Banner University Health Plans

Provider Newsbrief – June 21, 2021

Monoclonal Antibody Update

The Food and Drug Administration recently expanded the indications of COVID monoclonal antibody treatment to include more conditions that would qualify a patient for treatment. Copies of the revised guidelines and orders can be found following this cover page.

- Additional pages follow -

Pharmacy and Therapeutics Clinical Consensus Group
COVID-19 Monoclonal Antibody Guidelines
June 10, 2021

SARS-CoV-2 Specific Monoclonal Antibody Treatment

- Several monoclonal antibodies are being investigated
- Bamlanivimab, casirivimab/imdevimab and bamlanivimab/etesevimab granted Emergency Use Authorization (EUA)
- On April 16, 2021, the U.S. Food and Drug Administration revoked the emergency use authorization (EUA) for bamlanivimab, **when administered alone.**
- *Based on its ongoing analysis of emerging scientific data, specifically the sustained increase of SARS-CoV-2 viral variants that are resistant to bamlanivimab alone resulting in the increased risk for treatment failure, the FDA has determined that the known and potential benefits of bamlanivimab, when administered alone, no longer outweigh the known and potential risks for its authorized use.*
- On May 26, 2021, Department of Health and Human Services (HHS) recommended pausing distribution of bamlanivimab/estevimab in Arizona, California, Florida, Indiana, Oregon and Washington, Illinois and Massachusetts due to rising prevalence of P.1 Variant. The EUA for bamlanivimab/estevimab has not yet been evoked by the FDA.
- Information on safety and efficacy for COVID-19 is evolving with new literature released regularly
- Banner recommendations based on current literature, drug availability and disease severity

SARS-CoV-2 Specific Monoclonal Antibody Treatment Guidelines

- Casirivimab/imdevimab and bamlanivimab/etesevimab are investigational drugs and not currently FDA approved for any indication.
- The FDA issued an Emergency Use Authorization (EUA) to authorize the emergency use of casirivimab/imdevimab or bamlanivimab/etesevimab for the treatment of mild to moderate COVID-19 in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization. On May 14, 2021 the FDA updated the EUA for both monoclonal antibodies and expanded the indications for use.
- ***Casirivimab/imdevimab***
    - Casirivimab and Imdevimab EUA issued November 21, 2020, re-issued February 9 and February 25, 2021
    - Review Casirivimab and imdevimab EUA fact sheet for providers updated June 3, 2021
    - On June 3, 2021 the EUA updated the dose to casirivimab 600 mg and imdevimab 600 mg from 1200 mg
    - Although packaged separately, casirivimab (REGN10933) and imdevimab (REGN10987) must be administered together after dilution by single intravenous (IV) infusion only.
    - Data supporting EUA was based on review of the analysis of phase 1 and 2 data from the ongoing trial R10933-10987- COV-2067 (NCT04425629), a phase 1/2/3, randomized, double-blind, placebo-controlled trial that demonstrated possible clinical benefit. FDA's explanation for issuing EUA states: "it is reasonable to believe that casirivimab and imdevimab, administered together, may be effective".
- ***Bamlanivimab/etesevimab***
    - Bamlanivimab and Etesevimab EUA issued February 9, 2021, reissued February 25, 2021
    - Review Bamlanivimab and Etesevimab EUA fact sheet for providers
    - Bamlanivimab/etesevimab should no longer be administered in Arizona or California Banner facilities
    - Limited clinical data. Data supporting EUA based on the review of the data from the Phase 2/3 BLAZE-1 trial (NCT04427501), an ongoing randomized, double-blind, placebo-controlled clinical trial, and the Phase 2 BLAZE-4 trial (NCT04634409), an ongoing randomized, double-blind, placebo-controlled clinical trial that demonstrated possible clinical benefit.
- Benefit of SARS-CoV-2 specific monoclonal antibodies have not been observed in patients hospitalized due to COVID-19 and may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.
- SARS-CoV-2 specific monoclonal antibodies must be administered in settings in which health care providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and activate the emergency medical system (EMS).
- If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive therapy.

SARS-CoV-2 Specific Monoclonal Antibody for the Treatment of Mild to Moderate COVID-19 in Adult and Pediatric

Banner Emergency Authorization Criteria for Use for casirivimab/imdevimab and bamlanivimab/etesevimab

Inclusion Criteria

COVID positive by PCR or Antigen Testing
+
Within 10 days from symptom onset
+
18 years of age or older weighing at least 40 kg
+
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*:

- Body mass index (BMI) > 25
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease
- Receiving immunosuppressive treatment
- Age ≥ 65 years
- Cardiovascular disease
- Hypertension
- Chronic lung disease (e.g., COPD, cystic fibrosis)
- Pregnancy
- Sickle cell disease
- Neurodevelopment disorders or other conditions that confer medical complexity (e.g., genetic, or metabolic syndrome)
- Medical related technology dependence (e.g., gastrostomy)

Exclusion Criteria

- Hospitalized due to COVID-19
- Require oxygen therapy due to COVID-19
- 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
- Suspected or proven serious, active bacterial, fungal, viral or other infection (besides COVID-19)

Dosing and Administration

- Pharmacy to dispense casirivimab/imdevimab for patients in Arizona and California per P & T Protocol
- Pharmacy can interchange between casirivimab and imdevimab or bamlanivimab and etesevimab per P & T Protocol based on availability for facilities outside of Arizona or California **only**

casirivimab 600 mg and imdevimab 600 mg added to 100 mL 0.9% NaCl IV Infusion Once, Infuse over 22 minutes

Or

bamlanivimab 700 mg and etesevimab 1400 mg added to 100 mL 0.9% NaCl IV Infusion Once, Infuse over 31 minutes

- Use 0.2/0.22 micron in-line filter
- No dosage adjustments are recommended
- **Administer <u>as soon as possible</u> after positive COVID PCR or Antigen test and within 10 days of symptom onset**

Requirements for Use

- Order for Monoclonal Antibody must be signed by a Physician, Nurse Practitioner, or Physician Assistant
- Provider should discuss COVID Monoclonal antibody therapy with patient and provide patient fact sheet based on drug to be administered prior to administering med. (Available in Krames)
  - o casirivimab/imdevimab patient fact sheet
- Report all serious adverse events to FDA Medwatch

Monitoring

Clinically monitor patients (vital signs, infusion reactions) during infusion and observe patients for at least 1 hour after infusion complete

Report all adverse events through Banner Health Online Event Reporting

Additional Comments

- Bamlanivimab & etesevimab should no longer be utilized in either California or Arizona due to the rise in P.1 variant.
- There are insufficient data on the use of casirivimab/imdevimab or bamlanivimab/etesevimab during pregnancy. Casirivimab/imdevimab or bamlanivimab/etesevimab should only be used during pregnancy if the potential benefit outweighs the potential risk for the mother and the fetus.

SARS-CoV-2 Specific Monoclonal Antibody Allocation Process

- Availability of casirivimab/imdevimab and/or bamlanivimab/etesevimab based on HHS allocations.
- The EUA criteria for use of casirivimab/imdevimab or bamlanivimab/etesevimab are equivalent with comparable clinical efficacy and safety data. Pharmacy to dispense casirivimab/imdevimab or bamlanivimab/etesevimab based on availability. Pharmacy can interchange between casirivimab/imdevimab or bamlanivimab/etesevimab per P & T Protocol based on availability for Banner Health facilities outside of Arizona and California
- In Colorado, allocation will be managed through an online lottery process managed by the state health department

SARS-CoV-2 Specific Monoclonal Antibody: Additional Comments

- Although the EUA included criteria for patients ages 12-17, Banner AdHoc COVID P&T CCG is not including them in our recommendations because the one trial available for review included no one in that age group. Additionally, morbidity and mortality from COVID is lowest in that age group.
- The Banner AdHoc COVID P&T CCG is excluding patients with "suspected or proven serious, active bacterial, fungal, viral or other infection". We have no data on casirivimab/imdevimab or bamlanivimab/etesevimab use in such patients and existing monoclonal antibodies are generally withheld in patients with such infections.

COVID-19 Related Medication Treatment Summary

Adapted from Assessment of Evidence for COVID-19-Related Treatments. Bethesda, MD: American Society of Health-System Pharmacists, Inc.

Medication	Class	Comments	Banner Recommendation
SARS-CoV-2 Specific Monoclonal Antibodies			
casirivimab & imdevimab	Neutralizing Monoclonal Antibodies	The Study 1 study showed that viral load was significantly decreased by day #7 in the treatment arms compared to placebo. Medically attended visits (Hospitalizations/ER/Urgent Care/Clinic visits) were less in the casirivimab and imdevimab group (2.8%) compared to placebo (6.5%). This is the only clinical data available for casirivimab and imdevimab.	See P & T CCG Guidelines for Criteria for Use
Bamlanivimab & etesevimab		The combination arm of the BLAZE-1 trial showed Bamlanivimab 2800 mg and etesevimab 2800 mg had a significantly greater change in viral load at baseline to day 11 compared to placebo. In addition, the patients in the combination group had a lower number of hospitalization/ER visits at day 29 (0.9% compared to 5.8% in placebo). In the cohort of patients 65 yrs. or older or with a BMI $\geq$ 35, those in the combination group fared better in hospitalizations (combination 0% rate compared to 13.5% rate in placebo). The monotherapy bamlanivimab groups had lower rates as well (2.7% for the 700 mg, 3.3% for 2800 mg, and 5.9% for the 7000 mg groups). This is the only published study that presents data on bamlanivimab and etesevimab.	No longer recommended for use in Arizona or California due to rising resistance in P.1 variant

FAX

SUBJECT: COVID-19 Monoclonal Antibody Infusion Order

TO: Please select ONE infusion center location (avoid sending to multiple infusion centers)
Please note: hours of operation are subject to change

Arizona

☐ **BBMC (Baywood)**
Fax: 480-321-3939
Tel: 480-321-4032
Hours: Daily, 7:30am to 3:00pm

☐ **BUMC-Phoenix**
Fax: 602-839-2267
Tel: 602-839-6108
Hours: Daily, 7:00am to 3:00pm

☐ **BUMC-South (Abrams)**
Fax: 520-874-4824
Tel: 520-874-6082
Hours: Daily, 8:00am to 3:30pm

Colorado

☐ **MMC**
Fax: 970-820-6091
Tel: 970-820-4093
Hours: 8:00am to 4:00pm

☐ **NCMC**
Fax: 970-810-6992
Tel: 970-810-3940
Hours: 8:00am to 4:00pm

FROM:

Provider Name:_____ Date:_____

Provider Fax:_____ Provider Tel:_____

No. Pages:_____ Comments:_____

_____

ORDER Process:

Please follow the steps outlined below to evaluate patients for Monoclonal Antibody Infusion

1. Obtain positive direct SARS-CoV-2 test documentation
    a. PCR or direct antigen accepted, antibody tests are <u>not</u> accepted
2. Evaluate patient for high-risk criteria (can be evaluated by phone, face-to-face, or telehealth)
3. Complete clinical note that documents high-risk criteria and review of patient fact sheet
4. Complete order set and attach the following:
    - ☑ History & Physical note, including
        i. evaluation of risk factors
        ii. statement that patient does not have concurrent systemic infection (UTI, SSI, etc.)
    - ☑ Patient demographics including insurance information
    - ☑ Diagnostics labs (direct positive SARS CoV-2-test)
    - ☑ Documentation that patient has received fact sheet OR that the fact sheet has been verbally reviewed with the patient

The infusion center may contact you for any clarifications needed. To facilitate smooth and rapid scheduling for your patient, please be sure to include all documents listed below and accurate contact information.

PRINT SAVE AS EMAIL RESET

Banner Health

OUTPATIENT PROVIDER ORDERS – SARS-COV-2 SPECIFIC MONOCLONAL ANTIBODY

FORM MUST BE COMPLETE (no blanks) AND SIGNED BY THE PROVIDER FOR PATIENT TO BE CONSIDERED FOR casirivimab/imdevimab or bamlanivimab/etesevimab

FACILITY: _____ **INFUSION CENTER CONTACT INFORMATION:** _____

PLEASE PRINT

ORDER MUST BE FAXED FROM PROVIDER'S OFFICE

Date: _____

PATIENT NAME: _____ **DOB:** _____

Phone: _____ Height (cm): _____ Weight (kg): _____

Allergies: _____

Diagnosis Code: _____ Diagnosis Name (REQUIRED): _____

Authorization # (date received, name of person giving authorization, date range if applicable): _____

_____

Physician Name (PRINT FIRST & LAST): _____

Physician office phone #: _____ Physician Fax #: _____

Contact person and Ext # at physician office: _____

SARS-CoV-2 Specific Monoclonal Antibody Guidelines

- Banner SARS-CoV-2 Specific Monoclonal Antibody Guidelines available in Banner COVID Toolkit.
- **Casirivimab/imdevimab and bamlanivimab/etesevimab are investigational drugs and are not currently FDA approved for any indication.**
- The FDA issued two separate Emergency Use Authorization (EUA) to authorize the emergency use of casirivimab/imdevimab or bamlanivimab/etesevimab respectively for the treatment of mild to moderate COVID-19 with positive results of direct SARS-CoV-2 viral testing who are at high risk for progressing to severe COVID-19 and/or hospitalization.
  - Casirivimab and imdevimab EUA provider fact sheet available at https://www.fda.gov/media/143892/download
    Bamlanivimab and etesevimab EUA provider fact sheet available at: https://www.fda.gov/media/145802/download
  - Data supporting casirivimab and imdevimab EUA was based on an interim analysis from Phase 1/2 from Study 1 that demonstrated possible clinical benefit. Data supporting bamlanivimab and etesevimab EUA based on data from the Phase 2/3 BLAZE-1 trial and the Phase 2 BLAZE-4 trial that demonstrated possible clinical benefit. Limited clinical data available for casirivimab/imdevimab or bamlanivimab/etesevimab. The FDA's explanation for issuing EUA states that "it is reasonable to believe that casirivimab/imdevimab (administered together) or bamlanivimab/etesevimab (administered together) may be effective."
- On May 26, 2021, Department of Health and Human Services (HHS) recommended pausing distribution of bamlanivimab/estevimab in Arizona, California, Florida, Indiana, Oregon and Washington, Illinois and Massachusetts due to rising prevalence of P.1 Variant

SARS-CoV-2 Specific Monoclonal Antibody CRITERIA FOR USE

Patient must meet **ALL** criteria to be eligible for casirivimab/imdevimab or bamlanivimab/etesevimab consideration.

- ❑ 18 years of age or older weighing at least 40 kg
- ❑ COVID-19 positive by PCR or Antigen testing
- ❑ Within 10 days from symptom onset (Date of Symptom Onset: _____)
- ❑ Meets the following oxygen therapy requirements:
  - Not requiring oxygen therapy due to COVID-19 **OR**
  - If on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity, not requiring an increase in baseline oxygen flow rate due to COVID-19
- ❑ Does not have suspected or proven serious, active bacterial, fungal, viral, or other infection (excluding COVID-19)
- ❑ High risk - defined as meeting one or more of the following criteria (select **all** that apply):
  - ❑ Body Mass Index (BMI > 25)
  - ❑ Chronic Kidney Disease
  - ❑ Diabetes
  - ❑ Immunosuppressive Disease
  - ❑ Receiving immunosuppressive treatment
  - ❑ Age ≥ 65 years
  - ❑ Cardiovascular disease
  - ❑ Hypertension
  - ❑ COPD/other chronic respiratory disease
  - ❑ Pregnancy
  - ❑ Sickle cell disease
  - ❑ Neurodevelopment disorders or other conditions that confer medical complexity (e.g., genetic, or metabolic syndrome)
  - ❑ Medical related technology dependence (e.g., gastrostomy)
- ❑ Patient or caregiver received a copy of the casirivimab/imdevimab factsheet at https://www.fda.gov/media/143893/download, and bamlanivimab/etesevimab factsheet at https://www.fda.gov/media/145803/download (Also available in Krames in English and Spanish). Patient was informed of risks and benefits of therapy, availability of alternatives and that the drug is an unapproved drug authorized for use under the Emergency Use Authorization. Patient understands they have the option to accept or refuse treatments and, understanding the risks, benefits and alternatives, has agreed to accept treatment with casirivimab/imdevimab or bamlanivimab/etesevimab based on drug availability.

Banner Health

OUTPATIENT PROVIDER ORDERS – SARS-COV-2 SPECIFIC MONOCLONAL ANTIBODY

SARS-CoV-2 Specific Monoclonal Antibody Allocation

Banner Locations in Colorado

- Allocation through Online Lottery Process managed by the Colorado State Health Department, Provider License Number: _____

Labs

- ❑ HCG Qualitative, Urine prior to administration of casirivimab/imdevimab or bamlanivimab/etesevimab, if positive contact physician
- ❑ HCG Qualitative, Serum prior to administration of casirivimab/imdevimab or bamlanivimab/etesevimab, if positive contact physician
- ❑ Other: _____

SARS-CoV-2 Specific Monoclonal Antibody DOSING

Pharmacy to dispense casirivimab/imdevimab for patients in Arizona and California per P & T Protocol.
Pharmacy can interchange between casirivimab and imdevimab or bamlanivimab and etesevimab per P & T Protocol based on availability for facilities outside of Arizona or California **only.**

casirivimab 600 mg and imdevimab 600 mg added to 100 mL 0.9% NaCl IV Infusion Once, Infuse over 22 minutes use 0.2/0.22 micron in-line filter

or

bamlanivimab 700 mg and etesevimab 1400 mg added to 100 mL 0.9% NaCl IV Infusion Once, Infuse over 31 minutes, use 0.2/0.22 micron in-line filter

MONITORING

1. Obtain vital signs prior to casirivimab/imdevimab or bamlanivimab/etesevimab administration
2. Monitor vital signs every 15 minutes during infusion and every 30 minutes thereafter
3. Clinically monitor patients during infusion and for at least 1 hour after infusion completes
4. If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration and initiate appropriate medications and/or supportive therapy (see ADVERSE REACTIONS below)

ADVERSE REACTIONS

MINOR REACTIONS (e.g. nausea, itching, joint pain, rash)	**SEVERE REACTIONS** (e.g. bronchospasm, loss of airway, fainting, severe flushing)
STOP infusion	**CALL A CODE OR RAPID RESPONSE**
diphenhydrAMINE 50 mg IV Push Once	**STOP** infusion
famotidine 20 mg IV Push Once	EPINEPHrine 0.3 mg/0.3 mL SubCutaneous Once
dexaMETHasone 10 mg IV Push Once	Oxygen PRN
Notify Physician	Notify Physician

Physician signature Date / Time

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(06/2021)