Emergency Use Authorized Monoclonal Antibody Infusion (MaB) for Mild/Moderate COVID-19:

Guidance for Referring Duke Clinicians

- **COVID-19 MABs are investigational drugs with Emergency Use Authorization (EUA) from the FDA.**
- **MAB infusions are associated with reduced rates of hospitalization, especially among patients at HIGH RISK of disease progression.**
- **If administered, the medication is free**
  - **Patients may be charged for the actual infusion and monitoring. If the patient is enrolled in a CLINICAL TRIAL, the infusion and monitoring will be covered by the trial.**

More Information Regarding (links do not leave document, use control-click to jump to desired section)**:**

To refer a patient for monoclonal antibody infusion, providers should use:

Ambulatory Referral to COVID Infusion Clinic REF523

REFERRAL WORKFLOW for PATIENTS ELIGIBLE for EUA Monoclonal Antibody Infusion (back to top)

1. Referrals should be considered **for COVID-19 positive patients who meet the clinical criteria** plus they must also:
   - Be within **10 days of symptom onset**
   - **Express interest in an antibody infusion** and/or **the patient is at high risk** for development of severe disease progression or hospitalization
   - **Understand that these are products approved for emergency use**, be interested in learning more about them and potentially receiving them
   - Understand that **referral does not guarantee they will receive an infusion**
     Note: Infusion risks can be found here
2. **Provider** places referral: **Ambulatory Referral to COVID Infusion Clinic, REF523 and**
   - Tells patient they will be contacted within three days (usually sooner).
   - Tells patient they may be offered research studies as well (if they are eligible).
   - Documents discussion in the .LABCOVIDPOSITIVETELEPHONENOTE template.
   - Counsels the patient on steps to take if the symptoms worsen prior to the infusion appointment date.
3. **APP** from Infusion Center reviews the patient's clinical criteria and places a call to the patient
   - If the patient does not meet criteria for the MaB Infusion under the EUA, an In Basket message is sent back to the referring provider
     - The APP ***may*** refer the patient to the COVID Research Team for clinical trials
   - See additional post-referral logistics below
4. **The Infusion Center Referral will be reviewed by the Duke COVID Infusion team who will contact the patient and provide additional screening and education. Whether the patient is scheduled and receives an infusion will depend on this evaluation and the availability of the drugs.**

The job of the referring provider is to make sure the patient meets the criteria, provide the patient with basic information and place the referral. Placing the referral will move the process forward. There is no direct phone number for a provider to call to get additional information. **Do NOT call the clinical research team**. **The Infusion Center APP will refer the patient to the COVID Research team if the patient is appropriate for (and agrees to) evaluation for a clinical trial.**

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POST-REFERRAL LOGISTICS: (back to top)

1. The referral will be reviewed by the Duke COVID Infusion team who will contact the patient and provide additional screening and education, information about research options and decide whether antibody infusion is appropriate.
2. If patient is approved for infusion, the Infusion team will schedule the patient, write the infusion order and provide the patient with the FDA Fact Sheet for Patients/Caregivers.
3. The appointment will be at Duke Health Center at Southpoint, 6301 Herndon Rd, Durham, NC 27713
4. The appointment lasts at least 4 hours and must be scheduled within 10 days of symptom onset.
5. Patients must follow all instructions for infection prevention, including adherence to screening processes, mask-wearing, hand hygiene, social distancing, and remote communication strategies.
6. This requires a peripheral IV placement. The intravenous infusion lasts 60 minutes followed by a 60-minute observation period.
7. The COVID Infusion team will complete all required documentation, notification and follow up required by the FDA including placement of report through the DUHS Safety Reporting System (SRS) for any infusion-related events. Adverse events occurring after infusion clinic visit can be reported similarly if detected by other clinicians.

FDA EMERGENCY USE AUTHORIZATION OF MONOCLONAL ANTIBODIES (back to top)

Multiple monoclonal antibody products have been granted Emergency Use Authorization by the FDA in the ambulatory setting. **Guidelines now recommend use of COVID-19 MABs for high risk adults with mild/moderate COVID-19. Supportive data for combination MABs continue to emerge**. Which product a patient might receive depends on availability of the drugs. Duke patients have access to either bamlanivimab plus etesevimab (Eli Lilly) or casirivimab and imdevimab (Regeneron). See product-specific information below.

CLINICAL CRITERIA FOR MaB INFUSION UNDER THE EUA (back to top)

FDA and Duke Health clinical eligibility criteria for

- EUA bamlanivimab plus etesevimab (Eli Lilly) or
- EUA casiribimab plus imdevimab (Regeneron)

Must meet ALL of the following:

- Weight >= 40 kg,
- Age >=12
- Outpatient
- Lab-confirmed COVID-19 w/mild to moderate symptoms
- Less than 10 days since symptom onset
- Do NOT require an increase in baseline oxygen therapy or require O2 due to COVID
- **High risk for progressing to severe COVID-19 or hospitalization (see right column)**

High Risk for Progressive Disease –

Must have at least one of the following

- Obesity, with Body Mass Index (BMI) >=35
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease
- Currently receiving immunosuppressive treatment
- Aged >=65 years
- Aged >=55 years AND have at least one of the following:
  - Cardiovascular disease OR
  - Hypertension OR
  - COPD/other chronic respiratory disease.
- Aged 12-17 years AND have at least one of the following:
  - BMI ≥85th percentile for their age and gender based on CDC growth charts, 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.

POTENTIAL RISKS of MaB INFUSION (back to top)

- Hypersensitivity including anaphylaxis
- Infusion-related reactions have been observed: fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, dizziness.
- Theoretical risks of blunted long-term immune response to infection which may increase risk of recurrence.
- COVID-19 vaccination should be deferred for 90 days after the infusion.

CLINICAL RESEARCH AND TRIALS (back to top)

Non-HIGH RISK Duke patients interested in these investigational agents should be encouraged to consider existing clinical trials if they are open.

- **Interest in research will be reviewed with the patient by the APP on the COVID Infusion Team.**
- A lay-friendly summary of existing clinical trials is available at dukecovidstudies.org
    - These links can also be provided to the patient in
        - .LABCOVIDPOSITIVETELEPHONENOTE (to document phone conversation after positive test) or
        - .LABCOVIDPOSITIVEINFO (to communicate with patient via MyChart or letter).

You may also refer patients directly to the Pickett Road COVID Research Triage Team by sending a Staff Message to "P COVID Research" and then adding the smartphrase ".COVIDResearch".

COVID RESEARCH STUDY CALL CENTER

Providers or patients may contact myRESEARCHpartners@duke.edu or call 919-681-5698 for general information about open or upcoming COVID clinical trials. A lay-friendly summary of existing clinical trials is available at dukecovidstudies.org.

Please note: The myRESEARCHpartners (MRP) team does not have any additional information about referring patients to obtain the MaB infusion under the EUA. MRP team members are not DUHS employees and are not authorized to dispense clinical advice or make recommendations.

Additional clinical trial information:

Duke providers can review detailed information on existing clinical trials by visiting Adult Infectious Diseases Research (must be onsite on the Duke network or on VPN). The "Attachments" box on the right-hand side provides a link to current information.

PRODUCT-SPECIFIC INFORMATION (back to top)	
Casirivimab and Imdevimab (Regeneron) Casirivimab and imdevimab infusion is a combination of two recombinant human IgG1 monoclonal antibodies that target the receptor binding domain of the spike protein of SARS-CoV-2. It was granted Emergency Use Authorization on 11/21/2020 for treatment of mild to moderate COVID-19 in outpatients. Dose: 2,400mg infusion over 60 minutes (1,200mg casirivimab +1,200mg imdevimab) Duration: Once ***There is a Duke clinical trial available for this product. Learn more here or by emailing the study coordinator at*** ed_research@dm.duke.edu**.**	**Bamlanivimab & Etesevimab (Eli Lilly)** Bamlanivimab and etesevimab is a combination of two monoclonal antibiodies that target spike glycoprotein receptor-binding domains mediating viral entry into host cells. Emergency Use authorization was granted 2/9/2021 for treatment of mild to moderate COVID-19 in outpatients. Dose: 700mg bamlanivimab + 1,400mg etesevimab infusion. Administration time varies 21-60 minutes depending on body weight and volume of infusion. Duration: Once
***Neither casiribimab/indevimab nor bamlanivimab/etesevimab should be used in hospitalized patients with severe COVID-19 disease. Monoclonal antibodies may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 who require high-flow oxygen or mechanical ventilation.**	

References (back to top)

FDA EUA for Bamlanivimab plus etesevimab 2/9/2021. https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-monoclonal-antibodies-treatment-covid-19-0

FDA EUA for Casirivimab and Imdevimab 11/21/20. https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-monoclonal-antibodies-treatment-covid-19

NIH COVID-19 guideline statement on the Emergency Use Authorization of Anti-SARS-CoV-2 Monoclonal Antibodies for the Treatment of COVID-19. 4/8/2021. https://www.covid19treatmentguidelines.nih.gov/statement-on-anti-sars-cov-2-monoclonal-antibodies-eua/