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 dobutamine, the scientific conclusions are as follows:

In view of available data on stress cardiomyopathy (Takotsubo syndrome) from clinical trials, the literature, spontaneous reports, the PRAC considers a causal relationship between dobutamine and stress cardiomyopathy (Takotsubo syndrome) is at least a reasonable possibility. The PRAC concluded that the product information of products containing dobutamine 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 dobutamine the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing dobutamine 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 dobutamine 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 added as follows:

Special warnings and precautions for use

Stress cardiomyopathy (Takotsubo syndrome) is a possible severe complication of the use of dobutamine during stress echocardiography (see section 4.8). The administration of dobutamine for stress echocardiography should be only undertaken by a physician experienced with the procedure. The physician should be vigilant during the test and the recovery period and be prepared for appropriate therapeutic intervention during the test. In the event of stress cardiomyopathy (Takotsubo syndrome) dobutamine should be stopped immediately.

- Section 4.8

The following adverse reaction(s) should be added under the SOC Cardiac disorders with a frequency not known:

stress cardiomyopathy (Takotsubo syndrome) (see section 4.4)

Package Leaflet

- Section 4

Not known: frequency cannot be estimated from the available data

- Problems with your heart muscle (stress cardiomyopathy also known as Takotsubo syndrome) that present with chest pain, shortness of breath, dizziness, fainting, irregular heartbeat when dobutamine is used for stress echocardiography test

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	11 November 2021 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	3 January 2022
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	24 February 2022