EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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COVID-19: reminder of risk of serious side effects with chloroquine and hydroxychloroquine

Chloroquine and hydroxychloroquine are known to potentially cause heart rhythm problems, and these could be exacerbated if treatment is combined with other medicines, such as the antibiotic azithromycin, that have similar effects on the heart.

Recent studies[2,3] have reported serious, in some cases fatal, heart rhythm problems with chloroquine or hydroxychloroquine, particularly when taken at high doses or in combination with the antibiotic azithromycin.

Chloroquine and hydroxychloroquine are currently authorised for treating malaria and certain autoimmune diseases. In addition to side effects affecting the heart, they are known to potentially cause liver and kidney problems, nerve cell damage that can lead to seizures (fits) and low blood sugar (hypoglycaemia).

These medicines are being used in the context of the ongoing pandemic for treating patients with COVID-19 and investigated in clinical trials. However, clinical data are still very limited and inconclusive, and the beneficial effects of these medicines in COVID-19 have not been demonstrated. Results from large, well-designed studies are needed to make any conclusions.

Some clinical trials currently investigating the effectiveness of chloroquine or hydroxychloroquine in treating COVID-19 use higher doses than those recommended for the authorised indications. While serious side effects can occur with recommended doses, higher doses can increase the risk of these side effects, including abnormal electrical activity that affects the heart rhythm (QT-prolongation).

Healthcare professionals are recommended to closely monitor patients with COVID-19 receiving chloroquine or hydroxychloroquine and to take into account pre-existing heart problems that can make patients more prone to heart rhythm issues. They should carefully consider the possibility of side effects, particularly with higher doses, and exercise extra caution when combining treatment with other medicines such as azithromycin that may cause similar side effects on the heart.

[1] The text was updated on 23 April 2020 to correct the scope of the cited studies
[2] Mayla Gabriela Silva Borba, Fernando Fonseca Almeida Val, Vanderson Sousa Sampaio et al. Chloroquine diphosphate in two different dosages as adjunctive therapy of hospitalized patients with severe respiratory syndrome in the context of coronavirus (SARS-CoV-2) infection: Preliminary safety results of a randomized, double-blinded, phase IIb clinical trial (CloroCovid-19 Study). medRxiv doi: 10.1101/2020.04.07.20056424
[3] Lane J.C.E., Weaver J., Kosta K. et al. Safety of hydroxychloroquine, alone and in combination with azithromycin, in light of rapid wide-spread use for COVID-19: a multinational, network cohort and self-controlled case series study. medRxiv doi: 10.1101/2020.04.08.20054551

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Patients and healthcare professionals are reminded to report any suspected side effects to their national regulatory authorities.

A number of large, randomised clinical trials are looking at the benefits and risks of chloroquine and hydroxychloroquine in patients with COVID-19. In the context of COVID-19, these medicines should only be used as part of clinical trials or in line with nationally agreed protocols. They must not be used without a prescription and without supervision by a doctor.

EMA and the national competent authorities are monitoring the situation closely and have enhanced their safety monitoring of medicines used in the treatment of COVID-19 in order to take timely action when necessary.

This EMA public health statement has been issued by the COVID-19 EMA pandemic Task Force (COVID-ETF) in consultation with EMA's safety Committee (PRAC), in light of the ongoing discussions on the use of chloroquine and hydroxychloroquine in the treatment of COVID-19.

EMA is committed to providing available information to help healthcare professionals and their patients make informed decisions while awaiting clinical trial data on whether the medicines have a positive benefit-risk balance in the treatment of COVID-19.