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 milnacipran, the scientific conclusions are as follows:

Based on the review of literature data and post-marketing cases of Takotsubo cardiomyopathy associated with milnacipran, the plausible involvement of catecholamine pathway suggestive of the role of milnacipran in the occurrence of this adverse drug reaction and the fact that several other cases of Takotsubo cardiomyopathy have been reported with others Serotonin–norepinephrine reuptake inhibitors (SNRIs) (supporting a possible Serotonin–norepinephrine reuptake inhibitors class effect), the PRAC has requested an update of the product information of milnacipran medicinal products to add Takotsubo cardiomyopathy as an adverse drug reaction.

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 milnacipran the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing milnacipran 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 milnacipran are currently authorised in the EU or are subject to future authorisation procedures in the EU, the CMDh recommends that 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(s) should be added under the SOC Cardiac disorders with a frequency not known:

Takotsubo cardiomyopathy

Package Leaflet

The following adverse reaction should be added under section 4. Possible side effects with a frequency not known:

Takotsubo cardiomyopathy (Stress cardiomyopathy)

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	January 2019 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position :	16 March 2019
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	15 May 2019