### Overview of Outpatient Management:

<table>
<thead>
<tr>
<th>PATIENT DISPOSITION</th>
<th>RECOMMENDATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outpatient, not requiring hospitalization or supplemental oxygen</td>
<td><strong>COVID-19 monoclonal antibodies (mAb)</strong> are recommended for high-risk, symptomatic patients within 10 days of symptom onset.</td>
</tr>
<tr>
<td>Discharged from hospital, not requiring supplemental oxygen</td>
<td><strong>No specific antiviral or immunomodulatory therapy recommended.</strong></td>
</tr>
<tr>
<td>Discharged from hospital, requiring supplemental oxygen <em>(for those stable enough for discharge but still requiring oxygen)</em></td>
<td><strong>Consider continuing dexamethasone</strong> for the duration of supplemental oxygen requirement, up to 10 days total dexamethasone duration, with close monitoring for adverse events.</td>
</tr>
<tr>
<td>Discharged from ED or urgent care, despite new oxygen requirement <em>(when hospital resources are limited, inpatient admission is not possible, and close follow-up is ensured)</em></td>
<td><strong>Dexamethasone</strong> 6 mg PO daily for the duration of supplemental oxygen need, up to 10 days maximum, with close monitoring for adverse events.</td>
</tr>
</tbody>
</table>

### Overview of Inpatient Management:

<table>
<thead>
<tr>
<th>DISEASE SEVERITY</th>
<th>RECOMMENDATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalized, not requiring supplemental oxygen</td>
<td><strong>No specific antiviral or immunomodulatory therapy recommended.</strong> <strong>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.</strong></td>
</tr>
<tr>
<td>Hospitalized, requiring low-flow supplemental oxygen</td>
<td><strong>Use: Remdesivir plus Dexamethasone</strong></td>
</tr>
<tr>
<td>Hospitalized, requiring oxygen via high-flow device or noninvasive ventilation</td>
<td><strong>Use: Dexamethasone</strong> <strong>Consider: Remdesivir</strong> in patients who are early in their disease course (&lt;10 days of symptom onset); otherwise low likelihood of benefit at this disease severity. **Consider: Tocilizumab, in combination with dexamethasone, for patients who were recently hospitalized with rapidly increasing oxygen needs and systemic inflammation. Consider assessing response to corticosteroids before deciding whether tocilizumab is needed. Baricitinib not available at UCH.</td>
</tr>
<tr>
<td>Hospitalized, requiring invasive mechanical ventilation or ECMO</td>
<td><strong>For most patients, use: Dexamethasone</strong> <strong>For patients who are within 24hrs of ICU admission, consider: Tocilizumab</strong>, in combination with dexamethasone, for patients who were recently hospitalized with rapidly increasing oxygen needs and systemic inflammation. Consider assessing response to corticosteroids before deciding whether tocilizumab is needed. Baricitinib not available at UCH.</td>
</tr>
</tbody>
</table>

Adapted from NIH COVID-19 Treatment Guideline
COVID-19 Therapies at UCHealth: Indications, Drug Information, Ordering Information

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

Criteria for use:
1. Confirmed COVID-19 (by SARS-CoV-2 PCR or antigen)
2. Mild-moderate (symptomatic) disease
3. Duration of symptoms ≤ 10 days
4. High risk for severe disease. FDA EUA high-risk criteria (updated 5/14/21):
   - Older age (age ≥ 65 years)
   - Obesity or overweight (BMI ≥ 25 kg/m$^2$ or BMI ≥ 85$^{th}$ 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)

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

Available mAbs:
1. Casirivimab/Imdevimab (REG-COV-2; Regeneron mAb combination). Preferred agent at UCHealth. 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 variants.
3. Sotrovimab: Active against currently circulating variants but not currently available at UCHealth.

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 increase risk of serious or non-serious safety events (including renal or hepatotoxicity) have been observed in several retrospective studies.

Approval
- At UCHealth 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
- 66 kg to 90 kg = 600mg
- > 90kg = 800mg

**Baricitinib (Olumiant)**

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 remdesivir in patients requiring supplemental O2 (ACTT-2, Dec 2020), and a suggestion of mortality benefit when given with standard of care (either dexamethasone or dexamethasone + remdesivir) in patients requiring low-flow supplemental O2 (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
- In the rare circumstance when corticosteroids cannot be used, may use baricitinib + RDV for hospitalized, non-intubated pts requiring supplemental O2

At UCH, baricitinib is not available so tocilizumab may be offered for patients who meet criteria for rapid clinical progression.
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 – 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 that have received EUA are:

- Casirivimab/imdevimab (Regeneron)
- Bamlanivimab/etezavimab (Lilly) – no longer available or recommended due loss of activity against circulating SARS-CoV-2 variants

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 ≥ 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 COVID-19 vaccination for 90 days, to avoid potential interference with vaccine-induced immune response.
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.

Dosing and Administration

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

- Patient/Caregiver Information:

- CAS/IMD may be given subcutaneously if IV administration is not feasible
- 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

- 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](https://redcap.link/COVIDMedsAllocationTool)
  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=1d8OtoixYFTgAvku_671LGMZsQbnnDED&usp=sharing](https://www.google.com/maps/d/viewer?mid=1d8OtoixYFTgAvku_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 on the following pages
     - Providers outside of UCHealth or who do not use Epic may send infusion orders using the attached paper 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

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
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 generally 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 since 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](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
COVID-19 OUTPATIENT MONOCLONAL ANTIBODY INFUSION ORDER

Complete this form and fax to the appropriate infusion location after entering patient information into the Colorado Monoclonal Antibody Connector Tool: [https://redcap.link/COVIDMeds AllocationTool](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. Ensure that patient meets all EUA criteria – check boxes below:
   - Positive SARS-CoV-2 PCR or antigen 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/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: ___________
COVID-19 OUTPATIENT MONOCLONAL ANTIBODY INFUSION ORDER

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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):

☐ 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.

Provider Signature: _____________________________ Date/Time: _____________________________

Provider Name (Print): ___________________________ Phone: __________________ Fax: __________________
University of Colorado Hospital / University of Colorado Health
Anticoagulation Subcommittee

ANTICOAGULATION RECOMMENDATIONS FOR HOSPITALIZED COVID-19 PATIENTS

I. General Information
- Patients infected with the COVID-19 virus are potentially at increased risk of both venous thromboembolism and micro thrombosis in multiple vascular beds due to hospitalization, immobilization/isolation, and the thrombo-inflammatory state generated by COVID-19 infection itself
- COVID-19 has been associated with a coagulopathic presentation that when severe can mimic DIC. Coagulopathy typically increases thrombosis and not bleeding
- Lab derangements may include elevated d-dimers, prolonged prothrombin time ratios, elevated fibrinogen, elevated ferritin and thrombocytopenia

II. Recommendations for Subcutaneous VTE Prophylaxis

<table>
<thead>
<tr>
<th>Floor Patients</th>
<th>D-dimer &lt;1500* AND</th>
<th>D-dimer &gt; 1500* OR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TEG (MA) ≤ 70&lt;sub&gt;k&lt;/sub&gt; (Only if available, see info below)</td>
<td>TEG (MA) &gt; 70&lt;sub&gt;k&lt;/sub&gt; (Only if available, see info below)</td>
</tr>
<tr>
<td>Weight &lt;100 kg</td>
<td>Enoxaparin 40 mg once daily</td>
<td>Enoxaparin 30 mg BID</td>
</tr>
<tr>
<td>Weight 100-150 kg</td>
<td>Enoxaparin 30 mg BID</td>
<td>Enoxaparin 40 mg BID</td>
</tr>
<tr>
<td>Weight &gt; 150 kg</td>
<td>Enoxaparin 40 mg BID</td>
<td>Enoxaparin 0.5 mg/kg BID</td>
</tr>
<tr>
<td>AKI (GFR&lt;30 ml/min)&lt;sup&gt;#&lt;/sup&gt;</td>
<td>UFH 5000 U TID</td>
<td>UFH 7500 U TID</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICU Patients</th>
<th>D-dimer &lt;1500* AND</th>
<th>D-dimer &gt; 1500* OR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TEG (MA) ≤ 0&lt;sub&gt;k&lt;/sub&gt; (Only if available, see info below)</td>
<td>TEG (MA) &gt; 0&lt;sub&gt;k&lt;/sub&gt; (Only if available, see info below)</td>
</tr>
<tr>
<td>Weight &lt;100 kg</td>
<td>Enoxaparin 40 mg once daily</td>
<td>Enoxaparin 40 mg BID</td>
</tr>
<tr>
<td>Weight 100-150 kg</td>
<td>Enoxaparin 40 mg BID</td>
<td>Enoxaparin 0.5 mg/kg BID</td>
</tr>
<tr>
<td>Weight &gt; 150 kg</td>
<td>Enoxaparin 60 mg BID</td>
<td>Enoxaparin 0.5 mg/kg BID</td>
</tr>
<tr>
<td>AKI (GFR&lt;30 ml/min)&lt;sup&gt;#&lt;/sup&gt;</td>
<td>UFH 5000 U TID</td>
<td>UFH 7500 U TID</td>
</tr>
</tbody>
</table>

* Based on scarce available mortality data and preliminary data from anti-Xa activity levels in UCH pts

<sup>1</sup> This guideline does not endorse performing Thromboelastography (TEG) to be routinely done in COVID-19 patients, particularly those on the floor, but use of results may be considered if it is performed. Available in data from other populations indicate hypercoagulability is present in patients with TEG MA values above 70, although no outcomes data in COVID-19 to date. In addition, no clear data to date to incorporate other markers of inflammation like fibrinogen or ferritin at this time to drive anticoagulation choices, but these have been noted to be elevated in severely sick COVID-19 patients

<sup>#</sup> Considerations for patients with AKI:
- Patients on renal replacement therapy (HD, CRRT) may require more aggressive anticoagulation therapy in order to prevent clotting of the filter. Renal service should be consulted for final recommendation.
- Estimated GFR should not be used alone to assess renal function as patients with AKI may still have estimated GFR > 30 ml/min.
III. Additional Considerations for Prophylactic or Therapeutic Anticoagulation in COVID-19 Patients.
   a. COVID-19 patients with a *history of thromboembolic disease and/or on chronic anticoagulation prior to admit* should continue home anticoagulation regimen if clinically appropriate, or transition to alternative agent (most cases IV UFH) for therapeutic anticoagulation.
   b. COVID-19 patients who develop *new arterial or venous thromboembolic events* should be treated with therapeutic anticoagulation (UFH, LMWH) as standard of practice would dictate.
   c. *For high clinical suspicion of new thromboembolic events*, consider empiric therapeutic anticoagulation using heparin gtt and order a truncated, lower extremity DVT protocol (POCUS) as a confirmatory test.
      i. Initiation of therapeutic anticoagulation without confirmed or high clinical suspicion of DVT/PE, is controversial and is *not* recommended by *national/international guidelines (see below)*
      ii. In the setting of extremely high D-dimers (e.g. >3000 ng/ml), persistent clotting of lines and/or worsening clinical course, therapeutic anticoagulation may be considered and a multidisciplinary discussion with critical care attending, anti-thrombosis services and others (path, heme) is recommended.
   d. Primary teams are recommended to consult the inpatient anticoagulation service (metro) or pharmacy (North and South) to *assist with dose optimization* (AKI, drug-drug interactions, extremes of body weight, other) or *therapeutic selection* (appropriate heparin order set, use of alternative anticoagulants such as DOACS or injectable DTIs). Issues include
      i. For Enoxaparin: measure anti-Xa level 4 hours after 3rd dose. Goal = 0.3-0.5. Increase dose as needed guided by anti-Xa level. Consider using TEG.
      ii. When TEG monitoring available: Use Kaolin / heparinase.

IV. *Available Guidance on Anticoagulation is available through the following organizations*
   a. International Society of Thrombosis and Haemostasis
   b. American Society of Hematology c Anticoagulation Forum
   American College of Cardiology