

COVID-19: Inpatient Evaluation and Management Guidelines

<p>Goal</p> <p>Guide clinicians on the inpatient management of COVID-19 with regards to therapeutic management, determining appropriate level of care, and early recognition of those at risk for severe disease</p>	<p>Key Points</p> <ul style="list-style-type: none"> Recommendations for management of COVID-19 are evolving and guidelines will be updated regularly Patient isolation and proper use and maintenance of personal protective equipment are critical
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Initial Evaluation and Management		
<p>Testing</p>	<ul style="list-style-type: none"> Two Options: SARS-CoV-2 RAPID or Novel Coronavirus PCR (both detect viral RNA) Both tests are performed by nasopharyngeal swab (PCR can also be run on body fluids) The sensitivity / specificity is different for each test. <ul style="list-style-type: none"> Review OSWMC's Laboratory Testing and Specimen Collection guidelines to determine the most appropriate test based on the patient's indication and pretest probability. 	
<p>Indications for Admission</p>	<ul style="list-style-type: none"> Dyspnea at rest or dyspnea impairing ability to tolerate PO intake Persistent tachypnea / increased work of breathing New supplemental oxygen requirements or an increase in baseline supplemental oxygen requirements Signs of SIRS/sepsis - particularly high-grade fevers ($\geq 101^{\circ}\text{F}$ or 38.3°C) Evidence of organ failure - particularly AKI or elevated lactate Altered mental status 	<ul style="list-style-type: none"> Multiple risk factors for progression to severe COVID-19: <ul style="list-style-type: none"> Age 65 or older Cardiovascular disease (CAD, CHF, or cardiomyopathies) Chronic lung disease Diabetes Cancer (in particular hematologic malignancies, lung cancer, and metastatic disease) Obesity ($\text{BMI} \geq 30 \text{ kg/m}^2$) Chronic kidney disease Hemoglobin disorders such as sickle cell disease Receiving immunosuppressive therapy
<p>Orders for Admission</p> <p><i>Strongly recommend using the COVID-19 Admission Order Set</i></p>	<p>Initial Testing:</p> <ul style="list-style-type: none"> CBC, Chem 7, LFTs, coagulation profile, D-dimer Consider COVID IgG and type and screen (if may be candidate for convalescent plasma) ECG (consider troponin if otherwise indicated) CXR (portable is preferred due to exposure risks) Consider CTPE if D-dimer is elevated ($>2.0 \text{ mcg/mL}$) AND there is high clinical suspicion Consider procalcitonin, sputum culture, <i>S. pneumoniae</i> and Legionella antigen assays, MRSA nares swab Consider blood cultures if febrile / septic or other reasons to suspect concomitant bacterial process 	<ul style="list-style-type: none"> Level of care (see section below) Oxygen support to keep $\text{SpO}_2 \geq 90\%$ (or $\geq 88\%$ if chronic lung disease or concomitant hypercarbia) Pulse oximetry – continuous for at least the first 48hrs Prone order set Therapeutics (see section below) DVT prophylaxis is imperative and specific dosing is recommended for COVID-19 patients. See the COVID-19 Anticoagulation Management, VTE Prophylaxis and Treatment guideline or Appendix A Routine ID consult is NOT recommended. See indications outlined below. Routine Pulmonology consult is NOT recommended. See indications outlined below. Isolation Orders (Enhanced Droplet / Contact Precautions) Code Status

Treatment Recommendations	
General Principles for Supportive Care	<ul style="list-style-type: none"> ▪ Conservative Fluid Resuscitation: IV fluids can be utilized if clinically indicated but a conservative approach is recommended if PO intake and urine output are adequate due to risk for progression to ARDS ▪ Electrolyte Monitoring and Repletion: Imbalances are commonly seen and repletion is recommended to avoid other complications ▪ Supplemental Oxygen: Recommendations suggest goal SpO₂ ≥ 90% in most patients with goal SpO₂ ≥ 88% if patient has chronic lung disease or concomitant hypercarbia ▪ Awake Proning: Often helpful for patients requiring supplemental oxygen. See Prone Positioning for Non-Mechanically Ventilated Patients guideline. ▪ VTE Prophylaxis: This is particularly important as COVID-19 has been established as a hypercoagulable state. See COVID-19 Anticoagulation Management, VTE Prophylaxis and Treatment guideline or Appendix A. ▪ Antitussives and Expectorants: Often helpful for symptom management ▪ Antipyretics: Acetaminophen is first line, okay to consider NSAIDs if not otherwise contraindicated ▪ Bronchodilators: Not routinely recommended but can be useful, especially if pre-existing reactive airway disease. Notably, nebulizers are considered aerosol-generating procedures and are restricted to private rooms. ▪ Evaluation for Superimposed Bacterial Infection ▪ Consider Clinical Trial if your patient meets criteria. See Clinical Trials Workflow.
Advanced Care Planning (ACP)	<ul style="list-style-type: none"> ▪ Discussion regarding code status and intubation wishes should be completed on admission and can be documented in IHIS using the .COVID19ACP dotphrase. Ohio DNR forms should be completed if indicated. See the Palliative Care Resources for further details.
Infectious Disease Consultation	<ul style="list-style-type: none"> ▪ ID consult is no longer mandatory for COVID-19 patients or medication approval (such as remdesivir) ▪ Consider ID consultation in the following scenarios: <ul style="list-style-type: none"> ○ High risk asymptomatic COVID-19 patients that do not require supplemental oxygen (e.g. HIV, on immunosuppressive therapy, or active cancer) as they may be considered for remdesivir based on ID recommendations ○ Considering use of convalescent plasma (see below) ○ Considering use of Tocilizimab (see below) ○ Concerned for secondary bacterial infection
Pulmonology Consultation	<ul style="list-style-type: none"> ▪ Routine Pulmonology consult is not recommended. ▪ Pulmonology consultation is indicated in the following scenarios: <ul style="list-style-type: none"> ○ Patient requiring Heated High Flow Nasal Cannula (HHFNC) ○ Patient requiring continuous CPAP / BiPAP ○ Cystic Fibrosis patients ▪ Consider Pulmonology consultation in the following scenarios: <ul style="list-style-type: none"> ○ Pre-existing high risk chronic lung diseases (Pulmonary Fibrosis / ILD, tracheobronchomalacia, chronic hypercarbia, or advanced COPD) ○ Considering use of Tocilizimab (see below)
Infection Prevention and Control	<ul style="list-style-type: none"> ▪ Immediately place a surgical mask on patient to reduce transmission rates ▪ Place patients on Enhanced Droplet and Contact Isolation ▪ Use PPE appropriately: Gown, gloves, N-95 or acceptable alternative, and eye-protection ▪ Practice proper PPE donning and doffing technique and proper hand hygiene; review PPE Instructions



Treatment Recommendations

Corticosteroids [1]

General (Non-ICU) Patient Population	Pregnant Patient Population
<ul style="list-style-type: none"> Recommended only if patient requires supplemental oxygen Dexamethasone dosing is 6 mg (IV or PO) daily x 10 days or until discharge (whichever comes first) Frequently causes hyperglycemia in pre-diabetic / diabetic patients. As such, recommend monitoring accuchecks ACHS for at least 4 occurrences. Consider GI prophylaxis (with PPI or H2 blocker) if history of or high risk for PUD <p>See COVID-19 Critically Ill Adult Patient Management guideline for additional treatment options for ICU patients</p>	<ul style="list-style-type: none"> Corticosteroids are recommended in women requiring supplemental oxygen or mechanical ventilation Patients < 23 weeks or ≥ 34 weeks gestational age or postpartum: Recommend methylprednisolone 32 mg per day orally or intravenously for a total of 10 days or until discharge (whichever occurs first). Patients between 23 0/7 weeks and 33 6/7 weeks gestational age: Recommend 6 mg intramuscular q12h for 48 hours followed by methylprednisolone 32 mg per day for an additional 8 days for a total of 10 days or until discharge (whichever occurs first). Methylprednisolone is recommended over dexamethasone in breastfeeding patients

Remdesivir [2]

Indications	Dosing
<ul style="list-style-type: none"> FDA approved for the treatment of COVID-19 in adult and pediatric (12 years of age and older and weighing at least 40 kg) for patients within 14 days of symptoms onset with one of the following: <ul style="list-style-type: none"> Need for supplemental oxygen Immunocompromised Pregnant 2 or more risk factors for severe disease Requires ASP approval – though first dose can be ordered without approval if being entered after hours Page ASP at 9394 between 8am-5pm for approval code 	<ul style="list-style-type: none"> 200 mg IV x 1, followed by 100 mg IV daily x 4 doses (5 day total duration) <ul style="list-style-type: none"> If patient has not shown clinical improvement after 5 days of therapy, treatment may be extended up to 10 days
	Monitoring
	<ul style="list-style-type: none"> Remdesivir is not recommended if CrCl < 30 mL/hr unless benefit outweighs risk Requires baseline labs: Chem, LFTs, and PT/INR, and ongoing monitoring as clinically appropriate Remdesivir should be discontinued if ALT rises > 10x the upper limit of normal

Tocilizumab [3]

Indications	Dosing
<ul style="list-style-type: none"> Tocilizumab is a recombinant humanized monoclonal IL-6 antibody, approved for certain rheumatological diseases and Chimeric Antigen Receptor (CAR) T cell-induced cytokine release syndrome Tocilizumab may be considered in hospitalized patients already receiving corticosteroids with both of the following: <ul style="list-style-type: none"> Elevated CRP ≥ 75 Rapid and significant respiratory deterioration Consider consultation with pulmonology, critical care and/or infectious diseases as clinically appropriate 	<ul style="list-style-type: none"> 8 mg/kg/dose (800 mg maximum) intravenously Second dose may be repeated 12-24 hours later based on clinical response. Not to exceed 2 doses. Should not be initiated greater than 21 days from symptom onset
	Monitoring
	<ul style="list-style-type: none"> Monitor closely for secondary infections as fever can be masked IL-6 levels normally increase after tocilizumab administration and do not indicate treatment failure Further dosing should be guided by clinical status rather than inflammatory markers Monitor for hepatotoxicity which typically occurs 10-14 days following therapy.

Precautions

- Avoid use in patients with uncontrolled active infection** other than COVID-19
- Black box warning for severe infection
- Long half-life with potential for ongoing immunosuppression
- Caution in patients with hepatic insufficiency. Some clinical trials excluded patients with elevated LFTs (ALT/AST ≥5-10X upper limit of normal).

**Treatment Recommendations****COVID Convalescent Plasma (CCP) [4]** – See [CCP Clinical Trial and EUA Guideline](#) for more information

Currently, there is insufficient data to recommend either for or against the use of convalescent plasma. The benefit remains unclear and likely depends on the antibody titer present in the plasma. This treatment is available under FDA EUA issuance and as part of a clinical trial. Current data suggest that the earlier it is given, the more likely it is to be potentially beneficial.

Inclusion Criteria	Baseline Information and Consent for CCP
<ul style="list-style-type: none">▪ Laboratory confirmed COVID-19 Plus BOTH of the following:<ul style="list-style-type: none">○ Oxygen requirement of at least 2 LPM OR high risk for decompensation○ Duration of symptoms < 7 days OR negative COVID-19 IgG Ab test▪ It is important to note that patients may not qualify for some clinical trials if they have already been consented for convalescent plasma. As such, patients should be reviewed for clinical trial candidacy before considering convalescent plasma therapy.	<p>If considering convalescent plasma therapy:</p> <ul style="list-style-type: none">▪ Order type and screen (if not already performed)▪ Consider checking COVID-19 IgG▪ Consent patient for blood transfusion (will need to manually write “convalescent plasma” on the form under section 3, indicating “types of blood or blood products” consented to)▪ Go over convalescent plasma consent form with patient

Non-Antimicrobial Medications

- Additional recommendations for non-antimicrobial medications associated with complications and comorbidities linked to COVID-19 (e.g. IVIG, ACEI/ARBs, NSAIDs, etc.) refer to [Further COVID-19 Medication Considerations and FAQ](#).



Assessing Response to Therapy

Key Clinical / Laboratory Features to Monitor

- **Oxygen requirements** – can take several days to see significant improvement
- **Work of breathing** – can be early sign of decompensation
- **Fever curve** – often see oxygen needs fluctuate while still febrile
- **Chem 7, LFTs, PT/INR** – needed at baseline if remdesivir. Regular chemistry / electrolyte monitoring is encouraged when not receiving remdesivir as well, given high incidence of derangements.
- **Consider acute phase reactants (CRP and Ferritin)** – this is not routinely recommended but can be helpful in some situations. A downtrend can be reassuring whereas a lack of improvement may indicate still in the “fragile” stages of the illness.

Re-evaluation and Management Considerations in Patients that Fail to Improve Clinically

Considerations if patient has escalating oxygen requirements or fails to make improvement in oxygen requirements:

- ☐ **Encourage awake proning** or increased prone frequency if already proning
- ☐ **Consider scheduled antipyretics** if still having regular fevers
- ☐ **Repeat CXR** to assess for progression of airspace disease
- ☐ **Reassess risks for pulmonary embolism:**
 - Consider CTPE if not obtained on admission or repeat CTPE if not receiving anticoagulation for one reason or another
 - Can consider repeating D-dimer. A rise from normal to abnormal or a very rapid rise should further raise concern for VTE.
 - Consider empiric therapeutic anticoagulation if contraindications to CTPE and low bleeding risk. Can reassess CTPE candidacy later during admission.
 - Can consider checking Anti-Xa levels if patient is receiving enoxaparin
- ☐ **Reassess for evidence of superimposed infection:**
 - Consider repeating procalcitonin, sputum, or blood cultures
 - Influenza testing / immunocompromised respiratory viral panel
 - Dysphagia or other risk factors for aspiration
- ☐ **Assess volume status:**
 - Can check BNP
 - Can trend weights
 - Consider diuretic trial if concern for volume overload / pulmonary edema
 - Echos on COVID-19 patients are restricted (to reduce exposure risk), but may be ordered on a case-by-case basis
- ☐ **Re-consider Infectious Disease consultation** (especially in high-risk populations: HIV, transplant recipients, immunocompromised patients, active cancer treatment)
- ☐ **Re-consider Pulmonology consultation** (especially in high-risk populations: advanced COPD / asthma, chronic hypercarbia, pulmonary fibrosis / interstitial lung disease, tracheobronchomalacia)



Management of COVID-19 Related Complications

Bacterial Superinfection	<ul style="list-style-type: none"> ▪ The incidence of bacterial superinfection in patients with COVID-19 is unknown and it may be difficult to identify concomitant bacterial pneumonia, at times, due to overlapping symptoms ▪ If antibiotics are initiated, base selection upon the following guideline recommendations according to risk factors present: <ul style="list-style-type: none"> ○ OSUWMC Evaluation and Initial Management of Community-Acquired Pneumonia (CAP) ○ OSUWMC Evaluation and Initiation Management of Hospital-Acquired and Ventilator Associated Pneumonia (HAP/VAP) ○ MICU Algorithm for Empiric Antibiotics in CAP/HAP/VAP (critical care guideline only) ▪ De-escalation of antibiotics within 48 hours should be addressed based on available culture data and clinical status^{11,15} ▪ Refer to Utilization of Procalcitonin to Guide Duration of Antibiotic Therapy in Inpatients Diagnosed with Sepsis and/or a Respiratory Tract Infection pharmacy guideline
Liver Impairment	<ul style="list-style-type: none"> ▪ Abnormal LFTs are common in COVID-19 and can be seen in > 90% of patients during the disease course [7]. Typically, a mild hepatocellular pattern is seen. ▪ Assessment and monitoring <ul style="list-style-type: none"> ○ Baseline LFTs and INR ○ If baseline normal, monitor every 3 days ○ If abnormal, review medication list for hepatotoxic drugs and consider sending viral hepatitis serologies ○ If on hepatotoxic therapies monitor daily and consult pharmacy for dosing adjustment recommendations ○ Imaging is not required for mild asymptomatic hepatocellular abnormalities but should be considered if there are concerning signs such as ascites, RUQ pain, cholestatic pattern of LFTs, or concern for portal vein thrombosis
Venous Thromboembolism	<ul style="list-style-type: none"> ▪ COVID-19 has been correlated with increased risk for VTE, presumed to be a result of a prothrombotic inflammatory state. Unless contraindicated, patients should be placed on VTE prophylaxis while inpatient. See COVID-19 Anticoagulation Management, VTE Prophylaxis and Treatment guideline or Appendix A. ▪ Data suggest that certain groups of patients also benefit from 30 days of extended VTE prophylaxis after discharge. Follow the following steps to determine if your patient qualifies. See Anticoagulation Management, VTE Prophylaxis and Treatment guideline or Appendix B for criteria / dosing information. ▪ Management of confirmed VTE is similar to that of non-COVID-19 patients (see OSUWMC PE guideline)
Cardiovascular Complications (Acute coronary syndrome, acute myocarditis, cardiogenic shock, arrhythmias)	<ul style="list-style-type: none"> ▪ A significant number of patients develop arrhythmias, heart failure, and acute cardiac injury. However, this is usually in the setting of a prolonged severe illness. ▪ See Cardiovascular Disease, Evaluation and Management guideline
Critically Ill Patients	<ul style="list-style-type: none"> ▪ Some patients develop ARDS similar to other critically ill patients with respiratory failure and ultimately require intubation, proning, and paralytics ▪ See COVID-19 Critically Ill Adult Patient Management guideline

Levels of Care: Criteria for Transfer to Progressive Care Unit (PCU) and Intensive Care Unit (ICU)

Consider transfer to PCU if:	Consider transfer to ICU if:
<ul style="list-style-type: none"> ▪ Patient requiring > 6 LPM via NC ▪ Patient requiring CPAP / BiPAP ▪ Heated high flow NC (HHFNC) can now be provided in the PCU <ul style="list-style-type: none"> ○ <u>However, if patient has a new HHFNC requirement, a pulmonary consult should be placed to discuss whether ICU may be more appropriate</u> ○ ABG monitoring for patients on HHFNC is at physician discretion ▪ Typical indications for transfer to PCU still apply – increased level of care per nursing concerns, other comorbidities requiring closer monitoring (i.e. A fib with RVR, IV drips, etc.), more frequent vitals (up to every 2 hours) 	<ul style="list-style-type: none"> ▪ Rapidly progressive oxygenation requirements, especially new HHFNC or prolonged NIPPV ▪ Altered mentation in setting of rapidly progressive oxygen requirements ▪ Concern for impending respiratory failure ▪ Typical indications for transfer to ICU still apply – shock, need for mechanical ventilation, hemodynamic instability (SBP < 90, MAP < 65), ABG with pH < 7.3 or PCO₂ > 50 mmHg or above patient's baseline

Discharge Considerations

Inpatient Isolation Discontinuation	<ul style="list-style-type: none"> ▪ See guidelines regarding discontinuation of isolation precautions ▪ If any questions, can reach out to Epidemiology for guidance (pager 2399)
Repeat Testing	<ul style="list-style-type: none"> ▪ Repeat testing is not required nor recommended for discharge (as PCR testing can detect non-viable viral RNA after infection has resolved) ▪ However, some facilities (skilled nursing facilities or even home health care agencies) may require repeat testing prior to accepting a patient. Usually, these organizations will inform you about which tests (PCR vs rapid testing) they require.
COVID-19 Discharge Criteria	<p>Consider discharge for patients who meet the following clinical criteria:</p> <ul style="list-style-type: none"> ▪ Resolution of fever ≥ 48 hours (without the use of antipyretics) ▪ Improvement / stability in illness signs and symptoms (cough, SOB, and oxygen requirement) x 48 hours ▪ Oxygen requirements ≤ 4 LPM per NC ▪ As above, for patients going to a skilled nursing or rehab facility, isolation discontinuation protocols may be requested by the facility prior to discharge. ▪ Consider enrolling patient in COVID-19 Home Monitoring (including home monitoring kit) if their PCP is associated with OSUWMC (MyChart Care Companion COVID-19 Home Monitoring – Inpatient Tip Sheet) ▪ Recommend using the Discharge Checklist
Extended VTE Prophylaxis	<ul style="list-style-type: none"> ▪ Data supports continued VTE prophylaxis for 30 days in certain patient populations. ▪ See Anticoagulation Management, VTE Prophylaxis and Treatment guideline or Appendix B for criteria / dosing information.

Appendix A: Pharmacologic VTE Prophylaxis in COVID-19 Patients

PHARMACOLOGIC VTE PROPHYLAXIS IN COVID-19 PATIENTS*							
BMI < 40 and Weight ≤ 50kg		BMI < 40 and Weight > 50kg		BMI ≥ 40 and Weight < 150kg		BMI ≥ 40 and Weight ≥ 150kg	
CrCl < 30	CrCl ≥ 30	CrCl < 30	CrCl ≥ 30	CrCl < 30	CrCl ≥ 30	CrCl < 30	CrCl ≥ 30
Heparin 5,000 units SQ Q12H	Enoxaparin 30mg SQ Q24H	Heparin 5,000 units SQ Q8H	Enoxaparin 30mg SQ Q12H	Heparin 7,500 units SQ Q8H	Enoxaparin 40mg SQ Q12H	Heparin 7,500 units SQ Q8H	Enoxaparin 0.3mg/kg ^Δ SQ Q12H

* This applies to non-pregnant COVID-19 patients. For pregnant patients or other special populations, please refer to the [COVID-19 Anticoagulation Management Guidelines](#) and / or the [VTE Prevention Guidelines](#).

Δ The initial maximum dose is 60mg Q12H. For weight based enoxaparin, round to the nearest 10mg increments (e.g. 45mg should be rounded to 50mg Q12H and 43mg should be rounded to 40mg Q12H)

For patients receiving enoxaparin, refer to the [Enoxaparin Antifactor Xa Level policy](#) for guidance on monitoring

Note: As both documents are likely to be frequently updated, refer to the COVID-19 Anticoagulation Management Guidelines if a discrepancy has developed

Appendix B: VTE Prophylaxis at Discharge for COVID-19 Patients

DISCHARGE VTE PROPHYLAXIS IN COVID-19 PATIENTS*		
Data suggest that certain groups of patients benefit from 30 days of extended VTE prophylaxis after discharge. Follow the steps below to determine if your patient qualifies.		
1. Evaluate patient for presence of any of the following, which would make them NOT a candidate <ul style="list-style-type: none"> On Dual Antiplatelet Therapy at baseline Gastroduodenal Ulcers Active bleeding within the last 3 months that was at a critical site (i.e., intracranial) or required hospitalization, transfusion, or other interventions 		
2. If no risk conditions from step 1, complete the IMPROVEDD VTE and IMPROVE Bleeding Risk score assessments		
IMPROVEDD VTE Score ≥ 4 OR IMPROVEDD VTE Score 2 – 4 with D-dimer > 1mcg/mL AND Bleeding Risk Score < 7	IMPROVEDD VTE Score ≥ 4 OR IMPROVEDD VTE Score 2 – 4 with D-dimer > 1mcg/mL AND Bleeding Risk Score ≥ 7	IMPROVEDD VTE Score < 4 AND D-dimer ≤ 1mcg/mL
<ul style="list-style-type: none"> 30 days of extended VTE ppx is recommended at discharge. See dosing below 	<ul style="list-style-type: none"> Weigh risks and benefits of extended VTE ppx Include patient in discussions and decision making process If decision is made to discharge on extended VTE prophylaxis, see dosing below 	<ul style="list-style-type: none"> Extended VTE ppx is NOT recommended
Extended VTE Prophylaxis Dosing <ul style="list-style-type: none"> Apixaban 2.5mg BID (preferred in patients with CrCl < 30 mL/min) OR Rivaroxaban 10mg daily If patient is not a candidate for a DOAC, consult pharmacy 		
* Referring to non-pregnant patients. If patient is pregnant, refer to the COVID-19 Anticoagulation Management Guidelines		

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IHIS Order Sets

- MED: Admission COVID-19
- IP/ED: 2019 NOVEL CORONAVIRUS (2019-NCOV) LAB ORDERS (aka COVID-19)

IHIS Smart Phrases

- .HMECOVIDHANDP
- .COVID19DISCHARGEINSTRUCTIONS
- .HMECOVIDPROG

OSUWMC Resources

- [Further COVID-19 Treatment Considerations and FAQ](#)
- [COVID-19 Critically Ill Adult Patient Management](#)
- [Prone Positioning for Non-Mechanically Ventilated Patients](#)
- [Anticoagulation Management, VTE Prophylaxis and Treatment](#)
- [Discharge Checklist](#)

Isolation and Personal Protective Equipment (PPE)

- [Employee Exposure Guidelines, PPE Instructions and PPE Guidance](#)
- [Isolation Recommendation Guidance](#)
- [Medication Administration Bundling](#)
- [Code Blue Protocol](#)
- [Aerosol Generating Procedures](#)

CDC and WHO Resources

- [CDC resource for health care providers](#)
- [WHO technical guidance for health care providers](#)

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3. Fact Sheet for Health Care Providers: EUA of COVID-19 **Convalescent Plasma** for Treatment of COVID-19 in Hospitalized Patients <https://www.fda.gov/media/141478/download>
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COVID-19: Critically Ill Adult Patient Management

Key Points

- Consider [drug shortages](#) in the selection of all therapies
- Given the recent pandemic, all treatment strategies and recommendations are provided based on the best evidence available
- For more information regarding therapies that are not currently recommended and medications associated with complications and comorbidities linked to COVID-19 (e.g. IVIG, ACEI/ARBs, NSAIDs, etc.) refer to [Further COVID-19 Treatment Considerations: Therapies Not Currently Recommended and Frequently Asked Questions](#)
- Consider corticosteroids for patients on supplemental oxygen or mechanical ventilation
- [Cardiovascular](#) and [thromboembolic](#) complications are increased in this patient population. Refer to the respective patient population guidelines.

Treatment Recommendations

Refer to the [Inpatient Evaluation and Management Guideline](#) for information on presentation, initial workup and management

Corticosteroids

- Recommended in patients requiring supplemental oxygen and/or mechanical ventilation
 - In patients requiring supplemental oxygen or mechanically ventilated, **recommend** dexamethasone 6 mg oral or intravenous daily for 10 days⁵
- In patients meeting criteria for ARDS⁵⁻¹⁰ recommend** dexamethasone 20 mg daily for 5 days followed by 10 mg daily for 5 days **or** 6 mg daily for 10 days either oral or intravenous^{5,10}
 - In patient with ARDS who is clinical decompensating while on dexamethasone 6 mg daily, consider escalating dosing the dexamethasone 20 mg daily for 5 days followed by 10 mg daily for 5 days
- Corticosteroids are unlikely to be beneficial and may be harmful in late ARDS (> 7 days from onset)⁸

Pregnant Patient Population

- Corticosteroids are recommended in women requiring **supplemental oxygen or mechanical ventilation**
- Patients < 23 weeks or ≥ 34 weeks gestational age or postpartum: Recommend methylprednisolone 32 mg per day orally or intravenously for a total of 10 days or until discharge (whichever occurs first).
- Patients between 23 0/7 weeks and 33 6/7 weeks gestational age: Recommend 6 mg intramuscular q12h for 48 hours followed by methylprednisolone 32 mg per day for an additional 8 days for a total of 10 days or until discharge (whichever occurs first).
- Methylprednisolone is recommended over dexamethasone in breastfeeding patients

Remdesivir

Indication for Use	Dosing	Monitoring
<ul style="list-style-type: none"> FDA approved for the treatment of COVID-19 in adult and pediatric (12 years of age and older and weighing at least 40 kg) for patients within 14 days of symptoms onset with one of the following: <ul style="list-style-type: none"> Need for supplemental oxygen Immunocompromised Pregnant 2 or more risk factors for severe disease 	<ul style="list-style-type: none"> 200 mg IV x 1, followed by 100mg IV daily x 4 doses (5 days total duration) <ul style="list-style-type: none"> If patient has not shown clinical improvement after 5 days of therapy, treatment may be extended up to 10 days 	<ul style="list-style-type: none"> Remdesivir is not recommended if CrCl < 30 mL/hr unless benefit outweighs risk Requires baseline labs: Chem, LFTs, and PT/INR, and ongoing monitoring as clinically appropriate Remdesivir should be discontinued if ALT rises > 10x the upper limit of normal

Requires ASP approval – though first dose can be ordered without approval if being entered after hours
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Treatment Recommendations

Tocilizumab

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<ul style="list-style-type: none"> Tocilizumab is a recombinant humanized monoclonal IL-6 antibody, approved for certain rheumatological diseases and Chimeric Antigen Receptor (CAR) T cell-induced cytokine release syndrome Tocilizumab may be considered in hospitalized patients already receiving corticosteroids with both of the following: <ul style="list-style-type: none"> Elevated CRP ≥ 75 Rapid and significant respiratory deterioration Consider consultation with pulmonology and/or infectious diseases as clinically appropriate 	<ul style="list-style-type: none"> 8 mg/kg/dose (800 mg maximum) intravenously Second dose may be repeated 12-24 hours later based on clinical response. Not to exceed 2 doses. Should not be initiated greater than 21 days from symptom onset 	<ul style="list-style-type: none"> Monitor closely for secondary infections as fever can be masked IL-6 levels normally increase after tocilizumab administration and do not indicate treatment failure Further dosing should be guided by clinical status rather than inflammatory markers Monitor for hepatotoxicity which typically occurs 10-14 days following therapy
	Precautions <ul style="list-style-type: none"> Avoid use in patients with uncontrolled active infection other than COVID-19 Black box warning for severe infection Long half-life with potential for ongoing immunosuppression Caution in patients with hepatic insufficiency. Some clinical trials excluded patients with elevated LFTs (ALT/AST ≥ 5-10X upper limit of normal). 	

COVID Convalescent Plasma (CCP) – See [CCP Clinical Trial and EUA Guideline](#) for more information

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<ul style="list-style-type: none"> Laboratory confirmed COVID-19 Plus BOTH of the following: <ul style="list-style-type: none"> Oxygen requirement of at least 2 LPM OR high risk for decompensation Duration of symptoms < 7 days OR negative COVID-19 IgG Ab test It is important to note that patients may not qualify for some clinical trials if they have already been consented for convalescent plasma. As such, patients should be reviewed for clinical trial candidacy before considering convalescent plasma therapy. 	<p>If considering convalescent plasma therapy:</p> <ul style="list-style-type: none"> Order type and screen (if not already performed) Consider checking COVID-19 IgG Consent patient for blood transfusion (will need to manually write "convalescent plasma" on the form under section 3, indicating "types of blood or blood products" consented to) Go over convalescent plasma consent form with patient

Antibiotic Selection for Superinfection

- The incidence of bacterial superinfection in patients with COVID-19 is unknown and it may be difficult to identify concomitant bacterial pneumonia, at times, due to overlapping symptoms
- If antibiotics are initiated, base selection upon the following guideline recommendations according to risk factors present:
 - [OSUWMC Evaluation and Initial Management of Community-Acquired Pneumonia \(CAP\)](#)
 - [OSUWMC Evaluation and Initiation Management of Hospital-Acquired and Ventilator Associated Pneumonia \(HAP/VAP\)](#)
 - [MICU Algorithm for Empiric Antibiotics in CAP/HAP/VAP](#) (critical care guideline only)
- De-escalation of antibiotics within 48 hours should be addressed based on available culture data and clinical status^{11,15}
 - Refer to [Utilization of Procalcitonin to Guide Duration of Antibiotic Therapy in Inpatients Diagnosed with Sepsis and/or a Respiratory Tract Infection](#) pharmacy guideline

Management in Acute Respiratory Distress Syndrome (ARDS) - Steroids as recommended above (see page 1)

Fluid Management in ARDS

- In the absence of shock, following initial resuscitation a **conservative fluid management strategy is recommended** to achieve a negative fluid balance of 0.5 to 1.0 liters per day¹¹⁻¹³
 - Consider de-resuscitative strategies such as IV diuretics
- In the presence of shock, achieve fluid balance through renal replacement therapy, especially in the presence of acute kidney injury and oliguria¹³
- Conservative fluid strategy has shown increased ventilator free days and decreased ICU length of stay in ARDS patients when compared with a liberal fluid strategy
 - Cardiac failure is attributed as a large portion of deaths in COVID-19 patients (conservative fluid strategy is recommended to prevent myocardial injury and pulmonary edema)

SeaStar NxStage® Protocol for Cytokine Storm Syndrome

- The Italian Society of Nephrology has endorsed the use of cytokine filters in COVID-19 patients requiring RRT¹⁸
- See [SeaStar Medical's Selective Cytopheretic Device webpage](#) for more information
- The SeaStar® filter can be used in the NxStage® CRRT machine to allow cytokine filtration ([Appendix C](#))

Neuromuscular Blockade

- NMB should be considered in patients with ARDS with a PaO₂/FiO₂ ratio <150 and persistent ventilator dyssynchrony despite deep sedation (RASS -4 to -5), prone ventilation, or persistently high plateau pressures¹⁴
- Using intermittent IV push doses of NMB agents is preferred when able to conserve drug supply
 - Recommend vecuronium or rocuronium if using intermittent IV push due to longer duration of action than cisatracurium or atracurium
- Refer to the [Continuous Pharmacologic Neuromuscular Blockade of the Critically Ill Patient](#) and [Continuous Neuromuscular Blocking Agent Pharmacy Checklist](#) when initiating

Pulmonary Vasodilators

Inhaled Epoprostenol	Inhaled Nitric Oxide (NO)
<ul style="list-style-type: none"> ▪ Refer to Inhaled Epoprostenol policy for general considerations ▪ ONLY initiate if the patient is requiring mechanical ventilation <ul style="list-style-type: none"> ○ While inhaled epoprostenol is able to be administered with NIPPV, it is not recommended in PUI/Confirmed COVID-19 patients to decrease risk of aerosolization and spread ▪ Even in intubated patients, there is a risk of aerosolization when the circuit is broke during administration. Practitioners should take appropriate precautions when administering. 	<ul style="list-style-type: none"> ▪ NO should be reserved for severe refractory hypoxemia ▪ Typical starting dose is 20 ppm and titrate to lowest effective dose to avoid methemoglobinemia ▪ Refer to Inhaled Nitric Oxide policy for more information ▪ Recommend monitoring for methemoglobin daily while on therapy ▪ Inhaled NO has not been studied in patients with mild ARDS. However, NIPPV is not needed for administration of inhaled NO as it is for inhaled epoprostenol. <ul style="list-style-type: none"> ○ Inhaled NO may decrease viral replication leading to theoretical benefit ▪ Prior to initiation of iNO for mild-moderate ARDS there should be attending approval and/or enrollment in a clinical study
<ul style="list-style-type: none"> ▪ These have not shown improved outcomes in ARDS. They do increase oxygenation and reduce pulmonary arterial pressure ▪ Inhaled vasodilators may be considered as rescue therapy in patients with refractory hypoxemia despite lung protective ventilation ▪ If no clinical improvement within 4 hours of therapy, the pulmonary vasodilator should be discontinued, as continued therapy will not likely provide benefit ▪ Nebulizer therapy is considered an aerosol producing procedure (Aerosol Generating Procedure Guidance) 	

Management in Acute Respiratory Distress Syndrome (ARDS) - Steroids as recommended above (see page 1)

Extracorporeal Membrane Oxygenation (ECMO)²⁰

- In severe ARDS patients, failing conventional management, ECMO may have a role in improving oxygenation and gas exchange while also allowing for further reduction of intensity of mechanical ventilation, and further reducing risk of ventilator-induced lung injury
- Refer to [OSUWMC Refractory Hypoxemia](#) guideline for patients who remain hypoxic despite lung protective ventilation
- Refer to [OSUWMC Extracorporeal Life Support \(ECLS\): Evaluation, Initiation and Management](#) guideline for patient eligibility for ECMO
 - ECMO is a finite resource compounded in the setting of this pandemic
 - As concerns for depletion of equipment or personnel with training for patient care, selection criteria may evolve
- Early initiation of ECMO (within 7 days of mechanical ventilation) facilitates positive outcomes. Consider use of the rescue therapies listed above but these should not delay ECMO consult.
- If ECMO is considered, immediate evaluation is required
 - Consult "Inpatient Consult to ECMO"
 - Direct physician-to-physician communication is also required

Vitamin C

- **Not recommended** due to lacking evidence. If Vitamin C is given, a dose of 50 mg/kg (maximum of 5,000 mg) every 6 hours for 4 days should be used based on the available literature in non-COVID ARDS

Proning

- Non-Intubated Patient:
 - Consider if patient would benefit from proning. See the [awake proning guideline](#) for further information.
- Mechanically Ventilated Patient:
 - Patients with severe hypoxemia ($\text{PaO}_2/\text{FiO}_2$ ratio < 150) benefit from proning
 - [OSUWMC Refractory Hypoxemia](#) provides guidance
 - Discuss with the critical care fellow or attending prior to initiation of proning and complete the Proning Checklist ([Appendix B](#))
- Use [Standard Operating Procedure: CPR in Prone Patients](#), as needed

Palliative Care in COVID-19

- A fundamental goal of medicine is to relieve human suffering, and while saving lives is crucial, it may not be the only way to achieve this goal²⁰
- In times of humanitarian emergencies and crises, such as the current COVID-19 pandemic, palliative care is crucial
- Palliative care and symptom control should be integrated as much as possible to life-saving treatment
- The most common severe type of suffering in humanitarian emergencies and crisis is pain, which should be treated aggressively. When the decision is made to switch from life-sustaining therapy to end-of life (EOL) care, pain, dyspnea, delirium, constipation, and secretions should be managed.
 - Patients with COVID-19 may experience dyspnea and agitation to greater proportion than others at EOL
- Refer to [OSUWMC Palliative Medicine End of Life Care](#) guidelines

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**Appendix A: Prone Huddle Checklist**

Checklist		
	Prior to turning patient prone, all team members should huddle and discuss the following:	Comments:
<input type="checkbox"/>	Explain process to patient/family	
<input type="checkbox"/>	Prepare the patient for pronation per OSUWMC clinical standards	
<input type="checkbox"/>	Will the patient remain prone for 16 hours?	Time to return to supine: _____
<input type="checkbox"/>	Draw ABG when patient has been prone for 30 minutes	
<input type="checkbox"/>	Wean ventilator settings per protocol to titrate $\text{FiO}_2 \leq 0.6$ $\text{PEEP} \leq 10$ to maintain $\text{SpO}_2 > 88\%$	
<input type="checkbox"/>	Maintain sedation to target a RASS of -4 to -5	
<input type="checkbox"/>	Will tube feedings be restarted?	
<input type="checkbox"/>	Prior to turning patient supine, all team members should discuss the following:	Time to return to prone: _____
<input type="checkbox"/>	Will the patient remain in the supine position for at least 6 hours?	
<input type="checkbox"/>	Draw ABG when patient has been in supine position for 30 minutes	
<input type="checkbox"/>	What criteria would prompt re-proning?	
<input type="checkbox"/>	Can sedation be weaned after supination?	
<input type="checkbox"/>	If paralyzed, will the patient stay paralyzed after supination?	
<input type="checkbox"/>	Omit spontaneous awakening trial (SAT) or spontaneous breathing trial (SBT)?	
<input type="checkbox"/>	Sandbag at bedside (for use during cardiac arrest)?	



Appendix C: OSUWMC SeaStar NxStage CRRT Filter Protocol

OSUWMC SeaStar NxStage CRRT Filter Protocol	
What is it?	The SeaStar filter is a high-cut off membrane filter used for CRRT. When compared to standard CRRT filters, the SeaStar filter removes larger molecules with a size of 0.5-0.6 kilo Daltons. This allows filtration of inflammatory cytokines such as IL-6, IL-8 and TNF- α ⁴⁵
Evidence for its use	SeaStar's filter has been used in cytokine filtration for brain-dead organ donors. It has FDA approval "for use in patients with fluid overload, uremia and/or electrolyte disturbances associated with oligoanuria acute renal failure. It may also be used when removal of excess fluid is indicated, such as patients in pulmonary edema or congestive heart failure refractory to diuretic therapy."
COVID-19 Specific Use	With the COVID-19 pandemic, numerous reports have cited IL-6 and a cytokine cascade as a potential pathogenesis for COVID induced ARDS, myocarditis and multi-organ failure. ^{54,55} In addition, an IL-6 blocker (tocilizumab) has been described as a therapeutic option for patients with ARDS secondary to COVID-19. Use of the SeaStar filter would attenuate this cascade and potentially assist with recovery. The Italian Society of Nephrology has also endorsed the use of cytokine filters in COVID patients requiring RRT. ⁴⁶
OSUWMC Protocol	
Inclusion Criteria	<ol style="list-style-type: none"> 1. Confirmed COVID-19 infection 2. Intubation and either: <ol style="list-style-type: none"> a. Moderate to Severe ARDS: defined by Berlin criteria and a P:F ratio <200 b. Mild ARDS + evidence of multi-organ failure: P:F <300 + shock, renal failure, etc.
Procedure for use	<ol style="list-style-type: none"> 1. Contact Anesthesia Critical Care service (Pager #9714, 614-293-ECMO) 2. Place Nephrology consult 3. Obtain baseline inflammatory markers (IL-6, ferritin, ESR, CRP, procalcitonin, troponin, BNP, albumin and D-dimer) prior to initiation and at a daily interval afterwards 4. Obtain vascular access with a hemodialysis catheter (RIJ preferred over LIJ) 5. Initiate SeaStar therapy: <ol style="list-style-type: none"> a. Therapy is performed for at least 6 hours per day. Optimal therapy is 12 hours per day. (See below for the C2Rx CRRT prescription) b. Consider ultrafiltration if necessary to augment volume removal 6. Discontinue SeaStar therapy once P:F ratio is >250 or if inflammatory markers have normalized (CRP/IL-6)
OSU Clinical and Nursing Implications	<ol style="list-style-type: none"> 1. The SeaStar filter runs on our current NxStage CRRT machines. Patient must be located in the Doan or Ross in order to initiate therapy. 2. Patients requiring CRRT can receive therapy with SeaStar filters. They do not need to be transitioned to other filters. 3. Filter clotting is diminished using a predilution delivery, but given the hypercoagulable state of COVID-19, citrate anticoagulation or heparin infusion may need to be initiated 4. With time, high-cutoff filters can leak albumin. Continue to monitor daily levels and consider supplementation if necessary. 5. Antibiotic dosing is adjusted as is customary for CRRT.
CLR 2.0 Hemofiltration Treatment C2Rx) Prescription	<ol style="list-style-type: none"> 1. C2Rx hemofiltration dose is indexed to patient admission body weight. <ol style="list-style-type: none"> a. Therapy Fluid Rate (TFR)¹ will index to the patient's hospital admission body weight at a dose of 35 ml/kg/hr. <ul style="list-style-type: none"> • Example: in a 75 kg patient, TFR = 75 kg x 35 ml/kg/hr = 2625 ml/hr b. Blood flow rate (BFR) will index to TFR to maintain Filtration Fraction (FF) ≤ 0.1. <ul style="list-style-type: none"> • FF = TFR (in ml/min) / BFR (in ml/min), or BFR = TFR / 0.10 • Example: 87 kg patient <ul style="list-style-type: none"> ○ TFR = 87 kg x 35 ml/kg/hr = 3,045 ml/hr ○ TFR ml/min = 3045 ml/hr / 60 min/hr = 51 ml/min ○ BFR = 51 ml/min / 0.1 = 510 ml/min 2. On the NxStage System One platform the Therapy Fluid Rate is set in the Therapy Fluid window (top window, green arrows) and the machine automatically matches filtrate output rate to Therapy Fluid input rate to provide a neutral balanced treatment by default. 3. If net fluid removal is desired, the desired hourly Ultrafiltration Rate is set in the middle window (yellow arrows).

