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 gentamicin systemic use, the scientific conclusions are as follows:

Based on review of data from post-marketing surveillance and literature, the PRAC considers that a causal relationship between the use of gentamicin (systemic use) and the occurrence of acute renal failure, Fanconi-like syndrome in patients treated with a prolonged course of high-dose, as well as irreversible hearing loss and deafness could not be excluded and therefore requests that the product information is updated to reflect these adverse drug reactions. The frequency "very rare" should be applied to acute renal failure and Fanconi-like syndrome in patients treated with a prolonged course of high-dose, while the frequency of "not known" should be applied to irreversible hearing loss and deafness.

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 gentamicin systemic use the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing gentamicin systemic use 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 gentamicin systemic use are currently authorised in the EU or are subject to future authorisation procedures in the EU, the CMDh recommends that 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 4.8

All gentamicin (systemic use) containing medicinal products, which do not already mention acute renal failure among the adverse drug reactions

The following adverse reaction should be added under the SOC Renal and Urinary disorders with a frequency "very rare":

Acute renal failure

All gentamicin (systemic use) containing medicinal products, which do not already mention Fanconi-like syndrome among the adverse drug reactions

The following adverse reaction should be added under the SOC Renal and Urinary disorders with a frequency "very rare":

Fanconi-like syndrome in patients treated with a prolonged course of high-dose

All gentamicin (systemic use) containing medicinal products, which do not already mention irreversible hearing loss, deafness among the adverse drug reactions:

The following adverse reactions should be added under the SOC Ear and labyrinth disorders with a frequency "unknown":

Irreversible hearing loss, deafness

Package Leaflet

Section 4

All gentamicin (systemic use) containing medicinal products, which do not already mention acute renal failure among the adverse drug reactions

Frequency very rare: **Acute kidney failure**

All gentamicin (systemic use) containing medicinal products, which do not already mention Fanconi-like syndrome among the adverse drug reactions

Frequency very rare: **High urine levels of phosphate and amino acids (so called Fanconi-like syndrome, associated with high doses given over long time)**

All gentamicin (systemic use) containing medicinal products, which do not already mention irreversible hearing loss, deafness among the adverse drug reactions:

Frequency Unknown: **Irreversible hearing loss, deafness**

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	December 2017 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	27 January 2018
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	28 March 2018