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 bisoprolol / hydrochlorothiazide, the scientific conclusions are as follows:

In view of the available data from the literature (Dimakos et al.) on the risk of hypoglycaemia with the concomitant use with sulfonylureas and in line with the PRAC decisions following the assessment of other β-blockers PSUSA (hydrochlorothiazide / nebivolol PSUSA (PSUSA/00001658/202311), nebivolol PSUSA (PSUSA/00002129/202403) and timolol (PSUSA/00010432/202410)), the PRAC considers that a causal relationship between the increased risk of hypoglycaemia and the concomitant use of β-blockers and sulfonylureas is at least a reasonable possibility. The PRAC concludes that the product information of products containing bisoprolol / hydrochlorothiazide should be amended accordingly. Taking into account the already existing wordings in some nationally authorised products, the text may need to be adapted by marketing authorisation holders to individual products. In some cases, relevant information may already appear in the PI (e.g. advice for patients to self-monitor blood glucose levels), whereas in others, it may be entirely missing (e.g. a detailed warning about the risk of hypoglycaemia in the package leaflet). MAHs are therefore expected to incorporate the following wording recommendations where appropriate.

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 bisoprolol / hydrochlorothiazide the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing bisoprolol / hydrochlorothiazide 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:

Bisoprolol

Diabetic patients

Diabetes mellitus with severely fluctuating blood sugar levels: symptoms of hypoglycaemia may be masked. **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:

Combinations to be used with caution

Insulin and oral anti-diabetic agents

Increased hypoglycemic effect. Blockade of beta-adrenoreceptors may mask signs of hypoglycaemia. **The concomitant use of beta-blockers with sulfonylureas could increase the risk of severe hypoglycaemia (see section 4.4).**

Package Leaflet

- Section 2

The existing information should be amended as follows:

Other medicines and {(Invented) name}

…

In particular, tell your doctor if you are taking any of the following:

…

- medication for diabetes including insulin and sulfonylureas (e.g. glibenclamide, gliquidone, gliclazide, glipizide, glimepiride or tolbutamide). **Bisoprolol could increase the risk of severely low blood glucose levels when used with these medicines.**

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	July 2025 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	7 September 2025
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	6 November 2025