

What are the data regarding use of hydroxychloroquine sulfate (Plaquenil®) in combination with azithromycin (Zithromax®/Z-Pak®) for the treatment of COVID-19?

Initial response: March 25, 2020

Update 2: April 24, 2020

Summary of changes:

- Multiple governmental and professional organizations have updated their guidance regarding the use of hydroxychloroquine sulfate (HCQ) for the treatment of COVID-19.¹⁻⁸ At this time, no investigational drug has been shown to be safe and effective for the treatment of COVID-19.
- The Food and Drug Administration (FDA) continues to evaluate drugs for the treatment of COVID-19 and to-date has not approved any drug for the treatment of COVID-19.
- Studies evaluating the use of HCQ for the treatment of COVID-19 are underway.

Recommendations from governmental and professional organizations.¹⁻⁸

Organization, publication	Date	HCQ-related recommendations
<i>Governmental</i>		
FDA Safety announcement	Apr 24	<ul style="list-style-type: none"> • HCQ and chloroquine have not been shown to be safe and effective for treating or preventing COVID-19 and are associated with a number of risks including QT prolongation. Their use for COVID-19 has only been authorized under limited circumstances through the EUA. • If considering these drugs, check clinicaltrials.gov for a suitable trial and consider enrollment. • Patients should be monitored; parameters may include baseline ECG, electrolytes, renal function, and hepatic tests.
EMA Safety announcement	Apr 23	<ul style="list-style-type: none"> • Closely monitor patients with COVID-19 receiving HCQ or chloroquine for heart rhythm problems as well as other adverse events, and account for pre-existing CV problems. • Patients and healthcare professionals to report any suspected side effects to national regulatory authorities.
NIH Guidelines	Apr 21	<ul style="list-style-type: none"> • There are insufficient clinical data regarding the use of HCQ for COVID-19. • If HCQ is used, patients must be monitored for potential adverse effects, especially QT interval prolongation. Adverse drug events or medication errors should be reported to MedWatch.
FDA EUA	Apr 3	<ul style="list-style-type: none"> • HCQ and chloroquine products can be used to treat adult and adolescent patients who weigh ≥ 50 kg (≥ 110 lb) and are hospitalized with COVID-19, and for whom a clinical trial is not available, or participation is not feasible. • Fact sheets must be available for patients and prescribers, with this information: <ul style="list-style-type: none"> ○ Chloroquine phosphate 1 g on day 1, followed by 500 mg/d for 4 to 7 days. ○ HCQ 800 mg on day 1, followed by 400 mg/d for 4 to 7 days. ○ Optimal dosing and duration of treatment are unknown.
<i>Professional</i>		
IDSA Guidelines	Apr 11	<ul style="list-style-type: none"> • Due to uncertainty regarding risks and benefits, HCQ alone and HCQ + azithromycin should only be used in hospitalized patients in the context of a clinical trial.
ATS Guidance	Apr 3	<ul style="list-style-type: none"> • HCQ, on a case-by-case basis, can be prescribed to hospitalized patients with COVID-19 pneumonia if all of the following criteria are met: shared decision-making is possible in which patient is informed of possible risks vs. benefits of HCQ; data can be collected for interim comparisons of patients receiving and not receiving HCQ; illness is severe enough to warrant investigational therapy; and HCQ is not in short supply.
ACC/AHA/HRS Statement on CV risks of HCQ	Mar 29	<ul style="list-style-type: none"> • HCQ should be prescribed in the context of a clinical trial; if not possible, an ID or COVID-19 expert, with cardiology input regarding QT monitoring, should be consulted. • The intensity of QT and arrhythmia monitoring should be considered in the context of potential drug benefit, drug safety, resource availability and quarantine considerations.

ACC=American College of Cardiology; AHA=American Heart Association; ATS=American Thoracic Society; CV=cardiovascular; ECG=electrocardiogram; EMA=European Medicines Agency; EUA=emergency use authorization; FDA=Food and Drug Administration; HCQ=hydroxychloroquine; HRS=Heart Rhythm Society; ID=infectious disease; IDSA=Infectious Diseases Society of America; NIH=National Institutes of Health.

References: 1. Food and Drug Administration. <https://www.fda.gov/media/137250/download>. 2. European Medicines Agency. <https://www.ema.europa.eu/en/news/covid-19-reminder-risk-serious-side-effects-chloroquine-hydroxychloroquine>. 3. National Institutes of Health. <https://covid19treatmentguidelines.nih.gov/therapeutic-options-under-investigation/>. 4. Food and Drug Administration. <https://www.fda.gov/media/136535/download>. 5. Food and Drug Administration. <https://www.fda.gov/media/136537/download>. 6. Infectious Disease Society of America. <https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/>. 7. American Thoracic Society-led international taskforce. <https://www.thoracic.org/covid/covid-19-guidance.pdf>. 8. American College of Cardiology. <https://www.acc.org/latest-in-cardiology/articles/2020/03/27/14/00/ventricular-arrhythmia-risk-due-to-hydroxychloroquine-azithromycin-treatment-for-covid-19#outpatient>.