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 candesartan, candesartan / hydrochlorothiazide, the scientific conclusions are as follows:

There have been reported fourteen cases of diarrhoea with positive de-challenge and four cases with positive rechallenge. There were also four cases with a reasonable temporal association between candesartan and diarrhoea. The event occurred in two cases at same time with angioedema, which may suggest angioedema in the intestine. Moreover, diarrhoea is labeled for the other Angiotensin II Receptor Blockers (ARBs) in the class. The number of cases in EudraVigilance candesartan (n=175) is roughly in the range as for other ARBs in the class. Therefore, the PRAC considers necessary to add the adverse drug reaction "diarrhoea" in section 4.8 of the summary of product characteristics (SmPC) under the SOC Gastrointestinal disorders with a frequency not known. The package leaflet (PL) should be updated 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 candesartan, candesartan / hydrochlorothiazide the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing candesartan, candesartan / hydrochlorothiazide 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 candesartan, candesartan / hydrochlorothiazide 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 4.8

The following adverse reaction should be added under the SOC Gastrointestinal disorders with a frequency not known: **Diarrhoea**

Package Leaflet

- Section 4, Possible side effects under header "Not known (frequency cannot be estimated from the available data)":

Diarrhoea

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	January 2018 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	9 March 2018
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	8 May 2018