

## **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 ramipril / bisoprolol, the scientific conclusions are as follows:

In view of available data on the risk of severe hypoglycaemia with concomitant use of beta-blockers with sulfonylureas from the literature and in view of a plausible mechanism of action, the PRAC considers a causal relationship between the concomitant use of ramipril / bisoprolol and sulfonylureas, and the increased risk of severe hypoglycaemia is at least a reasonable possibility. The PRAC concluded that the product information of products containing ramipril / 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 ramipril / bisoprolol the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing ramipril / 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

A warning should be amended as follows:

#### Diabetic patients

- Caution is advised when <Invented Name> is used in patients with diabetes mellitus with large fluctuations in blood glucose values. Symptoms of hypoglycaemia can be masked by beta-blockers. **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

An interaction should be amended as follows:

#### Antidiabetic agents including insulin

[...]

Concomitant administration of bisoprolol with insulin and oral antidiabetic drugs may increase 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>

[...]

In particular, tell your doctor or pharmacist 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:                                                                                               | June 2026 CMDh meeting |
| Transmission to National Competent Authorities of the translations of the annexes to the position:                       | 10 August 2026         |
| Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder): | 9 October 2026         |