COVID-19 Monoclonal Antibodies – UCHealth Provider Information

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) *currently preferred mAb due to available stock and activity against all variants*
- Bamlanivimab/etesevimab (Lilly)
- Sotrovimab (GSK)

Evidence for Efficacy and Safety

Casirivimab/imdevimab (CAS/IMD)

COVID-19 Treatment

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.

Post-exposure Prophylaxis

Phase 3, double-blind RCT (medRxiv Preprint)

- Subcutaneous CAS/IMD 1200mg (n=753) vs. placebo (n=752) in seronegative outpatients with household contact diagnosed with SARS-COV-2.
- CAS/IMD met primary endpoint, significantly reducing symptomatic SARS-CoV-2 infection compared to placebo (1.5% vs. 7.8%, respectively; P<0.0001).
- Median time to resolution of symptoms was 2 weeks shorted with CAS/IMD compared to placebo (1.2 vs. 3.2 weeks, 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 only mAb product offered 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 COVID-19 vaccination for 90 days, to avoid potential interference with vaccine-induced immune response.

Criteria for mAb Use

Covid-19 Treatment

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 ethnicity, 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

(NEW)

The current COVID-19 Delta variant surge has dramatically increased demand for COVID-19 mAb therapy across all regions. UCHealth is rapidly expanding infusion access, but mAbs remain a limited resource currently. Accordingly, priority for mAbs will be given to patient groups at the highest risk of hospitalization or death. These are:

- Age 65 or older
- Immunocompromised patients* (see criteria below))
- 3 or more primary risk factors for severe COVID-#

Lower risk groups who qualify for mAb based on the emergency use authorization (EUA) criteria will be accommodated as space allows. If you are unsure whether your patient qualifies as a high risk patient and they potentially would benefit from mAb therapy, please route your patient to the Virtual Health Center for eligibility screening and prioritization using the process found beginning with **page 11**.

*Immunocompromised patients are defined as:

- Hematologic malignancy
- Solid malignancy on chemotherapy
- Solid organ transplant
- Advanced HIV (CD4 count < 200)
- Immune deficiencies
- Condition requiring treatment with immunosuppressive agents:
- Maintenance prednisone >0.5mg/kg or equivalent (≥ 40mg/day prednisone or equivalent in patients 70kg and above)
- Thymoglobulin in last 6 months
- Alemtuzumab in last year
- Rituximab in last 6 months
- TNF-α inhibitor in last 3 months (e.g. infliximab, etanercept, golimumab, adalimumab, certolizumab)
- Calcineurin inhibitors (tacrolimus and cyclosporine – excludes topical/ophthalmic administration routes)

- mTOR-inhibitors (everolimus, sirolimus – excludes topical routes)
- Mycophenolate, azathioprine, cyclophosphamide in the last 1 month
- Belatacept in past 2 months
- Eculizumab in last 6 months

#Primary risk factors for COVID-19 progression

- *Age >50 years*
- *Obesity, defined as body mass index >30*
- *Cardiovascular disease, including hypertension*
- *Chronic lung disease, including asthma*
- *Chronic metabolic disease, including diabetes*
- *Chronic kidney disease, including those on dialysis*
- *Chronic liver disease*

***Post Exposure Prophylaxis* (NEW)**

CAS/IMD may be given as **Post-exposure prophylaxis** for individuals who are:

- High risk for progression to severe disease (see criteria above)
- Not fully vaccinated **or** who are not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination (e.g., people with immunocompromising conditions/those taking immunosuppressive medications), **AND**
    - Have been exposed to an individual infected with SARS-CoV-2 consistent with close contact criteria per Centers for Disease Control and Prevention (CDC), **OR**
    - Who are at high risk of exposure to an individual infected with SARS-CoV-2 because of occurrence of SARS-CoV-2 infection in other individuals in the same institutional setting (for example, nursing homes or prisons)

The CDC defines close contact as someone who has been within six feet of an infected person (laboratory-confirmed or a clinically compatible illness) for a cumulative total of 15 minutes or more over a 24-hour period.

*UCHealth is aware of this indication. Our priority currently is to offer this therapy to patients with known COVID-19 infections. Options for expanding access are being investigated.

CAS/IMD is NOT authorized for pre-exposure prophylaxis.

Dosing and Administration

CAS/IMD: 600/600 mg IV x 1 dose

- 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

- 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. Send a medication order via the standard IV infusion order process as follows:
        - UCHealth *Epic* users: Enter a Therapy Plan for "COVID OUTPATIENT MONOCLONAL INFUSION OIC"; see instructions **(Page 10)**
        - Due to the high demand for mAb infusions and limited capacity at all UCHealth infusion sites, UCHealth is not able to offer infusion to external referring providers at this time. We will reevaluate this position as the demand lessens.
    2. Provide the patient with the UCHealth COVID-19 Monoclonal Antibody Patient Instruction sheet
    3. After receiving the medication order or referral, the VHC will contact the patient directly to determine the patients risk category and that the patient still meets criteria. If so, the patient will be scheduled at an available infusion site. The patient will be provided with instructions for their appointment.

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

- **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 preferred treatment department
    a. North Region: PVH Infusion OP
    b. South Region: MHC Infusion OP
    c. Denver Metro Region:
        i. BFH Infusion Unit
        ii. LTN Infusion Unit
        iii. AMC OIC (will be available based on resource availability)
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

NOTE: UCHealth-credentialed physicians and advanced practice providers may access the full version of this document, including a screenshot on the Source website by logging in**:**

- **Affiliates (Sydney, Steamboat, Stride, Estes Park) and Community Connect** – Sign in with your Epic username followed by @uchealth.org, no space between your Epic username and @uchealth.org. (EpicUserName@uchealth.org)
- **Non-employed contracted providers at UCHealth community hospitals (PVH, MCR, etc.)** – Sign in with your UCHealth email address (FirstName.LastName@uchealth.org) and your Epic password.
- **CU and Children’s** – Sign in with your UCD or Children’s email and password. If you’re still unable to sign in, please contact the UCHealth IT help desk at 720-848-4000.