BAMLANIVIMAB/ETESEVIMAB and REGENERON INFORMATION FOR

DELTA HEALTH PROVIDERS

What are Bamlanivimab/Etesevimab and Regeneron?

Bamlanivimab and Etesevimab are neutralizing human IgG-1 monoclonal antibodies to the SARS-CoV-2 spike protein which binds and blocks spike protein interaction with human ACE2 receptor thus preventing cellular entry of virus.

Regeneron is a combination of 2 monoclonal antibodies (Casirivimab and Imdevimab) which act by a similar mechanism.

Evidence for Effectiveness and Safety Data

The EUA for Bamlanivimab plus Etesevimab for the treatment of outpatients with mild to moderate COVID-19 who are at high risk of progressing to severe COVID-19 and/or hospitalization is based on data from several studies, including the Blocking Viral Attachment and Cell Entry with SARS-CoV-2 Neutralizing Antibodies BLAZE-1 and BLAZE-4 trials. In particular, the supporting data is from BLAZE-1, a Phase 3 trial that included more than 1,000 randomized high-risk participants with almost 50 primary outcome clinical events (i.e. hospitalization or death). The number of clinical events reported for this study supporting the EUA for Bamlanivimab plus Etesevimab is greater than that currently reported for Phase 2 studies of Bamlanivimab monotherapy or the Casirivimab plus Imdevimab combination. Futhermore, the clinical events reported in the Bamlanivimab monotherapy and the Casirivimab plus Imdevimab studies included emergency department visits, as well as hospitalizations and deaths. Based on the larger sample size and greater number of clinical events in the BLAZE-1 Phase 3 trial, the Panel has greater confidence in the currently available evidence for the clinical efficacy of the Bamlanivimab plus Etesevimab combination than in the evidence for the other monoclonal antibody options. For this reason when available, Bamlanivimab plus Etesevimab should be used for high-risk outpatients according to the EUA.

The data for Regeneron has not yet been published, but it has an ongoing phase 3 trial and early data suggests similar benefit in reduced viral load and need for hospitalization, as well as a similar side effect profile.

Both Bamlanivimab and Regeneron were granted EUA status in November 2020. Bamlanivimab and Etesevimab in combination were granted EUA status in February 2021.

Note: EUA status may be granted to investigational agents that are "possibly effective" and for settings in which no alternatives exist. EUA is not equivalent to FDA-approval and Bamlanivimab/Etesevimab or Regeneron is currently not considered standard of care. Clinical judgment should be exercised when deciding if Bamlanivimab/Etesevimab or Regeneron might be appropriate for a patient.

Dosing and Administration

· Bamlanivimab/Etesevimab: 700 mg of Bamlanivimab and 1400 mg of Etesevimab in combination as IV infusion for one dose given over 1 hour in 200 cc NS, with at least 1 hour observation post-infusion.

Regeneron: 1.2 mg of each antibody in combination as IV infusion over 1 hour in 250 cc NS, with at least 1 hour observation post- infusion.

· No dosage adjustments are indicated for renal or hepatic impairment.

· Note: currently the medication is provided at no cost; however, infusion facility fees may apply.

Criteria for Use

The FDA granted EUAs for Bamlanivimab/Etesevimab and Regeneron for adults and children 12 years and older weighing at least 40 kg with mild-moderate COVID-19 infection who are at high risk for complications, and in whom treatment can be given within 10 days from the date of symptom onset.

Patients whom have had post exposure prophylaxis (high risk for disease progression without vaccination or expected to have adequate response with significant exposure to COVID + person (>12 years, >40 kg) would qualify for treatment.

EUA high-risk criteria:

- BMI ≥ 25
- Pregnancy
- Chronic kidney disease
- Obesity or being overweight (ex. BMI >25kg/m2 or if age 12-17, have BMU > or equal to 85th percentile
- Diabetes mellitus
- Immunosuppressive disease or immunosuppressive treatment
- Age ≥ 65 years *OR*
- Cardiovascular disease (including congenital heart disease) or hypertension
- COPD/other chronic respiratory disease to include moderate to severe asthma, pulmonary hypertension, cystic fibrosis
- Neurodevelopmental disorders or other conditions that confer medical complexity
- Having medical-related technological dependence (tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID)
- Age 12-17 years *WITH* BMI ≥ 85% OR
- Sickle cell disease, Congenital OR Acquired heart disease, Neurodevelopmental disorders, Medical-related technological dependence (ex. tracheostomy)

Bamlanivimab/Etesevimab OR Regeneron are NOT indicated for patients who:

· Are hospitalized due to COVID-19

· Require new oxygen therapy or an increase in baseline oxygen flow rate due to COVID-19 (SpO2 <90%)

Bamlanivimab/Etesevimab OR Regeneron: Important Information for Providers to Tell Their Patients

· These medications are investigational drugs that are available for people with COVID-19 who are early in their course of infection, have mild-moderate symptoms, do not require supplemental oxygen, and are at high risk for developing severe disease.

· These medications are not FDA-approved and are not considered standard of care, but may prevent hospitalization in people who are at high risk for severe disease.

· **In order to receive the infusion, eligible patients must 1) be selected in a statewide random allocation process (i.e. lottery), AND 2) be able to be scheduled at the infusion location. Due to limited drug supply not all patients who are selected in the random allocation process may actually be able to receive the medication. Please set this expectation with patients.**

· These medications are a one-time IV infusion that must be given at a designated infusion. The infusion takes 1 hour, followed by a 1-hour observation period. Patients should anticipate a total appointment time of about 3 hours.

· In preliminary studies, the medication was overall well tolerated and seemed to be safe. The most common side effects were nausea, diarrhea, and dizziness. More serious adverse events are possible, such as severe allergic reaction (e.g. anaphylaxis). Provide FDA fact sheet and review with the patient.

Other Helpful Talking Points With Patients

- This medication may or may not improve the symptoms related to COVID-19. The goal of this medication is to prevent the need for hospitalization or going to the ER.
- If selected, these mediations should be given as soon as possible to be effective. After >10 days from symptom onset, it is unlikely to be beneficial.
- If this is a medication you would like to try, we can attempt to obtain the medication through the statewide random allocation process.
- I will enter you into the state random allocation system and I will let you know if you are selected. If selected, you will be required to schedule the infusion before day 10 of your symptom onset.
- Even if you have been selected, you may not be able to receive the infusion if:
    - o Your oxygen saturation is less than 90% when you arrive for your appointment,
    - o There is no remaining supply,
    - o More than 10 days have passed since your symptoms started.
- Whether or not you are able to get the infusion, you should continue isolation and supportive measures at home – rest, hydrate, etc. and let me know if you have worsening symptoms.
- If you receive the infusion, I would like to schedule a follow-up appointment with you 1-2 weeks afterward to see how you are doing. Please let me know if you experience any adverse events or require hospitalization.

Adverse Event Reporting

- The prescribing health care provider (and/or the provider's designee) is responsible for mandatory reporting of all medication errors and serious adverse events potentially related to Bamlanivimab/Etesevimab OR Regeneron treatment within 7 calendar days from the onset of the event.
- Events may be reported directly to FDA via Medwatch http://www.fda.gov/medwatch/report.htm