

Annex I

**Scientific conclusions and grounds for the variation to the terms of the Marketing
Authorisation(s)**

Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for chloroquine, the scientific conclusions are as follows:

In view of available data on the recent literature publication of Lane et al 2020, showing an increased cardiovascular mortality following the concomitant use of hydroxychloroquine and the macrolide antibiotic azithromycin, as well as the already well established risk for QT-prolongation and subsequent risk for ventricular arrhythmia, with both chloroquine and macrolides, the PRAC considers a causal relationship between the concomitant use of chloroquine and macrolides including azithromycin, and an increased risk of ventricular arrhythmia. The PRAC concluded that the product information of products containing chloroquine should be amended accordingly.

The CMDh agrees with the scientific conclusions made by the PRAC.

Grounds for the variation to the terms of the Marketing Authorisation(s)

On the basis of the scientific conclusions for chloroquine the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing chloroquine is unchanged subject to the proposed changes to the product information.

The CMDh reaches the position that the marketing authorisation(s) of products in the scope of this single PSUR assessment should be varied. To the extent that additional medicinal products containing chloroquine are currently authorised in the EU or are subject to future authorisation procedures in the EU, the CMDh recommends that the concerned Member States and applicant/marketing authorisation holders take due consideration of this CMDh position.

Annex II

Amendments to the product information of the nationally authorised medicinal product(s)

Amendments to be included in the relevant sections of the Product Information (new text underlined and in bold, deleted text ~~strike through~~)

Summary of Product Characteristics

- Section 4.5

The interactions/s should be added as follows:

[...] Chloroquine should be used with caution in patients receiving drugs known to prolong the QT interval e.g. Class IA and III antiarrhythmics, tricyclic antidepressants, antipsychotics, some anti-infectives **(e.g. macrolides including azithromycin)** due to increased risk of ventricular arrhythmia (see sections 4.4 and 4.9). Halofantrine should not be administered with chloroquine.

Package Leaflet

- Section 2

Tell your doctor if you take any of these medicines

[...] Against bacterial infections **(e.g. a group of medicines called macrolides including azithromycin)** [...]

Annex III

Timetable for the implementation of this position

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Adoption of CMDh position:	December 2021 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	31 January 2022
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	30 March 2022