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 quetiapine, the scientific conclusions are as follows:

In view of available data on **cardiomyopathy and myocarditis** from spontaneous reports including nine post-marketing cases with a plausible temporal relationship and positive de-challenge, as well as in view of a plausible mechanism of action, the PRAC considers that a causal relationship between quetiapine and cardiomyopathy as well as myocarditis is at least a reasonable possibility. The PRAC concluded that the product information of products containing quetiapine should be amended accordingly.

In view of available data on **cutaneous vasculitis** from two biopsy-confirmed literature cases with a strong temporal relationship including positive de-challenge and a third post-marketing spontaneous report with a plausible temporal relationship, the PRAC considers that a causal relationship between quetiapine and vasculitis is at least a reasonable possibility. The PRAC concluded that the product information of products containing quetiapine 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 quetiapine the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) quetiapine 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 quetiapine 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 4.4

A warning should be amended as follows:

Cardiomyopathy and myocarditis

Cardiomyopathy and myocarditis have been reported in clinical trials and during the post-marketing experience~~, however, a causal relationship to quetiapine has not been established~~ ***(see section 4.8).*** *~~Treatment with quetiapine should be~~ ~~reassessed in~~* ***In*** *patients with suspected cardiomyopathy or myocarditis* ***discontinuation of quetiapine should be considered****.*

- Section 4.8

The following adverse reactions should be added under the SOC Cardiac disorders with a frequency *not known:* ***cardiomyopathy*** *and* ***myocarditis***

The following adverse reaction should be added under the SOC Skin and subcutaneous tissue disorders with a frequency *not known:* ***Cutaneous vasculitis***

Package Leaflet

- Section 2. What you need to know before you take <product name>, Warnings and Precautions

The following bullet should be added under "Tell your doctor immediately if you experience any of the following after taking <product name>:"

- **have a fast and irregular heartbeat, even when you are at rest, palpitations, breathing problems, chest pain or unexplained tiredness. Your doctor will need to check your heart and if necessary, refer you to a cardiologist immediately.**

- Section 4. Possible side effects

The following adverse reactions should be added under frequency category: Not known (frequency cannot be estimated from the available data)

Disorder of the heart muscle (cardiomyopathy)

Inflammation of the heart muscle (myocarditis)

Inflammation of blood vessels (Vasculitis), often with skin rash with small red or purple bumps

Annex III

Timetable for the implementation of this position

Adoption of CMDh position:	March CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	9 May 2021
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	8 July 2021