

## New Mexico Medical Advisory Team Assessment

**MAT Workgroup Name:** Clinical Care

**Date:** April 9, 2020

### Question or request:

1. Should New Mexico obtain hydroxychloroquine (HCQ) sulfate for treatment of COVID-19 under the newly issued FDA emergency use authorization (EUA)?

### Recommendation/s in bullet form:

- The MAT recommends securing 50,000 Tablets (200 mg) of Hydroxychloroquine sulfate (HCQ).
- Some protocols also discuss using HCQ with Azithromycin. MAT does NOT recommend the addition of Azithromycin due to lack of adequate supporting evidence and potential side effects. No action is needed by the State of New Mexico to secure Azithromycin.
- MAT recommends seeking a source other than the FDA stockpile due to reporting requirements, via FEMA through the EOC or through Senator Heinrich's Office.
- Treatment of COVID-19 disease with HCQ should be **considered** by all clinicians and healthcare systems using the emergency use access approval guidelines provided by the FDA, with the understanding that evidence for the effectiveness of HCQ in the treatment of COVID-19 is still limited.

### Assessment:

Although there are no FDA-approved medications indicated for the treatment of COVID-19, treatment with Hydroxychloroquine Sulfate (HCQ) is recommended for select population groups.

- Emerging early studies have shown HCQ to have clinical benefit for COVID-19 patients with moderate to severe disease.<sup>1, 2, 3, 4, 5, 6, 7</sup>
- HCQ can be prescribed off label at the physician's discretion; physicians are not required to participate in a clinical trial to prescribe this medication.
- Under the emergency use access approval by FDA, the suggested dose for HCQ sulfate to treat adults and adolescents who weigh 50kg or more and are hospitalized with COVID-19 is 800mg of HCQ on the first day of treatment followed by 400mg daily for 4 to 7 days of total treatment based on clinical evaluation.
- The State of New Mexico should work with industry to secure 50,000 tablets of HCQ that can be used to treat patients with moderate to severe COVID-19 disease. If industry supply is not available, then medication should be obtained through the Strategic National Stockpile. However, there are significant stipulations and reporting requirements for use of HCQ obtained through the Strategic National Stockpile which may not be feasible for smaller health systems.
- UNMH and Presbyterian are offering treatment at their facilities through participation in clinical trials.
- Please see attached Presbyterian Healthcare Services COVID-19 (SARS-CoV-2) Summary of Adult Pharmacotherapy Considerations.

### EVIDENCE:

#### Use of Hydroxychloroquine (HCQ) for COVID-19:

HCQ has been shown, in preliminary data from one small randomized trial in China, to shorten the time to clinical recovery, whereas another small randomized trial in China showed no clinical benefit<sup>8,9</sup> Neither study was a randomized controlled trial (RCT). Clinicians at acute care facilities treating COVID-19 patients should consider the

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potential benefits of HCQ for patients who meet the conditions outlined in the assessment and for whom HCQ treatment is not contraindicated.

If the pharmaceutical industry is not able to supply the HCQ, the State of New Mexico should request this medication through the Strategic National Stockpile. However, drugs obtained through the Strategic National Stockpile have tighter controls and will require administering facilities to report on the use of the medications; this can be an onerous process for those acute care facilities who are not accustomed to participating in clinical trials.<sup>10</sup>

### Validity of HCQ for Treatment of COVID-19 Patients

In-vitro evidence has demonstrated that HCQ is more potent against SARS-COV-2 than chloroquine at inhibiting the virus and therefore it is the preferred treatment approach.<sup>2, 3, 5, 7, 11</sup> Interestingly, of the 80 patients with SLE in Wuhan being treated with HCQ, none contracted COVID. As a result of this in vitro data and the clinical study data from China discussed above, many academic medical centers and acute care facilities include the use of HCQ to treat specific types of COVID-19 patients.<sup>2, 3, 5, 6, 7</sup> Justification for inclusion in these guidelines is based on in vitro activity of HCQ rather than on results of clinical trials, and they caution about the potential for adverse effects. The Vanderbilt treatment guidelines specifically caution about HIV and Chikungunya trials suggesting that HCQ may worsen outcomes by increasing viral load.<sup>7</sup>

**Dosing:** The preferred dosing is 800mg by mouth on Day 1) followed by 200mg every 12 hours (400mg daily) for days 2 to 7 for a 5 to 8 day total duration.<sup>12</sup>

**Side Effects:** HCQ is not without risk, and may exacerbate cardiovascular and hepatic comorbidities and cause renal and hepatic injury. However, HCQ has been prescribed to lupus and rheumatologic arthritis patients long-term and has shown significant clinical benefit.

**Hydroxychloroquine/Azithromycin Combination:** HCQ and azithromycin combined have been shown to significantly increase the risk of cardiovascular mortality, chest pain/angina and heart failure compared to HCQ and are therefore not being recommended at this time.<sup>13</sup>

### **Red flags and concerns:**

- Ideally HCQ would be obtained from industry and NOT from the FDA stockpile, as the reporting requirements will make a statewide distribution and the required tracking of complication difficult.
- Please see attached Presbyterian Healthcare Services COVID-19 (SARS-CoV-2) Summary of Adult Antimicrobial Pharmacotherapy Considerations.

Although HCQ has a variety of side effects including cardiovascular problems (QT prolongation), bone marrow suppression, neuropathy and many drug-drug interactions, these side effects are infrequent and many patients use HCQ chronically for autoimmune diseases.<sup>6</sup> Despite the potential side effects and higher risk profile for those with COVID-19, we continue to recommend use of HCQ as a therapeutic measure for patients and feel that the benefits of treatment with HCQ outweigh the risks of delaying or avoiding treatment. We will continue to monitor the scientific literature regarding therapeutic studies and approaches and will update these recommendations as additional information is made available.

**Contributors:** There was moderate consensus on these recommendations among the following contributors.

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### Resources/Reference:

- <sup>1</sup>Center for Evidence-Based Medicine at the University of Oxford, Chloroquine and hydroxychloroquine: Current evidence for their effectiveness in treating COVID-19, published March 25, 2020; Available from: <https://www.cebm.net/covid-19/chloroquine-and-hydroxychloroquine-current-evidence-for-their-effectiveness-in-treating-covid-19/> [Accessed April 1, 2020]
- <sup>2</sup>Cortegiani, A., Ingoglia, G., Ippolito, M., Giarratano, A., & Einav, S. (2020). A systematic review on the efficacy and safety of chloroquine for the treatment of COVID-19. *Journal of critical care*. Available from: <https://www.sciencedirect.com/science/article/pii/S0883944120303907>. [Accessed April 7, 2020]
- <sup>3</sup> Harvard University, Treatments for COVID-19 Available from: <https://www.health.harvard.edu/diseases-and-conditions/treatments-for-covid-19>. [Accessed April 6, 2020]
- <sup>4</sup> Kalil, A. C. (2020). Treating COVID-19—Off-Label Drug Use, Compassionate Use, and Randomized Clinical Trials During Pandemics. *JAMA*. doi:10.1001/jama.2020.4742 [Accessed April 2, 2020].
- <sup>5</sup> Massachusetts General Hospital COVID-19 Treatment Guidelines Available from: <https://www.massgeneral.org/assets/MGH/pdf/news/coronavirus/mass-general-COVID-19-treatment-guidance.pdf> [Accessed April 7, 2020]
- <sup>6</sup> Vanderbilt University Faculty in Infectious Diseases, Emergency Medicine, Pulmonary/Critical Care, Hospital/General Medicine, Cardiology & Radiology, “Clinical Recommendations for Treatment of COVID-19 Adult Patients” March 22, 2020. Available from: <https://www.vumc.org/coronavirus/sites/default/files/COVID%20Documents/Weekly%20COVID-19%20Clinical%20Guidelines%20Update%20Summary%20-%202020-03-22-2020-%20FINAL.pdf>. [Accessed April 6, 2020]
- <sup>7</sup> Yale University, COVID-19 Treatment Algorithm Updated April 3, 2020. Available from: [https://medicine.yale.edu/intmed/COVID-19%20TREATMENT%20ADULT%20Algorithm%204.3.20\\_382832\\_5\\_v2.pdf](https://medicine.yale.edu/intmed/COVID-19%20TREATMENT%20ADULT%20Algorithm%204.3.20_382832_5_v2.pdf) [Accessed April 7, 2020]
- <sup>8</sup>Chen, Z., Hu, J., Zhang, Z., Jiang, S., Han, S., Yan, D., ... & Zhang, Z. (2020). Efficacy of hydroxychloroquine in patients with COVID-19: results of a randomized clinical trial. medRxiv. Available from: <https://www.medrxiv.org/content/10.1101/2020.03.22.20040758v2> [Accessed April 6, 2020]
- <sup>9</sup> Chen J, Lui D, Liu L, et al. A pilot study of hydroxychloroquine in treatment of patients with common coronavirus disease-19 (COVID-19) *J of Zhejiang U*. 2020; DOI : 10.3785/j.issn.1008-9292.2020.03.03. (Accessed March 25, 2020)
- <sup>10</sup> U.S. Food and Drug Administration, “Request for Emergency Use Authorization For Use of Chloroquine Phosphate or Hydroxychloroquine Sulfate Supplied From the Strategic National Stockpile for Treatment of 2019 Coronavirus Disease” Available from: <https://www.fda.gov/media/136534/download>. [Accessed March 28, 2020]
- <sup>11</sup> Wang M, Cao R, Zhang L et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Res*. 2020; 30:269-271. (PubMed 32020029) (DOI

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10.1038/s41422-020-0282-0)

<sup>12</sup> Sophie Perinel, Manon Launay, Élisabeth Botelho-Nevers, Éric Diconne, Aurore Louf-Durier, Raphaël Lachand, Martin Murgier, Dominique Page, Régine Vermesch, Guillaume Thierry, Xavier Delavenne, Towards Optimization of Hydroxychloroquine Dosing in Intensive Care Unit COVID-19 Patients, *Clinical Infectious Diseases*, , ciaa394, <https://doi.org/10.1093/cid/ciaa394>

<sup>13</sup> Lambert, Christophe (2020) Safety of hydroxychloroquine, alone and in combination with azithromycin, in light of rapid wide-spread use for COVID-19: a multinational, network cohort and self-controlled case series study. Available from: <https://data.ohdsi.org/Covid19EstimationHydroxychloroquine/>. [Accessed April 7, 2020]  
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