

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 azithromycin (systemic use formulations), the scientific conclusions are as follows:

In view of the increasing understanding on drug-drug interactions, and more specifically available data from the literature and spontaneous reports, on interaction between azithromycin (systemic use formulations) and colchicine leading to possible increase of colchicine serum level, the PRAC considers that colchicine should be added as example of P-glycoprotein substrates in the existing warning of their possible increased serum levels in case of co-administration with azithromycin.

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 azithromycin (systemic use formulations) the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing azithromycin (systemic use formulations) 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 azithromycin (systemic use formulations) 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 Interaction with other medicinal products and other forms of interaction

[A warning should be revised as follows]

Digoxin **and colchicine**: concomitant administration of macrolide antibiotics, including azithromycin, with P-glycoprotein substrates such as digoxin **and colchicine**, has been reported to result in increased serum levels of the P-glycoprotein substrate. Therefore, if azithromycin and P-glycoprotein substrates such as digoxin are administered concomitantly, the possibility of elevated serum digoxin concentrations should be considered. Clinical monitoring, and possibly serum digoxin levels, during treatment with azithromycin and after its discontinuation are necessary.

Package Leaflet

- Section 2. What you need to know before you take <invented name>

[A warning should be revised as follows]

Other medicines and <invented name>

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines:

[...]

- Digoxin (used for treatment of cardiac impairment)

- Colchicine (used for gout and familial Mediterranean fever)

Annex III

Timetable for the implementation of this position

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Adoption of CMDh position:	January 2018 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	10 March 2018
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	9 May 2018