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 - haemagglutinin complex, the scientific conclusions are as follows:

Regarding development of botulism following overdose, there is rather limited evidence in support of beneficial effects of use of antitoxin. The overall impression suggests that the administration of antitoxin may, at least in some cases, have a favourable effect in halting the progression of the paralysis. Further, there are recommendations in certain guidelines including the European Centre for Disease Prevention and Control, on using antitoxin in some cases of botulism. Nevertheless, use of antitoxin is associated with risks of serious adverse effects including anaphylactic / anaphylactoid reactions. Furthermore, there is variety of types of antitoxin, and uncertainty regarding availability of antitoxin in different member states. Taken together, the PRAC did not find sufficient support to include a recommendation to consider use of antitoxin for limiting the progression and duration of signs and symptoms of botulism. Nevertheless, the PRAC concluded there is sufficient evidence to remove the current statement that 'There is no specific antidote; antitoxin should not be expected to be beneficial'; and to refer to only general supportive care.

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 - haemagglutinin complex the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing botulinum toxin a - haemagglutinin complex 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 - haemagglutinin complex 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~~)

Summary of Product Characteristics

- 4.9 Overdose

Excessive doses may produce distant and profound neuromuscular paralysis. Overdose could lead to an increased risk of the neurotoxin entering the bloodstream and may cause complications associated with the effects of oral botulinum poisoning (e.g. dysphagia and dysphonia). Respiratory support may be required where excessive doses cause paralysis of respiratory muscles. ~~There is no specific antidote; antitoxin should not be expected to be beneficial and. g~~ General supportive care is advised.

In the event of overdose the patient should be medically monitored for any signs and/or symptoms of excessive muscle weakness or muscle paralysis. Symptomatic treatment should be instigated if necessary.

Symptoms of overdose may not present immediately following injection. Should accidental injection or oral ingestion occur the patient should be medically supervised for several weeks for any signs and/or symptoms of excessive muscle weakness or muscle paralysis.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	September 2019 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	03/11/2019
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	02/01/2020