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 nebivolol, the scientific conclusions are as follows:

In view of available data on risk of hypoglycaemia with concomitant use with sulfonylureas from the literature, in view of a plausible mechanism of action, and in line with the PRAC decision following the assessment of hydrochlorotiazide/ nebivolol PSUSA (PSUSA/00001658/202311) to include the safety information from Dimakos et al. in all nebivolol products, the PRAC considers a causal relationship between the increased risk of hypoglycaemia and the concomitant use of beta-blockers and sulfonylureas is at least a reasonable possibility. The PRAC concluded that the product information of products containing nebivolol should be amended accordingly taking into account the already existing wording in some nationally authorised products the text may need to be adapted by marketing authorisation holders to individual products.

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 nebivolol the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing nebivolol 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

The existing warning should be amended as follows:

Nebivolol

Metabolic/Endocrinological:

Nebivolol does not affect glucose levels in diabetic patients. Care should be taken in diabetic patients however, as nebivolol may mask certain symptoms of hypoglycaemia (tachycardia, palpitations*).* **Beta-blockers could further increase the risk of severe hypoglycaemia when used concurrently with sulfonylureas. Diabetic patients should be advised to carefully monitor blood glucose levels. (see Section 4.5).**

- Section 4.5

The existing information on the interaction with antidiabetics should be amended as follows:

Nebivolol

Insulin and oral antidiabetic drugs: although nebivolol does not affect glucose level, concomitant use may mask certain symptoms of hypoglycaemia (palpitations, tachycardia). **The concomitant use of beta-blockers with sulfonylureas could increase the risk of severe hypoglycaemia. (see Section 4.4).**

Package Leaflet

Warnings and precautions

Talk to your doctor before taking <Product>.

Inform your doctor if you have or develop one of the following conditions:

if you are diabetic, as nebivolol may hide the symptoms of low blood sugar (hypoglycaemia) **and could increase the risk of severe hypoglycaemia when used with certain type of antidiabetic drugs called sulfonylureas (e.g. gliquidone, gliclazide, glibenclamide, glipizide, glimepiride or tolbutamide)**

Other medicines and X

Tell your doctor or pharmacist if you are taking or recently used any of the following medicines with <Product>:

- **medicines for diabetes such as insulin or oral antidiabetics drugs**

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	12 December 2024 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	26 January 2025
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	27 March 2025