### Infectious Diseases Consults and Approval

- Infectious Diseases approval NOT required for hydroxychloroquine and azithromycin for hospitalized patients with **confirmed** COVID-19
- Infectious Diseases consult available for all hospitalized patients with confirmed COVID-19

### Patient group | Current Potential Therapy Options | Notes
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**Mild disease:**  
Not requiring hospitalization  
OR  
Hospitalized patient with (SPO2 > 93%), and NO radiographic evidence of pneumonia  

Not hospitalized: Supportive care  

Hospitalized: Start Hydroxychloroquine  
400 mg PO q 12 hrs x 2 doses then 12 hours later start  
400 mg PO q 24 hrs x 4 doses for a total of 5 days of therapy  

***May add azithromycin  
500 mg PO x 1 dose then 24 hours later start  
250 mg PO q 24 hours x 4 doses for a total of 5 days of therapy  
OR  
500 mg PO q 24 hours x 3 doses for a total of 3 days of therapy  

Hospitalized patient with (SPO2 > 94%), and radiographic evidence of pneumonia: **Consider remdesivir trial**  

If discharged, discontinue hydroxychloroquine and azithromycin.  

- Check ECG prior to hydroxychloroquine initiation for QT prolongation. Risk is increased when used with other QT prolonging drugs.  
- Follow QT monitoring algorithm below.  
- Review potential medication interactions and other possible side effects  

*** Combination Azithromycin and Hydroxychloroquine: contraindicated in persons with known WPW and prolonged QT

**Moderate disease:**  
Hospitalized patients with hypoxia (SPO2 ≤ 94 %)  
OR  
Radiographic evidence of pneumonia  

Start Hydroxychloroquine  
400 mg PO q 12 hrs x 2 doses then 12 hours later start  
400 mg PO q 24 hrs x 4 doses for a total of 5 days of therapy  

***May add azithromycin  
500 mg PO x 1 dose then 24 hours later start  
250 mg PO q 24 hours x 4 doses for a total of 5 days of therapy  
OR  
500 mg PO q 24 hours x 3 doses for a total of 3 days of therapy  

If discharged, discontinue hydroxychloroquine and azithromycin.  

- Check ECG prior to hydroxychloroquine initiation for QT prolongation. Risk is increased when used with other QT prolonging drugs.  
- Follow QT monitoring algorithm below.  
- Review potential medication interactions and other possible side effects  

*** Combination Azithromycin and Hydroxychloroquine: contraindicated in persons with known WPW and prolonged QT

**Severe disease with respiratory failure but no other end organ damage:**  
Patient requiring high flow, NRB, BIPAP or mechanical ventilation  
AND  
Not on pressors, CrCl > 30 ml/min, ALT < 5x upper limit of normal  

Start Hydroxychloroquine:  
400 mg PO q 12 hrs x 2 doses then 12 hours later start  
400 mg PO q 24 hrs x 4 doses for a total of 5 days of therapy  

***May add azithromycin  
500 mg PO x 1 dose then 24 hours later start  
250 mg PO q 24 hours x 4 doses for a total of 5 days of therapy  
OR  
500 mg PO q 24 hours x 3 doses for a total of 3 days of therapy  

Consider  
- Remdesivir clinical trial  
- Convalescent plasma  
- Mesenchymal stem cells  
- Tocilizumab*  

If discharged, discontinue hydroxychloroquine and azithromycin.  

- Check ECG prior to hydroxychloroquine initiation for QT prolongation. Risk is increased when used with other QT prolonging drugs.  
- Follow QT monitoring algorithm below.  
- Review potential medication interactions and other possible side effects  

*** Combination AZ and HCQ contraindicated in persons with known WPW and prolonged QT

* Requires non-formulary Infectious Diseases Approval and not to be used if patient requires mechanical ventilation.

*Current recommendation is for patients with specific clinical parameters (RR ≥ 30, SPO2 ≤ 93%, PaO2/FiO2 < 300, > 50% lung infiltrates in 24-48 hours) and lab findings (CRP > 150 and D-dimer >2.5).
**Patient group**

Severe disease with respiratory failure and other end organ damage:
- Patient requiring mechanical ventilation
- AND
- Requiring pressors or CrCl < 30 ml/min or receiving HD or CVVH or ALT > 5x upper limit of normal

<table>
<thead>
<tr>
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<th>Notes</th>
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<tbody>
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If discharged, discontinue hydroxychloroquine and azithromycin.

- Consider
  - Remdesivir clinical trial
  - Convalescent plasma
  - Mesenchymal stem cells

**Evidence of systemic inflammation**

Worsening of respiratory function with evidence of systemic inflammation including elevations of IL-6, fibrinogen, D-dimer, CRP

Consider
- Remdesivir clinical trial
- Convalescent plasma
- Mesenchymal stem cells

If discharged, discontinue hydroxychloroquine and azithromycin.

### Obtain Baseline ECG

A: if not on any QT prolonging agents, K / Mg within normal limits, and most recent ECG is within 30 days, a new ECG may not be necessary. B: Ideally, discontinue QT prolonging agents.

- **Normal Baseline QT**
  - QTc < 470 ms
  - Administer Hydroxychloroquine
  - Obtain ECG 2 hours after 2nd dose (of 400 mg)

- **Marginal Baseline QT**
  - QTc 470 – 500 ms
  - Caution Required

- **Abnormal Baseline QT**
  - QTc > 500 ms
  - Do not start Hydroxychloroquine or Discuss risk/benefit pre-initiation

### Notes:

- Adjust for a baseline wide QRS: QTc = QTc – (QRS-100ms). For example, if the baseline QRS is 180ms, a QTc of 570ms translates to 490ms (570 – (180-100)).
- High risk patients for development of Torsade de Pointes, who should be considered for continuous telemetry monitoring include those with LV dysfunction (LV EF <30%) Must discontinue drug for any evidence of Torsade de Pointes
- Consider mobile telemetric monitoring for outpatients.

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*Credit: Dr. Vivek Reddy and Dr. Valetin Fuster*
**Medications:**

**Corticosteroids:**
- While there is insufficient data to provide recommendations for all patients with COVID-19, some patients may benefit from corticosteroids, please consult pulmonary and/or critical care for guidance.

**Hydroxychloroquine (Plaquenil®):**
- Hydroxychloroquine is preapproved for patients with PCR-confirmed COVID-19. ID approval required at ALL TIMES if utilized for the treatment of COVID-19 without PCR-confirmation.
- Hydroxychloroquine is NOT recommended for use in patients without PCR-confirmed COVID-19.
- Epic Hospitals: **Utilize COVID-19 order set to enter load and maintenance dose**

**Dosing:**
400 mg PO q 12 hours x 2 doses then 12 hours later start
400 mg PO q 24 hours x 4 doses for a **total of 5 days of therapy**

- Pregnancy Category: D
- Renal and hepatic dose adjustments not recommended
- If GI discomfort, can change 400 mg daily to 200 mg BID
- Tablet can be crushed

**Monitoring:**
- Risk is increased when used with other QT prolonging drugs.
- Utilize QT monitoring algorithm to guide therapy

**Drug interaction Resources:**
- University of Liverpool Interactions with Experimental COVID-19 Therapies
- University of Liverpool Interactions with Experimental COVID-19 Therapies Summary Table

**Potential Side Effects:** Cardiomyopathy, hypoglycemia, bone marrow suppression, dermatitis

**Updated:** April 10, 2020
Remdesivir:

- Remdesivir is available for compassionate use for pregnant patients and patients less than 18 years of age.
- Actively enrolling patients into a clinical trial
- Email COVIDGILEAD@mssm.edu for trial enrollment consideration or compassionate use
- If tocilizumab administered to patient, must wait 24 hours after tocilizumab administration to give remdesivir

ACE inhibitors (angiotensin converting enzyme inhibitors) and ARBs (angiotensin-receptor blockers):\textsuperscript{13}

- It is strongly recommended that those patients prescribed ACE inhibitors and ARBs for preexisting conditions should be continued on their ACE inhibitor and ARB therapy.
- Patients should NOT be started on an ACE inhibitor or an ARB for the treatment of COVID-19.

Azithromycin\textsuperscript{20}:

Dosing:

- 500 mg PO x 1 dose then 24 hours later start 250 mg PO q 24 hours x 4 doses for a total of 5 days of therapy
  OR
- 500 mg PO q 24 hours x 3 days for a total of 3 days of therapy

- If patient able to tolerate oral hydroxychloroquine, then patient should receive oral azithromycin. Intravenous azithromycin use is discouraged.
- A non-randomized prospective cohort of patients who received either hydroxychloroquine and azithromycin, hydroxychloroquine monotherapy or control found that viral eradication rates in the combo group at day 6 were 100%. The study contains a flaw as 6 patients were not considered in the final study analysis and there was confounding by indication. Hydroxychloroquine and azithromycin have shared cardiovascular toxicities, particularly QTc prolongation.

Tocilizumab (Actmera\textsuperscript{®})

- Limited availability and requires non-formulary approval AT ALL TIMES for off-label use
- Not FDA-approved for the treatment of COVID-19 related cytokine storm
- Monoclonal antibody consent required prior to administration.
- Infectious Diseases must be consulted for the consideration of initiation of tocilizumab for the treatment of COVID-19 related cytokine storm. An ID provider must request non-formulary approval from one of the ID non-formulary approvers.

Dosing:

- Patients ≥30 kg: 8 mg/kg (actual body weight) IV x single dose (Maximum dose: 800 mg)
- 162 mg subcutaneous (SC) pre-filled syringe to be injected into left and right leg – a total of TWO syringes are to be injected once

Drug interaction Resource:

- [University of Liverpool Interactions with Experimental COVID-19 Therapies](#)
- [University of Liverpool Interactions with Experimental COVID-19 Therapies Summary Table](#)

- Tocilizumab may reduce levels of apixaban and rivaroxaban but does NOT interfere with enoxaparin or heparin.
- Please address in patients on anticoagulation for COVID-associated coagulopathy

Caution:

- Associated with lower gastrointestinal perforations in patients on concomitant steroids, NSAIDS, and/or methotrexate and in patients with diverticulitis
- Avoid use in patients with platelets <50,000 and those with ANC <500

Updated: April 10, 2020
References:

11. Fang Lei. Are Patients with Hypertension and Diabetes Mellitus at increased risk for COVID-19 infection? The Lancet Published: March 11, 2020DOI:https://doi.org/10.1016/S2213-2600(20)30116-8

Updated: April 10, 2020