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 hydrocortisone (systemic formulations except for products indicated in adrenal insufficiency in a modified release tablet formulation and except for centrally authorised products for adrenal insufficiency, paediatric use only), the scientific conclusions are as follows:

In view of available data on thyrotoxic periodic paralysis from the literature, including in all cases a close temporal relationship, positive dechallenge and in view of a plausible mechanism of action, the PRAC considers a causal relationship between hydrocortisone (systemic formulations except for products indicated in adrenal insufficiency in a modified release tablet formulation and except for centrally authorised products for adrenal insufficiency, paediatric use only) and thyrotoxic periodic paralysis is at least a reasonable possibility. The PRAC concluded that the product information products containing hydrocortisone (systemic formulations except for products indicated in adrenal insufficiency in a modified release tablet formulation and except for centrally authorised products for adrenal insufficiency, paediatric use only) 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 hydrocortisone (systemic formulations except for products indicated in adrenal insufficiency in a modified release tablet formulation and except for centrally authorised products for adrenal insufficiency, paediatric use only) the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing hydrocortisone (systemic formulations except for products indicated in adrenal insufficiency in a modified release tablet formulation and except for centrally authorised products for adrenal insufficiency, paediatric use only) 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:

Thyrotoxic Periodic Paralysis (TPP) can occur in patients with hyperthyroidism and with hydrocortisone-induced hypokalaemia. TPP must be suspected in patients treated with hydrocortisone presenting signs or symptoms of muscle weakness, especially in patients with hyperthyroidism.

If TPP is suspected, levels of blood potassium must be immediately monitored and adequately managed to ensure the restoration of normal levels of blood potassium.

Package Leaflet

- 2. What you need to know before you <take> <use> [invented name]

Warnings and precautions

Talk to your doctor or pharmacist before <taking> <using> [Invented name]
[…]

- If you have an over-active thyroid gland (hyperthyroidism)
[…]

Contact your doctor promptly if you experience muscle weakness, muscle aches, cramps and stiffness while using hydrocortisone. These can be symptoms of a condition called Thyrotoxic Periodic Paralysis, which may occur in patients with an over-active thyroid gland (hyperthyroidism) who are treated with hydrocortisone. You may need additional treatment to alleviate this condition.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	April 2025 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	8 June 2025
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	7 August 2025