

Alert - June 15, 2020: Based on FDA’s continued review of the scientific evidence available for hydroxychloroquine sulfate (HCQ) and chloroquine phosphate (CQ) to treat COVID-19, FDA has determined that the statutory criteria for EUA as outlined in Section 564(c)(2) of the Food, Drug, and Cosmetic Act are no longer met. Specifically, FDA has determined that CQ and HCQ are unlikely to be effective in treating COVID-19 for the authorized uses in the EUA. Additionally, in light of ongoing [serious cardiac adverse events](#) and other serious side effects, the known and potential benefits of CQ and HCQ no longer outweigh the known and potential risks for the authorized use. This warrants [revocation of the EUA](#) for HCQ and CQ for the treatment of COVID-19

**FACT SHEET FOR HEALTH CARE PROVIDERS
EMERGENCY USE AUTHORIZATION (EUA) OF CHLOROQUINE PHOSPHATE
SUPPLIED FROM THE STRATEGIC NATIONAL STOCKPILE FOR TREATMENT OF
COVID-19 IN CERTAIN HOSPITALIZED PATIENTS**

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of chloroquine phosphate supplied from the Strategic National Stockpile to treat adults and adolescents who weigh 50 kg or more and are hospitalized with COVID-19 for whom a clinical trial is not available, or participation is not feasible.

Revoked

This EUA is for the unapproved use of chloroquine phosphate supplied from the Strategic National Stockpile to treat adults and adolescents who weigh 50 kg or more and are hospitalized with COVID-19 for whom a clinical trial is not available, or participation is not feasible.

Chloroquine phosphate must be administered orally

To request chloroquine phosphate under Emergency Use Authorization (EUA):
Contact your Local or State Health Department

Health care providers must submit a report on all medication errors, **ALL SERIOUS ADVERSE EVENTS**, and **CLINICAL OUTCOMES** related to chloroquine phosphate. See specific reporting instructions below.

The optimal dosing and duration of treatment for COVID-19 is unknown.

The suggested dose under this EUA for chloroquine phosphate to treat adults and adolescents who weigh 50 kg or more and are hospitalized with COVID-19 for whom a clinical trial is not available, or participation is not feasible, is 1 gram of chloroquine phosphate on day one, followed by 500 milligrams daily for four to seven days of total treatment based on clinical evaluation.

The suggested dose and duration may be updated as data from clinical trials becomes available.

For information on clinical trials that are testing the use of chloroquine phosphate in COVID-19, please see www.clinicaltrials.gov.

INSTRUCTIONS FOR ADMINISTRATION

This section provides essential information on the unapproved use of chloroquine phosphate under this EUA in adults and adolescents who weigh 50 kg or more and are hospitalized with COVID-19 for whom a clinical trial is not available, or participation is not feasible.

Please refer to this fact sheet for information on use of chloroquine phosphate under the EUA. Indication for COVID-19 is not part of the FDA-approved labeling but chloroquine phosphate information for other FDA-approved indications, including pharmacokinetics and safety profile, may be found in an FDA-approved package insert for chloroquine phosphate at <https://dailymed.nlm.nih.gov/dailymed/>.

The chloroquine phosphate product from the SNS may contain a package insert that is not the FDA approved labeling. Please refer to this fact sheet for information on use of chloroquine phosphate under the EUA and the above link for FDA approved labeling for additional information.

Contraindications

Chloroquine phosphate is contraindicated in the presence of retinal or visual field changes of any etiology and in patients with known hypersensitivity to 4-aminoquinoline compounds. Chloroquine phosphate should not be used in patients with a prolonged QT interval at baseline or at increased risk for arrhythmia. Health care providers should carefully review **Warnings** and **Drug Interactions** below before prescribing Chloroquine phosphate.

Dosing

The optimal dosing and duration of treatment for COVID-19 is unknown.

The suggested dose under this EUA for chloroquine phosphate to treat adults and adolescents who weigh 50 kg or more and are hospitalized with COVID-19, for whom a clinical trial is not available, or participation is not feasible, is 1 gram of chloroquine phosphate on day one, followed by 500 milligrams daily for four to seven days of total treatment based on clinical evaluation.¹

The suggested dose and duration may be updated as data from clinical trials becomes available.

¹ The dosage of chloroquine phosphate is often expressed in terms of equivalent chloroquine base. Each 250 milligram tablet of chloroquine phosphate is equivalent to 150 milligram base and each 500 milligram tablet of chloroquine phosphate is equivalent to 300 milligram base. The dosing suggested in the Fact Sheet is for chloroquine phosphate.

Recommended Laboratory and Monitoring Procedures

A baseline electrocardiogram should be obtained to assess for QT interval prolongation and other abnormalities. Baseline evaluation of renal and hepatic function is recommended.

Warnings

Cardiac Effects: QT interval prolongation. Use with caution in patients with cardiac disease, QT prolongation, a history of ventricular arrhythmias, bradycardia, uncorrected potassium or magnesium imbalance, and during concomitant administration with QT interval prolonging drugs such as azithromycin and some other antibacterial drugs. Monitor the electrocardiogram during treatment.

Myocarditis, pericarditis, and cardiomyopathy may increase risk for arrhythmia. Monitor for cardiac injury.

Severe hypoglycemia: Chloroquine phosphate has been reported to decrease insulin clearance and resistance. Loss of consciousness in patients with or without the use of antidiabetic medications has been reported.

Hematologic effects: Hemolysis in G6PD deficient patients, pancytopenia, aplastic anemia and neutropenia have been reported.

Hepatic impairment: Since chloroquine phosphate is known to concentrate in the liver, it should be used with caution in patients with hepatitis, other hepatic disease, alcoholism or in conjunction with known hepatotoxic drugs.

Renal impairment: Chloroquine phosphate is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function.²

Central nervous system effects: chloroquine phosphate may increase the risk of convulsions in patients with a history of seizures. Acute extrapyramidal disorders may occur with chloroquine phosphate. Psychosis, delirium, agitation, confusion, suicidal behavior, and hallucinations may occur with chloroquine phosphate.

Worsening of psoriasis and porphyria: Use of chloroquine phosphate in patients with psoriasis may precipitate a severe attack of psoriasis. When used in patients with porphyria, the condition may be exacerbated. Chloroquine phosphate should not be used in these conditions unless the benefit to the patient outweighs the potential risks.

Retinopathy: Retinal damage has been observed in some patients receiving long-term treatment with chloroquine phosphate.

Drug Interactions

² Some experts recommend a dose reduction of 50% for GFR < 10 mL/minute, hemodialysis, or peritoneal dialysis; no dose reduction is recommended if GFR ≥ 10 mL/minute.

Digoxin: Concomitant chloroquine phosphate and digoxin therapy may result in increased serum digoxin levels. Serum digoxin levels should be closely monitored in patients receiving both drugs.

Antacids and kaolin: Antacids and kaolin can reduce absorption of chloroquine phosphate; an interval of at least 4 hours between intake of these agents and chloroquine phosphate should be observed.

Cimetidine: Cimetidine can inhibit the metabolism of chloroquine phosphate, increasing its plasma level. Concomitant use of cimetidine should be avoided.

Insulin and other antidiabetic drugs: As chloroquine phosphate may enhance the effects of a hypoglycemic treatment, a decrease in doses of insulin or other antidiabetic drugs may be required.

Arrhythmogenic drugs: There may be an increased risk of inducing ventricular arrhythmias if chloroquine phosphate is used concomitantly with other arrhythmogenic drugs, such as amiodarone, azithromycin or moxifloxacin.

Ampicillin: In a study of healthy volunteers, chloroquine phosphate significantly reduced the bioavailability of ampicillin. An interval of at least two hours between intake of ampicillin and chloroquine phosphate should be observed.

Cyclosporine: After introduction of chloroquine phosphate, a sudden increase in serum cyclosporine level has been reported. Therefore, close monitoring of serum cyclosporine level is recommended and, if necessary, chloroquine phosphate should be discontinued.

Mefloquine: Co-administration of chloroquine phosphate and mefloquine may increase the risk of convulsions.

Praziquantel: In a single-dose interaction study, chloroquine phosphate has been reported to reduce the bioavailability of praziquantel.

Tamoxifen: Concomitant use of chloroquine phosphate with drugs known to induce retinal toxicity such as tamoxifen is not recommended.

Antiepileptics: The activity of antiepileptic drugs might be impaired if co-administered with chloroquine phosphate.

Usage in Pregnancy

In animal studies, embryo-fetal developmental toxicity was shown at doses approximately 3 to 16 times the maximum recommended therapeutic dose based on a body surface area comparison. Preclinical data showed a potential risk of genotoxicity in some test systems. In humans, at recommended doses for prophylaxis and treatment of malaria, observational studies as well as a meta-analysis, including a small number of prospective studies with chloroquine phosphate exposure during pregnancy, have shown no increase in the rate of birth defects or spontaneous abortions.

The individual benefit-risk balance should be reviewed before prescribing chloroquine phosphate in pregnant women.

INSTRUCTIONS FOR HEALTH CARE PROVIDERS

As the health care provider administering chloroquine phosphate, you should, prior to prescribing/dispensing in accordance with applicable state and local law, provide your patients with the Fact Sheet for Patients and the pamphlet titled “Emergency Use Authorization (EUA) of Chloroquine Phosphate - Fact Sheet for Patients and Parent/Caregivers” and communicate the following information to the patient:

1. That the Secretary of HHS has authorized emergency use of chloroquine phosphate, some of which is supplied in packages containing blister packs of 10 pills with prescribing information that is not FDA-approved labeling for chloroquine phosphate
2. That the patient has the option to accept or refuse administration of chloroquine phosphate
3. The potential consequences of refusing chloroquine phosphate
4. The significant known and potential risks and benefits of chloroquine phosphate, as supplied under this EUA
5. The alternative products that are available and their benefits and risks, including clinical trials

If providing this information will delay the administration of chloroquine phosphate to a degree that would endanger the lives of patients, the information must be provided to the patients as soon as practicable after chloroquine phosphate is administered.

If the drug is dispensed separate from the blister pack for inpatient use, the dispensing container should clearly identify the drug and dosage strength.

MANDATORY REQUIREMENTS FOR CHLOROQUINE PHOSPHATE ADMINISTRATION UNDER EUA

In order to mitigate the risks of using this product for an unapproved use under EUA and to optimize the potential benefit of chloroquine phosphate, the following items are required. Use of chloroquine phosphate under this EUA is limited to the following (all requirements **must** be met):

1. Adults and adolescents who weigh 50 kg or more and are hospitalized with COVID-19 for whom a clinical trial is not available, or participation is not feasible.
2. As the health care provider, communicate to your patient or parent/caregiver information consistent with the “Fact Sheet for Patients and Parents/Caregivers” prior to the patient receiving chloroquine phosphate. Health care providers (to the extent practicable given the circumstances of the emergency) must document in the patient’s medical record that the patient/caregiver has been:
 - a. Given the Fact Sheet for Patients and Parents/Caregivers,
 - b. Informed of alternatives to receiving authorized chloroquine phosphate, and
 - c. Informed that chloroquine phosphate is an unapproved drug that is authorized for the unapproved use under this Emergency Use Authorization.

3. The prescribing health care provider and/or the provider's designee are/is to provide responses to requests from FDA for information about adverse events and medication errors following receipt of chloroquine phosphate.
4. The prescribing health care provider and/or the provider's designee are/is responsible for reporting medication errors and adverse events (death, serious adverse events*) occurring during chloroquine phosphate treatment within 7 calendar days from the onset of the event. The reports should include unique identifiers and the words "**Chloroquine phosphate treatment under Emergency Use Authorization (EUA)**" in the description section of the report.
 - Submit adverse event reports to FDA MedWatch using one of the following methods:
 - Complete and submit the report online: www.fda.gov/medwatch/report.htm, or
 - By using a postage-paid Form FDA 3500 (available at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf>) and returning by mail (MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787), or by fax (1-800-FDA-0178), or
 - Call 1-800-FDA-1088 to request a reporting form
 - Submitted reports should include in the field name, "Describe Event, Problem, or Product Use/Medication Error" a statement "**Chloroquine phosphate treatment under EUA.**"

*Serious Adverse Events are defined as:

- death;
- a life-threatening adverse event;
- inpatient hospitalization or prolongation of existing hospitalization;
- a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- a congenital anomaly/birth defect;
- a medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly.

5. The prescribing health care provider and/or the provider's designee are/is responsible for submitting patient outcomes reports:
 - Complete and submit the report online: **Mandatory Patient Outcome Reporting Survey - EUA for Chloroquine Phosphate and Hydroxychloroquine Sulfate** <https://euachloroquine-hydroxychloroquine-outcome.ppd.com/>.

APPROVED AVAILABLE ALTERNATIVES

There are no approved available alternative products. There is an EUA for treatment of the same population with hydroxychloroquine sulfate. Additional information on COVID-19 treatments can be found at <https://www.cdc.gov/coronavirus/2019-ncov/index.html>. The health care provider should visit <https://clinicaltrials.gov/> to determine whether

enrollment of the patient(s) in a clinical trial is more appropriate than product use under this EUA.

AUTHORITY FOR ISSUANCE OF THE EUA

The Secretary of the Department of Health and Human Services (HHS) has declared an emergency that justifies the emergency use of chloroquine phosphate supplied from the Strategic National Stockpile to treat adults and adolescents who weigh 50 kg or more and are hospitalized with COVID-19 for whom a clinical trial is not available, or participation is not feasible. In response, the Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) for the unapproved use of the FDA product chloroquine phosphate supplied from the Strategic National Stockpile for adults and adolescents who weigh 50 kg or more and are hospitalized with COVID-19 for whom a clinical trial is not available, or participation is not feasible. As a health care provider, you must comply with the mandatory requirements of the EUA listed above.

FDA issued this EUA, requested by Biomedical Advanced Research and Development Authority (BARDA).

Although limited scientific information is available, it is reasonable to believe that chloroquine phosphate may be effective for treatment of adults and adolescents who weigh 50 kg or more and are hospitalized with COVID-19 for whom a clinical trial is not available, or participation is not feasible as specified in this Fact Sheet. You may be contacted and asked to provide information to help with the assessment of the use of the product during this emergency. Serious adverse events related to the use of chloroquine phosphate must be reported to FDA through FDA's MEDWATCH Voluntary Online reporting www.fda.gov/medwatch/report.htm. Please include in the field name, "Describe Event, Problem, or Product Use/Medication Error" the following statement: **Chloroquine phosphate treatment under Emergency Use Authorization (EUA).**

This EUA for chloroquine phosphate will end when the Secretary determines that the circumstances justifying the EUA no longer exist or when there is a change in the approval status of the product such that an EUA is no longer needed.