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 COVID-19 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.

**O2 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.

**O2/Mechanical Ventilation**
- Target SpO2 >92%. Consider HFNC at 15-30LPM with surgical mask over patient’s face.
- Once intubated, maintain plateau pressures < 30cm H2O. Low Vt and high PEEP strategies are controversial.
- If PaO2/FiO2 < 150, consider early proning and use of paralytics
- If PaO2/FiO2 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

**Adults**

- Admission to floor
  - Without 
  
  \(O_2\) Requirement or Risk Factors
  - Admission to ICU
    - With 
    \(O_2\) Requirement and/or Risk Factors
      - Admission to PICU or floor

**EVALUATE FOR ENROLLMENT IN AVAILABLE CLINICAL TRIALS**

The use of experimental treatments for COVID-19 outside of clinical trials is not recommended at this time. When information from ongoing clinical trials is published, recommendations will be updated.


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/](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.

## Clinical Trials

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

<table>
<thead>
<tr>
<th>Trial</th>
<th>Study Summary</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Active</strong></td>
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<tr>
<td>Outcomes Related to COVID-19 Treated with Hydroxychloroquine among In-patients with Symptomatic Disease (ORCHID)</td>
<td>Hospitalized adults with confirmed SARS-CoV-2 or high suspicion for COVID-19</td>
<td>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</td>
<td>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 &gt;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 of &gt;1 dose of hydroxychloroquine or chloroquine in the 10 days prior to enrollment 8. Inability to receive enteral medications</td>
</tr>
<tr>
<td>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)</td>
<td>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</td>
<td>1. ≥18 Bilateral lung infection 2. 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.</td>
<td>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.</td>
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<tr>
<td>Pending</td>
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<tr>
<td>Randomized Controlled Trial of Losartan for Inpatients with COVID-19</td>
<td>Evaluation of impact of early losartan compared to placebo on change in respiratory failure</td>
<td>1. ≥18 years of age 2. Hospital admission with a respiratory SOFA ≥1 and increased oxygen requirement compared to baseline 1. Randomization within 24 hours of hospital presentation or 48 hours of a positive test result</td>
<td>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 1. Most recent mean arterial blood pressure prior to enrollment</td>
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**International, Multicenter, Randomized, Double-Blind, Placebo-Controlled Phase III Study Evaluating the Efficacy and Safety of Dapagliflozin in Respiratory Failure in Relation to COVID-19 (DARE 19)**

**PI:** Vishnu Garla, MD  
**Contact:** Bronwyn Briseno

| Evaluation of the effects of dapagliflozin compared with placebo on risk of death or disease progression in patients hospitalized with COVID-19 | 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;  
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  
6. Chest radiography or CT findings consistent with COVID-19. | 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;  
3. eGFR or receiving renal replacement therapy/dialysis;  
4. Current participation 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. |


**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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose and Duration</th>
<th>Comments</th>
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<tbody>
<tr>
<td><strong>Investigational Therapies</strong></td>
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<tr>
<td>Hydroxychloroquine (HCQ)</td>
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<tr>
<td>• Only recommend in the context of a clinical trial</td>
<td>Adult</td>
<td>400 mg PO BID x2 doses followed by 200 mg PO BID x4 days</td>
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<tr>
<td></td>
<td>Pediatric</td>
<td>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</td>
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<tr>
<td></td>
<td>Duration: 5 days total</td>
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</table>
|                               | 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                    |                   |          |
| • 200 mg IV x 1 followed by 100 mg IV q24h | Adult | 400 mg IV x1 dose |
| • 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 | 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 |
| Tocilizumab (Actemra)         |                   |          |
| • Adjunctive agent that targets IL-6 | Adult | 400 mg IV x1 dose |
| • Consider in critically ill patients with suspected cytokine storm | 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) |
| Azithromycin                  |                   |          |
| • No intrinsic activity for SARS-COV-2 | Adult | 500 mg IV/PO on day 1, followed by 250 mg IV/PO daily x 4 days + HCQ |
| • Published evidence for has significant limitations | 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) |
| • Clear toxicity risk | Additional assessment | • Assess for serious drug-drug interactions (DDI)  
|                               |                     | • Assess baseline QTc and Mg2+ with follow-up QTc in 24-48 hours |
|                               | Contraindications | • QTc >500 |
| Lopinavir-Ritonavir (Kaletra®) |                   |          |
| • In vitro studies suggest activity | Adult | 400mg-100mg PO BID |
| • Current published evidence failed to demonstrate efficacy | 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/](http://www.covid19-druginteractions.org/)