our region. Santé along with Fresno County has arranged infusion sites and continues to help develop locations for MAB**s** treatment.

Where can my patients receive Monoclonal Antibody infusions?

Initial Fresno County Locations:

- St. Agnes Medical Center - Paul LeBlanc – paul.leblanc@samc.com
- Kaiser - Tim J. Sayles – Tim.J.Sayles@kp.org
- Adventist Reedley/Selma - Ed Abukhazneh – AbukhaAF@ah.org
- Premium Urgent Care – Three locations – Dr. Eric Green – (504) 236-1486

Additional Outpatient Locations Offering MABs Treatment:

- **Fresno Nephrology Center**
  568 E. Herndon Ave. #101, Fresno, CA 93720
  Phone: (559) 431-0066

- **Nighat Sarwar MD, Inc**
  7407 N. Cedar Ave. Ste. #103, Fresno, CA 93720
  Phone: (559) 431-4007 **ATTN**: Victoria

- **Bautista Medical Group**
  1805 E. Fir, Suite 101, Fresno, CA 93720
  Phone: (559) 252-7301 **ATTN:** Araceli

- **UCSF COVID-19 Equity Project**
  - 550 E Shaw Ave. Fresno CA 93710
  - **Phone** (559) 349-8082

Please contact your preferred infusion location to obtain an appointment time and coordinate site-specific instructions for your patients to receive treatment. You may be required to attest the patient meets the high-risk criteria to be eligible for the infusion. The infusions are not available on a walk-in basis.

Thank you on behalf of all of us at Santé for making this potentially life-saving treatment available to your COVID-19 patients. We are and continue to be so grateful to you, our valuable providers and staff, for assisting in the campaign against COVID-19.

Monoclonal Antibody Product Links:
Regeneron - https://www.regeneron.com/sites/default/files/treatment-covid19-eua-fact-sheet-for-hcp.pdf
bamlanivimab / etesevimab - bam-and-ete-eua-factsheet-patient.pdf (lilly.com)

Attachment: Health Advisory *Monoclonal Antibody Treatments for COVID -19* September 24, 2021, Fresno County Department of Public Health

Health Update

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Monoclonal Antibody Treatments for COVID-19

On January 4, 2021, The Fresno County Department of Public Health (FCDPH) recommended monoclonal antibodies as COVID-19 treatment options available to healthcare providers. **This health update provides current information on BAM/ETE and clarifies that Sotrovimab is not currently available for ordering. There are (2) NEW Monoclonal Antibody provider sites in Fresno County: UCSF COVID-19 Equity Project (CEP) and Dr. Nighat Sarwar. Sites offering MAB treatments are located on page 6 of this Health Update.**

Monoclonal antibodies are an important tool in keeping patients from deteriorating and to assist the health care system from becoming overwhelmed. Preliminary data suggests a 70-80% reduction in hospitalizations and deaths among high-risk COVID-19 positive patients who received monoclonal antibodies. Currently approved MABs have been shown to be effective against current variants including Delta.
Anti-SARS-CoV-2 Monoclonal Antibodies | COVID-19 Treatment Guidelines (nih.gov)

There are three approved MABs, Sotrovimab,REGEN-COV, and BAM/ETE. Sotrovimab is not available for ordering in Fresno County and is not approved for post-exposure prophylaxis so this Health Update focuses on REGEN-COV and BAM/ETE.

On June 25, 2021, the distribution of bamlanivimab plus etesevimab was paused in the United States because of the increase in the combined frequencies of two SARS-CoV-2 variants of concern (VOC) circulating across the country: Gamma (P.1) and Beta (B.1.351). In recent months, the Delta (B.1617.2, non-AY.1/AY.2) variant has become the predominant variant circulating in all states. Because the combination of bamlanivimab plus etesevimab retains activity against the Delta variant, as of September 2, 2021, the use and distribution of these anti-SARS-CoV-2 monoclonal antibodies (mAbs) have been resumed in all U.S. states, territories, and jurisdictions.

Statement on Bamlanivimab Plus Etesevimab | COVID-19 Treatment Guidelines (nih.gov)

Categories of Health Alert Messages:

Health Alert: Conveys the highest level of importance; warrants immediate action or attention
Health Advisory: Provides important information for a specific incident or situation; may not require immediate action
Health Update: Provides updated information regarding an incident or situation; unlikely to require immediate action
Health Information: Provides general health information which is not considered to be of emergent nature

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Who is Eligible to Receive Monoclonal Antibodies?

Monoclonal antibodies have Federal Drug Administration (FDA) emergency use approval for the treatment of mild to moderate COVID-19 positive patients within the first 10 days of diagnosis who are at high risk for progressing to severe COVID-19 and/or hospitalization. High risk is defined as patients who meet at least one of the following criteria:

- Have a body mass index (BMI) ≥25
- Have chronic kidney disease
- Have diabetes
- Have immunosuppressive disease
- Are currently receiving immunosuppressive treatment
- Are ≥65 years of age
- Are ≥55 years of age AND have
    - Cardiovascular disease, OR
    - Hypertension, OR
    - Chronic obstructive pulmonary disease/other chronic respiratory disease
- Are 12 – 17 years of age AND have
    - BMI ≥85th percentile for their age and gender based on Centers for Disease Control and Prevention (CDC) growth charts: 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

Monoclonal antibodies are not authorized for use in patients who are hospitalized due to COVID-19 or who require oxygen therapy due to COVID-19, or who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.
There are no contraindications to providing the monoclonal antibodies.

What information can I give my patients about monoclonal antibodies?

As a healthcare provider, you must communicate to your patient or parent/caregiver, as age appropriate, information consistent with the "Fact Sheet for Patients, Parents and Caregivers" (and provide a copy of the Fact Sheet- links to both monoclonal antibodies are provided below) prior to the patient receiving monoclonal antibodies, including:

- The FDA has authorized the emergency use of monoclonal antibodies for the treatment of mild to moderate COVID-19 in adult patients with positive results of COVID-19 testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization
- The patient or parent/caregiver has the option to accept or refuse the monoclonal antibody treatment

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- The significant known and potential risks and benefits of monoclonal antibodies, and the extent to which such potential risks and benefits are unknown
- Information on available alternative treatments and the risks and benefits of those alternatives, including clinical trials.
- Patients treated with monoclonal antibodies should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect "high touch" surfaces, and frequent handwashing) according to CDC guidelines.

Patient Fact Sheet Links:

REGEN-COV - https://www.regeneron.com/sites/default/files/treatment-covid19-eua-fact-sheet-for-patient.pdf
BAM/ETE- bam-and-ete-eua-factsheet-patient.pdf (lilly.com)

MAB for Post-exposure Prophylaxis

Both BAM/ETE and REGEN-COV have been approved for post-exposure prophylaxis, REGEN-COV In July 2021, and BAM/ETE in September 2021: https://www.fda.gov/media/145610/download The indications for emergency use as post-exposure prophylaxis (prevention) for COVID-19 is the same for both BAM/ETE and REGEN-COV:
adults and pediatric individuals (12 years of age and older weighing at least 40 kg) who are at high risk for progression to severe COVID-19, including hospitalization or death. REGEN-COV is not authorized for pre-exposure prophylaxis to prevent COVID-19 before being exposed to the SARS-CoV-2 virus -- only after exposure to the virus.

The EUAs for BAM/ETE and REGEN-COV have been updated to state they should only be used as post-exposure prophylaxis for individuals who are:

- Not fully vaccinated **or** who are not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination (for example, people with immunocompromising conditions, including those taking immunosuppressive medications), **and**
    - Have been exposed to an individual infected with SARS-CoV-2 consistent with close contact criteria 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 or prisons)

The primary data supporting the EUA reissuance for post-exposure prophylaxis of COVID-19 are from a Phase 3 trial. The trial was a randomized, double-blind, placebo-controlled clinical trial studying a single dose of REGEN-COV for prevention of COVID-19 in household contacts of individuals infected with SARS-CoV-2. Cases were confirmed using real-time reverse transcription–polymerase chain reaction (RT-PCR), one of the most accurate laboratory methods for detecting, tracking, and studying COVID-19. An 81% reduction in confirmed symptomatic COVID-19 cases was observed with REGEN-COV compared to placebo at day 29 in cases who were RT-PCR negative and seronegative at baseline (the primary analysis population). In the overall trial population, there was a 62% reduction in RT-PCR confirmed symptomatic COVID-19 cases in the REGEN-COV group compared to placebo at day 29.

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FDA authorizes REGEN-COV monoclonal antibody therapy for post-exposure prophylaxis (prevention) for COVID-19 | FDA

DOSAGE AND ADMINISTRATION

REGEN-COV

People who had a previous severe allergic reaction to REGEN-COV should not use it again. Other important information for these trials including other outcomes and side effect information is available in the health care provider fact sheet: https://www.fda.gov/media/145611/download

REGEN-COV consists of the monoclonal antibodies casirivimab and imdevimab, administered together. Monoclonal antibodies are laboratory-made proteins that mimic the immune system's ability to fight off harmful pathogens, such as viruses like SARS-CoV-2.

The authorized dose for REGEN-COV for both treatment and as post-exposure prophylaxis is 600 mg of casirivimab and 600 mg of imdevimab administered together.

- For treatment, intravenous infusion is strongly recommended; subcutaneous (under the skin) injection is authorized as an alternative route of administration when intravenous infusion is not feasible and would lead to delay in treatment.
- For post-exposure prophylaxis, either intravenous infusion or subcutaneous injection is appropriate. For individuals who remain at high risk of exposure to another individual with SARS-CoV-2 for longer than 4 weeks, and who are not expected to mount an adequate immune response to full SARS-CoV-2 vaccination, following an initial dose of 600 mg of casirivimab and 600 mg of imdevimab, repeat doses of 300 mg of casirivimab and 300 mg of imdevimab once every 4 weeks are appropriate for the duration of ongoing exposure.

  treatment-covid19-eua-fact-sheet-for-hcp.pdf (regeneron.com)

BAM/ETE

Unlike REGEN-COV which can be given either as IV infusion or subcutaneous injection, BAM/ETE can only be given as an Intravenous Infusion.

Bamlanivimab and etesevimab are both available as solutions in separate vials and must be diluted and combined prior to administration.

- To prepare the dose you will need 1 vial of bamlanivimab and 2 vials of etesevimab.
- Administer bamlanivimab and etesevimab together as a single intravenous (IV) infusion via pump or gravity
- Clinically monitor patients during administration and observe patients for at least 1 hour after infusion is complete. Bamlanivimab and etesevimab may only be administered in settings in which health care providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary

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Fact Sheet for Health Care Providers Emergency Use Authorization (EUA) Of Bamlanivimab And Etesevimab 09162021 (fda.gov)

SIDE EFFECTS

REGEN-COV

The most common side effects were injection site reactions. The signs and symptoms of injection site reactions which occurred in at least 1% of subjects in the REGEN-COV group were skin redness (erythema), an uncomfortable, irritating sensation that creates an urge to scratch (pruritus), and ecchymosis (discoloration of the skin resulting from bleeding underneath, caused by bruising). There were no cases of severe hypersensitivity reactions, or potentially life-threatening allergic reactions (such as anaphylaxis).

BAM/ETE

The safety of bamlanivimab administered with etesevimab is primarily based on exposure of approximately 1,400 ambulatory (non-hospitalized) subjects who received doses of bamlanivimab and etesevimab together, at the recommended dose or higher, in BLAZE-1 and BLAZE-4. BLAZE-1 is a Phase 2/3, randomized, double-blind, placebocontrolled clinical trial studying bamlanivimab and etesevimab administered together for the treatment of subjects with mild to moderate COVID-19. In the Phase 3 portion of the trial, enrolled participants had at least one risk factor for the development of severe COVID-19 illness. BLAZE-4 is a Phase 2, randomized, double-blind, placebo-controlled clinical trial studying bamlanivimab and etesevimab for the treatment of subjects with mild to moderate COVID-19. Subjects ≥65 years old or with BMI ≥35 were excluded from enrollment. In clinical trials, approximately 4,000 subjects have received bamlanivimab (either alone or with etesevimab) at doses ranging from 700 to 7,000 mg. Bamlanivimab and etesevimab at the authorized doses of 700 mg and 1,400 mg have been administered together to approximately 800 subjects in clinical trials [see Clinical Pharmacology (14.2)].

The following adverse reactions (i.e., adverse events assessed as causally related) have been observed in those who have received bamlanivimab and etesevimab together at the authorized dose or higher:

- anaphylaxis (n=1, 0.07%)
- infusion-related reactions (n=16, 1.1%) 26 In the case of anaphylaxis and serious infusion-related reactions, all infusions were stopped, and treatment was administered. One case required epinephrine. All events resolved. The most common treatment-emergent adverse events in the bamlanivimab and etesevimab treatment group in BLAZE-1 and BLAZE-4 included nausea, dizziness, and pruritus. No treatment-emergent adverse events occurred in more than 1% of participants and the rates were comparable in the treatment and placebo groups

Where can my patients receive monoclonal antibodies?

INFUSIONS ARE NOT AVAILABLE ON A "WALK-IN" BASIS. Please contact the individuals or sites beforehand to coordinate inclusion criteria, and an appointment date and time.

Local hospitals have received allotments of monoclonal antibodies. Several community-based providers are also offering monoclonal antibodies. See contact information below:

Location	Name	Email Address and/or Phone Number

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Saint Agnes Medical Center	Paul LeBlanc	paul.leblanc@samc.com
Kaiser Permanente	Tim J. Sayles	Tim.J.Sayles@kp.org
Adventist Reedley/Selma (*Contact the Adventist Health Emergency room in Reedley and Selma to arrange for an infusion*)	Ed Abukhazneh	AbukhaAF@ah.org
Premium Urgent Care	Dr. Erick Green Brenda Velasquez or Sandra Mandrigal **Address:** 2021 Herndon Ave Suite 101 Alyssa **Address:** 6643 N. Milburn Ave Suite 104 Green Sport Medicine Kristie Butler **Address:** 2021 Herndon Ave Suite 201	(504) 236-1486 (559) 797-4315 (559) 412-2535 (559) 813-3005
Baz Allergy, Asthma and Sinus Center	Dr. Malik Baz	(559) 436-4500
Fresno Nephrology Group	Office Staff	(559) 431-0066
Bautista Medical Group (Sunnyside)	Araceli	(559) 252-7301 sunnysidebmg@gmail.com
UCSF COVID-19 Equity Project (CEP)	Office Staff **Address:** 550 E. Shaw Ave 93710	(559) 349-8082 fresno-mobileheal@ucsf.edu
Dr. Nighat Sarwar	Victoria Evans **Address:** 7407 N. Cedar Suite 103	(559) 431-4007

These infusion sites may request that you verify that the patient is eligible for monoclonal antibody infusion, including that COVID-19 positive in last 10 days, meets high risk criteria, currently with no, mild, or moderate symptoms (no O2 requirement) and that the patient has been given information about monoclonal infusions (see above section with links to patient information).

Can I give monoclonal antibodies in my office or health care setting?

Yes, you can. Monoclonal antibodies are administered over 20-50 minutes with an IV infusion and must be monitored for one hour after for any reactions. REGEN-COV can also be given with four subcutaneous injections. The mechanics of

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storing, mixing, dosing, and administering monoclonal antibodies is described in the below fact sheets for healthcare providers.

Monoclonal Antibody Product Links:

https://www.regeneron.com/sites/default/files/treatment-covid19-eua-fact-sheet-for-hcp.pdf
GSK Sotrovimab Fact Sheet for HCP 07092021 (fda.gov)
bam-and-ete-eua-factsheet-hcp.pdf (lilly.com)

Payment

The Centers for Medicare and Medicaid Services (CMS) reimburses healthcare providers for the infusion: https://www.cms.gov/files/document/covid-infographic-coverage-monoclonal-antibody-products-treat-covid-19.pdf

Ordering MAB Doses

MAB is offered to health care providers at no cost for administration to eligible patients. Prior to receiving MAB, health care providers must complete two forms and email these to C19therapies@amerisourcebergen.com

- AmerisourceBergen Letter of Authorization (LOA) Form: https://www.co.fresno.ca.us/home/showdocument?id=59253&t=637680728287981606
- AmerisourceBergen Application: https://docs.google.com/spreadsheets/d/150qbdn1_2h7rJjUAk3i0qHVsxW4Vq0hY/edit?usp=sharing&ouid=105793088427972894257&rtpof=true&sd=true

Currently, both REGEN-COV and BAM/ETE are available through a federal distribution plan, while Sotrovimab is not, with allocations to states, and in California to counties including Fresno County. To submit a request for either REGEN-COV or BAM/ETE, health care providers are asked to complete the following form. There is a link embedded in the form to submit your request to FCDPH: https://forms.office.com/g/2dnQuRA0gK

More Information

If you have any questions or challenges with accessing or administering monoclonal antibodies, please contact FCDPH Public Health Physicians. Contact information is included below:

- Dr. John Zweifler jzweifler@fresnocountyca.gov
- Dr. Robin Linscheid rlinscheidjanzen@fresnocountyca.gov

Thank you for making this life-saving treatment available to your COVID-19 positive patients.