

Outpatient Prevention:

PATIENT DISPOSITION	•RECOMMENDATION
Outpatient, post-exposure prophylaxis	<ul style="list-style-type: none"> •COVID-19 monoclonal antibodies (mAb) are recommended for high-risk, patients who are not fully vaccinated or who are not expected to mount an adequate immune response to complete vaccination and have been exposed to an individual infected with SARS-CoV-2, or who are at high risk of exposure because of occurrence of infection in the same institutional setting.

Outpatient Treatment:

PATIENT DISPOSITION	•RECOMMENDATION
Outpatient, not requiring hospitalization or supplemental oxygen	<ul style="list-style-type: none"> •COVID-19 monoclonal antibodies (mAb) are recommended for high-risk, symptomatic patients within 10 days of symptom onset.
Discharged from hospital, not requiring supplemental oxygen	<ul style="list-style-type: none"> •No specific antiviral or immunomodulatory therapy recommended.
Discharged from hospital, requiring supplemental oxygen <i>(for those stable enough for discharge but still requiring oxygen)</i>	<ul style="list-style-type: none"> •Consider continuing dexamethasone for the duration of supplemental oxygen requirement, up to 10 days total dexamethasone duration, with close monitoring for adverse events.
Discharged from ED or urgent care, despite new oxygen requirement <i>(when hospital resources are limited, inpatient admission is not possible, and close follow-up is ensured)</i>	<ul style="list-style-type: none"> •Dexamethasone 6 mg PO daily for the duration of supplemental oxygen need, up to 10 days maximum, with close monitoring for adverse events.

Inpatient Treatment:

DISEASE SEVERITY	•RECOMMENDATION
Hospitalized, not requiring supplemental oxygen	<ul style="list-style-type: none"> •No specific antiviral or immunomodulatory therapy recommended. •Consider passive antibody treatment with mAb (if meets EUA criteria) or convalescent plasma in patients who are known or suspected to have poor intrinsic humoral immunity.
Hospitalized, requiring low-flow supplemental oxygen	<ul style="list-style-type: none"> •Use: Remdesivir plus Dexamethasone
Hospitalized, requiring oxygen via high-flow device or noninvasive ventilation	<ul style="list-style-type: none"> •Use: Dexamethasone •Consider: Remdesivir in patients who are early in their disease course (<10 days of symptom onset); otherwise low likelihood of benefit at this disease severity. •Consider: Baricitinib, in combo with dexamethasone, for recently hospitalized patients with rapidly increasing oxygen needs and systemic inflammation. Tocilizumab may be considered if baricitinib is contraindicated. Consider assessing response to steroids before deciding whether tocilizumab is needed.
Hospitalized, requiring invasive mechanical ventilation or ECMO	<ul style="list-style-type: none"> •For most patients, use: Dexamethasone •For patients who are within 24hrs of ICU admission and mechanical ventilation, consider: Tocilizumab, in combination with dexamethasone.

**Tocilizumab is presently in extreme short supply. Baricitinib will be the preferred add-on immunomodulatory agent for patients with severe COVID-19 with inadequate response to dexamethasone. Available tocilizumab supply is reserved for those mechanically ventilated at baseline (within 24 hours of intubation) and those with severe disease and baricitinib contraindication

COVID-19 Therapies at UHealth: Indications, Drug Information, Ordering Information

Monoclonal Antibodies

COVID-19 monoclonal antibodies (mAbs) are laboratory-derived neutralizing antibodies against the SARS-CoV-2 spike protein. mAbs are used primarily for outpatient treatment or post-exposure prophylaxis, with potential for inpatient use in select cases. Given early, mAbs can shorten duration of symptoms and prevent hospitalization. mAbs are available under Emergency Use Authorization (EUA) for COVID-19 treatment and post-exposure prophylaxis.

Treatment Criteria (for age ≥ 12 years, weight ≥ 40 kg):

1. Confirmed COVID-19 (by PCR or antigen test)
2. Mild-moderate (symptomatic) disease
3. Duration of symptoms ≤ 10 days
4. High risk for progression to severe disease (see EUA high-risk criteria below)

Treatment Exclusions:

- Hospitalization due to COVID-19
- New oxygen requirement or increase in oxygen flow rate from baseline (SpO₂ <90%)

Post-exposure Prophylaxis Criteria* (for age ≥ 12 years, weight ≥ 40 kg):

1. High risk for progression to severe disease (see EUA high-risk criteria below)
2. Not fully vaccinated or not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination (e.g., individuals with immunocompromising conditions including immunocompromising medications) AND one of the following:
 - a. Exposure to an individual infected with SARS-CoV-2 (within 6 feet for a total of 15 minutes or more, providing care to someone who is sick, direct physical contact, sharing utensils, or exposure to respiratory droplets)
 - b. High risk of exposure to an individual infected with SARS-CoV-2 because of occurrence of infection in other individuals in the same institutional setting (e.g. nursing homes, prisons).

*UHealth 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.

FDA EUA Criteria for high risk of progression to severe disease (Updated 5/14/21)

- Older age (age ≥ 65 years)
- Obesity or overweight (BMI ≥ 25 kg/m², or BMI $\geq 85^{\text{th}}$ 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)

Available mAbs:

1. **Casirivimab/Imdevimab** (REG-COV-2; Regeneron mAb combination). This is the preferred agent at UHealth. Retains activity against currently circulating variants including alpha, beta, gamma, and delta.
2. No longer recommended: Bamlanivimab monotherapy and bamlanivimab/etesevimab combination, due to loss of activity against some SARS-CoV-2 variants.

3. Sotrovimab: Active against currently circulating variants but not available at UCHHealth presently.

Ordering: see attached pages for outpatient ordering instructions

Notes:

- Select **inpatients** may be considered for mAbs who meet the above criteria and:
 - Are hospitalized for another reason (i.e., are not hospitalized due to COVID-19)
 - Are known to be seronegative or postulated to have impaired humoral immune response
 - *At AMC please send inpatient requests via secure chat to “AMC Antimicrobial 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.

Remdesivir (Veklury; RDV):

Remdesivir is FDA-approved for the treatment of COVID-19 requiring hospitalization in adults and pediatrics (≥ 12 years and weighing ≥ 40 kg).

Criteria for use:

1. Confirmed COVID-19 by SARS-CoV-2 PCR
2. Symptom duration ≤ 14 days (longer duration considered if transplant recipient or other severely immunocompromised host)
3. Hypoxia requiring supplemental O₂
 - Patients requiring high-flow oxygen, non-invasive ventilation, invasive mechanical ventilation, and/or ECMO at baseline are unlikely to benefit from RDV based on current evidence.
 - May continued RDV if patients progress to mechanical ventilation or ECMO.
4. ALT $< 10x$ ULN

Dose: 200 mg on day 1, then 100 mg on days 2-5

Duration: 5 days or until hospital discharge (whichever is sooner)

Ordering and monitoring:

- Monitor LFTs daily. Consider discontinuation if ALT $> 10x$ ULN.
- Renal impairment (including CrCl < 30 mL/min and renal replacement therapy (e.g. CRRT, iHD, PD)) is not a contraindication to RDV. The RDV package insert recommends against use among patients with CrCl < 30 mL/min due to the potential for cyclodextrin and RDV accumulation leading to worsening renal failure. However, given the small amount of cyclodextrin in RDV and short duration of exposure, adverse events are unlikely, and no increased risk of serious or non-serious safety events (including renal or hepatotoxicity) have been observed in several retrospective studies.

Approval

- At UCHHealth AMC, RDV is a tier-2 protected antimicrobial (i.e., order is approved by verifying pharmacist if criteria above are met).
- Requests not meeting the above criteria can be made via the Antimicrobial Stewardship secure chat group to “AMC Antimicrobial Stewardship.”

Dexamethasone

Dexamethasone is indicated in patients requiring supplemental O₂ for COVID-19, including mechanical ventilation or ECMO. It is NOT recommended in those not requiring supplemental O₂.

Dose: 6 mg IV or PO per day

Duration: 10 days, or until hospital discharge. If patient requires a brief hospitalization and still requiring increased oxygen support, consider discharging to complete a 5-7 days course. Alternative glucocorticoids can be considered if dexamethasone is unavailable:

- Prednisone 40 mg per day
- Methylprednisolone 32 mg per day (once daily or 2 divided doses)
- Hydrocortisone 160 mg per day (2-4 divided doses)

Note: Recommend consultation with OB/GYN regarding the use of steroids in pregnant patients.

Tocilizumab (Actemra)

Tocilizumab is an IL-6 receptor antagonist used for treatment of rheumatoid arthritis and cytokine-release syndrome associated with CAR-T cell therapy. It had prior mixed results for COVID-19 treatment, but two recent trials (REMAP-CAP, RECOVERY) suggest a mortality benefit when used **with corticosteroids** in a select population of hospitalized patients who are exhibiting rapid respiratory decompensation. Consider as an adjunct therapy to steroids for patients who are recently admitted (hospitalization <3 days) and are:

- Newly admitted to the ICU (within 24hr) with high O₂ need (HFNC FiO₂ >0.4/flow rate 30L/min, NIV, MV)
- Not yet admitted to ICU but with rapidly increasing O₂ need requiring HFNC or NIV, AND have significantly elevated inflammatory markers (CRP ≥ 75 mg/L)

Other considerations:

- Consider assessing response to corticosteroids (e.g. 48 hrs) prior to deciding whether tocilizumab is needed
- Tocilizumab has not been shown to have benefit in patients already requiring mechanical ventilation (unless newly intubated <24 hrs)
- Tocilizumab should be AVOIDED in:
 - Severely immunocompromised hosts
 - Suspected or confirmed other concurrent infection
 - AST/ALT >5x ULN
 - ANC <500, platelets <50K
 - High risk for GI perforation
 - Pregnancy: weigh risk vs potential benefit
- Monitor for development of new, or re-activation of latent, infections
- Consider screening for latent infections depending on risk factors (e.g. TB, strongyloides, others)
- Consider prophylactic treatment with ivermectin in patients from strongyloides-endemic areas
- Monitor following tocilizumab administration: neutrophils, platelets, LFTs

Dosing: 8mg/kg x 1 dose, rounded as below. Unclear benefit of additional doses.

- 40 kg to 65 kg = 400mg using IV formulation → 324mg if using the SQ syringe for compounding
- 66 kg to 90 kg = 600mg using IV formulation → 648mg if using the SQ syringe for compounding
- > 90kg = 800mg using IV formulation → 810mg if using the SQ syringe for compounding

Baricitinib (Olmiant)

Baricitinib is an oral Janus kinase (JAK) inhibitor that is used for rheumatoid arthritis treatment (non-formulary at UCH). Some data has shown improved time to recovery when given with RDV in patients requiring supplemental O₂ (ACTT-2, Dec 2020), and lower 28-day all-cause mortality when given with either dexamethasone or dexamethasone + RDV in patients requiring supplemental oxygen or high-flow/NIV (excluded baseline mechanical ventilation). The benefit of baricitinib in this trial was most pronounced among those requiring HFNC/NIV at baseline. (COV-BARRIER, May 2021 pre-print).

Based on this, NIH Guideline recommends that for hospitalized patients on high-flow oxygen or NIV who have evidence of clinical progression or increased markers of inflammation, may use either Baricitinib OR tocilizumab plus dexamethasone alone, or Baricitinib OR tocilizumab plus dexamethasone + remdesivir

Indication:

At UCH, baricitinib will be the preferred add-on treatment to dexamethasone for patients with COVID-19 who are:

- Hospitalized < 72 hours
- Experience worsening respiratory function despite dexamethasone who require HFNC or NIV
- Persistently elevated/increasing C-reactive protein

Dosing:

- 4mg once daily x 14 days (may discontinue use sooner than 14 days if patient otherwise recovered and discharging from hospital – do not continue after hospital discharge)
- eGFR:
 - ≥ 60 mL/min/1.73m² = 4mg once daily
 - 30-59 mL/min/1.73m² = 2mg once daily
 - 15-29 mL/min/1.73m² = 1mg daily or 2mg q48h
 - < 15 mL/min/1.73m² = hold and resume dosing once eGFR > 15 mL/min/1.73m²
- ALC < 200: hold dose, can resume once ALC > 200
- ANC < 500: hold dose, can resume once ANC > 500
- Increase in AST or ALT to >5-10x ULN concerning for DILI: hold dose until diagnosis of DILI is excluded

Other considerations:

- Consider assessing response to corticosteroids (e.g. 48 hrs) prior to deciding whether baricitinib is needed
- Baricitinib has not been evaluated among patients requiring mechanical ventilation at baseline, but may be continued among patients initiated on baricitinib in whom subsequently progress to mechanical ventilation who.
- Baricitinib should be AVOIDED in:
 - eGFR (non-race based result) < 15 mL/min/1.73m²
 - Any form of renal replacement therapy
 - Known active tuberculosis (routine quantiferon screening not required if no epidemiologic risk factors)
 - Absolute lymphocyte count (ALC) < 200 cells/ μ L (aka 0.2×10^9 /L) – may be started/resumed once ALC improves to > 200
 - Absolute neutrophil count (ANC) < 500 cells/ μ L (aka 0.5×10^9 /L) – may be started/resumed once ANC improves to > 500
 - Hemoglobin < 8g/dL
 - Pregnancy: weigh risk vs potential benefit
- Screen for drug-drug interactions
- Monitor CBC and BMP daily, LFTs weekly, and for development of new, or re-activation of latent, infections

Convalescent Plasma

COVID-19 convalescent plasma (CCP) is plasma obtained from donors who have previously recovered from COVID-19, and contains neutralizing antibodies to SARS-CoV-2. CCP has previously received emergency use authorization (EUA) for COVID-19 treatment; however, studies have shown mixed results and recent studies show no clinical benefits in hospitalized patients, including with high-titer plasma.

- Convalescent plasma is not recommended for routine use in hospitalized or non-hospitalized patients; rather, it is recommended to be used in the context of a clinical trial.
- EUA convalescent plasma is available through the blood bank (all units have high-titer neutralizing antibody) if use is desired outside of a clinical trial (e.g., if patient is felt to benefit from passive immunity but is not eligible for mAb therapy).

COVID-19 Monoclonal Antibodies – UHealth 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)
- Bamlanivimab/etesevimab (Lilly) – no longer recommended due loss of activity against some SARS-CoV-2 variants
- 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 ≥ 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 shorter 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 UHealth 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/m², 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

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

- 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=1d80toixYFITgAvku_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.
 - UHealth *Epic* users: Enter a Therapy Plan for “COVID OUTPATIENT MONOCLONAL INFUSION OIC”; see instructions (Page 4)
 - Providers outside of UHealth 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 UHealth COVID-19 Monoclonal Antibody Patient Instruction sheet

UHealth COVID-19 Monoclonal Antibody Infusion Sites

Broomfield Hospital

1820 Destination Dr, Broomfield, CO 80021

Phone: (719) 444-2273

Email: infusionAMC@uhealth.org

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

Memorial Central Outpatient Infusion

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

Phone: (719) 365-5650

Fax: (719) 365-6274

Email: infusionMHC@uhealth.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@uhealth.org

Yampa Valley Medical Center

1024 Central Park Drive, Steamboat Springs, CO 80487

Phone: (970)-870-1040

Fax: (970)-871-2315

Email: uhealthymvc-pharmacy@uhealth.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 UCHHealth 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

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

The screenshot shows the Epic EMR interface for a patient visit on 11/23/2020. The 'Orders Only' tab is active. In the top right corner of the main content area, there are two buttons labeled '1. Therapy Plan OIC' and '2. Therapy Plan OIC', which are highlighted with a red rectangular box. A black arrow points from the first instruction in the list above to this red box. The interface also displays various tabs like 'BestPractice', 'Allergies', 'SmartSets', and 'Verify Rx Benefits'. The patient information on the left includes 'Thomas Demo', 'Male, 11 m.o., 12/5/2019', and 'MRN: 8009574'. The bottom of the screen has a 'Start Review' button and 'ADD ORDER' and 'ADD DX (0)' options.

COVID-19 OUPATIENT MONOCLONAL ANTIBODY INFUSION ORDERS

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

Complete this form and fax to the appropriate infusion location after entering patient information into the Colorado Monoclonal Antibody Connector Tool: <https://redcap.link/COVIDMedsAllocationTool>

Select Infusion location (for orders to BFH, place order within Epic):

- PVH Fax: (970) 495-7627
- MHC Fax: (719) 365-6274
- YVMC Fax: (970) 871-2315

Start Date: _____ Weight: _____ kg Height: _____ cm
 Allergies: _____

PROVIDER COMMUNICATION AND INSTRUCTIONS:

1. Send face sheet, copy of insurance card, and H&P or most recent provider progress note.

2. Please select the indication:
 - Treatment** – Use is authorized for patients aged ≥12 years, weight ≥40 kg, with mild-moderate COVID-19 (symptomatic, not requiring hospitalization or new oxygen requirement), who are at high-risk for progression to severe disease. Check **ALL** boxes below to ensure patient meets EUA criteria for treatment:
 - Positive SARS-CoV-2 viral test (PCR or antigen) Date of positive test: _____
 - Within 10 days of symptom onset Date of symptom onset: _____
 - Not requiring supplemental oxygen due to COVID-19 (if pt uses oxygen at baseline, no increase in flow rate)

3. EUA high-risk criteria. Please select all which high-risk criteria that apply to the patient meets. Must choose at least one:
 - BMI ≥ 25 kg/m²
 - Age ≥ 65 years
 - Pregnancy
 - Chronic kidney disease
 - Diabetes mellitus
 - Immunocompromised disease or treatment, including HIV infection
 - Cardiovascular disease including hypertension, stroke, cerebrovascular disease, congenital heart disease
 - Chronic lung disease including 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)
Please specify: _____

MEDICATION ORDER:

1. 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 and record: vital signs including pulse oximetry on room air (or on baseline oxygen flow rate) prior to infusion, at end of infusion, and at end of observation period.
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 for Healthcare Providers:** <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, or will be, provided a copy of the **FDA Fact Sheet for Patients and Caregivers** (links below):
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>
- I acknowledge that any adverse event (AE) or death following initiation of treatment must be immediately reported pursuant to FDA requirements. UHealth sites will use RL solutions to report AEs.

Provider Signature: _____ Date/Time: _____
Provider Name (Print): _____ Phone: _____ Fax: _____