June 25, 2021

From: COVID-19 Scientific Research Committee

To: COVID-19 Pandemic Response Team

Dear Committee:

The Scientific Research Committee was asked to review literature surrounding therapeutic treatment of COVID-19 in adult patients.

As a committee, we believe the documented algorithm is thought to be the most up to date, comprehensive and scientifically current treatment algorithm. The committee supports the adaptation of the algorithm prepared and approved by the Chief Medical Officer approval board.

Sincerely,

COVID-19 Scientific Committee

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AdventHealth Treatment Algorithm for COVID-19 in Adult Patients

Disclaimer: The Scientific Research Committee ensures timely review of emerging experimental therapies, therefore, off-label use of therapies with only published *in vitro* data should NOT be implemented until reviewed and sanctioned by this committee. The recommendations below are subject to change based on emerging data or drug shortage information.

The medications listed below (outside of treatment table) have been reviewed, but due to lack of evidence, these medications are not currently recommended for the treatment of COVID-19.

All patients should receive supportive care (IV fluids, anti-pyretics, anti-emetics, etc.).

- **ACE I/ARB:**
  - The HFSA, ACC and AHA emphasize the lack of experimental or clinical data on these class of drugs in COVID-19 and recommend that patients currently taking these medications for known beneficial indications (HF, HTN, or ischemic heart disease, for example) be advised to continue. They advise against adding/removing beyond what would be done in standard practice and urge individualized treatment decisions based on patient's clinical presentation and hemodynamics.
- **NSAIDs**:
  - There is no evidence for or against the management of fever with NSAIDs. Acetaminophen is preferred for management of fever, but each clinical scenario should be carefully evaluated.
- **Nebulized respiratory medications for patients:**
  - Nebulized respiratory medications should be avoided in non-intubated patients unless otherwise indicated in patients with bronchospasms to prevent the spread of the COVID-19. For COVID-19 negative non-intubated patients, nebulized respiratory medications are preferred over MDIs.
  - If indicated, inhalers (MDIs) with spacers are preferred for non-intubated patients.
  - If indicated, nebulized medications with a closed circuit may be used in intubated patients.
- **Azithromycin:**
  - Based on current evidence demonstrating lack of benefit in preventing invasive mechanical ventilation or death in hospitalized patients, use of azithromycin for treatment of COVID-19 is not recommended.
- **Ivermectin:**
  - At this time, ivermectin not recommended for COVID-19, but this recommendation will be re-evaluated when results of ongoing randomized controlled trials are available.
  - Current evidence for benefit of ivermectin is weak and does not support the use of ivermectin for COVID-19; however, no significant risk of harm has been identified.
  - International COVID-19 Guidelines & Statements on the Use of Ivermectin for the Treatment of COVID-19:
    Merck Statement on Ivermectin use in COVID-19 IDSA Guidelines for Treatment of COVID-19 - Ivermectin
    Statement on Ivermectin | COVID-19 Treatment Guidelines
- **Micronutrients (Vitamin C and Zinc)**
  - Adjunctive use of micronutrients in COVID-19 patients beyond the recommended daily allowances for supplementation is not supported by scientific evidence.

- If utilization is necessary for the treatment of nutritional deficiencies, a once daily dosing strategy should be employed.

- **Lopinavir/ritonavir:**
  - Use of lopinavir/ritonavir is not recommended because of unfavorable pharmacodynamics and negative clinical trial data.
- **Hydroxychloroquine or chloroquine:**
  - Based on studies demonstrating harm and little clinical benefit, the use of hydroxychloroquine for the treatment of COVID-19 is NOT recommended outside of a clinical trial.
- **Tissue Plasminogen Activator (tPA)**
  - Widespread use of tPA in critically ill COVID-19 patients is not supported by the currently published studies and, therefore, is not recommended.

Therapeutic options should be based on severity using the following scale:

- 0 = Patient on room air
- 1 = Patient requires supplemental O2 via NC up to a max of 6L
- 2 = Patient requires supplemental O2 in addition to ≥1 of the following:
  - Dyspnea or staccato speech at rest or after minimal activity
  - RR > 22 on 6L
  - PaO2 <65 mmHg with 6L
  - Worsening infiltrates on imaging (CT preferred)
- 3 = Patient requires HFNC, CPAP, or NIV
- 4 = Patient intubated with minimal support PaO2/FiO2, or using PS
- 5 = Patient intubated with PaO2/FiO2 > 150 mmHg
- 6 = Patient intubated with PaO2/FiO2 < 150 mmHg
- 7 = Patient intubated with PaO2/FiO2 < 150 mmHg AND requiring vasopressor support
- 8 = Patient intubated in prone position or ECMO

Severity Score	Treatment for Hospitalized Patients*^
0	Supportive care only - If clinically stable, consider discharge for self-quarantine
1	Remdesivir (based on criteria) Dexamethasone 6 mg po or IV daily for up to 10 days
2	Remdesivir (based on criteria) Corticosteroids If patient cannot tolerate or does not respond to corticosteroids, consider Baricitinib
3	Corticosteroids ± Tocilizumab or Baricitinib ± Remdesivir (based on criteria)
≥4	Corticosteroids ± Tocilizumab

**Patients can be discharged whenever clinically indicated. Full duration of therapy does not need to be completed if patient is suitable for discharge to home. Isolation should be maintained at home if patient returns home before the time period recommended for discontinuation.*

^The decision to modify the recommendation for Convalescent Plasma was based on the RECOVERY study results indicating lack of mortality benefit when compared to placebo in hospitalized patients; however, immunodeficient patients were not included in this study and may still derive a benefit with convalescent plasma for severity score 2 or 3.

Recommended Laboratory Monitoring for all Hospitalized Patients with COVID-19:

- Daily CMP, magnesium, and CBC with differential
- Procalcitonin (PCT) at baseline and then every 2 days as needed
- CRP at baseline and then every 3 days
- D-dimer at baseline and then every 3 days

Recommended Therapies for Hospitalized Patients (Click Here for Outpatient Recommendations)

Drug	Dosing	Formulations	Monitoring	Adverse Effects	Notes
Remdesivir *Criteria for use (see below)* **Use beyond 5 days requires CMO approval*	200 mg IV x 1 on day 1 followed by 100 mg IV daily Duration: Up to 5 days or until hospital discharge, whichever is first	**IV infusion** Infuse over 30 minutes using dedicated IV line	• Prior to 1st dose: eGFR, hepatic laboratory, and prothrombin time • During therapy: as clinically appropriate	• Increased Risk of Transaminase Elevations	Risk of reduced antiviral activity when co-administered with chloroquine or hydroxychloroquine
Dexamethasone *(or alternative, see corticosteroid below)*	6 mg po or IV daily Duration: Up to 10 days	**Oral tablet, liquid IV infusion**	• Glucose	• Minimal adverse effects with low-dose and short-term use	Safe in pregnancy
Tocilizumab *Restricted to infectious diseases or critical care providers* *See below*	8 mg/kg (max 800 mg) x1 Duration: 1-2 doses Dose may be repeated at 24 hours if no signs of clinical improvement	**IV infusion**	• LFTs • CBC • Hypersensitivity	• Neutropenia, anemia • Hepatotoxicity • Hypersensitivity • Risk of infection	Do not administer to patients with active bacterial infections Avoid in pregnancy
Baricitinib	4 mg once daily* (dose adjustment required for eGFR<60 mL/min/1.73 m^2) Duration: Up to 14 days or until hospital discharge, whichever is first	**Oral tablet** **May be dispersed in water for administration via G tube or NG tube**	Routine	• Serious infections • Thrombosis • Abnormal laboratory values • Serious venous thrombosis	

Remdesivir (RDV)

- Remdesivir was approved by the FDA on October 22, 2020, for adults and pediatric patients (≥12 years older and weighing ≥40 kg) for the treatment of COVID-19 requiring hospitalization. Refer to RDV Prescribing Information & RDV - Dear Healthcare Provider Letter.
- Emergency Use Authorization for RDV to treat hospitalized pediatric patients weighing 3.5 kg to <40 kg or pediatric patients <12 years of age weighing ≥3.5 kg with suspected or laboratory-confirmed COVID-19. Refer to RDV - EUA for Pediatric Patients or RDV - Fact Sheet for HCP (Pediatrics).

Criteria for Use*: *Based on the available scientific evidence, the Scientific Review Committee supports the use of remdesivir in patients requiring supplemental oxygen; however, the FDA approval for RDV permits treatment for adults and pediatric patients (≥12 years older and weighing ≥40 kg) for the treatment of COVID-19 requiring hospitalization.* ***For patients who are not requiring supplemental oxygen due to hypoxemia (SpO2<94%) and for patients who require mechanical ventilation/ECMO, current data has not demonstrated a reduction in time to clinical recovery or mortality.****

Treatment of suspected or laboratory confirmed COVID-19 in adults and children hospitalized with severe disease. Severe disease is defined as:

- Requiring supplemental oxygen
- Requiring non-invasive ventilation or high-flow oxygen (supplemental oxygen through a high-flow device)

Remdesivir should not be initiated routinely in the patients with the following at baseline:

- Patients on room air
- Patients on mechanical ventilation or ECMO
- Patients with known hypersensitivity to any ingredient of remdesivir
- Those expected to expire within 24 hours or in hospice care
- Patients with hepatic impairment, defined as ALT ≥ 10x ULN

Prescribing information states "Remdesivir is not recommended in patients with eGFR <30 mL/min.", however, expert consensus is that the benefits of RDV may outweigh the risk for most patients with impaired renal function. (Reference: J Am Soc Nephrol. 2020;31(7):1384-1386. doi:10.1681/ASN.2020050589.)

Tocilizumab

While definitive data is not currently available, review of the emerging literature indicates there may be a role for tocilizumab in treatment of COVID-19 in select patients.
When standard of care (i.e., dexamethasone) has already been initiated, then at physician discretion, tocilizumab may be considered for patients with severity score ≥3 (high-flow oxygen or mechanical ventilation).

Tocilizumab 8 mg/kg IV (max 800 mg/dose)

- Use restricted to infectious diseases or critical care providers
- A second dose may be administered at 24 hours if clinical signs/symptoms worsened or have not improved (i.e., worsening of severity score).

Caution: Some trials have excluded patients with suspected active bacterial, fungal, or viral infection (other than SARS-CoV-2 or well-controlled HIV). While some studies have reported no difference in secondary infection rate, other studies have reported a higher prevalence of secondary infection in patients receiving tocilizumab compared with patients who received placebo.

Baricitinib

FDA issued Emergency Use Authorization for Baricitinib in combination with remdesivir for the treatment of COVID-19 in hospitalized adults and pediatric patients ≥2 years of age and requiring supplemental oxygen, invasive mechanical ventilation or ECMO. Baricitinib EUA Fact Sheet for Healthcare Providers.

Scientific evidence suggests potential benefit of baricitinib + remdesivir only in hospitalized patients requiring high-flow oxygen support.

Renal Impairment:

eGFR	**Dose**
≥60 mL/min/1.73 m^2	4 mg once daily
<60 to 30 mL/min/1.73 m^2	2 mg once daily
<30 to 15 mL/min/1.73 m^2	1 mg once daily
<15 mL/min/1.73 m^2	Not recommended

Corticosteroid Considerations for Use:

All patients requiring supplemental oxygen

- Initiate low dose steroids with dexamethasone 6 mg po or IV daily for up to 10 days
- If dexamethasone unavailable, utilize one of the following options
    - Prednisone 40 mg once daily or two divided doses (20 mg PO BID)
    - Methylprednisolone 32 mg once daily or two divided doses (16 mg PO BID)

Patients with refractory shock, ARDS or Cytokine Release Syndrome (CRS), early initiation of low dose glucocorticoids have been recommended

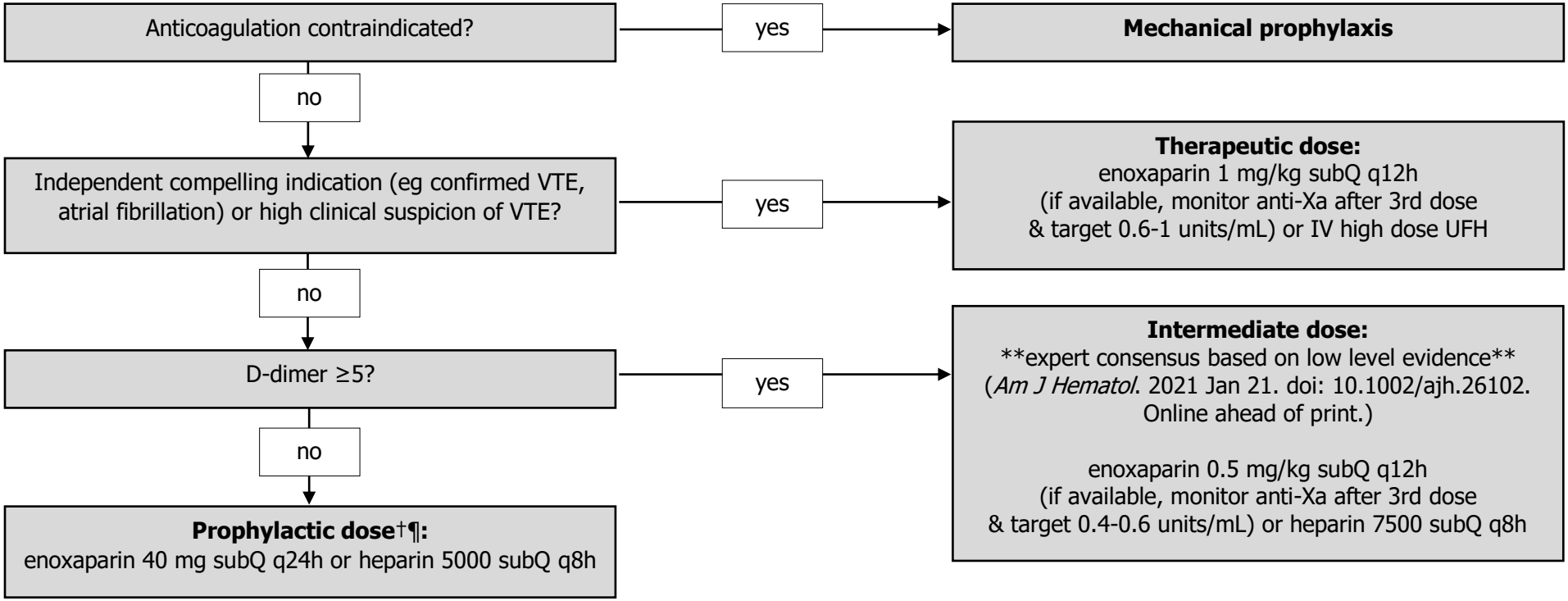
- Methylprednisolone 40 mg IV, q8h x 7 days
- Dexamethasone 10 mg IV BID x 5 days, then 10 mg daily x 5 days

To determine a patient's risk for developing CRS, the following chart may be used as guidance:

		Low Probability of CRS Benefit	**Moderate Probability of CRS Benefit**	**High Probability of CRS Benefit**
Timing	*Initiation*	**Late** (> 10 days after decompensation)	**Mid-period** (5-10 days after decompensation)	**Early** (< 5 days after decompensation)
	Duration	**Long** (> 10 days)	**Moderate** (6-10 days)	**Short** (≤ 5 days)
Signs and symptoms	*Fever*	< 37°C	37-38°C	> 38°C
	Cough	No	Yes	-
	ALI	No ALI (P/F > 300)	ALI (P/F 200-300)	ARDS (P/F < 200)
	O_2	< 4L NC	0.4-0.7	>0.7
	Vent	No	Variable	Yes
	CT/CXR	Minimal infiltrates	Patchy infiltrates (25-50%)	Diffuse infiltrates (>50%)
	Shock	No	No	Yes
Inflammatory Markers	*CRP*	< 4	4-10	> 10
	ESR	< 50	50-70	> 70
	Ferritin	< 250	250-500	> 500
	D-dimer	< 1	1-3	> 3
	Lymphocytes	> 1000	750-1000	< 750

COVID-19 Inpatient Anticoagulation Pathway

__**EARLY (first 24 hrs of hospital admission)**__ initiation of prophylactic anticoagulation compared with no anticoagulation among patients admitted to hospital with COVID-19 was associated with a decreased risk of 30 day mortality and no increased risk of serious bleeding events. (*BMJ. 2021 Feb 11;372:n311. doi: 10.1136/bmj.n311.*)



*Higher intensity of anticoagulation must be weighed against the risk for bleeding. Currently, the National Institute of Health and American Society of Hematology are awaiting publication of 3 platform RCTs to finalize therapeutic anticoagulation recommendation, which will be included on the algorithm after the update. Evidence for intermediate dose anticoagulation is based on an observational study cited below, therefore it is of low-quality evidence, use clinical judgement when prescribing. If higher intensity dosing is utilized, consider ordering diagnostic tests to rule out VTE.
†Heparin preferred in AKI, dialysis, or when unable to reach anti-Xa targets with enoxaparin.
¶Patients with BMI≥40, use enoxaparin 40 mg subQ q12h or heparin 7500 subQ q8h.

Outpatient Anticoagulation for COVID-19 patients

Patients receiving chronic anticoagulant or antiplatelet therapy for existing conditions should remain on their current regimen if positive for COVID-19, unless a new clot has developed, or ICU level of care requires a switch to parenteral/SubQ therapy.

All other patients should be assessed as follows:

1. Confirmed VTE or high clinical suspicion with attending MD (i.e. evidence of DVT/PE/positive Doppler or high clinical suspicion)
    a. Therapeutic anticoagulation needed
        i. Calculate duration of therapy already completed
            1. Continue for minimum of 3 months (long term/indefinite term for idiopathic VTE and low bleeding risk)
        ii. Confirm regimen and dose (all regimens listed below must be adjusted for renal impairment). Subtract any days of treatment initiated as inpatient to determine remaining loading dose and/or maintenance dose.
            1. Apixaban 10 mg PO BID x7 days, followed by 5 mg BID
                a. May be utilized in patients with cancer on a case-by-case basis
            2. Rivaroxaban 15 mg PO BID x 21 days, followed by 20 mg daily with dinner
            3. Enoxaparin 1 mg/kg SubQ BID with CrCL >30 ml/min (alternative for patients with cancer or pregnancy)
                a. NOT preferred due to cost
                b. Round to the nearest syringe (30 mg, 40 mg, 60 mg, 80 mg, 100 mg, 120 mg, 150 mg)
        iii. Obtain prescription
            1. Pharmacist to consult care management to initiate outpatient medication procurement
                a. "Case Management Consult for Medications/Medical Follow Up" à Special Instructions: *Enter drug name*
            2. Care management to send to Rxpress or Hospital outpatient pharmacy (preferred) or patient outpatient pharmacy (if patient preference)
                a. Apixaban Eligibility
                    i. for 30-day trial: never filled Eliquis before
                    ii. for Co-pay card: must have commercial insurance (not state or federal insurance, e.g. Medicare)
                b. Rivaroxaban Eligibility
                    i. Commercial or private insurance
                    ii. Not for state or federal insurance, e.g. Medicare
                    iii. Unable to use for 10 mg tabs
            3. Deliver meds to bedside prior to discharge
            4. Pharmacist provides education
            5. Care management sets up outpatient follow up with 7 days

2. High Risk of VTE: Modified International Medical Prevention Registry on Venous Thromboembolism (IMPROVE) VTE risk score ≥4; or Modified IMPROVE VTE risk score ≥2 and D-dimer level >2 times the upper limit of normal.
Recommendation is based on low level evidence from consensus documents only, use clinical judgement when prescribing

Modified IMPROVE VTE Risk Score	
VTE Risk Factor	**VTE Risk Score**
Previous VTE	3
Known thrombophilia (a)	2
Current lower limb paralysis or paresis(b)	2
History of cancer(c)	2
ICU/CCU stay	1
Complete immobilization(d) ≥1 day	1
Age ≥60 years	1
CCU= cardiac care unit; ICU= intensive care unit; VTE= venous thromboembolism. a: A congenital or acquired condition leading to excess risk of thrombosis (eg, factor V Leiden, lupus anticoagulant, factor C or factor S deficiency). b: Leg falls to bed by 5 seconds but has some effort against gravity (taken from NIH stroke scale). c: Cancer (excluding non-melanoma skin cancer) present at any time in the last 5 years (cancer must be in remission to meet eligibility criteria) d: Immobilization is being confined to bed or chair with or without bathroom privileges.	

   a. Prophylactic anticoagulation needed
      i. Calculate duration of therapy already completed
         1. Continue for a total of 4 weeks
      ii. Confirm regimen and dose
         1. Apixaban 2.5 mg PO BID (regardless of renal function)
         2. Rivaroxaban 10 mg PO daily (regardless of renal function)
         3. Enoxaparin 40 mg SubQ daily (for BMI ≥40: 40 mg SubQ BID)
            a. NOT preferred due to cost
            b. Round to the nearest syringe (30 mg, 40 mg, 60 mg, 80 mg, 100 mg, 120 mg, 150 mg)
      iii. Obtain prescription
         1. Pharmacist to consult care management to initiate outpatient medication procurement
            a. "Case Management Consult for Medications/Medical Follow Up" à Special Instructions: *Enter drug name*
         2. Care management to send to Rxpress or Hospital outpatient pharmacy (preferred) or patient outpatient pharmacy (if patient preference)
         3. Deliver meds to bedside prior to discharge
         4. Pharmacist provides education

5. Care management sets up outpatient follow up with 7 days

3. Low risk of VTE or contraindication to anticoagulation
    a. No OAC at discharge
    b. Extended VTE prophylaxis is not routinely recommended and should only be prescribed on a case-by-case basis

COVID19 Convalescent Plasma (CCP)

CCP is available only under FDA emergency use authorization (EUA); however, current evidence and guidelines do not recommend the use of CCP in hospitalized patients. While the RECOVERY trial did not demonstrate a mortality benefit with CCP in hospitalized patients when compared to placebo, immunodeficient patients were not included and may still derive a benefit from this therapy. If, based on clinical judgement, a provider wishes to use CCP, patients must meet the EUA criteria for use and ordering physician must attest to the criteria via Cerner PowerPlan. Per the FDA, this authorization is limited to use of **only** high titer plasma.

Guideline Recommendations for use of CCP in Hospitalized Patients with COVID-19:

- **NIH (Updated April 21, 2021):** The panel recommends against the use of high titer or low titer CCP in patients hospitalized with COVID-19, except those enrolled in a clinical trial
- **IDSA (Updated April 7, 2021):** Among hospitalized patients with COVID-19, the panel suggest against the use of CCP.

AdventHealth Transfusion Consent must be obtained from the patient/LAR prior to CCP administration (following routine SOP). Nurse must give patient/LAR CCP fact sheet prior to CCP administration. Note: Availability of CCP is dependent upon collection and distribution of donated plasma from individuals who have recovered from COVID19 and may not be readily available.

Orlando Campus: If patient is being considered for enrollment in COVID-19 clinical trials, be aware that prior or concomitant use of convalescent plasma may exclude patient(s) from participation. Contact respective clinical trial research coordinator for detailed information about restrictions associated with each clinical trial. **

Criteria for Use

1. Patients hospitalized with COVID-19, early in the disease course, and those with impaired humoral immunity
   a) FDA defines early course as **prior to** respiratory failure requiring intubation and mechanical ventilation
   b) Transfusions administered late in the course of COVID-19, defined as requiring intubation or mechanical ventilation, has not been associated with clinical benefit

Treatment Timing

1. As soon as possible, ideally within 3 days of admission or new oxygen requirement

Administration

1. Treatment with CCP consists of one unit of high titer plasma, approximately 200 mL given over 1 hour
2. Premedicate with acetaminophen 650 mg PO and diphenhydramine 50 mg PO 30 minutes prior to start of CCP. May repeat x1 if >12 hours from premedication administration and CCP transfusion not yet complete.

Treatment for Non-Hospitalized Patients

Colchicine

Colchicine is a commonly utilized anti-inflammatory medication with antiviral properties that may attenuate the effects of cytokine storm. Recently, a large, randomized, controlled trial (COLCORONA) demonstrated a benefit in reducing hospitalization and death with use of colchicine in patients > 40 years of age with certain risk factors. Currently, the data is insufficient to recommend for or against routine use of colchicine in *hospitalized* patients; however, colchicine may be considered for non-hospitalized patients with documented COVID-19, plus one of the following risk factors: advanced age (≥ 70 years old), obesity, diabetes, hypertension, chronic respiratory disease, heart failure, coronary artery disease, fever (≥ 100.4º) within last 48 hours, dyspnea, and laboratory abnormalities (pancytopenia, high neutrophil count, low lymphocyte count).

Dose: 0.6 mg orally twice daily x 3 days, then 0.6 mg daily for up to 30 days
Common adverse effects: diarrhea, nausea, abdominal pain, vomiting

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Monoclonal Antibodies (Outpatient only)

Based on current level of SARS-CoV-2 variant penetrance in the U.S., particularly the P.1/Gamma variant and the B.1.351/Beta variant, distribution of bamlanivimab/etesevimab has been pasued nationwide. Casirivimab/imdevimab or Sotrovimab are the recommended MABs in the U.S. as of June 25, 2021. The distribution of local variants will continued to be closely monitored via the CDC website, thus changes to this recommendation will be adjusted accordingly.

Guideline Recommendations on MABs for COVID-19:

- **NIH (updated June 17, 2021):** According to The National Institutes of Health COVID-19 Treatment Guidelines, the panel recommends using one of the combination (bamlanivimab/etesevimab OR casirivimab/imdevimab) anti-SARS-Cov-2 MABs to treat outpatients with mild-moderate COVID-19 who are at risk of clinical progression. Therapy should be initiated as soon as positive result and within 10 days of symptom onset. In regions where SARS-CoV-2 variants with reduced in vitro susceptibility to bamlanivimab/etesevimab are common, some panel members would preferentially use casirivimab/imdevimab while acknowledging that it is not known whether in vitro susceptibility data correlate with clinical outcomes.
- **IDSA (June 16, 2021):** According to the Infectious Diseases Society for America Guidelines on the Treatment and Management of Patients with COVID-19, the panel suggest use of bamlanivimab/etesevimab, casirivimab/imdevimab, OR sotrovimab rather than no neutralizing antibodies among ambulatory patients with mild-moderate COVID-19 at high risk for progression to severe disease. Local variant susceptibility may be considered in the choice of the most appropriate neutralizing antibody.

**No comparative data exists to guide treatment decisions, thus preferred MAB should be based on local variants and access to certain MABs*

As of June 25, 2021, two MAB options are being distributed in the U.S. under an FDA EUA: casirivimab/imdevimab and sotrovimab. On June 25, 2021, the Assistant Secretary for Preparedness and Response and the FDA announced that distribution of bamlanivimab/etesevimab will be paused ***nationwide*** based on increased rates of variants displaying reduced susceptibility to bamlanivimab/etesevimab.

Casirivimab/imdevimab, and sotrovimab are immunoglobulin G-1 (IgG1) MABs that bind to the receptor binding domain of the spike protein of SARS-CoV-2, thus preventing attachment of the virus into human cells.

"In order to mitigate the risks of using this unapproved product under the EUA and to optimize the potential benefit of casirivimab/imdevimab or sotrovimab, the following items are required. Use of casirivimab/imdevimab or sotrovimab under these EUAs is limited to the following (all requirements **must** be met)."

This authorization only permits casirivimab/imdevimab, or sotrovimab to be used to treat mild to moderate COVID-19 in:

- Mild symptoms are defined as: fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, and loss of taste and smell
- Moderate includes the symptoms listed above plus may also include shortness of breath
- Adults & pediatric patients (age ≥12 and weight ≥40 kg)
- Positive SARS-CoV-2 viral testing
- **High risk*** for progressing to severe COVID-19 and/or hospitalization (see criteria below)
- **Outpatient setting** with immediate access to medications to treat severe infusion reactions (anaphylaxis) and the ability to activate EMS

***High Risk Criteria**

At least one of the following criteria must be met for both adult and pediatric patients (12-17 weighing at least 40 kg):

- Older age (i.e., ≥65 years)
- Obese or being overweight
  - Age ≥ 18 and BMI ≥ 25kg/m^2
  - Age 12-17 and BMI ≥ 85th percentile
- CKD
- Pregnancy
- Diabetes
- Immunosuppressive disease
- Receiving immunosuppressive treatment
- Cardiovascular disease including congenital heart disease and hypertension
- Chronic lung disease (e.g., COPD, asthma, cystic fibrosis, pulmonary hypertension, interstitial lung disease)
- Sickle cell disease
- Having a medical-related technological dependence (e.g., tracheostomy, gastrostomy, positive pressure ventilation not related to COVID-19)
- Neurodevelopmental disorders (e.g., cerebral palsy)
- **In addition to the criteria listed above, a provider may prescribe a MAB for *any other medical condition or factor* (e.g., race, ethnicity) that may place an individual at high risk for progression of COVID-19.**

Not authorized for:

- Patients who are **hospitalized** due to COVID-19
- Patients who require oxygen therapy due to COVID-19
- Patients who require an increase in baseline oxygen flow rate due to COVID-19
- Prevention of COVID-19

Casirivimab/Imdevimab (PREFERRED MAB IN FLORIDA)

November 21, 2020: FDA issues Emergency Use Authorization for casirivimab/imdevimab for the treatment of mild to moderate COVID-19.
Refer to EUA Letter – Casirivimab/Imdeivmab & Fact Sheet for Health Care Providers
Patient Fact Sheet in English OR Patient Fact Sheet in Spanish
Dose: 600 mg of casirivimab + 600 mg of imdevimab administered together as a single IV infusion OR subcutaneously

IV Infusion Rates (preferred route):

- 50 mL = 20 minutes
- 100 mL = 21 minutes
- 150 mL = 31 minutes
- 250 mL = 50 minutes

Subcutaneous Administration (alternative route if IV route unavailable or would lead to delay in care):

- Dose should be prepared into a total of four syringes

No dosage adjustment is recommended based on age, sex, race, body weight, renal or mild hepatic impairment, during pregnancy or while lactating, or for disease severity or inflammation.

- Timing: Administer dose as soon as possible after positive viral test and within 10 days of symptom onset
- Monitoring: Observe patients during infusion and for ≥1 hour after infusion is complete

Sotrovimab

May 26, 2021: FDA issues Emergency Use Authorization for sotrivimab for the treamtebt of mild to moderate COVID-19.
Refer to EUA Letter – Sotrivimab & Fact Sheet for Health Care Providers
Patient Fact Sheet in English
Dose: 500 mg administered as a single IV infusion over 30 minutes

Instructions for Healthcare Providers:

- Document in the medical record that patient has been counseled and provided with copy of Fact Sheet for Patients. As the healthcare provider, you must communicate to your patient or parent/caregiver, as age appropriate, information consistent with the "Fact Sheet for Patients, Parents and Caregivers" prior to the patient receiving any MAB, including:
    - FDA has authorized the emergency use of casirivimab/imdevimab, bamlanivimab/etesevimab, and sotrovimab for the treatment of mild to moderate COVID-19 in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.
    - The patient or parent/caregiver has the option to accept or refuse casirivimab/imdevimab, bamlanivimab/etesevimab, or sotrivimab.
    - The significant known and potential risks and benefits of casirivimab/imdevimab, bamlanivimab/etesetimab, or sotrivmab and the extent to which such potential risks and benefits are unknown.
    - Information on available alternative treatments and the risks and benefits of those alternatives, including clinical trials.

- Patients treated with casirivimab/imdevimab, bamlanivimab/etesevimab, or Sotrovimab should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect "high touch" surfaces, and frequent handwashing) according to CDC guidelines.

- Mandatory reporting of all medication errors and serious adverse events potentially related to casirivimab/imdevimab or sotrovimab to FDA MedWatch & Regeneron within 7 calendar days

References:

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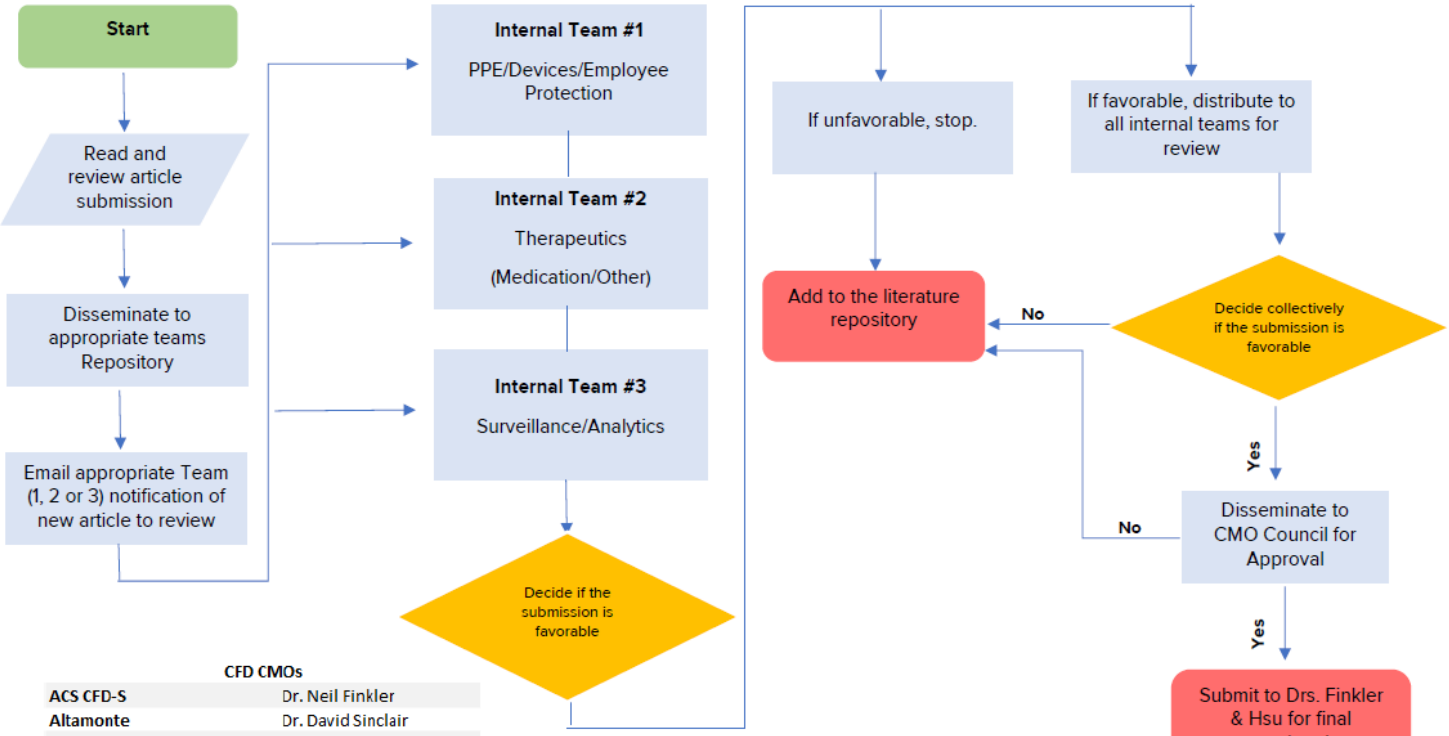
Disclaimer: The Scientific Committee was formed under the Medical Management Branch of the COVID-19 Pandemic Response Team. The committee's goal is to create a repository, interrogate research literature as it pertains to the treatment of COVID-19 and provides a rapid approval process. The algorithm below is the decision-making process that governs our decisions.

Scientific Subcommittee Approval Process



CFD CMOs	
ACS CFD-S	Dr. Neil Finkler
Altamonte	Dr. David Sinclair
Apopka/WG	Dr. Omayra Mansfield
Celebration	Dr. Jay Ball
Mission Control	Dr. Sanjay Pattani
East Orlando	Dr. Alric Simmonds Jr.
Orlando	Dr. Victor Herrera
Children's	Dr. Michael Keating
Heart of Florida / Lake Wales	Dr. Vincent Carifi
Winter Park	Dr. Jennifer Keehbauch
Kissimmee	Dr. Dennis DeLeon

Internal Team Legend	
Internal Team #1	Drs. Simmonds & Rizwan
Internal Team #2	Drs. Parikh & Smith
Internal Team #3	Drs. Parikh & West
	Drs. Mansfield & Herrera to be added

Summary of Revisions

- 03/15/2020
  - General treatment options, dosing, and monitoring
- 03/19/2020
  - Testing guidance for asymptomatic and symptomatic patients
  - Added therapeutic options based on severity using scale and laboratory monitoring for patients with COVID-19
  - Updated dosing for hydroxychloroquine
  - Corticosteroids: use of steroids in patients with severe disease could be considered as part of the supportive care regimen for *patients with ARDS on a case-by-case basis*
  - ACEi/ARB: advised against adding/removing beyond in standard practice
  - NSAIDs: no evidence for against the management of fever with NSAIDs
  - Guidance for use of nebulized respiratory medications
  - Removed chloroquine, ribavirin, atazanavir/ritonavir, atazanavir/cobicistat, darunavir/cobicistat
  - Added Tocilizumab
  - Post-exposure prophylaxis for patients and health care workers
- 03/21/2020
  - Added: Discharge patients should be offered supportive care (anti-pyretics, MDI, etc.)
- 03/25/2020
  - Updated treatment options based on severity score:
    - Severity score 1: removed hydroxychloroquine, lopinavir/ritonavir, darunavir/ritonavir
    - Severity score 2-3: no change
    - Severity score ≥ 4: Remdesivir for eligible patients first, if not: hydroxychloroquine. Removed combination of hydroxychloroquine plus lopinavir/ritonavir or darunavir/ritonavir
  - Lower dose glucocorticoids (equivalent to methylprednisolone 1-2 mg/kg/day for 3-5 days or ≤0.5-1 mg/kg/day methylprednisolone for ≤ 7 days) have been recommended after *careful consideration of risks and benefits.*
  - Azithromycin: insufficient evidence to recommend the use of azithromycin in addition to hydroxychloroquine
  - ECG monitoring at baseline for all hospitalized patients
- 03/31/2020
  - Revised the duration of treatment
    - Severity score: 2-3: changed from 10 days to 5-7 days
    - Severity score ≥ 4: changed from 10-14 days to 7-10 days
  - Corticosteroids: early initiation of lower dose glucocorticoids (equivalent to methylprednisolone 1-2 mg/kg/day for 3-5 days or ≤0.5-1 mg/kg/day methylprednisolone for ≤ 7 days) have been recommended for *patients with refractory shock and/or ARDS*
  - Removed darunavir/ritonavir
  - Added Sarilumab with criteria for use
- 4/15/2020
  - Added: statement regarding use of off-label experimental therapies with only *in vitro* data
  - Added recommendation against use of ivermectin
  - Added anticoagulation pathway
  - Added guidance on cardiac monitoring

- Added additional steroid guidance and chart with risk factors for CRS
- Added restriction to ID for lopinavir/ritonavir
- Revised daily monitoring parameters

- 4/20/2020
  - Added statement regarding use of micronutrients, Zinc and Vitamin C
- 4/27/2020
  - Removed lopinavir/ritonavir from algorithm
  - Added comment regarding use of hydroxychloroquine
  - Updated remdesivir information for compassionate use
- 4/29/2020
  - Updated anticoagulation algorithm, removal of ROTEM
  - Added statement regarding use of tPA
- 5/12/2020
  - Removed hydroxychloroquine from algorithm
- 5/18/2020
  - Added guidance for outpatient anticoagulation
  - Removed cardiac monitoring for patients receiving hydroxychloroquine
  - Removed statement regarding empiric initiation of experimental/investigational therapies for severity score ≥ 4
  - Included information on remdesivir emergency use authorization
  - Included information on convalescent plasma
- 5/26/2020
  - Clarification of outpatient anticoagulation recommendations
- 6/4/2020
  - Updated allocation information on remdesivir
- 6/9/2020
  - Updated DOH link to request remdesivir for State of Florida (outside of CFDS)
- 6/18/2020
  - Addition of low-dose dexamethasone recommendation
  - Removal of remdesivir compassionate use information
  - Edited remdesivir allocation information
- 6/30/2020
  - Added warning against use of hydroxychloroquine
  - Modified IL6 antagonist recommendation to include use for severity score ≥ 2
  - Updated remdesivir access process
- 7/3/2020
  - Removal of sarilumab from algorithm
  - Updated tocilizumab recommendation to include use for severity score ≥ 3
- 7/14/2020
  - Modified remdesivir criteria for use
- 8/5/2020
  - Revised remdesivir criteria for use
  - Updated multi-state convalescent plasma inclusion criteria

- Removal of HERO study details as trial has stopped enrollment
- Addition of statement regarding insufficient data on use of tocilizumab

- 8/25/2020
  - Updated convalescent plasma criteria based on FDA's EUA announcement
- 9/3/2020
  - Updated verbiage regarding remdesivir criteria for use
- 10/27/2020
  - Updated remdesivir information to reflect changes in regulatory requirements based on FDA approval of remdesivir on 10/22/20
  - Removed tocilizumab and recommended against routine use
- 11/12/2020
  - Added bamlanivimab
- 11/19/2020
  - Added NIH and IDSA recommendations and references for use of bamlanivimab in outpatients
- 11/24/2020
  - Reviewed available data and EUA information on baricitinib
- 12/3/2020
  - Added casirivimab/imdevimab
- 12/22/2020
  - Revised language regarding baricitinib
- 1/7/2021
  - Updated verbiage regarding use of ivermectin
- 1/12/2021
  - Added tocilizumab back into treatment algorithm
- 2/4/2021
  - Included information on colchicine for non-hospitalized patients
- 2/9/2021
  - Modified tocilizumab recommendation to include only patients with severity score ≥3
  - Updated convalescent plasma EUA criteria
- 2/11/2021
  - Updated EUA information on convalescent plasma
  - Added EUA information for bamlanivimab/etesevimab combination
  - Added additional links to ivermectin
- 2/18/2021
  - Updated information on convalescent plasma severity score recommendations based on EUA
- 3/02/2021
  - Updated inpatient and outpatient anticoagulation algorithm
- 3/10/2021
  - Added additional study evaluating ivermectin
  - Updated information and recommendations on MABs
- 3/25/2021
  - Updated criteria for use for remdesivir to include option to use in patients on high flow oxygen
  - Updated information and recommendations on MABs
- 4/20/2021

- Updated guideline recommendations on MABs
- Included FDA EUA updates and information on the revoked EUA for bamlanivimab monotherapy

- 5/3/2021
  - Updated tocilizumab criteria to reflect provider restrictions
- 5/25/2021
  - Updated EUA requirements for MABs
- 5/27/2021
  - Updated bamlanivimab-etesevimab information on distribution to the state of Florida
- 6/3/2021
  - Modified recommendation for use of COVID-19 convalescent plasma
- 6/7/2021
  - Updated FDA EUA information for casirivimab/imdevimab: new dosing and route of administration
- 6/15/2021
  - Clarified language regarding scientific basis for avoiding routine use of remdesivir in patients on room air or mechanical ventilation
  - Removed statement about insufficient data for baricitinib and the warning against use of baricitinib with corticosteroids
  - Updated FDA EUA information for new MAB, Sotrovimab
- 6/25/2021
  - Updated information regarding distribution of bamlanivimab-etesevimab in the U.S.