THE SOCIETY FOR POST-ACUTE AND LONG-TERM CARE MEDICINE
amda

Readiness Document for Clinicians for Use of Monoclonal Antibody Infusions for Treatment of COVID-19

Overview

Two investigational SARS-CoV-2 neutralizing antibody treatments, bamlanivimab and casirivimab plus imdevimab are now available through Emergency Use Authorization (EUA) from the FDA for use in eligible outpatients with mild to moderate disease who are at high risk for disease progression and/or hospitalization. Both neutralizing antibodies might reduce the rate of hospitalizations and emergency room visits in high-risk patients defined as age >65 years and underlying illnesses listed below.
https://www.covid19treatmentguidelines.nih.gov/therapeutic-management/

At the present time, due to insufficient data, the National Institute of Health (NIH) COVID-19 Treatment Guidelines Panel (the Panel) does not recommend either for or against the use of neutralizing antibodies (bamlanivimab or casirivimab plus imdevimab), though preliminary data suggests that outpatients may benefit from receiving anti-SARS-CoV-2 monoclonal antibodies early in the course of infection.
https://www.covid19treatmentguidelines.nih.gov/therapeutic-management/

Monoclonal antibody infusions are not a prophylaxis against COVID-19.

EUA approved use:
In patients who are ≥12 years of age and weighing ≥40 kilograms (about 88 pounds), and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

Anti-SARS-CoV-2 antibody-based therapies may have their greatest likelihood of having an effect in the earliest stages of infection, before the host has mounted an effective immune response. The treatment is a single dose, infused therapy that should be administered as soon as possible after COVID-19 symptoms have appeared and a confirmed positive SARS-CoV-2 test result is obtained.

Safety:

Infusion-related reactions have been observed and there is potential for severe reactions, including anaphylaxis. Monoclonal antibody treatment may only be administered in settings in which health care providers have immediate access to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS). Post-acute and long-term care settings with access to such expertise and resources may be able to administer monoclonal antibody in their own facilities.

https://www.fda.gov/media/143603/download

https://www.fda.gov/media/143892/download

Vaccine consideration:

The CDC's Advisory Committee on Immunization Practices has recommended that COVID-19 vaccine should be deferred until 90 days after the administration of monoclonal antibody treatment.
https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2020-12/slides-12-12/COVID-03-Mbaeyi.pdf

MONOCLONAL ANTIBODY ELIGIBILITY CRITERIA CHECKLIST (Page 1 of 2)

Several monoclonal antibodies have received emergency use authorization from the FDA for the treatment of mild to moderate COVID-19 in adults with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

Resident Name: _____ Room: _____ Date: _____

Inclusion Criteria ***(Must Meet All 3 Criteria)***	**Yes**	**No**
Mild to moderately symptomatic COVID-19[1]		
Within 10 days of symptom onset, preferably in the first 3 days		
Positive direct test for SARS-CoV-2 *(either A or B)* A) If no outbreak present in the building, PCR positive B) If outbreak is present in the building, PCR or antigen positive		

High Risk Criteria for Adults ***(Must Have 1 of the Following)***	**Yes**	**No**
Body mass index ≥ 35		
Age ≥ 65		
Chronic kidney disease		
Diabetes		
Immunosuppressive disease or currently receiving immunosuppressive treatment		
≥ 55 years of age AND have: • cardiovascular disease, OR • hypertension, OR • chronic obstructive pulmonary disease/other chronic respiratory disease		

Exclusion Criteria ***(May Not Have Any of the Following)***	**Yes**	**No**
Patient is hospitalized or meets hospitalization criteria[2]		
Patient requires oxygen due to COVID-19 (Pulse ox ≤ 93% on room air)		
If on chronic oxygen, patient requires an increase in oxygen therapy due to COVID-19		
Patient is on hospice, is hospice eligible, had a palliative care/hospice consult within the prior 6 months, or has a life expectancy less than 6 months (clinician judgement or MDS J1400), inclusions of these residents can be decided on a case by case basis		

MONOCLONAL ANTIBODY ELIGIBILITY CRITERIA CHECKLIST (continued)

DEFINITIONS

[1]Mild to Moderate Symptoms (1 or more of the following)	[2]Hospitalization Criteria Definition (1 or more of the following)
• Fever (99.0 or greater) • New cough • Sore throat • Malaise • Headaches • Muscle pain/aches • Gastrointestinal symptoms • Shortness of breath with exertion • Loss of smell and taste	• RR≥30 • HR ≥ 130 • SBP < 90 despite fluid resuscitation

Infusion-related reactions have been observed and there is potential for severe reactions, including anaphylaxis. Monoclonal antibody treatment may only be administered in settings in which health care providers have immediate access to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS). Post-acute and long-term care settings with access to such expertise and resources may be able to administer monoclonal antibody in their own facilities.

Administration of monoclonal antibody treatment requires documentation of:

1. Patient has been given FDA Fact sheet for patients
2. Patient has been informed of alternatives to receiving monoclonal antibody treatment
3. Patient has been informed that this is an unapproved drug that is authorized for use under the FDA Emergency Use Authorization (EUA)
4. Reporting of adverse events to FDA MedWatch, following the requirements under Emergency Use Authorizations (see last page for details)

Fact sheets for patients:

https://www.fda.gov/media/143604/download (bamlavinimab)

https://www.fda.gov/media/143893/download (casirivimab plus imdevimab)

Resources for clinicians:

Further information for healthcare providers including instructions on preparation of infusions and side effects are available in the following factsheets

https://www.fda.gov/media/143603/download (bamlavinimab)

https://www.fda.gov/media/143892/download (casirivimab plus imdevimab)

https://asap.nebraskamed.com/monoclonal-antibody-project/

COVID-19 OUTPATIENT MONOCLONAL ANTIBODY INFUSION ORDERS

- ✓ **Place peripheral IV**

- ✓ **Monoclonal Antibody Infusion Orders**
  - bamlanivimab 700 mg IV over 1 hour once
  - casirivimab – imdevimab 2400 mg IV over 1 hour once

- ✓ **Hypersensitivity Reaction Management**
  - ✓ For ALL Reactions:
    - Provide supplemental oxygen via nasal cannula to keep O2 saturation >94%
    - Obtain vital signs and O2 saturation every 10 minutes
    - Refer to orders below for symptomatic management
    - Contact physician
    - Complete FDA Medwatch Event Report

  - ✓ For fever or chills:
    - acetaminophen 1000 mg PO once

  - ✓ For itching, rash, hives or flushing:
    - diphenhydramine 25 mg IV once
    - famotidine 20 mg IV once
    - If patient desires to complete infusion, decrease monoclonal antibody infusion rate by half
      - Change bamlanivimab infusion rate to 100 mL/hour until bag complete
      - Change casirivimab – imdevimab infusion rate to 125 mL/hour until bag complete

  - ✓ For shortness of breath, wheezing, or chest tightness:
    - Discontinue monoclonal antibody infusion
    - diphenhydramine 50 mg IV once
    - albuterol neb 2.5 mg INH once
    - methylprednisolone 125mg IVP once

  - ✓ For stridor, severe bronchospasm, sensation of throat closure or choking, or SBP <90
    - Discontinue monoclonal antibody infusion
    - Evaluate airway
    - epinephrine 0.3 mg IM once into anterolateral thigh
    - Place patient into recumbent position with lower extremities elevated
    - 0.9% sodium chloride 500 mL IV bolus once
    - Call “Condition” / Call 911

Monitoring for nurses and prescribers

- Patients treated with monoclonal antibody treatment 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.
- Clinically monitor patients, including vital signs during administration and observe patients for at least 1 hour after infusion is complete.
- There is a potential for serious hypersensitivity reaction, including anaphylaxis, with administration of monoclonal antibody treatment. If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration, and initiate appropriate medications and/or supportive care.

Suggested medications to be available in Nursing home infusion site: E-Box for MAb infusions:

Medication	**Number of doses**
epinephrine 0.3 mg IM	
methylprednisolone 125mg	
albuterol neb 2.5 mg INH	
diphenhydramine 50 mg IV	
famotidine 20 mg IV	
Albuterol syr 2 mg PO	
Diphenhydramine 25mg PO	

Additional MANDATORY REQUIREMENTS FOR MONOCLONAL ANTIBODY TREATMENT ADMINISTRATION UNDER EMERGENCY USE AUTHORIZATION:

- The prescribing health care provider and/or the provider's designee are/is responsible for mandatory reporting of all medication errors and serious adverse events* potentially related to **bamlanivimab** treatment within 7 calendar days from the onset of the event. The reports should include unique identifiers and the words "Bamlanivimab treatment under Emergency Use Authorization (EUA)" in the description section of the report.
- Submit adverse event reports to FDA MedWatch using one of the following methods:
  - Complete and submit the report online: www.fda.gov/medwatch/report.htm, or
  - By using a postage-paid Form FDA 3500 (available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf) and returning by mail (MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787), or by fax (1-800-FDA-0178), or
  - Call 1-800-FDA-1088 to request a reporting form
  - Submitted reports should include in the field name, "Describe Event, Problem, or Product Use/Medication Error," the statement "Bamlanivimab treatment under Emergency Use Authorization (EUA)"

*Serious Adverse Events are defined as:

- death;
- a life-threatening adverse event;
- inpatient hospitalization or prolongation of existing hospitalization;
- a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- a congenital anomaly/birth defect;
- a medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly.

- The prescribing health care provider and/or the provider's designee are/is to provide mandatory responses to requests from FDA for information about adverse events and medication errors following receipt of bamlanivimab.

- OTHER REPORTING REQUIREMENTS
  In addition, please provide a copy of all FDA MedWatch forms to:
  Eli Lilly and Company, Global Patient Safety
  Fax: 1-317-277-0853
  E-mail: mailindata_gsmtindy@lilly.com
  Or call Eli Lilly and Company at 1-855-LillyC19 (1-855-545-5921) to report adverse events.

- The prescribing health care provider and/or the provider's designee are/is responsible for mandatory reporting of all medication errors and serious adverse events* potentially related to **casirivimab and imdevimab** treatment within 7 calendar days from the onset of the event. The reports should include unique identifiers and the words "Casirivimab and imdevimab treatment under Emergency Use Authorization (EUA)" in the description section of the report.

- Submit adverse event reports to FDA MedWatch using one of the following methods:
  - Complete and submit the report online: www.fda.gov/medwatch/report.htm, or
  - By using a postage-paid Form FDA 3500 (available at: http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf) and returning by mail (MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787),
  - or by fax (1-800-FDA-0178), or
  - Call 1-800-FDA-1088 to request a reporting form

- Submitted reports should include in the field name, "Describe Event, Problem, or Product Use/Medication Error" a statement "Casirivimab and imdevimab treatment under Emergency Use Authorization (EUA)."

*Serious Adverse Events are defined as:

- death;
- a life-threatening adverse event;
- inpatient hospitalization or prolongation of existing hospitalization;
- a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- a congenital anomaly/birth defect;
- a medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly.

OTHER REPORTING REQUIREMENTS:

In addition, please provide a copy of all FDA MedWatch forms to: Regeneron Pharmaceuticals, Inc Fax: 1-888-876-2736 E-mail: medical.information@regeneron.com or call Regeneron Pharmaceuticals at 1-844-734-6643 to report adverse events.
(https://www.fda.gov/media/143892/download)