PharMerica

CLINICAL ADVISORY

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Hydroxychloroquine Use and Drug Interactions

Issue

There are currently no FDA-approved medications for prophylaxis and/or treatment of SARS-CoV-2 (COVID-19), however, there has been much discussion recently about certain therapies being used off-label.[1] At this time, the clinical management of this disease includes infection prevention and control, supportive care, and mechanical ventilator support when necessary.[2]

Hydroxychloroquine has received the most attention to date and is currently under investigation in clinical trials for pre-exposure or post-exposure prophylaxis of SARS-CoV-2 infection, and treatment of patients with mild, moderate, and severe COVID-19. There is currently no evidence, beyond anecdotal, that hydroxychloroquine is effective for treating persons infected with COVID-19, and there is also no data to recommend the use of hydroxychloroquine as prophylaxis for COVID-19.[3]

The Society for Post-Acute and Long-Term Care Medicine (PALTC) cautions that hydroxychloroquine also has the potential to result in serious side effects, which may be more severe in the PALTC population, especially when used in combination with azithromycin and other medications. Therefore, in a benefit versus risk decision, a prescriber would be weighing the lack of any solid evidence of a benefit versus a very real risk of serious side effects.[3]

A recent FDA Emergency Use Authorization was issued that allows use of hydroxychloroquine supplied from the Strategic National Stockpile (SNS) to treat adults and adolescents who weigh >50 kg and are hospitalized with COVID-19 for whom a clinical trial is not available, or participation is not feasible.

Additionally, many State Boards of Pharmacy have enacted regulations with regards to the prescribing of hydroxychloroquine limiting treatment to COVID-19 positive patients enrolled in clinical trials and prohibiting use for prophylaxis.

Informational Guide

The following hydroxychloroquine guidelines contain information gathered from the FDA-approved labeling, case studies, and observational reports to date and must be reviewed by your healthcare professionals. They may need to be modified as necessary to meet unique standards of practice within your nursing care center and are not to be construed as a substitute for the professional judgment of health care professionals.

PharMerica, along with the writers, editors, and reviewers of this informational guide cannot be held responsible for the continued currency of information, for any errors or omissions and for any consequences arising from this guideline.

1. Gautret P, Lagier JC, Parola P, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. International Journal of Antimicrobial Agents. In Press March 17, 2020.
2. Centers for Disease Control and Prevention (CDC). Information for clinicians on therapeutic options for COVID-19 patients. Updated March 21, 2020. Accessed March 23, 2020. https://www.cdc.gov/coronavirus/2019-ncov/hcp/therapeutic-options.html
3. AMDA Statement on the Current Use of Hydroxychloroquine in Persons with COVID-19. American Medical Director's Association The Society for Post Acute and Long Term Care Medicine. Updated April 7, 2020. Accessed April 10, 2020.

Use of Hydroxychloroquine for COVID-19

FDA Emergency Use Authorization (EUA): allows use of hydroxychloroquine sulfate supplied from the Strategic National Stockpile (SNS) to treat adults and adolescents who weigh ≥50 kg and are hospitalized with COVID-19 for whom a clinical trial is not available, or participation is not feasible[1]

Dosing Recommendations (Based on Hydroxychloroquine Sulfate[1,2]

- **FDA EUA**: 800 mg on 1st day of treatment, then 400 mg daily for 4-7 days
- **Lexi-Comp Alternatives:**
  - 200 mg TID for 10 days
  - 400 mg BID on day 1 followed by 400 mg once daily for 5 days
  - 600 mg BID on day 1 followed by 400 mg once daily for 4 days

Contraindications[1]

- Presence of retinal or visual field changes of any etiology
- Known hypersensitivity to aminoquinoline compounds (i.e. hydroxychloroquine, chloroquine)

Laboratory Monitoring[1,2] ***Refer to Lexi-Comp for more information***

- Baseline ECG (to assess QT interval)
- Baseline evaluation of renal and hepatic function

Warnings[1]

- **QT prolongation:** caution in pts w/ cardiac disease, QT prolongation, hx of ventricular arrhythmias, K+ or Mg+ imbalance, other QT prolonging agents
- **Severe Hypoglycemia**
- **Hematologic Effects:** reports of hemolysis in G6PD deficient patients; anemia, neutropenia
- **Hepatic Impairment:** caution in pts w/ hepatic impairment (hepatitis, liver dx, alcoholism) and w/ use of other hepatotoxic agents
- **Worsening of Psoriasis**
- **Retinopathy:** irreversible retinal damage

Use in Pregnancy[1] ***Refer to Lexi-Comp and/or CDC for more information***

- Evaluate risk vs. benefit before initiating this drug in pregnant patients

Important Instructions for Healthcare Providers[1]

- Required to provide patients with Fact Sheet titled "Emergency Use Authorization of Hydroxychloroquine Sulfate Fact Sheet for Patients and Parents/Caregivers" **PRIOR to prescribing/dispensing in accordance to law**
- Communicate the following information to the patient**
  - Emergency use of hydroxychloroquine sulfate has been authorized by the Secretary of HHS
  - Administration of hydroxychloroquine may be accepted or refused by the patient
  - Drug specific information:
    - Potential consequences of refusing hydroxychloroquine sulfate
    - Significant known and potential risks and benefits of hydroxychloroquine
    - Alternative products available and benefits/risks, including clinical trials

Mandatory Requirements for Hydroxychloroquine Sulfate Administration under Emergency Use Authorization[1]

- **ALL CRITERIA MUST BE MET**
  - Adults and adolescents who weigh ≥50kg AND are hospitalized for COVID-19 whom a clinical trial is NOT available or participation is not feasible
  - Healthcare providers must communicate information consistent with the Fact Sheet prior to the patient receiving hydroxychloroquine
    - Requires documentation in patient's medical record
  - For Provider and/or provider's designee:
    - Provide responses to requests from the FDA for information about adverse events and medical errors
    - Report medical errors and adverse events **within 7 calendar days from the onset of the event via FDA MedWatch**
    - Submit patient outcomes report online- **Mandatory Patient Outcome Reporting Survey – EUA for Chloroquine Phosphate and Hydroxychloroquine Sulfate**

Information on Approved Available Treatments[1]

- NO approved alternative products available
- Similar EUA for chloroquine phosphate has been issued
- Additional Information: CDC and ClinicalTrials.gov

References:

1. Fact Sheet for Healthcare Providers: Emergency Use Authorization of Hydroxychloroquine Sulfate Supplied from the Strategic National Stockpile for Treatment of COVID-19 in Certain Hospitalized Patients. Food and Drug Administration (FDA). 2020. https://www.fda.gov/media/136537/download
2. Hydroxychloroquine. Lexi-Drugs. Lexi-Comp. Drug Monograph. 2020 Wolters Kluwer Clinical Drug Information. https://online.lexi.com/lco/action/doc/retrieve/docid/patch_f/7057?cesid=0Ct52lnp6Mc&searchUrl=%2Flco%2Faction%2Fsearch%3Fq%3Dhydroxychloroquine%26t%3Dname%26va%3Dhydroxychloroquine

Hydroxychloroquine Drug Interactions[2]

DRUGS	EFFECT OF CONCOMITANT USE WITH HYDROXYCHLOROQUINE	MANAGEMENT
Anti-Malarial Agents: Artemether, Lumefantrine, Mefloquine	Enhances toxic effects	AVOID concurrent use of other anti-malarial agents
Dapsone	Increases risk of hemolytic reactions Higher Risk: pts with G6PD deficiency, methemoglobin reductase deficiency, or Hgb M	Monitor for signs and symptoms of hemolytic reactions May consider dc therapy in higher risk patients
Androgens: Fluoxymesterone, Mesterolone,, Methyltestosterone, Oxandrolone, Oxymetholone, Testosterone ***EXCEPTION: Danazol***	May enhance hypoglycemic effects	Monitor for hypoglycemia and/or decreased requirements of antidiabetic agents
Antidiabetic Agents	May enhance hypoglycemic effects	Monitor for hypoglycemia
Anti-Psychotics (Phenothiazines): Chlorpromazine, Fluphenazine, Methotrimeprazine, Periciazine, Perphenazine, Prochlorperazine, Promazine, Thioridazine, Trifluoperazine	May increase the serum concentration of anti-psychotic agents	Monitor for toxic effects of phenothiazine anti-psychotics upon initiation or dose increase in HCQ Monitor for decreased effects if dose reduction or discontinuation of HCQ
Haloperidol **Greater significance with IV**	Enhances QT prolonging effect	Monitor for QT prolongation and ventricular arrhythmias Pts with risk factors are at greater risk
Beta Blockers ***EXCEPTIONS: Atenolol, Carteolol (ophthalmic), Levobunolol, Nadolol, Sotalol***	May decrease metabolism of beta blockers via CYP2D6	Monitor for increased effects of beta blocker upon initiation or dose increase in HCQ Monitor for decrease effects if dose reduction or discontinuation of HCQ
Digoxin	May increase serum concentrations of digoxin	Monitor for increased serum concentrations/toxic effects of digoxin upon initiation or dose increase in HCQ Monitor for decreased serum concentrations/effects if dose reduction or discontinuation of HCQ
SSRIs: Citalopram, Escitalopram, Fluoxetine, Paroxetine, Sertraline, Fluvoxamine, Vortioxetine, Dapoxetine	Enhance hypoglycemic effect Escitalopram and Citalopram: enhance QT prolonging effects	Monitor for hypoglycemia and QT prolongation May consider dosage adjustments of BG-lowering agent upon SSRI initiation or discontinuation
MAOIs: Isocarboxazid, Linezolid, Phenylzine, Rasigiline, Safinamide, Selegiline, Tranylcypromine, Methylene Blue	May enhance hypoglycemic effects	Monitor for hypoglycemia
Fluoroquinolones	May enhance hypoglycemic effects	Monitor for hypo- or hyperglycemia during concomitant Highest Risk of Hypoglycemia: first few days of abx therapy Highest Risk of Hyperglycemia: after several days of abx therapy
Salicylates: Aspirin, Aminosalicylic acid, Bismuth salicylate, Sodium salicylate	May enhance hypoglycemic effects	Monitor for hypoglycemia Concern for pts receiving ≥3 grams/day (salicylates) – may consider dose reduction
Tamoxifen	May increase risk of retinal toxicity	Concomitant use with drugs known to induce retinal toxicity are not recommended
QT Prolonging Agents: Azithromycin, Amiodarone, Chlorpromazine, Cisapride, Disopyramide, Dronedarone, Methadone, Procainamide, Qunidine, Quinine, Sotalol, Ziprasidone	Enhance QT prolonging effect	Monitor for QT prolongation and ventricular arrhythmias including torsades de pointes Increased Risk: older age, female sex, bradycardia, hypokalemia, hypomagnesemia, heart disease, higher drug concentrations
Mucomyst (Acetylcysteine)	No drug interaction	
Inhalants: Albuterol, Ipratropium, Ipratropium-Albuterol, Ipratropium-Fenoterol, Tiotropium, Budesonide, Budesonide-Formeterol	No drug interaction	

References:

1. Fact Sheet for Healthcare Providers: Emergency Use Authorization of Hydroxychloroquine Sulfate Supplied from the Strategic National Stockpile for Treatment of COVID-19 in Certain Hospitalized Patients. Food and Drug Administration (FDA). 2020. https://www.fda.gov/media/136537/download
2. Hydroxychloroquine. Lexi-Drugs. Lexi-Comp. Drug Monograph. 2020 Wolters Kluwer Clinical Drug Information. https://online.lexi.com/lco/action/doc/retrieve/docid/patch_f/7057?cesid=0Ct52lnp6Mc&searchUrl=%2Flco%2Faction%2Fsearch%3Fq%3Dhydroxychloroquine%26t%3Dname%26va%3Dhydroxychloroquine