Iowa Board of Pharmacy

Iowa Board of Medicine

Iowa Board of Dentistry

Iowa Board of Nursing

Iowa Board of Physician Assistants

July 8, 2020

Petition by Sen. David L. Hartsuch, MD MS for formal consideration by the Boards of their Joint Statement dated March 26, 2020 regarding the prescribing of Hydroxychloroquine, and for revision of this joint statement.

} ***Petition to Formally Consider and Revise Joint Statement.***

Background -

Hydroxychloroquine (HCQ) was first formulated in 1936 and approved for medical use in 1955. It is widely used worldwide as an anti-malarial drug, and domestically for the treatment of Lupus. Over a million prescriptions per year are commonly prescribed in the US. It's widespread use with minimal complications makes it one of the safest drugs.

While commonly known worldwide as an anti-malarial drug, it has been identified as having efficacy as an anti-viral drug both in vitro and in vivo. Randomized controlled trials and other reports have demonstrated the efficacy of treating COVID-19 and many more trials are currently underway to confirm these results and to delineate the boundaries of its use for this application. Furthermore, trials have shown that early use of HCQ significantly reduces the mortality of patients with COVID-19. Furthermore, there are few therapeutic alternatives to hydroxychloroquine.

On March 19, 2020, President Donald Trump called the drug a "game-changer" immediately removing the use of the drug from the realm of science into the realm of politics. In the week that followed, the number of prescriptions for the drug tripled; across the nation, Boards of Medicine and Pharmacy responded in order to limit the use of the drug. This bolus of prescribing lasted about a week and subsequently subsided to baseline.

On March 26, 2020, The Iowa Boards of Medicine, Pharmacy, Dentistry, Nursing, and Physician Assistants issued a "Joint Statement" expressing what practitioners and pharmacists "should" do. Certainly not a requirement that practitioners "must do". However, in light of the significant legal authority of the Boards, this appears to have the force of law possibly leading

to disciplinary action for practicing as one "should not". It has had a chilling effect in our State preventing the prescribing and filling of prescriptions of HCQ for COVID-19 patients. Certainly, this has had its desired effect since most pharmacists require the diagnosis of COVID-19 without any true law requiring it. It is not clear what actual discussion or deliberation the boards had of this statement prior to its publication. There does not appear to be any such discussions mentioned in the minutes of any of the Boards. It is not clear how the statement arose at all, although it is amazingly similar to statements issued by those of other states.

This statement does not impose any legal obligation upon any provider or pharmacist. The statement is rightfully informs providers and pharmacist that Hydroxychloroquine, like any drug, should be properly prescribed and not stockpiled. However, its use of words like "should", "encouraged", or "discouraged". Its general tenor has gone beyond this and appears to threaten practitioners that might not follow the Boards' recommendations. Consequently, it functionally has discouraged the use of the drug, if not acted as an outright ban on prescribing for this purpose. Specifically, the Boards have suggested that pharmacists should not fill these prescriptions unless they have a diagnosis on the prescription—a requirement that is certainly not based in law, custom, or within the authority of the Boards. Furthermore, this may impinge upon patients' privacy rights. Licensees are rightfully concerned that this Saber rattling by the Boards would turn into actual disciplinary action.

Diagnosis of COVID-19 -

The Statement by the board has stated that physicians "should" write the diagnosis of "COVID-19" on the prescription. The policy says, "Prescribers should include the diagnosis code or diagnosis with prescriptions issued for hydroxychloroquine, chloroquine, and azithromycin.", with the stated benefit to "prevent communications from the pharmacy which in turn will expedite the time to treat." The statement also "recommends" that pharmacists confirm the diagnosis implying that prescriptions should not be filled without a firm diagnosis stated on the prescription. Normally, there is no legal requirement to associate a diagnosis with a prescription although often third-party payors will require this.

In the case of COVID-19, the diagnostic criteria are not well established. As you know, COVID-19 is a highly lethal and contagious disease. It has a prolonged latency period perhaps lasting a week or more during which the asymptomatic carrier can infect others. Furthermore, there has been widespread shortages of testing; often these test results are delayed; and the available tests often have not been shown to have sufficient sensitivity or specificity. Consequently, large numbers of patient are recommended to merely self-isolate without a definitive diagnosis. We have seen a fairly high mortality among Persons Under Investigation (PUI) who were either not tested or tested negative for COVID-19.

The result is that clinicians must weight the risk and benefits of treatment based upon the index of suspicion rather than upon objective criteria. As such, there are patients

that should be treated according to the professional opinion of physicians who do not have a definitive diagnosis of COVID-19 acceptable to the Boards. This decision to treat these patients must rest with the patient and the practitioner rather than with the Boards themselves. Furthermore, writing a diagnosis of COVID-19 on the prescription in the absence of objective criteria could subject the practitioner to charges of fraud.

The statement of the Boards discourages "prophylactic" prescribing of HCQ but offers no definition of what this means. Some might interpret this to mean any prescription without an actual positive test. Others might interpret this to mean prescribing to patients who might have had significant exposure but without objective signs or symptoms. Again, the tenor makes it appear that the Boards intend to second guess the judgment of practitioners and discipline them for what the Boards regard as "prophylactic" use of the drug.

While your statement is not legally binding, it appears to be; It has been effectively translated into law as pharmacy chains now require writing the diagnosis on prescriptions pursuant to your recommendations. This has discouraged the legitimate prescribing of this important drug and placed the health of patients in jeopardy.

Public Health Concerns -

While the United States has only 4.3% of the World population, we now have over 25% of the world cases of COVID-19 and an equally disproportionate share of its deaths. Countries such as Australia, and New Zealand have actually placed HCQ on their nations' treatment guidelines and have nearly eradicated COVID-19 from their shores. Nations with high incidence of malaria with many patients on the drug such as India with much higher populations have had a nearly insignificant number of cases of COVID-19. In the United States, however, treatment guidelines from the CDC and NIH have largely ignored the research on the use of HCQ and have favored Remdesivir (RDV). Though expensive and in limited supply this drug has shown no survival benefit in hospitalized patients.

In contrast, early treatment with HCQ has been shown to significantly reduce hospitalizations and save lives. Clinical trials to date have shown a significant reduction (50%) in hospitalizations in those patients treated as outpatients. The cost of the drug on GoodRx which is a reasonable estimate of market value is 25 cents per tablet or approximately $3 for the recommended 5 day course of the drug due to its long half-life. The public health impact of this drug should be apparent. Furthermore, despite the claim of the Boards, there does not appear to be significant shortages of the drug.

I have attached two papers in support of the safety and efficacy of HCQ. I would like to highlight that in 1,948 patients who were given HCQ at Henry Ford Hospital in Detroit, none of the patients exhibited the dreaded arrhythmias which comprise the main safety concern by HCQ's opponents. With this evidence alone, we can be 95% confident that this condition will not arise in more than 1.6 patients per thousand treated. Considering

the millions of doses of this drug safely given just in America, the Boards should realize that these safety concerns are unfounded.

We are faced with a lethal and highly contagious disease and must apply the best science at hand even if possibly incomplete. The best science today demonstrates the safety and efficacy of HCQ for the treatment of COVID-19. Discouraging the use of this drug is more likely than not to negatively impact the public health of Iowans and encourage the spread of COVID-19.

Politization of HCQ -

Following the infamous statement by Donald Trump, the media, and oppositional political machine has disproportionately promoted the dangers of HCQ, such as arrhythmia, and showed a bias toward reporting a lack of efficacy against COVID-19. Many reports were made about a couple who ingested an aquarium cleaner product and died as evidence of its toxicity. Our own Iowa Department of Public Health has promoted these dangers by placing a warning notice from the Poison Control Center which demonstrate arrhythmia from an overdose of the drug. These are not true representations of the risk of the drug but do show the political nature of HCQ's assessment.

In Appendix A, I have included the financial disclosures of the NIH treatment guidelines committee. As you will notice, there are a significant number of members with financial ties to Gilead pharmaceutical company which received orphan drug status on RDV. Successful use of HCQ would greatly reduce the market potential for RDV and reduce the profits of the company. It should be apparent from the disconnect between treatment guidelines and underlying research that these financial relationships have had their desired effect.

Powers of the Boards –

According to the Iowa Code, the Boards were created in order to regulate the various medical and pharmacy professionals who practice within the State. They exist to ensure that medical professionals are qualified to practice and maintain professional conduct consistent with their varied professions. The Iowa code 155A.27 specifies what information is required to be included in a prescription. Currently, there is no empowering act which authorizes the Boards to require a diagnosis on each prescription for COVID-19 nor has there been any formal rulemaking in this regard.

Beyond the regulation of the professions, the Boards are not empowered to act to ration scarce resources, nor to enforce treatment guidelines such as those promoted by the NIH or managed care organizations. Currently, off label prescribing of medication is permitted by law unless there is some particular safety concern which I would again ask the Boards to clearly demonstrate for HCQ beyond mere speculation. It is beyond the scope of the Boards to determine whether a prescription for one use should be given precedence over an alternate use. Since the Boards should solely be concerned with

the health of our citizens, they are certainly not authorized by the legislature to engage in a political struggle to embarrass our President or any other person.

Finally, a descent respect for our Constitution, the Legislature, and Due Process demands that with regard to proclamations of this kind the Board should—if not must—act explicitly with formal public deliberation and documentation in their minutes. It is deceptive for the Boards to implement extra-legislative administrative rules through a declaration under a pretense of authority which leaves health professionals to worry about legal repercussions which might arise.

Petition for Redress-

The petitioner humbly requests:

1) The Boards should formally convene to discuss the subject of their statement with adequate public input.

2) The Boards should adopt formal rules where applicable after consideration of the relevant science and actual practice deficiencies seen in the community.

3) The Boards should respect the privacy rights of patients and remove the recommendation that prescriptions should contain a diagnosis and should instruct pharmacies to fill prescriptions without the need for a diagnosis consistent with the policy pertaining to all other drugs.

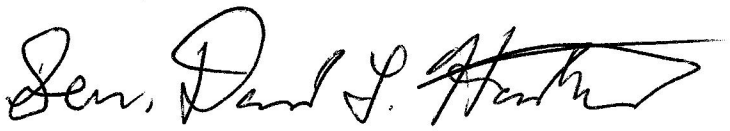
4) The Board should respect the right of individual prescribers to prescribe drugs for off label indications such as this.

5) The Boards should show data that shortages truly exist before making recommendations intended to ration this drug.

6) The Boards should base their policy decisions solely upon the scientific merits of the treatment rather than the political issues surrounding HCQ.

Thank you for regarding this petition. I look forward to your reasoned response.

Sincerely,



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Appendix A, Table 2. Panel on COVID-19 Treatment Guidelines Financial Disclosure for Companies Related to COVID-19 Treatment or Diagnostics (Reporting Period: May 1, 2019, to March 31, 2020)

Member	Financial Disclosure	
	Company	**Relationship**
Judith Aberg	Gilead Sciences	Research Support
	Regeneron	Research Support
Adaora Adimora	Gilead Sciences	Consultant, Research Support
Jason Baker	Gilead Science	Research Support
Roger Bedimo	Gilead Sciences	Honoraria
Eric Daar	Gilead Sciences	Consultant, Research Support
David Glidden	Gilead Sciences	Consultant
Gregory Martin	Regeneron	Consultant
Henry Masur	None	N/A
Susanna Naggie	AbbVie	Research Support
	Gilead Sciences	Research Support
	Vir Biotechnology	Advisory Board, Stock Options
Pablo Tebas	Gilead Sciences	Research Support
	Inovio Pharmaceuticals	Research Support
Phyllis Tien	None	N/A
Timothy Uyeki	None	N/A
Alpana A. Waghmare	Ansun BioPharma	Research Support
	KYORIN Pharmaceutical Co.	Advisory Board

JOINT STATEMENT FROM THE:

IOWA BOARD OF PHARMACY
IOWA BOARD OF NURSING
IOWA DENTAL BOARD
IOWA BOARD OF PHYSICIAN ASSISTANTS
IOWA BOARD OF MEDICINE

March 26, 2020

The Iowa Boards of Medicine, Nursing, Physician Assistants, Dentistry and Pharmacy have recently received increased reports of prescriptions being issued for hydroxychloroquine, chloroquine, and azithromycin for prophylactic purposes in response to the COVID-19 outbreak. Concerns have been raised that this activity may lead to stockpiling of medication, inappropriate use and potential drug shortages for patients with a legitimate need. To protect the public health and safety, licensees are reminded of the following:

For prescribers:

- Prescribing hydroxychloroquine, chloroquine and azithromycin for COVID-19 prophylactic use is discouraged and not recommend by the Boards at this time.
- Prescribing hydroxychloroquine, chloroquine, and azithromycin for yourself, family, friends and co-workers in anticipation of a COVID-19 related illness can significantly impact drug supplies, which may negatively impact the health of existing patients who are established on these medications for the treatment of indicated disease states as approved by the FDA. Further, such prescribing may lead to improper use of these medications which can cause harm. Prescribers should exercise caution and refrain from prophylactic prescribing in light of the State of Public Health Disaster Emergency.
- Prescribers should include the diagnosis code or diagnosis with prescriptions issued for hydroxychloroquine, chloroquine, and azithromycin. Including this information may prevent communications from the pharmacy which in turn will expedite the time to treat.
- Prescribers should limit the amount prescribed of hydroxychloroquine, chloroquine, and azithromycin, unless otherwise deemed appropriate by the prescriber (e.g., 14-day supply, etc.).

For pharmacies:

- Pharmacists should use their professional judgment and take appropriate steps to verify that newly issued prescriptions for hydroxychloroquine, chloroquine, and azithromycin are issued for a legitimate medical purpose. To prevent drug shortages, the Board of Pharmacy recommends

contacting prescribers to confirm the diagnosis of patients newly prescribed these medications during the State of Public Health Disaster Emergency.

- Multiple states[1] have adopted a 14-day supply limitation for the dispensing of these medications. While Iowa has not officially implemented a specific dosage unit or day supply limitation at this time, licensees are strongly encouraged to limit dispensing for patients newly prescribed hydroxychloroquine, chloroquine, and azithromycin during the State of Public Health Disaster Emergency if the prescription is not accompanied with a supporting diagnosis. The Board is not recommending that pharmacies refuse to fill legitimate prescriptions for hydroxychloroquine, chloroquine, or azithromycin; rather, the Board is recommending that pharmacies use caution and exercise professional judgment when deciding whether and how much to dispense of these medications.

While all Boards are recommending caution, licensees should avoid interruptions in care for patients previously established on these medications that have an appropriate diagnosis. The Boards recognize this may be a difficult balance; however, licensees should make a good faith effort to ensure appropriate prescribing, dispensing, and patient care.

[1] North Carolina, Nevada, Louisiana, Texas, Ohio, and Idaho.

Early Outpatient Treatment of Symptomatic, High-Risk Covid-19 Patients that Should be Ramped-Up Immediately as Key to the Pandemic Crisis

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Funding: None.

Conflict of Interest: Dr. Risch acknowledges past advisory consulting work with two of the more than 50 manufacturers of hydroxychloroquine, azithromycin and doxycycline. This past work was not related to any of these three medications and was completed more than two years ago. He has no ongoing, planned or projected relationships with any of these companies, nor any other potential conflicts-of-interest to disclose.

Running Head: Outpatient Treatment of High-Risk Covid-19

Abstract

More than 1.6 million Americans have been infected with SARS-CoV-2 and >10 times that number carry antibodies to it. High-risk patients presenting with progressing symptomatic disease have only hospitalization treatment with its high mortality. An outpatient treatment that prevents hospitalization is desperately needed. Two candidate medications have been widely discussed: remdesivir, and hydroxychloroquine+azithromycin. Remdesivir has shown mild effectiveness in hospitalized inpatients, but no trials have been registered in outpatients. Hydroxychloroquine+azithromycin has been widely misrepresented in both clinical reports and public media, and outpatient trials results are not expected until September. Early outpatient illness is very different than later hospitalized florid disease and the treatments differ. Evidence about use of hydroxychloroquine alone, or of hydroxychloroquine+azithromycin in inpatients, is irrelevant concerning efficacy of the pair in early high-risk outpatient disease. Five studies, including two controlled clinical trials, have demonstrated significant major outpatient treatment efficacy. Hydroxychloroquine+azithromycin has been used as standard-of-care in more than 300,000 older adults with multicomorbidities, with estimated proportion diagnosed with cardiac arrhythmias attributable to the medications 47/100,000 users, of which estimated mortality is <20%, 9/100,000 users, compared to the 10,000 Americans now dying each week. These medications need to be widely available and promoted immediately for physicians to prescribe.

Keywords: Azithromycin; Covid-19; Doxycycline; Hydroxychloroquine; Remdesivir; SARS-CoV-2; Zinc

Abbreviations: AZ, azithromycin; CDC, US Centers for Disease Control; FAERS, FDA Adverse Events Reporting System database; FDA, US Food and Drug Administration; HCQ, hydroxychloroquine; NIH, US National Institutes of Health; QTc, corrected electrocardiogram Q-T-wave duration; RCT, randomized controlled trial; RR, relative risk; R_t, epidemic reproduction number at time *t*.

Highlights:

- As of May27, 2020 there are over 1,678,843 confirmed cases of COVID-19 claiming more than 100,000 lives in the Unites States. Currently there is no known effective therapy or vaccine.
- -According to a protocol-based treatment algorithm, among hospitalized patients, use of hydroxychloroquine alone and in combination with azithromycin was associated with a significant reduction in-hospital mortality compared to not receiving hydroxychloroquine.
- -Findings of this observational study provide crucial data on experience with hydroxychloroquine therapy, providing necessary interim guidance for COVID-19 therapeutic practice.

Abstract:

Significance: The United States is in an acceleration phase of the COVID-19 pandemic. Currently there is no known effective therapy or vaccine for treatment of SARS-CoV-2, highlighting urgency around identifying effective therapies.

Objective: The purpose of this study was to evaluate the role of hydroxychloroquine therapy alone and in combination with azithromycin in hospitalized patients positive for COVID-19.

Design: Multi-center retrospective observational study

Setting: The Henry Ford Health System (HFHS) in Southeast Michigan: large six hospital integrated health system; the largest of hospitals is an 802-bed quaternary academic teaching hospital in urban Detroit, Michigan.

Participants: Consecutive patients hospitalized with a COVID-related admission in the health system from March 10,2020 to May 2,2020 were included. Only the first admission was included for patients with multiple admissions. All patients evaluated were 18 years of age and older and were treated as inpatients for at least 48 hours unless expired within 24 hours.

Exposure: Receipt of hydroxychloroquine alone, hydroxychloroquine in combination with azithromycin, azithromycin alone, or neither.

Main Outcome: The primary outcome was in-hospital mortality.

Results: Of 2,541 patients, with a median total hospitalization time of 6 days (IQR: 4-10 days), median age was 64 years (IQR:53-76 years), 51% male, 56% African American, with median time to follow-up of 28.5 days (IQR:3-53). Overall in-hospital mortality was 18.1% (95% CI:16.6%-19.7%); by treatment: hydroxychloroquine+azithromycin, 157/783 (20.1% [95% CI: 17.3%-23.0%]), hydroxychloroquine alone, 162/1202 (13.5% [95% CI: 11.6%-15.5%]), azithromycin alone, 33/147 (22.4% [95% CI: 16.0%-30.1%]), and neither drug, 108/409 (26.4% [95% CI: 22.2%-31.0%]). Primary cause of mortality was respiratory failure (88%); no patient had documented torsades de pointes. From Cox regression modeling, predictors of mortality were age ≥65 years (HR:2.6 [95% CI:1.9-3.3]), white race (HR:1.7 [95% CI:1.4-2.1]), CKD (HR:1.7 [95%CI:1.4-2.1]), reduced O2 saturation level on admission (HR:1.5 [95%CI:1.1-2.1]), and ventilator use during admission (HR: 2.2 [95%CI:1.4-3.3]). Hydroxychloroquine provided a 66% hazard ratio reduction, and hydroxychloroquine+azithromycin 71% compared to neither treatment ($p<0.001$).

Conclusions and Relevance: In this multi-hospital assessment, when controlling for COVID-19 risk factors, treatment with hydroxychloroquine alone and in combination with azithromycin was associated with reduction in COVID-19 associated mortality. Prospective trials are needed to examine this impact.