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 galantamine, the scientific conclusions are as follows:

In a view of available data on QTc prolongation / Torsade de pointes from spontaneous case reports where the relationship between galantamine and the event was assessed as probable in one case and possible in seven cases, two case reports from the literature, knowledge from overdose of galantamine and the cholinergic mechanism (which increases the propensity for bradycardia), the PRAC considers it warranted to update the current warning statement on cardiac disorders (SmPC Section 4.4 and corresponding parts of the PIL), to add wording on relation to QTc prolongation / Torsade de pointes. The PRAC thus conclude that the product information of all products containing galantamine should be amended accordingly.

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

Cardiac disorders

Because of their pharmacological action, cholinomimetics may have vagotonic effects on heart rate, including bradycardia and all types of atrioventricular node block (see section 4.8). The potential for this action may be particularly important to patients with "sick sinus syndrome" or other supraventricular cardiac conduction disturbances or in those who use medicinal products that significantly reduce heart rate concomitantly, such as digoxin and beta blockers or for patients with an uncorrected electrolyte disturbance (e.g. hyperkalaemia, hypokalaemia).

Caution should therefore be exercised when administering galantamine to patients with cardiovascular diseases, e.g. immediate post-myocardial infarction period, new-onset atrial fibrillation, second degree heart block or greater, unstable angina pectoris or congestive heart failure, especially NYHA group III-IV.

There have been reports of QTc prolongation in patients using therapeutic doses of galantamine and of torsade de pointes in association with overdoses (see section 4.9). Galantamine should therefore be used with caution in patients with prolongation of the QTc interval, in patients treated with drugs affecting the QTc interval, or in patients with relevant pre-existing cardiac disease or electrolyte disturbances.

In a pooled analysis of placebo-controlled studies in patients with Alzheimer´s dementia treated with galantamine an increased incidence of certain cardiovascular adverse events were observed (see section 4.8).

Package Leaflet

2. What you need to know before you take X

Warnings and precautions

Before you take X your doctor needs to know if you have, or have had, any of the following:

- a heart condition (such as chest discomfort that is often brought on by physical activity, a heart attack, heart failure, slow or uneven heart beat, **prolonged QTc interval**)

Other medicines and X
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Some medicines can make side effects more likely in people taking X. These include:

- **medicines affecting the QTc interval**

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	November 2020 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	27 December 2020
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	25 February 2021