Frequently Asked Questions on the Revocation of the Emergency Use Authorization for Hydroxychloroquine Sulfate and Chloroquine Phosphate

Q. Why was the Emergency Use Authorization (EUA) for hydroxychloroquine sulfate (HCQ) and chloroquine phosphate (CQ) revoked?

A. FDA has a responsibility to regularly review the appropriateness of an Emergency Use Authorization (EUA), including review of emerging scientific data associated with the emergency use of an authorized product. 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 conclusion warrants revocation of the EUA for HCQ and CQ for the treatment of COVID-19.

FDA's review of the available scientific evidence determined:

- The suggested dosing regimens for CQ and HCQ as detailed in the Fact Sheets are unlikely to produce an antiviral effect.
- Earlier reports of decreased viral shedding with HCQ or CQ treatment have not been consistently replicated and recent data from a randomized controlled trial assessing probability of negative conversion showed no difference between HCQ and standard of care alone.
- Current U.S. treatment guidelines do not recommend the use of HCQ or CQ in hospitalized patients with COVID-19 outside of a clinical trial, and the NIH guidelines now recommend against such use outside of a clinical trial.
- Recent data from a large randomized controlled trial showed no evidence of benefit of HCQ treatment in hospitalized patients with COVID-19 for mortality or other outcomes such as hospital length of stay or need for mechanical ventilation.

The decision to revoke this EUA was made in consultation with the Biomedical Advanced Research and Development Authority (BARDA) at the U.S. Department of Health and Human Services. BARDA had originally requested the EUA covering CQ and HCQ. FDA and BARDA are part of a USG-interagency effort to rapidly respond to this public health emergency and have been communicating as new scientific data emerged.

For more information, please see the Letter of Revocation.

Q. Will the revocation of the EUA impact the use of hydroxychloroquine sulfate (HCQ) or chloroquine phosphate (CQ) for their FDA-approved uses?

A. No, the revocation does not change the approvals of these drugs. Some versions of chloroquine phosphate (CQ) are approved for the treatment of malaria, and hydroxychloroquine sulfate (HCQ) is still approved for the treatment of malaria, lupus, and rheumatoid arthritis. FDA has determined that the drugs are safe and effective for these uses when used in accordance with their FDA-approved labeling, and patients prescribed these drugs for their approved uses should continue to take them as directed by their healthcare providers. There is no new information that impacts FDA's conclusions about the safety and efficacy of CQ or HCQ for their currently approved uses.

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If you are taking HCQ or CQ for their currently approved uses and are diagnosed with COVID-19, use of these drugs may decrease the effectiveness of other potential COVID-19 treatments, specifically, remdesivir. You should discuss options and specific situation with your health care provider.

Q. What if I am in the middle of treatment with hydroxychloroquine sulfate (HCQ) or chloroquine phosphate (CQ) for COVID-19 under the EUA? Can my treatment continue to completion?
A. As required by section 564(f)(2) of the Federal Food, Drug & Cosmetic Act, the chloroquine phosphate (CQ) and hydroxychloroquine sulfate (HCQ) authorized under the EUA remain authorized for continued emergency use to finish the treatment course of any hospitalized patient to whom the authorized CQ or HCQ was administered, to the extent found necessary by the patient's attending physician.

However, based on emerging and other scientific data, FDA does not recommend using HCQ or CQ to treat hospitalized patients with COVID-19 outside of a clinical trial. FDA revoked the EUA for CQ and HCQ after determining that it is unlikely that CQ and HCQ may be effective in treating COVID-19. In light of this determination, combined with ongoing reports of serious cardiac adverse events and other serious side effects, the agency also determined that the known and potential benefits of CQ and HCQ do not outweigh the known and potential risks for its authorized uses.

Q. Was the EUA for hydroxychloroquine sulfate (HCQ) and chloroquine phosphate (CQ) revoked due to a safety issue?
A. Based on emerging and other scientific data, FDA revoked the Emergency Use Authorization (EUA) for chloroquine phosphate (CQ) and hydroxychloroquine sulfate (HCQ) after determining that it is unlikely that CQ and HCQ may be effective in treating COVID-19. In light of this determination, combined with ongoing reports of serious cardiac adverse events and other serious side effects, the agency also determined that the known and potential benefits of CQ and HCQ do not outweigh the known and potential risks for its authorized uses.

Q. Should I be concerned if I was given hydroxychloroquine sulfate or chloroquine phosphate for COVID-19?
A. FDA is unaware of any residual side effects for patients who have received and completed their course of chloroquine phosphate (CQ) or hydroxychloroquine sulfate (HCQ) to treat COVID-19, as was authorized under the EUA. Please speak with your healthcare provider if you have any concerns about your treatment with these drugs for COVID-19.

Q. Can hospitals finish their current supplies of hydroxychloroquine sulfate (HCQ) and chloroquine phosphate (CQ)?
A. As required by section 564(f)(2) of the Federal Food, Drug & Cosmetic Act, hydroxychloroquine sulfate (HCQ) and chloroquine phosphate (CQ) that were distributed from the SNS under this EUA remain authorized for emergency use to continue to treat any hospitalized patient to whom the authorized product has already been administered during the COVID-19 public health emergency, to the extent found necessary by the patient's attending physician.

While HCQ that has been distributed from SNS is no longer authorized under the EUA to treat hospitalized patients for COVID-19 unless they had already started treatments, FDA-approved HCQ can be distributed in interstate commerce. Please refer to ASPR any questions regarding the return or further distribution of HCQ that was distributed under the EUA.

The CQ products covered by the EUA are not approved by FDA for any indication and therefore cannot be legally introduced into interstate commerce. It is our understanding that the CQ products covered by the EUA were not distributed by the SNS and will thus not be in the hands of health care facilities.

Q. Why did FDA grant the EUA for hydroxychloroquine sulfate (HCQ) and chloroquine phosphate (CQ) for the treatment of COVID-19 initially?
A. On March 28, 2020, BARDA requested and FDA issued an Emergency Use Authorization (EUA) for emergency use of oral formulations of chloroquine phosphate (CQ) and hydroxychloroquine sulfate (HCQ) for the treatment of COVID-19. Based on the scientific information available to FDA as of that date, the Agency determined that CQ and HCQ may be effective in treating COVID-19 and that the known and potential benefits of CQ and HCQ outweighed the known and potential risks for this use. The agency limited the use of authorized products to adults and adolescents who weigh 50 kg (approximately 110 pounds) or more, who were hospitalized with COVID-19, and for whom participation in a clinical trial was not available, or participation was not feasible.

Q. Did the agency wait for BARDA to request revocation of the EUA?
A. FDA has been continuously reviewing emerging data and published literature related to the authorized use of these products and has determined, at this time, that the products no longer meet the statutory criteria for issuance of an EUA. FDA and BARDA agreed that the scientific evidence supports revocation of the EUA. FDA and BARDA are part of a USG-interagency effort to rapidly respond to this public health emergency and have been communicating as new scientific data emerged. That the BARDA request for revocation and the FDA revocation issued on the same day illustrates the agreement between the two agencies on this issue.

Q. Did the new information about a potential drug interaction between remdesivir and hydroxychloroquine sulfate (HCQ) and chloroquine phosphate (CQ) contribute to the revocation of the EUA?
A. FDA's action to revoke the EUA authorizing the use of hydroxychloroquine sulfate (HCQ) and chloroquine phosphate (CQ) to treat certain hospitalized patients with COVID-19 was taken based on FDA's ongoing assessment of available scientific information associated with the authorized emergency use of these products. Revocation of an EUA may occur when the statutory criteria for authorization are no longer met. The potential drug interaction between remdesivir and HCQ/CQ is not the basis for the revocation of the EUA.

Q. Will clinical trials studying hydroxychloroquine sulfate and chloroquine phosphate for the treatment and prevention of COVID-19 continue?
A. Yes. Clinical trials are underway to determine if these drugs can benefit patients with COVID-19 or prevent infection after an exposure. Clinical trials are an important way for the FDA to gather data and make decisions about drugs for the treatment of COVID-19.

Q. What impact did FDA's revocation of the EUA covering chloroquine phosphate (CQ) and hydroxychloroquine sulfate (HCQ) have on ongoing clinical trials for the treatment or prevention of COVID-19 for these drug products?
A. On March 28, 2020, based on the totality of the scientific evidence available at the time, the FDA issued an Emergency Use Authorization (EUA) for emergency use of oral formulations of chloroquine phosphate (CQ) and hydroxychloroquine sulfate (HCQ) for the treatment of 2019 coronavirus disease (COVID-19). The authorization limited the use of the authorized products to adults and adolescents who

weighed 50 kg or more and were hospitalized with COVID-19 in instances in which participation in a clinical trial was not available, or participation was not feasible.

The initial authorization allowing the emergency use of these products identified the agency's preference toward the use of CQ and HCQ for patients with COVID-19 as part of a clinical trial, as clinical trials are designed to provide robust evidence regarding the efficacy and safety of a drug. Recognizing that there may be instances in which access to a clinical trial is not available, or participation of an individual is not feasible, the EUA specifically made available the emergency use of these drugs to those patients with COVID-19 in a hospitalized setting who weighed greater than 50 kg.

As part of the agency's ongoing review of the appropriateness of the EUA, FDA determined, based on the clinical and non-clinical scientific evidence available, that the criteria for issuance of an emergency authorization were no longer met and revoked the EUA covering CQ and HCQ. FDA's decision to revoke the EUA only impacted the availability of CQ and HCQ for its previously authorized emergency uses. The agency recognizes that clinical trials evaluating CQ and HCQ for the treatment or prevention of COVID-19 in various settings and patient populations are ongoing.

As new information is reported from clinical trials and other studies regarding new therapeutics for COVID-19, FDA reminds investigators and Institutional Review Boards (IRBs) of their responsibility to conduct continuing review of research studies under applicable FDA regulations. In doing so, the IRB must determine that the criteria for IRB approval of research under FDA regulations continue to be met. FDA strongly encourages investigators and sponsors to provide IRBs with meaningful information from other studies, particularly when doing so may assist IRBs in their continuing review of ongoing studies and ensuring the protection of human subjects.