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 manidipine, the scientific conclusions are as follows:

Based on cumulative data the PRAC considers that a causal relationship between the adverse drug reaction "myalgia" and manidipine cannot be excluded and recommends therefore that "myalgia" is added to section 4.8 of the SmPC with the frequency "not known".

In addition, based on cumulative data from spontaneous reporting as well as literature data, which is further supported by its mechanism of action, the PRAC considers that a causal relationship between manidipine and "gynaecomastia" is likely and therefore this adverse drug reaction should be added to section 4.8 of the SmPC with the frequency “not known”.

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 manidipine the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing manidipine 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 manidipine 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 reactions should be added under:

- the SOC "Musculoskeletal and connective tissue disorders"**: myalgia** with a frequency **not known**

- the SOC “Reproductive system and breast disorders”: **gynaecomastia** with a frequency **not known**.

Package Leaflet

Frequency not known:

Muscle pain

Breast swelling with or without tenderness in males (gynaecomastia)

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	27 February 2019 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	13 April 2019
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	12 June 2019

APPENDIX I

PRAC PSUR Assessment Report