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 amiodarone, the scientific conclusions are as follows:

In view of available data on Primary graft dysfunction post cardiac transplant from the literature, the PRAC considers a causal relationship between Amiodarone and primary graft dysfunction post cardiac transplant is at least a reasonable possibility. The PRAC concluded that the product information of products containing amiodarone should be amended accordingly.

Having reviewed the PRAC recommendation, the CMDh agrees with the PRAC overall conclusions and grounds for recommendation.

Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions for amiodarone the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing amiodarone is unchanged subject to the proposed changes to the product information

The CMDh recommends that the terms of the marketing authorisation(s) should be varied.

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:

Primary Graft Dysfunction post cardiac transplant

In retrospective studies, amiodarone use in the transplant recipient prior to heart transplant has been associated with an increased risk of primary graft dysfunction (PGD). PGD is a life-threatening complication of heart transplantation that presents as left, right or biventricular dysfunction occurring within the first 24 hours of transplant surgery for which there is no identifiable secondary cause (see Section 4.8). Severe PGD may be irreversible.
For patients who are on the heart transplant waiting list, consideration should be given to use an alternative antiarrhythmic drug as early as possible before transplant.

The following adverse reaction(s) should be added under the SOC Injury, poisoning and procedural complications with a frequency not known:

- Section 4.8

Primary graft dysfunction post cardiac transplant (see Section 4.4)

Package Leaflet

- Section 2

Warnings and precautions

Talk to your doctor, pharmacist or nurse before you are given this medicine:

If you are on a heart transplant waiting list, your doctor may change your treatment. This is because taking amiodarone before heart transplantation has shown an increased risk of a life-threatening complication (primary graft dysfunction) in which the transplanted heart stops working properly within the first 24 hours after surgery.

- Section 4

Frequency not known:

Life-threatening complication after heart transplantation (primary graft dysfunction) in which the transplanted heart stops working properly (see section 2, Warnings and precautions)

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	September 2024 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	4 November 2024
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	2 January 2025