

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 botulinum toxin a, the scientific conclusions are as follows:

Based on the evidence outlined in the PRAC Assessment Report, the following updates to the product information for VISTABEL and BOTOX are recommended.

The CMDh agrees with the scientific conclusions made by the PRAC.

Grounds for the variation to the terms of the Marketing Authorisation(s)

On the basis of the scientific conclusions for botulinum toxin a the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing botulinum toxin a is unchanged subject to the proposed changes to the product information.

The CMDh reaches the position that the marketing authorisation(s) of products in the scope of this single PSUR assessment should be varied. To the extent that additional medicinal products containing botulinum toxin a are currently authorised in the EU or are subject to future authorisation procedures in the EU, the CMDh recommends that the concerned Member States and applicant/marketing authorisation holders take due consideration of this CMDh position.

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~~)

The following changes to the product information of **VISTABEL** are recommended (new text **underlined and in bold**)

Summary of Product Characteristics

Section 4.8 Forehead Lines and Glabellar Lines with or without Crow's Feet Lines

System Organ Class: Musculoskeletal and connective tissue disorders

Preferred Term: **Mephisto sign (lateral elevation of eyebrows)**

Frequency: **Common**

Section 4.8 Glabellar Lines

System Organ Class: Musculoskeletal and connective tissue disorders

Preferred Term: **Mephisto sign (lateral elevation of eyebrows)**

Frequency: **Uncommon**

Package Leaflet

Section 4 Possible Side Effects

Injections for the temporary improvement in the forehead lines and vertical lines between the eyebrows seen at frown when treated with or without the fan-shaped lines from the corner of the eyes.

Common: **Mephisto sign (raising of the outer eyebrows)**

Injections for the temporary improvement in the vertical lines between the eyebrows

Uncommon: **Mephisto sign (raising of the outer eyebrows)**

The following updates are proposed for **BOTOX** (**new text underlined and in bold**):

Summary of Product Characteristics:

Section 4.8 Chronic migraine

System Organ Class: Musculoskeletal and connective tissue disorders

Preferred Term: **Mephisto sign (lateral elevation of eyebrows)**

Frequency: **Unknown**

Package Leaflet

Section 4 Possible side effects

Injections in the head and neck for the treatment of headache in patients who suffer from chronic migraine

Unknown: **Mephisto sign (raising of the outer eyebrows)**

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	Sep 2022 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	30 October 2022
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	29 December 2022