

Exhibit 12

E-Mail Joel Bundy 10/6/2021



Colleagues,

Please see the newest [COVID-19 Comprehensive Treatment Guidelines \(version 26\)](#). Updates are emphasized below.

- Remdesivir (Veklury) – clarified verbiage on oxygen status limits for inclusion.
- Tocilizumab (Actemra) – emphasized the risk of secondary infection and black box warning for immunosuppression. Highlighted the most appropriate candidates for toci based on NIH guidelines and 2 large studies (RECOVERY and REMAP-CAP). Early identification of these patients is important and post-administration monitoring for continued immunosuppression.
- Corticosteroids – expanded information around steroid dosing. Dexamethasone 6mg is still the recommended regimen but equivalent doses of other steroids listed. Alternatives for higher

doses of steroids listed although this is up to provider discretion and not yet supported in COVID specific trials.

- Non-critically ill patients may benefit from therapeutic anticoagulation, while critically ill did not see improved outcomes and should remain on VTE prophylaxis unless confirmed indications are present.
- Added a “do not endorse” section which includes medications that may cause harm and efficacy/safety is not supported in peer reviewed, published RCT. These medications will not be verified or dispensed for prevention or treatment of COVID: ivermectin, bicalutamide, etoposide, fluvoxamine, dutasteride, and finasteride. These medications should only be prescribed if the patient is enrolled in a clinical trial.
- Ascorbic acid (Vitamin C) IV is not endorsed for prevention or treatment of COVID-19 or sepsis/septic shock.

Best,

Joel Bundy, MD, FACP, CPE

Vice President

Chief Quality and Safety Officer

Sentara Healthcare

Sentara Comprehensive COVID-19 treatment guidelines – VERSION 26

Endorsed by COVID taskforce, Pharmacy, CC, HM, and ID

Mechanical Ventilation - Mortality increases after initiation of mechanical vent support; consider decreasing SaO2 target to greater than or equal to 85%.	
Proning	• Recommend proning for 16 hours per day while on ventilatory support with P/F ratio <150 (can consider earlier) • Consider setting up proning team at facilities that don't currently have it • Encourage awake proning for those not on mechanical ventilation
Respiratory/Ventilation	• Use static compliance, physiology, and radiographic evidence to guide selection of high peep vs. low peep strategy • Avoid volume overload; do not provide Surviving Sepsis 30 cc/kg IV fluid bolus to avoid worsening oxygenation • If intubation is required, should be performed by most experienced intubator available, with video laryngoscopy • Early discussion of goals of care and potential involvement of palliative medicine is recommended • If unable to wean off ventilator, consider tracheostomy
ENDORSED PHARMACOLOGIC THERAPIES	
DVT Prophylaxis	All COVID (+) patients should receive <u>enoxaparin</u> as prophylaxis for deep venous thrombosis, unless contraindicated. • Pharmacy may automatically interchange orders for heparin SC to enoxaparin for the COVID population when clinically appropriate.
Anticoagulation Treatment	COVID-19 positive patients appear to have a process consistent with hypercoagulable disseminated intravascular coagulation (DIC). Society recommendations differ for anticoagulation based on the severity and trajectory of disease. • Enoxaparin is the preferred agent • Consider monitoring anti-Xa levels for patients who are obese, critically ill, or CrCL < 50 (check 4 hours after 3rd dose) <u>ICU or critically-ill patients:</u> should <u>NOT</u> be empirically anticoagulated based on d-dimer alone • Anticoagulation should be utilized for all clinically indicated disease states, including VTE, atrial fibrillation, and others but not based on d-dimer alone in this population • Recommend standard VTE prophylaxis with enoxaparin as the preferred agent – enoxaparin 40mg SC q24h <u>Non-ICU Patients:</u> <u>MAY benefit</u> from being empirically anticoagulated for 14 days or until discharge based on elevated d-dimer of at least 2x the ULN in conjunction with additional risk factors • Weigh risk vs benefit for each patient, especially those on dual antiplatelet therapy or at high risk of bleeding • Enoxaparin is the preferred agent at 1mg/kg SC q12h or 1.5mg/kg SC q24h

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Remdesivir <i>*Course may be continued if patient's oxygen status worsens but should be held or stopped for renal or liver dysfunction.</i>	Initiation Use Criteria – Inpatients Only. <i>Discharge should NOT delayed to complete the 5-day course of Remdesivir.</i> • Lab confirmed diagnosis of COVID-19 • Symptom onset within the last 10 days • Oxygen requirements due to COVID: any supplemental nasal cannula or device up to 15 L/min <i>(This criteria is derived from patients who saw benefit in the ACTT-1 Trial)</i> ○ Not candidates if on CPAP, BiPAP, high flow device > 15L/min, or mechanical ventilatory support ○ Consider patient's baseline oxygen requirements when reviewing inclusion/exclusion criteria • CrCl > 30 ml/min • LFTs < 10x ULN
Systemic Corticosteroids	Systemic corticosteroids show mortality benefit in patients on mechanical ventilation or oxygen support. Caution is advised with previously immunosuppressed patients and/or increased risk of fungal infection. Increase steroid dose based on response. • Dexamethasone 6mg IV or PO daily x 10 days (Or methylprednisolone 32mg daily or prednisone 40mg daily) • Expert opinion/not supported yet in literature: Consider increasing methylprednisolone up to 80mg IV BID x 10 days as needed Higher dosing of steroids is beneficial in ARDS. • Methylprednisolone 1 mg per kg IV then 0.5 mg per kg every 12 hours for 7 days - consider BMI for dosing. • Follow with a slow taper of oral prednisone as dictated by clinical course. Optimal duration of taper is unknown. Patients receiving steroids who did not require oxygen support showed a trend towards patient harm. (RECOVERY trial)
Tocilizumab (Actemra) *EUA Approval for COVID* <i>Black Box Warning:</i> for a risk of serious infections that may lead to hospitalization or death, including tuberculosis (TB), bacterial, invasive fungal, viral, and other opportunistic infections.	Patients should be progressing despite high-dose steroids before considering tocilizumab. Trend IL-6 and CRP to ensure inflammation is not due to other causes, especially active or suspected infections. Serious risk of secondary infection following receipt of tocilizumab. Many patients may improve on increased steroid doses and not require tocilizumab. Weight-based dosing x 1 dose 40- 65kg = 400mg; 66 – 90 kg = 600mg; > 90 kg = 800mg *Medication is limited to pulmonary/critical care and must meet criteria below: • IL-6 $\geq 2x$ ULN (≥ 14 pg/mL) • CRP ≥ 7.5mg/dL or 75 mg/L • Hospitalized ≤ 3 days (all patients), and ICU admission < 24 hours (if applicable) • Rapidly increasing oxygen needs beyond nasal cannula Exclusions: 1. Immunosuppression 2. ALT/AST > 5x ULN 3. Platelets < 50 4. Not accepting all treatments

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THERAPIES THAT ARE <u>NOT</u> SUPPORTED OR ENDORSED	
Ivermectin	Concentrations needed to inhibit SARS-COV-2 would be difficult to achieve in humans and are extremely toxic. There is no available data on outcomes or efficacy in humans from a RCT. This medication is not recommended until further studies evaluating appropriate dosing regimens are found to be safe and effective. Several organizations, including AMA, ASHP, CDC, FDA and Merck, have issued statements recommending against the use of ivermectin for prevention or treatment of COVID-19. There is a Call for Immediate End to Prescribing, Dispensing, and Use of Ivermectin to Prevent or Treat COVID-19 Outside Clinical Trials.
Ascorbic Acid (Vitamin C)	Ascorbic acid IV is not endorsed for treatment or prevention of COVID-19 or sepsis/septic shock.
Bicalutamide (CASODEX) Etoposide (TOPOSAR) Fluvoxamine (LUVOX) Dutasteride (AVODART) Finasteride (PROSCAR)	- These medications are <u>NOT endorsed</u> for use in COVID-19. Many do not have published peer-reviewed, RCT available to assess both efficacy and safety in COVID-19. - Use is limited to patients enrolled in a clinical trial for treatment of COVID-19.
<i>There are other medications currently being studied for use in COVID-19 prevention and treatment. Until published literature is available to evaluate both safety and efficacy these medications will not be endorsed or recommended in Sentara's COVID-19 treatment guidelines. Literature will be evaluated on a continual basis and the guidelines updated as needed to reflect the on-going changes.</i>	

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