

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 acetylsalicylic acid / bisoprolol, the scientific conclusions are as follows:

In view of available data on risk of hypoglycaemia with concomitant use with sulfonylureas from the literature and in view of a plausible mechanism of action, 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 acetylsalicylic acid / bisoprolol 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 acetylsalicylic acid / bisoprolol the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing acetylsalicylic acid / bisoprolol 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

Bisoprolol must be used with caution in:

- diabetes mellitus with large fluctuations in blood glucose values; symptoms of hypoglycaemia (e.g. tachycardia, palpitations or sweating) can 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:

Bisoprolol

Combinations to be used with caution

...

Insulin and oral antidiabetic drugs: increase of blood sugar lowering effect. Blockade of beta-adrenoreceptors may mask symptoms 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} capsules

...

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

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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