Management of Inpatients with Suspected SARS-CoV-2 (COVID-19)

All UMMC patients suspected of having COVID-19 should immediately be reported to Mississippi MED-COM at (601) 984-4655.

The backbone of the treatment strategy for COVID19 is good quality supportive care as in any viral pneumonia. There is no current evidence from RCTs to recommend any specific anti-COVID-19 treatment for patients with suspected or confirmed COVID-19 infection. In the absence of strong evidence, we recommend the following based upon limited reported data. This document will be updated continually as new evidence emerges and based on the availability of treatment regimens. Currently, there is no evidence supporting outpatient management of patients with suspected or confirmed COVID-19, including the use of hydroxychloroquine and azithromycin.

Patient Admitted on Nasal Cannula		
Disposition: Consider admission to intensive care unit if older than 65 years of age with a new oxygen requirement, D-dimer > 1,000 ng/L, or RR > 22 breaths/min		
Fluids	Conservative fluid management strategy	
Medications	***Evaluate for enrollment in clinical trials***	
	Antimicrobials	Empiric early antibiotics for bacterial pneumonia; rule out influenza
	Bronchodilators	If needed, use metered dose inhalers and avoid nebulized therapies
Coagulopathy	Evaluate hematologic abnormalities and treat as appropriate. See "Anticoagulation Dosing Recommendations for COVID-19 Patients" document.	
O_2 Supplement	Target SpO2 >90%. If oxygen requirement increases to 5 L Call primary team and ICU for evaluation.	
	Consider high-flow nasal cannula at 15 – 30 LPM with surgical mask over patient's face.	
Patient Admitted to Intensive Care Unit		
Fluids	Conservative fluid management strategy such as daily net neutral fluid balance in patients without evidence of shock	
Medications	***Evaluate for enrollment in clinical trials***	
	Antimicrobials	Empiric early antibiotics for bacterial pneumonia; rule out influenza
Coagulopathy	Evaluate hematologic abnormalities and treat as appropriate. See "Anticoagulation Dosing Recommendations for COVID-19 Patients" document.	
O_2/Mechanical Ventilation	Target SpO2 >92%. Consider HFNC at 15-30LPM with surgical mask over patients face.	
	Once intubated, maintain plateau pressures < 30cm H_20. Low Vt and high PEEP strategies are controversial.	
	If PaO_2/FiO_2 < 150, consider early proning and use of paralytics	
	If PaO_2/FiO_2 remains < 150 after proning and paralysis, consider cautious use of inhaled vasodilators and ECMO consult	

Additional Comments:

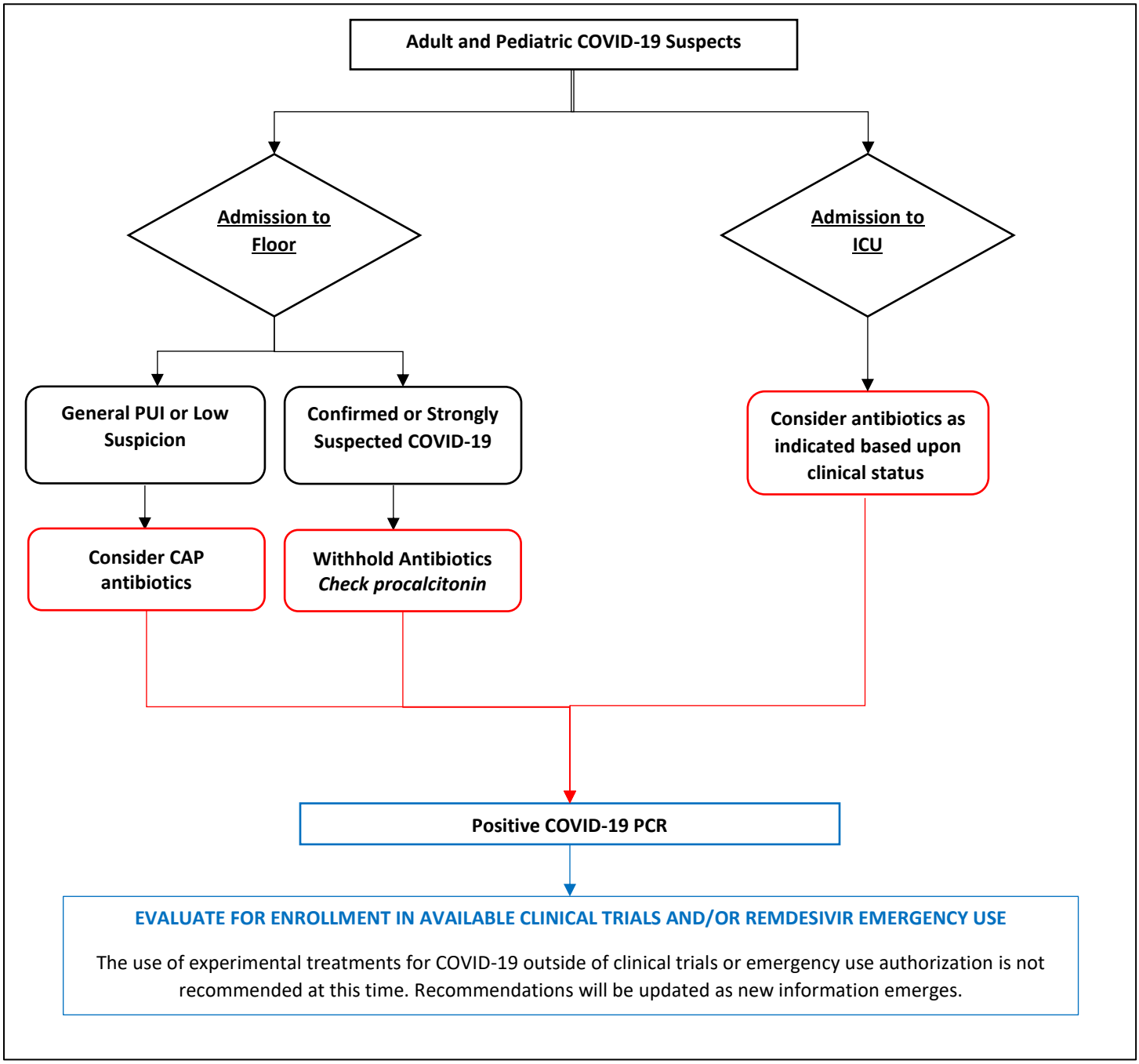
- Corticosteroids are not recommended for routine treatment of COVID-19. Consider use of corticosteroids in patients with ARDS due to COVID-19, refractory septic shock, or other compelling indication (COPD exacerbation, asthma exacerbation, etc.) Optimal dosing for ARDs due to COVID-19 is unknown but can consider using methylprednisolone 1 mg/kg/day.
- There is not enough information to comment on the withholding of NSAIDs or ACEi/ARB therapy
- Early intubation for hypoxemic respiratory failure is no longer required.

Agents not recommended for COVID-19 treatment

The agents listed below have no evidence supporting the use for treatment of COVID-19 but can be used for alternative diagnoses or in the context of clinical trials. * = drugs with low supply (recent shortage or currently on allocation) – contact pharmacy with questions.

- HIV protease inhibitors (more on lopinavir/ritonavir on page 4): darunavir, atazanavir
- H2-receptor blockers: famotidine*, cimetidine
- Supplements: zinc*, ascorbic acid*
- Miscellaneous: IVIG*, interferon, azithromycin

Algorithm for Management of Patients with suspected COVID-19



Information about ongoing or potential clinical trials at UMMC can be found at: https://intranet.umc.edu/Research/Research%20Offices/Clinical-Trials/COVID-19-Task-Force-Potential%20Studies.html

Consider enrolling pregnant patients in: PRIORITY (Pregnancy CoRonavIrus Outcomes RegIsTRY), a nationwide registry for pregnant and postpartum individuals with suspected COVID-19 or confirmed diagnosis https://priority.ucsf.edu/

Consider enrolling pediatric patients in: Pediatric Covid-19 National Survey (PIDTRAN-6_Covid-19), a nationwide registry for pediatric COVID-19 patients in the United States. Link to survey can be provided upon request by contacting apalmer@umc.edu.

Consider enrolling rheumatology patients in: COVID-19 Global Rheumatology Alliance registry at https://rheum-covid.org/

Clinical Trials

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https://intranet.umc.edu/Research/Research%20Offices/Clinical-Trials/COVID-19-Task-Force-Potential%20Studies.html

Trial	Study Summary	Inclusion Criteria	Exclusion Criteria
Active			
Outcomes Related to COVID-19 Treated with Hydroxychloroquine among In-patients with Symptomatic Disease (ORCHID) PI: Alan Jones, MD Coordinator: Rebekah Peacock OCT: Whitney Bondurant	Hospitalized adults with confirmed SARS-CoV-2 or high suspicion for COVID-19 Blinded, multicenter, placebo-controlled randomized clinical trial Intervention: hydroxychloroquine 400 mg twice daily for two doses (day 1), then 200 mg twice daily for days 2-5	1. ≥18 yo 2. Currently hospitalized or in ED with anticipated hospitalization 3. Symptoms of acute respiratory infection 4. Lab-confirmed SARS-CoV-2 infection within the past 10 days or lab test result pending plus a high suspicion for COVID-19 as indicated by all of the following: a. Cough with duration ≤10 days b. Bilateral pulmonary infiltrates on chest imaging or new hypoxemia c. No alternative explanation for symptoms	1. Pregnancy or breastfeeding 2. Unable to randomize within 10 days after onset of acute respiratory infection symptoms or within 48 hours after hospital arrival 3. Seizure disorder 4. Porphyria cutanea tarda 5. QTc >500 ms on ECG within 72 hours prior to enrollment or diagnosis of long QT syndrome 6. Allergy to hydroxychloroquine, chloroquine, or amodiaquine 7. Receipt in the 12 hours prior to enrollment or planned administration during the 5-day study period of any of the following: amiodarone, cimetidine, dofetilide, phenobarbital, phenytoin, sotalol 8. Receipt of >1 dose of hydroxychloroquine or choloroquine in the 10 days prior to enrollment 9. Inability to receive enteral medications
A Phase 1b/2, Randomized, Double-Blind, Placebo-Controlled, Multi-Center Study to Evaluate the Safety and Efficacy of TJ003234 in Subjects with Severe Coronavirus Disease 2019 (COVID-19) PI: Gailen Marshall, MD Coordinator: Heather Vaughn OCT: Donald Naylor	Evaluation of the safety and efficacy of TJ003234 administered as an intravenous (IV) infusion in subjects with severe COVID-19 under supportive care, and to assess the effect of TJ003234 on the levels of cytokines	1. ≥18 2. Bilateral lung infection 3. Lab-confirmed SARS-CoV-2 or COVID-19 4. One of the following criteria: a. Severe disease that meets one of the following conditions: (i) Finger blood oxygen saturation ≤ 93% or PaO2/FiO2 ≤ 300 mmHg; or (ii)Requiring non-invasive or invasive mechanical ventilation; or b. Hospitalized patients ≥60 with medical comorbidities.	1. COPD patients requiring inhaled corticosteroid, long-acting beta-adrenergic agonists or anticholinergics, or long-term oxygen therapy 2. Pulmonary interstitial disease, pulmonary alveolar proteinosis, and pulmonary granulomatosis 3. Cardiovascular event in the prior 3 months 4. Severe renal impairment or liver disease 5. Known hepatitis B or C infection or HIV 6. TB 7. Blood system disorders or abnormalities 8. Dependence on methylprednisolone 2 mg/kg/day or more or long-term use of anti-rejection or immunomodulatory drugs 9. ECMO 10. Pregnancy or breastfeeding.
Remdesivir for the Treatment of SARS-CoV2 Infection *Expanded Access* PI: Jason Parham OCT: David Cretella	Expanded access treatment protocol for use of RDV for the treatment of a participant with coronavirus disease-2019 (COVID-19) resulting from infection of SARS-CoV-2.	1. Age ≥18 years or aged ≥12 and <18 years of age weighing ≥40 kg 2. Hospitalized with confirmed SARS-CoV2 by PCR or known contact of confirmed case with syndrome consistent with COVID-19 with PCR pending 3. Requiring mechanical ventilation 4. ALT ≤5 x upper limit of normal	1. Multiorgan failure, including coagulopathy, hepatic failure, renal failure, or significant cardiomyopathy 2. Use of >1 pressor for septic shock 3. Renal failure with eGFR <30 ml/min, dialysis, or CVVH 4. Known hypersensitivity to remdesivir or its metabolites
International, Multicenter, Randomized, Double-Blind, Placebo-Controlled Phase III Study Evaluating the Efficacy and Safety of	Evaluation of the effects of dapagliflozin compared with placebo on risk of death or disease progression in	1. >18 years of age; 2. Lab-confirmed SARS-CoV-2 infection less than 72 hours prior to randomization or strongly suspected on presentation; 3. Currently hospitalized;	1. Severe COVID-19 (requiring mechanical ventilation and/or non-invasive ventilation or expected need for mechanical ventilation within 24 hours); 2. History of type 1 diabetes mellitus or diabetic ketoacidosis;

Dapagliflozin in Respiratory Failure in Relation to COVID-19 (DARE 19) PI: Vishnu Garla, MD Contact: Bronwyn Briseno	patients hospitalized with COVID-19	4. Mild-moderate disease (SpO2 ≥ 94% with low-flow supplemental oxygen); 5. Medical history of at least one of the following: hypertension, Type 2 diabetes, atherosclerotic cardiovascular disease, heart failure, or CKD stage 3 to 4; and Chest radiography or CT findings consistent with COVID-19.	3. eGFR or receiving renal replacement therapy/dialysis; 4. Current participation 1. in another interventional clinical trial (with an investigational drug); 5. Evidence of oliguria or serum creatinine >= 1.5 X baseline pre-hospitalization value; 6. Systolic blood pressure 7. Has received in the last 14 days experimental immune modulators and/or monoclonal antibody therapies for COVID-19; 8. Treatment with any SGLT2i (e.g., dapagliflozin, canagliflozin, empagliflozin, ertugliflozin) within the previous 4 weeks; and 9. Pregnancy or breastfeeding.
Pending			
Randomized Controlled Trial of Losartan for Inpatients with COVID-19 PI: Alan Jones, MD Contact: Rebekah Peacock	Evaluation of impact of early losartan compared to placebo on change in respiratory failure	1. ≥18 years of age 2. Hospital admission with a respiratory SOFA ≥1 and increased oxygen requirement compared to baseline 5. Randomization within 24 hours of hospital presentation or 48 hours of a positive test result	1. Currently taking an ACEi or ARB 2. Prior reaction or intolerance to an ARB or ACEi 3. Pregnant or breastfeeding 4. History of kidney disease or severe liver disease 5. Severe dehydration 5. Most recent mean arterial blood pressure prior to enrollment
Pilot Safety and Proof of Principle Study of Intravenous DNase Therapy in SARS-CoV-2 (COVID-19) PI: Matthew Kutcher, MD	Evaluation of IV DNase treatment of COVID-19 patients with evidence of early hypercoagulable disseminated intravascular coagulation to determine safety and efficacy in reducing levels of circulating cell-free DNA	1. ≥18 years of age 2. Inpatient status 3. SARS-CoV-2 PCR test positive for infection 4. D-dimer >500 ng/ml FEU	1. Known hypersensitivity to dornase alpha 2. Pregnant or lactating

Treatment Information

Drug	Dose and Duration	Comments
Investigational Therapies		
Hydroxychloroquine (HCQ) • Only recommend in the context of a clinical trial	**Adult** 400 mg PO BID x2 doses followed by 200 mg PO BID x4 days **Pediatric** 6.5 mg/kg (max: 400 mg/dose) q12h PO x2 doses followed by 3.5 mg/kg (max: 200 mg/dose) PO q12h x 4 days	**Additional assessment** • Assess QTc prior to initiation • Assess for serious drug-drug interactions (DDI) **Contraindications** • QTc >500 (see QTc monitoring table on page 2) **A/E:** retinopathy, rash, nausea, glucose fluctuations
Remdesivir • Direct acting antiviral that has now received emergency use authorization • Supply critically limited. • Enrollment and allocation decisions made on an individual basis	**Adult** 200 mg IV x 1 followed by 100 mg IV q24h **Pediatric** • <40 kg: 5 mg/kg IV load followed by 2.5 mg/kg IV q24h • ≥40kg: Refer to adult dosing Duration: Non-MV – 5 days Mechanically ventilated – 10 days	Available through either an expanded access protocol requiring study enrollment (above) or emergency use authorization **Additional assessment** • Requires baseline eGFR and ALT **A/E:** Increased ALT/AST. Caution for use in AKI
Tocilizumab (Actemra) • Adjunctive agent that targets IL-6 • Consider in critically ill patients with suspected cytokine storm	**Adult** 400 mg IV x1 dose **Pediatric – 2 Years of Age and Older** • <30 kg: 12 mg/g IV x1 dose (max 400 mg) • ≥30kg: 8 mg/kg IV x1 dose (max 400 mg) Duration: 1 dose	**Additional assessment** • Consider checking inflammatory markers (CRP, ferritin, LDH, fibrinogen, D-dimer) **A/E:** Increased ALT/AST, infusion related reactions, hematologic dyscrasias, increased LDL
Not Recommended: Risk/Benefit Ratio Does Not Favor Use		
Azithromycin • No intrinsic activity for SARS-COV-2 • Published evidence for has significant limitations • Clear toxicity risk	**Adult** 500 mg IV/PO on day 1, followed by 250 mg IV/PO daily x 4 days **+ HCQ** **Pediatric - >3 months** • 10 mg/kg IV/PO on day 1 (max 500 mg), followed by 5 mg/kg IV/PO daily x 4 days (max 250 mg)	**Additional assessment** • Assess for serious drug-drug interactions (DDI) • Assess baseline QTc and Mg^{2+} with follow-up QTc in 24-48 hours **Contraindications** • QTc >500
Lopinavir-Ritonavir (Kaletra®) • *In vitro* studies suggest activity • Current published evidence failed to demonstrate efficacy	**Adult** 400mg-100mg PO BID **Pediatric** *14 days to 6 months:* 16 mg/kg PO BID (lopinavir component) *6 months to 18 years:* • 15-25 kg: 200 mg-50 mg PO BID • 26-35 kg: 300 mg-75 mg PO BID • >35 kg: 400 mg-100 mg PO BID	**Additional assessment** • Check HIV antigen/antibody prior to first dose • Assess for serious DDI (CYP3A4 substrate/inhibitor) **A/E:** hepatotoxicity, pancreatitis, QTc prolongation, diarrhea Combination with ribavirin has been suggested based on synergistic action with lopinavir/ritonavir. Additional studies are needed before recommending this combination.

Information on drug interactions and administration for patients who cannot swallows can be found at: http://www.covid19-druginteractions.org/