What are COVID-19 Monoclonal Antibodies?

COVID-19 monoclonal antibodies (mAbs) are laboratory-made neutralizing antibodies directed against SARS-CoV. Currently available products bind to the virus spike protein to prevent their interaction with human cells. Several mAb products have received FDA emergency use authorization (EUA) for use among ambulatory patients with mild-moderate COVID-19 who are at high risk for developing severe disease. mAbs have been studied alone and in combination and continue to be under active investigation. mAbs that have received EUA are:

- Casirivimab/imdevimab (Regeneron)
- Bamlanivimab/etesevimab (Lilly) – no longer approved/recommended due loss of activity against current SARS-CoV-2 variants in circulation.

Evidence for Efficacy and Safety

Casirivimab/imdevimab (CAS/IMD)

Phase 2 double-blind RCT (Weinreich et al, 2021)

- CAS/IMD vs placebo given to 275 outpatients with symptomatic non-severe COVID-19 within 7 days of symptom onset and 72 hrs of PCR test
- Primary endpoint: decreased overall viral load at 7 days with CAS/IMD vs placebo
- Secondary outcome: decreased need for medical visits at 29 days with CAS/IMD (6/182, 3%) vs placebo (6/93, 6%)
- No overall difference in adverse events between CAS/IMD and placebo; one anaphylactic reaction in a CAS/IMD recipient.

Phase 3 double-blind RCT (Regeneron Press Release)

- CAS/IMD 1200mg (n=736) vs. CAS/IMD 2400mg (n=1355) vs. placebo (n=2089) in outpatients with non-severe COVID-19 and $\geq$ 1 risk factor (included obesity [58%], age ≥ 50 years [51%], and cardiovascular disease [36%]).
- CAS/IMD met primary endpoint which identified a 70% (1200mg) and 71% (2400mg) lower risk of death or hospitalization vs. placebo ($p < 0.01$).
- CAS/IMD met secondary endpoints, including mean symptom duration reduction of 4 days for both doses (10 vs. 14 days, $p < 0.0001$).
- Overall, no new safety signals and both doses well-tolerated. Serious adverse events were encountered in 1.1%, 1.3%, and 4% among 1200mg, 2400mg, and placebo recipients, respectively.

Notes:

- NIH COVID-19 Treatment Guidelines recommend CAS/IMD for treatment of for patients meeting EUA criteria, based on phase 3 clinical trial data (unpublished) demonstrating decreased incidence of hospitalization or death (class AIIa recommendation).
- mAbs are available by Emergency Use Authorization but are not FDA-approved products; clinical judgment and shared, informed decision-making should be exercised when considering use for individual patients
- ***CAS/IMD is the preferred mAb product at UCHealth due to its retained activity with current circulating variants***
- mAbs may be considered for patients who meet the high-risk criteria but are hospitalized for another reason (i.e., not hospitalized due to COVID-19); at AMC send inpatient requests via secure chat to “AMC Stewardship” group.
- Patients who receive passive antibody therapy (mAbs or convalescent plasma) are recommended to defer

Criteria for mAb Use

COVID-19 mAbs can be given under EUA to adults and pediatric patients (≥12 years and weighing ≥ 40kg with mild-moderate COVID-19, who are at high risk for progression to severe disease, and in whom treatment can be given within 10 days of symptom onset.

FDA EUA high-risk criteria (updated 5/14/21):

- Older age (age ≥ 65 years)
- Obesity or overweight (BMI ≥ 25 kg/m^2, or BMI ≥85th percentile if age 12-17 years)
- Pregnancy
- Chronic kidney disease
- Diabetes mellitus
- Immunosuppressive disease or treatment, including HIV infection
- Cardiovascular disease (including congenital heart disease and cerebrovascular disease) or hypertension
- Chronic lung disease (e.g.,COPD, asthma, interstitial lung disease, cystic fibrosis, pulmonary hypertension, or current/former smoker)
- Sickle cell disease
- Neurodevelopmental disorders including cerebral palsy or genetic, metabolic syndromes or severe congenital abnormalities
- Medical-related technological dependence (e.g., tracheostomy, gastrostomy, or positive pressure ventilation)
- Other medical conditions or factors placing an individual patient at high risk for progression to severe disease (e.g., race or ethinicity, people with disabilities, substance use disorder, others)

Monoclonal antibodies 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

Dosing and Administration

CAS/IMD: 600/600 mg IV x 1 dose **(Preferred due to no change in neutralization against current SARS-CoV-2 variants)**

- Provider Fact Sheet: https://www.regeneron.com/downloads/treatment-covid19-eua-fact-sheet-for-hcp.pdf
- Patient/Caregiver Information:
  - English: https://www.regeneron.com/sites/default/files/treatment-covid19-eua-fact-sheet-for-patient.pdf
  - Spanish: https://www.regeneron.com/sites/default/files/treatment-covid19-eua-fact-sheet-for-patient-spanish.pdf

- Following infusion, patients must remain at infusion site for 1 hour observation. Anticipated total appointment time is about 3 hours.
- No dosage adjustments are needed for kidney or liver impairment.
- Currently the medication is provided at no cost; however, infusion facility fees may apply.

How to Order: Provider Instructions

- The CDPHE COVID-19 Monoclonal Antibody Connector Tool can be used to guide providers through the process of determining patient eligibility and locating infusion sites.
- After an informed discussion with the patient, including review of the FDA EUA fact sheets for Providers and for Patients, Parents, and Caregivers, follow the steps below to obtain the medication for the patient:

1. Enter patient information into the Colorado Monoclonal Antibody Connector Tool: https://redcap.link/COVIDMedsAllocationTool
   - ➢ After completing the form you will be immediately notified if your patient is eligible to receive mAb treatment.
2. Select the preferred infusion site within the online form. For a map of active infusion sites in Colorado: https://www.google.com/maps/d/viewer?mid=1d8OtoixYFITgAvku_671LGMZsQbnnDED&usp=sharing
3. Send a medication order to the selected infusion site via the standard IV infusion order process for that site.
   - ➢ Each facility may have different policies regarding accepting medication orders from providers outside the healthcare system, infusing pediatric patients, etc. Please contact facilities directly to confirm details.
   - ➢ UCHealth *Epic* users: Enter a Therapy Plan for "COVID OUTPATIENT MONOCLONAL INFUSION OIC"; see instructions **(Page 4)**
   - ➢ Providers outside of UCHealth or who do not use *Epic* may send infusion orders using the Order Form, faxed to the appropriate location
4. After receiving the medication order, the infusion site will contact the patient directly to schedule the infusion, and provide the patient with instructions for their appointment.
5. Provide the patient with the UCHealth COVID-19 Monoclonal Antibody Patient Instruction sheet

UCHealth COVID-19 Monoclonal Antibody Infusion Sites

Broomfield Hospital

1820 Destination Dr, Broomfield, CO 80021

Phone: (719) 444-2273

Email: infusionAMC@uchealth.org

Note: Broomfield Hospital infusion center can only accept medication orders from providers credentialed with UCHealth

Memorial Central Outpatient Infusion

1400 E Boulder St Suite 1370, Colorado Springs, CO 80909

Phone: (719) 365-5650

Fax: (719) 365-6274

Email: infusionMHC@uchealth.org

Poudre Valley Hospital COVID Infusion Clinic

1024 S Lemay Ave 1st floor, Fort Collins, CO 80524

Phone: (970) 495-8388

Fax: (970) 495-7627

Email: infusionPVH@uchealth.org

Yampa Valley Medical Center

1024 Central Park Drive, Steamboat Springs, CO 80487

Phone: (970)-870-1040

Fax: (970)-871-2315

Email: uchealthyvmc-pharmacy@uchealth.org

Important Information To Discuss With Patients

- When given early in the course of infection, COVID-19 monoclonal antibodies may improve symptoms and prevent the need for hospitalization in patients who are at high-risk for developing severe disease.
- In preliminary studies, these medications were overall well-tolerated and seemed to be safe. The most common side effects were nausea, diarrhea, and dizziness. More serious adverse events are possible (e.g. anaphylaxis).
- Patients may not be able to receive the infusion if, by the time of their appointment:
    - They are hypoxic and require supplemental oxygen, and/or otherwise hemodynamically unstable,
    - There is no remaining supply,
    - More than 10 days have passed their symptoms started.
- Whether or not patients receive the infusion, they should continue isolation procedures and supportive measures at home, and report any new or worsening symptoms.
- COVID-19 vaccination should be deferred for 90 days after mAb infusion, to avoid potential interference of mAbs with the vaccine-induced immune response.

Adverse Event Reporting

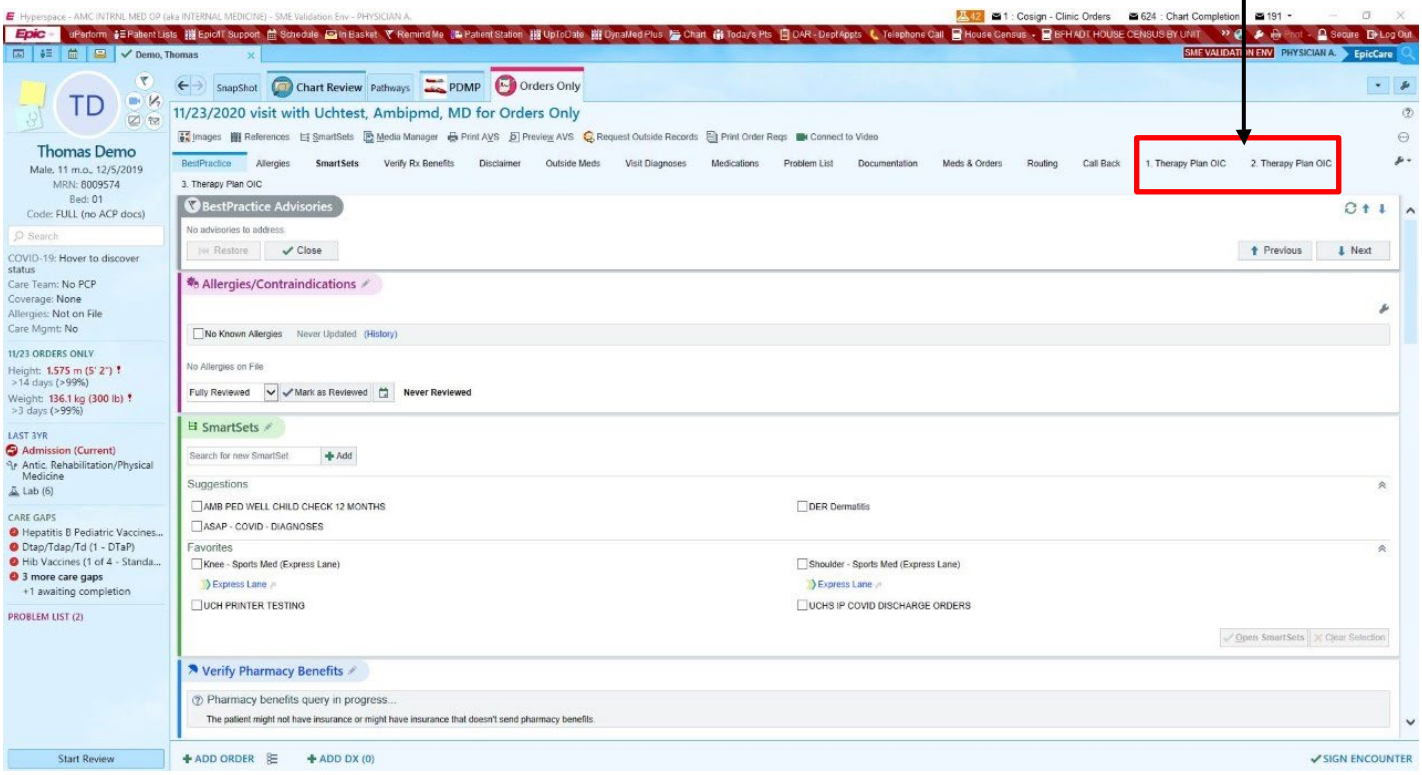
- The prescribing health care provider (and/or the provider's designee) is responsible for mandatory reporting of all medication errors and serious adverse events potentially related to mAb treatment within 7 days from the onset of the event.
- Events may be reported via RL Solutions (within UCHealth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

FAQs

- **If my patient cannot be scheduled at their preferred infusion site, can they try to be scheduled at another infusion site?** Yes, they can contact another infusion site and inquire about availability.
- **Are pregnant patients eligible?** Yes, however, pregnant patients were excluded from clinical trials, so there are currently no data on safety or efficacy in this population. Potential risks and benefits should be discussed with individual patients.
- **Can patients who are hospitalized for another reason but who tested positive for COVID-19 get a monoclonal antibody**? Yes, mAbs may be considered for patients who meet the EUA criteria but who are hospitalized for another reason (i.e., are not hospitalized due to COVID-19); however, policies for inpatient mAb infusions may vary by site.

Epic Therapy Plan Infusion Order Instructions

1. Within the patient visit, select Therapy Plan in header (see screen shot below)
2. Search “COVID OUTPATIENT MONOCLONAL INFUSION OIC”
3. Associate with correct diagnosis
4. Plan start date is today
5. Select corresponding treatment department
    a. North Region: PVH Infusion OP
    b. South Region: MHC Infusion OP
    c. Denver Metro Region: BFH Infusion Unit
6. Select Assign Plan
7. Do not uncheck any orders or change timing
8. Dosing is defaulted, please answer order questions accordingly
9. Accept and Sign-Plan



uchealth

Patient Name: _____
MRN: _____
Date of Birth: _____

COVID-19 OUPATIENT MONOCLONAL INFUSION ORDERS

Note: This order should only be placed after patient has been entered into the CDPHE random allocation system and has been selected for treatment.

Start Date: _____ Weight: _____kg Height: _____cm

Allergies: _____

Provider Communication:

GUIDELINES FOR PRESCRIBING:

1. Send FACE SHEET, copy of insurance card, and H&P or most recent provider progress note.
2. Ensure that patient meets **ALL** EUA criteria – check boxes below:

   - ☐ Positive SARS-CoV-2 viral test Date of positive test:_____
   - ☐ Within 10 days of symptom onset Date of symptom onset:_____
   - ☐ Not requiring supplemental oxygen due to COVID-19 (if on oxygen at baseline, no increase in oxygen flow rate due to COVID-19)
   - ☐ Weight at least 40 kg

3. Use is authorized for adults and children 12 years and older weighing at least 40kg with mild-moderate COVID-19 infection who are at high-risk for complications. High risk is defined as patients who meet AT LEAST ONE of the following criteria:

   - ☐ BMI ≥ 25 kg/m^2
   - ☐ Age ≥ 65 years
   - ☐ Pregnancy
   - ☐ Chronic kidney disease
   - ☐ Diabetes mellitus
   - ☐ Immunocompromised disease or treatment, including HIV infection and active substance use disorder
   - ☐ Cardiovascular disease including hypertension, stroke, or cerebrovascular disease
   - ☐ Chronic lung disease including COPD, asthma, interstitial lung disease, cystic fibrosis, pulmonary hypertension, or current/former smoker
   - ☐ Neurodevelopmental disorders including cerebral palsy or genetic, metabolic syndromes or severe congenital abnormalities
   - ☐ Medical-related technological dependence (tracheostomy, gastrostomy, or positive pressure ventilation)
   - ☐ Racial or Ethnic Minority
   - ☐ Person with disabilities

MEDICATION ORDER:

Please select a single monoclonal antibody product, casirivimab + imdevimab.

☐ Casirivimab 600 mg / Imdevimab 600 mg in sodium chloride 0.9% intravenous, 50 mL, ONCE over 20 minutes

NURSING ORDERS:

1. Place peripheral IV or access existing indwelling venous access. Discontinue peripheral IV or de-access indwelling venous access at conclusion of the visit. If applicable, perform central line care per Hospital Policy and Procedure. If needed for sequential visits, may leave peripheral IV in place; change site every 72-96 hours. Staff may use appropriate Flush SmartSet to add medications.
2. Perform the following: Pulse Oximetry on Room Air, Vital signs prior to infusion, at end of infusion and at end of observation period prior to discharge.
3. After infusion is complete flush the infusion line to ensure delivery of the required dose.
4. Clinically monitor patients during infusion and observe patients for at least 1 hour after infusion is complete. If infusion related reaction occurs, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care.

HYPERSENSITIVITY MEDICATIONS:

1. Infusion center staff may utilize the site-specific hypersensitivity/anaphylaxis protocol in the event of a hypersensitivity reaction.

By signing below, I affirm the following:

☐ I have read the FDA fact sheet at the following link for healthcare providers:
- Casirivimab/imdevimab - https://www.regeneron.com/sites/default/files/treatment-covid19-eua-fact-sheet-for-hcp.pdf

☐ The patient is aware of the risks/benefits of EUA and agrees to treatment.

☐ The patient has/will be provided a copy of the FDA patient and family member fact sheet.
Casirivimab/imdevimab
- English Patient/Caregiver Information - https://www.regeneron.com/sites/default/files/treatment-covid19-eua-fact-sheet-for-patient.pdf
- Spanish Patient/Caregiver Information - https://www.regeneron.com/sites/default/files/treatment-covid19-eua-fact-sheet-for-patient-spanish.pdf

☐ I acknowledge that any adverse event (AE) or death following initiation of treatment must be immediately reported pursuant to FDA requirements. UCHealth sites will use RL solutions to report AEs.

☐ I acknowledge that the facility will attempt to fulfill the requested product as ordered; however, if the prescribed monoclonal antibody product is unavailable the alternative agent will be substituted as supplies dictate.

Provider Signature:_____ Date/Time:_____

Provider Name (Print):_____ Phone: _____ Fax: _____