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 praziquantel, the scientific conclusions are as follows:

A publication[1] (Mutiti CS et al, 2021) regarding a non-randomized, open-label, single-dose, one sequence crossover study with 2 arms to evaluate the risk of drug-drug interactions (DDI) which may occur when praziquantel is administered to HIV patients on antiretroviral therapy containing efavirenz or ritonavir, demonstrates that Efavirenz had a significant effect on the pharmacokinetics of praziquantel, reducing the AUC by 77%. The DDI with efavirenz appears clinically relevant as this inductive effect presents a significant risk of treatment failure because of sub therapeutic levels of praziquantel in patients on efavirenz containing regimens. Taking all of the above into account, the PRAC Rapporteur concluded that the product information of products containing praziquantel 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 praziquantel the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing praziquantel 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 praziquantel 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.

[1] Mutiti CS, Kapungu NN, Kanji CR, et al. Clinically relevant enantiomer specific R- and S-praziquantel pharmacokinetic drug-drug interactions with efavirenz and ritonavir. Pharmacol Res Perspect. 2021;9(3)

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 interaction should be added as follows:

Concomitant use with efavirenz is not recommended due to significant decrease in plasma concentrations of praziquantel, with risk of treatment failure due to increased hepatic metabolism by efavirenz. In case the combination is needed, an increased dose of praziquantel could be considered.

Package Leaflet

- Section 2

Other medicines and praziquantel

Tell your doctor or pharmacist if you are using:

- efavirenz (medicine to treat HIV infection)

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

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