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 prulifloxacin, the scientific conclusions are as follows:

Fluoroquinolones are known to cause neuromuscular blockade by interfering with AChR ion channel and consequently fluoroquinolone exposure may result in potentially life-threatening myasthenia gravis exacerbations in patients with underlying disease. This risk is already described as associated to fluoroquinolones and is addressed in the product information of the majority of fluoroquinolone-containing products in the EU. In addition, a case was reported in the article "Prulifloxacin as trigger of myasthenia gravis" by Rossi et al. 2009. On the basis of the available evidence and the supposed class effect, it is considered appropriate to update the product information of prulifloxacin-containing products within this PSUSA procedure.

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

A warning should be added as follows:

Fluoroquinolones, including prulifloxacin, have neuromuscular blocking activity and may exacerbate muscle weakness in patients with myasthenia gravis. Prulifloxacin is not recommended in patients with a known history of myasthenia gravis.

- Section 4.8

The following adverse reaction should be added under the SOC "Musculoskeletal and connective tissue disorders" with a frequency "unknown":

Exacerbation of myasthenia gravis

Package Leaflet

2. What you need to know before you take (prulifloxacin) tablets

Warnings and precautions

Talk to your doctor or pharmacist before taking your medicine if:

- **You have myasthenia gravis (muscle weakness).**

4. Possible side effects

Tell your doctor if any of the following side effects gets serious or lasts longer than a few days:

Unknown

Muscle weakness. This is important in people with myasthenia gravis (a rare disease of the nervous system).

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	June 2018 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	11 August 2018
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	10 October 2018