

# ECU Health (formerly Vidant Health) COVID-19 Inpatient Adult Treatment

## Outpatient Options

- See separate outpatient treatment algorithm
- Outpatient **clinical trial** (call or text 252-414-2655 day of positive results)

## Supportive Care

- **Anticoagulation** (see separate anticoagulation algorithm)
- **Vitamin Supplementation**
  - Zinc sulfate 220 mg daily x 14 days
  - Multivitamin with minerals BID x 14 days
  - Ergocalciferol 50,000 IU twice weekly X 4 doses
    - If vitamin D < 40 ng/ml

## Risk Factors for Severe Disease

CV disease, HTN, age >55, underlying lung disease, smoking history, chronic liver disease, DM, CKD, cancer, HIV, transplant, immunosuppression, chemotherapy, SNF/LTAC residents, obesity, or pregnancy

## Inpatient Options

### Mild Disease

#### (Asymptomatic or No Oxygen Requirement)

- **Remdesivir** 200 mg on day 1 then 100 mg daily x **2 days** or until discharge
  - Requires ID approval if not within **5 days** of symptom onset

### Low-Flow Oxygen (<6L)

- **Dexamethasone** 6 mg daily x 10 days or until discharge
  - Consider famotidine 20 mg BID with steroids if not on PPI/H2 blocker
- **Remdesivir** 200 mg on day 1 then 100 mg daily x **2 days** or until discharge
  - Requires ID approval if not within **5 days** of symptom onset

### High-Flow Oxygen (≥6L) or Mechanically Ventilated

- **Dexamethasone** 6 mg daily x 10 days or until discharge
  - Consider famotidine 20 mg BID with steroids if not on PPI/H2 blocker
- **Baricitinib** 4 mg daily x 14 days or until discharge
  - Renal dose adjustment needed
  - Requires ID approval if not within 5 days of respiratory requirements
- **Tocilizumab** (alternative to baricitinib)
  - Requires ID approval (**on shortage**)

**Decision to use these agents should be made only with close attention to the patient's clinical status, comorbidities, interacting medications, and with the understanding that there are limited/controversial data available to support use. Use of some of these agents for COVID-19 requires ID or investigator approval (details below). See drug table below for detailed information on each therapy.**

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## Drug Information:

<p>Remdesivir (Veklury®)</p>	<ul style="list-style-type: none"><li>• <b>Adult use is allowed without ID approval if the patient meets the following criteria:</b> Adult use is allowed without ID approval if the patient meets all the following criteria: 1) Adult patient on room air or &lt; 6L low-flow oxygen AND, 2) within 5 days of symptom ONSET (not test date, but date of any respiratory or non-respiratory viral symptom) AND, 3) are unvaccinated (or not completely up-to-date on vaccination per latest CDC guidance) or immunocompromised (i.e. not expected to properly respond to vaccination**). **Conditions/treatments that may result in severe immunocompromise/inadequate response to vaccine include active treatment for solid tumor and hematologic malignancies, receipt of solid organ transplant and taking immunosuppression, receipt of chimeric antigen receptor (CAR)-T-cell or hematopoietic stem cell transplant, moderate or severe primary immunodeficiency, advanced or untreated HIV, active treatment with high-dose corticosteroids (i.e. <math>\geq 20</math> mg prednisone or equivalent per day), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents, TNF blockers, and other biologic agents that are immunosuppressive or immunomodulatory.</li><li>• <b>All other adult use requires ID approval by any ID attending. Call 252-814-4296 from 08:00–21:00 seven days a week. Any request after 21:00 will need to be approved and started the following morning. All pediatric use requires pediatric ID approval, contact Dr. William Alex Dalzell, Dr. Salma Syed, or Dr. Yamini Mandelia.</b></li><li>• <b>Recommended use:</b> Greatest benefit may be in patients early in the course of disease (&lt;7 days of symptoms). Remdesivir is unlikely to be beneficial in patients with diffuse infiltrates on CXR or CT scan, those requiring high supplemental oxygen, or those with markedly elevated inflammatory markers such as CRP or D-Dimer.</li><li>• <b>Mechanism:</b> Broad-spectrum antiviral nucleotide prodrug with potent in vitro activity against a range of RNA viruses including Ebola virus, Marburg, MERS-CoV, SARS-CoV, respiratory syncytial virus, Nipah virus, and Hendra virus. The mechanism of action of remdesivir is premature termination of viral RNA transcription.</li><li>• <b>Options for obtaining remdesivir:</b><ul style="list-style-type: none"><li>○ FDA approved on October 22, 2020 and available via wholesaler</li><li>○ Emergency Use Authorization (EUA) still required for hospitalized children weighing 3.5 kg-40 kg or hospitalized children less than 12 years of age</li></ul></li><li>• <b>Adult dosing:</b> Suggested dose is a single loading dose of remdesivir 200 mg IV on Day 1, followed by once-daily maintenance doses of remdesivir 100 mg IV for 2-4 days. Remdesivir is to be administered via IV infusion in a total volume of up to 250 mL 0.9% saline. Doses of 200 mg will be infused over 2 hours and doses of 100 mg will be infused over 1 hour. Duration can be shortened to 3 days total if otherwise ready for discharge.</li><li>• <b>Monitoring:</b> Suggest daily renal and hepatic function monitoring</li><li>• <b>Renal dysfunction:</b> There are now several case reports describing use of remdesivir in patients with AKI or ESRD. These patients can be considered on a case by case basis. Dose and duration should be the same. When given on HD days make sure dose is after HD (as drug is cleared by HD).</li></ul>
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<p>Baricitinib (Olumiant®)</p>	<ul style="list-style-type: none"> <li>• <b>Adult use is allowed without ID approval if the patient meets the following criteria:</b> Within 5 days of requiring at least &gt;6 L NC respiratory support for COVID-19 pneumonia, AND has at least one elevated inflammatory marker, AND eGRF &gt;15 mL/min.</li> <li>• <b>All other adult use requires ID approval by any ID attending. Call 252-814-4296 from 08:00–21:00 seven days a week. Any request after 21:00 will need to be approved and started the following morning. All pediatric use requires pediatric ID approval, contact Dr. William Alex Dalzell, Dr. Salma Syed, or Dr. Yamini Mandelia.</b></li> <li>• <u>Recommend use</u> in patients who are in the inflammatory component of their illness and are at least requiring 6 L oxygen, including those who are rapidly deteriorating despite dexamethasone. Factors that will be considered include: use of supplemental oxygen, CXR or CT scan findings, inflammatory markers particularly CRP and D-Dimer, and how long into inflammatory phase the patient is since drug more likely to be effective if given earlier in the course of the inflammatory process.</li> <li>• <u>Mechanism:</u> Inhibitor of JAK1 and JAK2. Baricitinib is proposed to reduce an inflammatory response and have potential antiviral activity against COVID-19.</li> <li>• <b>FDA approved on May 10, 2022 for use in hospitalized adult patients with COVID-19 requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or ECMO. Obtaining verbal consent and disseminating the fact sheet is no longer required for adults.</b></li> <li>• <u>Used via EUA only for pediatrics.</u> Baricitinib is authorized for emergency use by the US FDA for treatment of COVID-19 in hospitalized patients requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO). <u>It is the responsibility of the primary team to provide the Patient Fact Sheet for Patients, Parents, and Caregivers; obtain verbal consent from the patient/caregiver and document in the chart, place the appropriate drug order based on renal function, and monitor renal/hepatic function plus ANC/ALC daily during treatment. Documentation is included in the order by appropriately answering “Yes” when the above criteria have been satisfied.</u> Mandatory reporting of all medication errors and all serious adverse events is required.</li> <li>• <u>Dose:</u> 4 mg PO/per tube daily x 14 days or until discharge. Dose adjustment or drug interruption may be needed for decreasing eGFR, ALC &lt;200 cells/uL, ANC &lt;500 cells/uL, or if drug induced liver injury (AST/ALT increase) is suspected (see fact sheet for specific recommendations). Tocilizumab may be preferred in severe renal dysfunction or when PO/per tube is not feasible, but will be a patient specific decision.</li> <li>• <u>Remdesivir plus baricitinib:</u> In general, patients who begin to qualify for baricitinib will be entering a phase of their illness that will no longer benefit from remdesivir. Therefore, if a patient on remdesivir is being considered for baricitinib, it usually makes most sense that remdesivir is discontinued as baricitinib is initiated. An exception to this would be in a patient who is on remdesivir and would qualify for concomitant dexamethasone but cannot receive a corticosteroid due to contraindication (this patient could be on remdesivir plus baricitinib).</li> <li>• <u>Other considerations:</u> Risk of latent TB reactivation or other infection; and thrombosis.</li> </ul>
<p>Tocilizumab (Actemra®)</p>	<ul style="list-style-type: none"> <li>• Drug <u>shortage</u> is currently impacting supply.</li> <li>• <b>Adult use requires ID approval by any ID attending. Call 252-814-4296 from 08:00–21:00 seven days a week. Any request after 21:00 will need to be approved and started the following morning. All pediatric use requires pediatric ID approval, contact Dr. William Alex Dalzell, Dr. Salma Syed, or Dr. Yamini Mandelia.</b></li> </ul>

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	<ul style="list-style-type: none"> <li>• <b><u>EHR order may say “for outpatient use only except for heme/onc and transplant patients”, however, this can be bypassed if you have ID approval for COVID-19.</u></b></li> <li>• <b><u>Recommend use</u></b> in patients who are in the inflammatory component of their illness, are exhibiting rapid respiratory deterioration despite dexamethasone due to COVID-19, and are at least requiring 6 L oxygen. Factors that will be considered include: use of supplemental oxygen, CXR or CT scan findings, inflammatory markers particularly CRP and D-Dimer, and how long into inflammatory phase the patient is since drug more likely to be effective if given earlier in the course of the inflammatory process.</li> <li>• <b><u>Mechanism:</u></b> monoclonal anti-IL-6 receptor blocking antibody proposed as a therapeutic agent to mitigate hyperinflammation associated with COVID-19. FDA approved for various rheumatologic conditions as well as cytokine release syndrome associated with CAR-T cell therapy.</li> <li>• <b><u>This drug is now being used via EUA.</u></b> Tocilizumab is authorized for emergency use by the FDA for treatment of COVID-19 in hospitalized adult and pediatric patients (2 years of age and older) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or ECMO. Providers must communicate to the patient and/or caregiver information consistent with the Fact Sheet for Patients, Parents, and Caregivers and <b><u>provide them with a copy of this Fact Sheet</u></b> prior to the administration. However, if providing this information will delay the administration to a degree that would endanger the life of a patient, the information must be provided as soon as feasible after administration. Mandatory reporting of all medication errors and all serious adverse events is required.</li> <li>• <b><u>Dose:</u></b> 8mg/kg based on actual body weight (max dose 800 mg). Clinical assessment and laboratory assessment (including CRP) to guide need for repeat dosing, which can be done at least 8 hours after the initial dose. Round dose to nearest vial size (either 80 mg or 200 mg vials depending on availability).</li> <li>• <b><u>Other considerations:</u></b> Risk of latent TB reactivation or other infection; risk vs benefit for initiation in patients with neutropenia, thrombocytopenia, or elevated AST/ALT; and need for concomitant steroid therapy.</li> </ul>
<p>Monoclonal antibodies (MAB)</p> <p>Treatment: Sotrovimab Bebtelovimab</p> <p>Prevention: Tixagevimab/ cilgavimab (Evusheld®)</p>	<ul style="list-style-type: none"> <li>• <b><u>For referrals see outpatient treatment algorithm.</u></b></li> <li>• <b><u>Available for ordering by all providers for adult patients meeting criteria mentioned below.</u></b> Documentation (including verbal consent and fact sheet dissemination) is included in the order by selecting appropriate answers to the questions on the order.</li> <li>• <b><u>All pediatric use requires pediatric ID approval, contact Dr. William Alex Dalzell, Dr. Salma Syed, or Dr. Yamini Mandelia.</u></b></li> <li>• The FDA has had multiple EUA’s for neutralizing monoclonal antibodies, most recently: sotrovimab (May 26, 2021), tixagevimab/cilgavimab (Evusheld®, prevention only, Dec 8, 2021), and bebtelovimab (Feb 2022). We changed from bamlanivimab/etesevimab to casirivimab/imdevimab in Jul 2021 due to increasing delta variants. Due to increasing omicron variants, we changed to sotrovimab in Dec 2021. Evusheld® use for prevention only will begin Jan 2021.</li> <li>• <b><u>Mechanism of neutralizing antibodies:</u></b> Neutralizing antibodies directed at the receptor-binding domain of SARS-CoV-2 spike protein have been evaluated as prophylactic and therapeutic agents for COVID-19. In animal models there is evidence that antibody therapy may more rapidly reduce viral load in the upper and lower airways of infected animals resulting in reduced viral-induced pathology. Potential advantages of neutralizing antibodies include the ability to standardize the amount of neutralizing activity and the possibility of conferring protection more rapidly than with vaccine-induced immune responses (which generally take several weeks).</li> </ul>

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	<ul style="list-style-type: none"> <li>• <u>Sotrovimab and bebtelovimab are for treatment of mild-to-moderate COVID-19</u> in adult and pediatric outpatients (12 years of age or older and weighing at least 40 kg) at high risk for progression to severe COVID-19. See outpatient treatment algorithm for details.</li> <li>• <u>Tixagevimab/cilgavimab (Evusheld®) is for pre-exposure prophylaxis ONLY (not treatment)</u> in certain adult and pediatric outpatients (12 years of age or older and weighing at least 40 kg).             <ul style="list-style-type: none"> <li>○ Preferred route is IM in 2 separate syringes (into gluteal muscle)</li> <li>○ Longer half-life</li> <li>○ If meets criteria for moderately/severely immunocompromised and has had a COVID-19 vaccine, wait two weeks post vaccination before administering Evusheld®</li> <li>○ Criteria for use:                 <ul style="list-style-type: none"> <li>▪ NOT currently infected with SARS-CoV-2</li> <li>▪ NOT recently exposed to an individual infected with SARS-CoV-2</li> <li>▪ Moderately to severely compromised immune system due to a medical condition or due to taking immunosuppressive medications or treatments and may not mount an adequate response to vaccination (see conditions above in sotrovimab section)</li> <li>▪ History of severe adverse reactions to a COVID-19 vaccine and/or components (so vaccination not recommended)</li> </ul> </li> </ul> </li> <li>• <u>Administration and observation:</u> <ul style="list-style-type: none"> <li>○ Clinically monitor patients during infusion and observe patients for at least 1 hour after infusion is complete.</li> <li>○ Health care providers must submit a report on all medication errors and ALL SERIOUS ADVERSE EVENTS. The prescribing health care provider and/or the provider's designee are/is responsible for mandatory reporting of all medication errors and serious adverse events occurring within 7 calendar days from the onset of the event. Must be submitted to FDA MedWatch and the manufacturer.</li> </ul> </li> </ul>
<p>Nirmatrelvir/ ritonavir (Paxlovid®)</p>	<ul style="list-style-type: none"> <li>• <u>For referrals see outpatient treatment algorithm.</u></li> <li>• <u>EUA authorized Dec 2021</u> for mild-to-moderate COVID-19 in adults and pediatric outpatients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19.</li> <li>• <u>Mechanism:</u> Nirmatrelvir is a SARS-CoV-2 main protease (Mpro) inhibitor (also referred to as 3CLpro) which renders it incapable of processing polyprotein precursors and therefore prevents viral replication. Ritonavir is an HIV-1 protease inhibitor and CYP3A inhibitor that inhibits CYP3A-mediated metabolism of nirmatrelvir resulting in increased nirmatrelvir plasma concentrations.</li> <li>• <u>Dose:</u> 300 mg nirmatrelvir (two 150 mg tablets) + 100 mg ritonavir PO BID x 5 days with or without food</li> <li>• <u>Special considerations:</u> Renal dose adjustment needed for eGFR ≥30 to &lt;60 mL/min. Not recommended for patients with eGFR &lt;30 mL/min. Not recommended with severe hepatic impairment (Child-Pugh Cass C). Can increase risk of HIV-1 developing resistance to HIV protease inhibitors in individuals with uncontrolled or undiagnosed HIV-1 infection.</li> <li>• <u>DRUG INTERACTIONS:</u> Ritonavir is a strong CYP3A4 inhibitor and can significantly increase other CYP3A4 substrate concentrations. Co-administration with potent CYP3A4 inducers may impact Paxlovid® concentrations. <u>Medication profile MUST be reviewed for drug interactions prior to initiation.</u></li> </ul>

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	<ul style="list-style-type: none"> <li>• <u>As with other EUAs, dissemination of fact sheet, verbal consent, and reporting of all serious adverse events and/or medication errors is required.</u></li> <li>• <u>ECU Health criteria for use can be found on outpatient treatment algorithm</u></li> </ul>
Molnupiravir	<ul style="list-style-type: none"> <li>• <u>For referrals see outpatient treatment algorithm.</u></li> <li>• <u>EUA authorized Dec 23, 2021</u> for adult outpatients with mild-to-moderate COVID-19 with positive results of direct SARS-CoV-2 viral testing who are at high risk for progressing to severe COVID-19 and for whom alternative COVID-19 treatment options authorized by FDA are not accessible or clinically appropriate.</li> <li>• <u>Mechanism:</u> Nucleoside analogue that inhibits SARS-CoV-2 replication</li> <li>• <u>Dose:</u> 800 mg (four 200 mg capsules) PO BID x 5 days with or without food</li> <li>• <u>Special considerations:</u> NOT for use during pregnancy (animal reproductive studies showed possibility of fetal harm)</li> <li>• <u>As with other EUAs, dissemination of fact sheet, verbal consent, and reporting of all serious adverse events and/or medication errors is required.</u></li> <li>• <u>ECU Health criteria for use can be found on outpatient treatment algorithm</u></li> </ul>
Fluvoxamine	<ul style="list-style-type: none"> <li>• <u>IDSA guideline recommendation:</u> Among ambulatory patients with COVID-19, the IDSA guideline panel recommends fluvoxamine only in the context of a clinical trial.</li> <li>• <u>Mechanism:</u> Selective serotonin reuptake inhibitor (SSRI) that is FDA-approved for the treatment of obsessive-compulsive disorder. SSRI's have been shown to have affinity for Sigma-1 receptors, which modulate cytokine levels in animal models of septic shock and demonstrate in vitro activity against SARS-CoV-2. Of the SSRIs, fluvoxamine has high activity for these receptors. SSRIs may also decrease uptake of serotonin from platelets during thrombosis, resulting in decreased neutrophil recruitment and platelet aggregation.</li> </ul>
Ivermectin	<ul style="list-style-type: none"> <li>• <u>Ivermectin has not been added to these treatment recommendations.</u></li> <li>• <u>IDSA guideline recommendation:</u> In hospitalized patients with severe COVID-19, the IDSA panel suggests against ivermectin use outside of the context of a clinical trial (conditional recommendation, very low certainty of evidence). In outpatients with COVID-19, the IDSA panel suggests against ivermectin use outside of the context of a clinical trial (conditional recommendation, very low certainty of evidence). See guideline for data summary.</li> <li>• <u>Mechanism:</u> Anti-parasitic agent FDA approved for some indications. Has in-vitro activity against some viruses, including SARS-CoV-2 but no proven therapeutic utility. Concentrations needed to obtain the in-vitro IC50 for SARS-CoV-2 are considerably higher than those achieved in human plasma and lung tissue.</li> </ul>
Convalescent plasma	<ul style="list-style-type: none"> <li>• <u>Convalescent plasma was officially removed from this algorithm in the December 30, 2021 update</u></li> <li>• <u>IDSA guideline recommendation:</u> Among ambulatory patients the IDSA guideline panel recommends against COVID-19 convalescent plasma outside of the context of a clinical trial. Among hospitalized patients they recommended against it.</li> <li>• <u>Mechanism:</u> Passive immunotherapy (pathogen neutralization, antibody-dependent cellular cytotoxicity, enhanced phagocytosis)</li> </ul>

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Hydroxychloroquine (HCQ)	<ul style="list-style-type: none"> <li>• <u>HCQ was officially removed from this algorithm in the June 16, 2020 update.</u> On June 15, 2020, based on FDA’s continued review of the scientific evidence available for HCQ and chloroquine (CQ) to treat COVID-19, FDA has determined that the statutory criteria for EUA as outlined in Section 564(c)(2) of the Food, Drug, and Cosmetic Act are no longer met. Specifically, FDA has determined that CQ and HCQ are unlikely to be effective in treating COVID-19 for the authorized uses in the EUA. Additionally, in light of ongoing serious cardiac adverse events and other serious side effects, the known and potential benefits of CQ and HCQ no longer outweigh the known and potential risks for the authorized use. This warrants revocation of the EUA for HCQ and CQ for the treatment of COVID-19.</li> <li>• <u>IDSA guideline recommendation:</u> Among hospitalized patients with COVID-19, the IDSA guideline panel recommends against hydroxychloroquine. See guideline for data summary.</li> </ul>
HCQ + Azithromycin	<ul style="list-style-type: none"> <li>• <u>HCQ + azithromycin combination was officially removed from this algorithm in the April 30, 2020 update.</u></li> <li>• <u>IDSA guideline recommendation:</u> Among hospitalized patients with COVID-19, the IDSA guideline panel recommends against hydroxychloroquine plus azithromycin. See guideline for data summary.</li> </ul>
Lopinavir/ritonavir (Kaletra)	<ul style="list-style-type: none"> <li>• <u>Kaletra was officially removed from this algorithm in the May 8, 2020 update.</u></li> <li>• <u>IDSA guideline recommendation:</u> Among hospitalized patients with COVID-19, the IDSA guideline panel recommends against the use of the combination lopinavir/ritonavir. See guideline for data summary.</li> </ul>
Interferon Beta-1a	<ul style="list-style-type: none"> <li>• <u>Interferon Beta-1a has not been added to these treatment recommendations.</u></li> <li>• <u>Mechanism:</u> Subcutaneous interferon beta-1a is approved in the U.S. and more than 90 other countries for the treatment of multiple sclerosis. Interferon beta-1a has the same amino acid sequence as a naturally occurring protein called interferon beta, which is part of a class of proteins called type 1 interferons. Infected cells normally produce type 1 interferons to help the immune system fight pathogens, especially viruses. Interferon beta has both antiviral and anti-inflammatory properties.</li> <li>• A randomized, controlled clinical trial evaluating the safety and efficacy of a treatment regimen consisting of the antiviral remdesivir plus the immunomodulator interferon beta-1a in patients with coronavirus disease 2019 (COVID-19) has begun. The study, called the Adaptive COVID-19 Treatment Trial 3 (ACTT 3), is anticipated to enroll more than 1,000 hospitalized adults with COVID-19 at as many as 100 sites in the US and abroad. <u>Clinical trial is the only way to obtain drug. The closest site in NC is Duke. More data can be found here: <a href="https://clinicaltrials.gov/ct2/show/NCT04492475">https://clinicaltrials.gov/ct2/show/NCT04492475</a></u></li> </ul>

## General COVID-19 Information:

1. COVID-19 is the disease caused by SARS-Coronavirus-2 or SARS-CoV-2.
2. Incubation period ~5 days (ranges from 2-14 days).
3. Frequently signs and symptoms at illness onset include fever (83-98%), dry cough (76-82%), and myalgia/fatigue (11-44%). GI symptoms have also become a common occurrence (anorexia, diarrhea, vomiting, abdominal pain, anosmia, dysgeusia). In one report, 10% (n=20) presented without digestive or respiratory symptoms, 3% (n=7) with digestive symptoms but without respiratory symptoms (all except 1 did have fever), 42% (n=85) with respiratory symptoms but without digestive symptoms, and 45% (n=92) with both respiratory and digestive symptoms.

Last updated June 22, 2022 – this document is subject to frequent revisions

Updates since the March 4, 2022 version are noted by the red font color

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4. CXR have shown bilateral involvement in most patients. CT patterns have revealed patchy infiltrate, bilateral disease, and have been consistent with viral infection.
5. Potential for clinical deterioration during second week of illness.
6. Co-infection of COVID-19 with other viruses and bacteria is possible.
7. False negative COVID-19 results are possible. Poor quality of specimen can be a reason for false negative.

## **Recommended Labs and Monitoring:**

1. Daily: CBC with differential (follow lymphopenia) and complete metabolic panel (includes LFTs)
2. To help rule out bacterial co-infection: Procalcitonin
3. For risk stratification and worry of cytokine release syndrome: LDH, troponin, CPK, D-dimer, CRP, ESR, triglycerides, ferritin, and fibrinogen. May consider trending these as appropriate.
  - a. Ideally would obtain IL-6 levels but this lab is a send out that will take 4-7 days to result so we are not currently recommending it.
4. Pregnancy test
5. Vitamin D, total (VITDT)

## **General Drug Considerations:**

1. There are clinical trials of HCQ that include supplemental zinc, vitamin C, and vitamin D. For all COVID-19 positive patients suggest 14 days of the following nutritional supplements:
  - a. **Multivitamin with minerals** (Theragran-M tablet) twice daily. The preference is to use the Theragran-M tablet product, even if need to crush finely and administer per tube, due to the copper concentration in this vitamin (2 mg/tab) vs Centrum liquid (0 mg). If absolutely needed, can use the Centrum liquid multivitamin with iron-minerals. But, the copper supplementation may be important due to Zinc binding copper absorption.
  - b. **Zinc sulfate** 220 mg capsule daily (50 mg elemental zinc) or oral suspension if need liquid (220 mg/5mL). Zinc has anti-viral activity, including inhibition of viral RNA dependent RNA polymerase (like remdesivir). Zinc deficiency is common in elderly people and is associated with anosmia (an early sign of COVID-19 disease).
  - c. **Ergocalciferol** 50,000 IU twice weekly or ergocalciferol drops if liquid needed (50,000 IU/6.25 mL). Need for further supplementation should be based on vitamin D level results. Vitamin D is a known immunomodulator and deficiency is more common in African Americans, who are at higher risk for severe disease. Vitamin D inhibits proinflammatory cytokines, including IL-6. We are giving ergocalciferol over cholecalciferol based on the high dose and available supplies. The shorter half-life of the ergocalciferol also will help to see effects earlier and reach steady state more quickly.
2. The ECU Health **anticoagulation** subcommittee has developed a guideline for inpatient prophylaxis, discharge prophylaxis, and treatment of VTE in COVID-19 patients. Please see their separate document.



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3. **Dexamethasone 6 mg IV or PO for 10 days (or until discharge if earlier).** An equivalent glucocorticoid dose may be substituted if dexamethasone unavailable. Equivalent total daily doses of alternative glucocorticoids to dexamethasone 6 mg daily are methylprednisolone 32 mg and prednisone 40 mg. IDSA guideline recommendations are as follows: Among hospitalized critically ill patients with COVID-19, the IDSA guideline panel recommends dexamethasone rather than no dexamethasone (Strong recommendation, moderate certainty of evidence). Critical illness is defined as patients on mechanical ventilation and ECMO. Critical illness includes end organ dysfunction as is seen in sepsis/septic shock. In COVID-19, the most commonly reported form of end organ dysfunction is ARDS. Among hospitalized patients with severe, but non-critical COVID-19 the IDSA guideline panel suggests dexamethasone rather than no dexamethasone (Conditional recommendation, moderate certainty of evidence). Severe illness is defined as patients with SpO<sub>2</sub> ≤ 94% on room air, including patients on supplemental oxygen. Among hospitalized patients with non-severe COVID-19 without hypoxemia requiring supplemental oxygen, the IDSA guideline panel suggests against the use of glucocorticoids. Non-severe illness is defined as patients with a SpO<sub>2</sub> >94% not requiring supplemental oxygen. See guideline for data summary.
4. If no contraindications, continue **statins** or consider starting in those with a guideline indication for one.
5. Do not need to stop home **ACEI/ARB** therapy, unless there is another compelling reason.
6. Avoid starting new prescriptions for **NSAIDs**. Can see IDSA guideline for some discussion of NSAIDs.
7. Use **inhalers** over nebulizers.
8. Many institutions are noting that patients with COVID-19 tend to have higher than normal baseline triglyceride levels secondary to an HLH-type syndrome and many institutions are avoiding discontinuation of their **propofol** infusions in these patients until TG levels are closer to 750/1000 mg/dL. This would avoid having to change to an alternative/less desired sedative agent in these patients (ie: benzodiazepines which are less than ideal due to the longer elimination time and association with longer intubation times). It is recommended to continue to monitor these patients closely for any signs and symptoms of PRIS while on propofol therapy.
9. Due to the frequency of every one hour blood glucose checks for patients who are receiving intravenous **insulin** with Endotool, it would be preferred to manage these patients with basal/bolus regimen of insulin if possible or tolerate a blood glucose that is slightly above our goal. This will aide in decreasing the number of times the nurse has to enter the room to obtain a finger stick for insulin drip titrations. See separate document for subcutaneous insulin management of mild/moderate DKA in the COVID-19 patient.
10. In patients who are intubated **scheduled eye care** is administered in the form of Clear Eyes solution and petrolatum ointment both given every 4 hours alternating which results in an eye drop being administered every 2 hours to aide in lubrication secondary to dryness that results from the ventilator. In an effort to reduce nursing exposure and since most patients should be maintained at a light level of sedation, it is recommended to omit the petrolatum ointment and use only the Clear Eyes solution in these patients with a frequency of 'four times day' or 'three times a day' with the specific times correlating with other medication administration times.
11. In an effort **to minimize aerosolization during extubation** consider strategies of prevention of post extubation coughing and gagging. IV lidocaine 1 mg/kg (max 100 mg) can be given 3-5 minutes prior to extubation or 1 mg/kg of 2% lidocaine solution can be instilled intratracheally into the outer aperture of the ETT 5 minutes prior to extubation to blunt the post extubation cough response. In patients with heart block/bradycardia without a pacemaker AVOID IV lidocaine administration and can consider utilization of 0.5 mg/kg of 2% lidocaine solution via the ETT in these patients.
12. Anecdotal reports from China suggest that patients infected with coronavirus who were receiving **famotidine**, a H<sub>2</sub> receptor antagonist to treat conditions such as acid reflux and peptic ulcer disease, had improved survival vs those receiving proton pump inhibitors. This post hoc finding has led to interest in the

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drug, though no predominant theory describing a mechanism for its efficacy yet exists. One theory is that famotidine, like many other compounds, binds and therefore inhibits the coronavirus main protease, 3C-like main protease (3Clpro). **Among hospitalized patients with severe COVID-19, the IDSA panel suggests against famotidine use for the sole purpose of treating COVID-19 (conditional recommendation, low certainty of evidence).** See guideline for data summary. If stress ulcer prophylaxis is indicated, consider choosing famotidine over PPIs. This is already in agreement with current MICU practices for critically ill intubated patients.

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