Title: Essential COVID-19 information on the use of hydroxychloroquine (HQ) as a treatment and prophylaxis for SARS-CoV-2

Question: What is the evidence for and risks of using hydroxychloroquine (HQ) as a treatment and prophylaxis for SARS-CoV-2?

Context:

• There is widespread concern of contracting the virus that causes COVID-19 among both the public and among health care workers.
• HQ has been suggested as treatment and prophylaxis for COVID-19 illness in social media, news reports, some scientific data and announcements from politicians.
• In Alberta, there have been anecdotal reports of physicians prescribing HQ for their colleagues or staff. This has prompted an advisory from the Alberta College of Pharmacy for their members not to dispense HQ when stockpiling is suspected (Alberta College of Pharmacy, March 2020). A similar advisory was sent from the College of Physicians and Surgeons of Alberta to its members (April 2020).
• There is ongoing controversy about the role of HQ in the treatment of COVID with evolving signals of potential harm in COVID-19 patients. Recommendations that HQ be taken off order sets for COVID management in AHS outside the setting of monitored randomized controlled trials have been made to reflect changes to major national guidelines (Association of Medical Microbiology and Infectious Diseases Canada, Infectious Diseases Society of America, American Thoracic Society) in Canada and the US.

Recommendation – Provided by: AHS COVID-19 Scientific Advisory Group

1. Hydroxychloroquine (HQ) is not currently recommended to be used as prophylaxis for COVID-19 outside clinical trials, given the lack of established benefit to counterbalance potential harms, and no existing data on prophylaxis.
2. Given the significant increased risk of QT prolongation and cardiac arrhythmias, HQ should not be used with azithromycin or other macrolide antibiotics unless in the context of a clinical trial. These medications should also not be used sequentially given very long half-lives and continued QT prolongation risk.
3. As there are limited supplies of HQ within AHS, and concerns may eventually arise with supply in Alberta’s community pharmacies, its use should be prioritized to those patients who are on it for chronic rheumatologic conditions, where there is stronger evidence of benefit.
4. For patients with COVID-19 disease, in both the hospital and the community, preference for use of HQ as treatment is given to those enrolled in clinical trials investigating the effects of HQ in treating and preventing severe COVID-19 illness.
5. Off-label prescribing of HQ for treatment of COVID-19 positive inpatients should only be performed after careful consideration of the potential harms, consideration of expert consultation as needed (e.g., Infectious Disease, Respiratory Medicine, and General Internal Medicine) and discussion between the Most Responsible Physician and the patient.
6. If all criteria in #5 are met and the decision is made to use HQ:
   a. The use of a risk stratification tool (e.g., Tisdale et al, 2013) to access the risk of QTc prolongation must be considered when evaluating the benefit vs harm of using HQ as treatment in SARS-CoV-2 patients.
   b. A drug interaction check between HQ and the patient’s medications must be completed using the website https://www.covid19-druginteractions.org/ or a suitable alternative. Pharmacy Services can assist with performing the drug interaction check.
   c. While the patient is on HQ, baseline and intermittent ECGs to assess the corrected QT (QTc) interval during treatment should be considered depending on the patient’s baseline risk.
   d. Adverse events with respect to off-label use of HQ for inpatient treatment should be documented and reported by clinicians through the AHS Reporting and Learning System for Patient Safety at https://insite.albertahealthservices.ca/tools/rls/Page1820.aspx.
   e. These recommendations will be updated as the published data evolves.

Summary of evidence:
- The evidence of HQ effectiveness in treating COVID-19 illness is limited. Although there is plausible in vitro activity of HQ against COVID-19, there is equivocal in vivo data across observational studies and small randomized controlled trials with significant methodologic concerns.
- There is no evidence for HQ for use as prophylaxis for COVID-19 illness. There are multiple randomized trials underway to explore this in health care workers and close contacts to known cases.
- HQ risks, particularly when used for patients with cardiopulmonary compromise due to COVID-19 infection, include the potential for serious clinical and laboratory adverse effects, potential drug interactions, and carry a risk to children if unintentionally ingested.