

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 amantadine, the scientific conclusions are as follows:

During the reporting period serious reports of impulse-control disorders (ICD) were received. These are serious and increasingly recognized as complication in PD, occurring in up to 20 % of patients over the course of their illness. However, there is a plausible mechanism for amantadine to induce impulse-control disorders and therefore it is recommended to add 'Impulse control disorder' to sections 4.4 and 4.8 of the SmPC of all amantadine containing products.

Reported cases and publications of eye disorders with amantadine treatment provided enough evidence for related adverse reactions e.g. blurred vision, corneal lesion, etc to be listed in the SmPC. In addition a general warning in case of blurred vision has been added too.

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 amantadine the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing amantadine 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 amantadine 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

- Section 4.4

Warnings should be added or revised as follows:

[...]

“Impulse control disorders

Patients should be regularly monitored for the development of impulse control disorders. Patients and carers should be made aware that behavioural symptoms of impulse control disorders, including pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with products with a dopaminergic effect, including <product name>. Dose reduction or tapered discontinuation should be considered if such symptoms develop.”

[...]

“If blurred vision or other visual problems occur an ophthalmologist should be contacted to exclude corneal oedema. In case that corneal oedema is diagnosed treatment with amantadine should be discontinued.”

- Section 4.8

The following adverse reaction should be added under the SOC Psychiatric disorders with a frequency “not known (cannot be estimated from the available data)”:

Impulse control disorders

Pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with products with a dopaminergic effect, including <product name> (see section 4.4).

The following adverse reactions should be added under the SOC **Eye Disorders** with the respective frequency as follows:

Uncommon: blurred vision

Rare: corneal lesion, e.g. punctate subepithelial opacities which might be associated with superficial punctate keratitis, corneal epithelial oedema, and markedly reduced visual acuity.

Package Leaflet

- Section 2:

[...]

Tell your doctor if you or your family/carer notices that you are developing urges or cravings to behave in ways that are unusual for you and you cannot resist the impulse, drive or temptation to carry out certain activities that could harm yourself or others. These are called impulse control disorders and can include behaviours such as addictive gambling, excessive eating or spending, an abnormally high sex

drive or an increase in sexual thoughts or feelings.

Your doctor may need to adjust or stop your dose of <product name>.

[...]

If blurred vision or other visual problems occur please contact an eye doctor immediately.

[...]

- Section 4:

[...]

Not known (frequency cannot be estimated from the available data):

- *Urge to behave in an usual way - strong impulse to gamble excessively, altered or increased sexual interest, uncontrollable excessive shopping or spending, binge eating (eating large amounts of food in a short time period) or compulsive eating (eating more food than normal and more than is needed to satisfy your hunger)*

[...]

Uncommon: blurred vision

Rare: corneal lesion, corneal oedema, reduced visual acuity

Annex III

Timetable for the implementation of this position

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Adoption of CMDh position:	September 2018 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	3 November 2018
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	2 January 2019