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 ciprofloxacin (systemic use) the scientific conclusions are as follows:

Cases of syndrome of inappropriate secretion of antidiuretic hormone - SIADH were identified during the reported period of this PSUSA. These data provides sufficient evidence for listing SIADH in section 4.8 of the SmPC as an adverse drug reaction associated with ciprofloxacin (systemic) treatment with the frequency unknown. During the reporting period there were a few cases of hypoglycaemic coma identified by spontaneous reporting and literature publication. In view of this new information and due to this already being labelled in other products of the class, sections 4.4 and 4.8 of the SmPC should be updated to reflect that cases of hypoglycaemic coma have been reported. The package leaflet is updated in accordance.

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

MAHs should ensure that the below wording is reflected in the product information of their product:

Dysglycaemia

As with all quinolones, disturbances in blood glucose, including both hypoglycaemia and hyperglycaemia have been reported (see section 4.8), usually in diabetic patients receiving concomitant treatment with an oral hypoglycaemic agent (e.g., glibenclamide) or with insulin. Cases of hypoglycaemic coma have been reported. In diabetic patients, careful monitoring of blood glucose is recommended.

- Section 4.8

The following adverse reaction should be added under the SOC 'Endocrine disorders' with a frequency 'not known': **Syndrome of inappropriate secretion of antidiuretic hormone (SIADH).**

The following adverse reaction should be added under the SOC 'Metabolism and Nutrition Disorders' with a frequency 'not known': **Hypoglycaemic coma (see section 4.4).**

Package Leaflet

- Section 2 What you need to know before you…:

Quinolone antibiotics may cause ~~**disturbances in blood sugar**, including both a decrease in blood sugar below normal levels (hypoglycaemia) and~~ an increase **of your** ~~in~~ blood sugar **levels** above normal levels (hyperglycaemia)**, or lowering of your blood sugar levels below normal levels, potentially leading to loss of consciousness** ~~(see section 4. Possible side effects). Disturbances in blood sugar occurred usually in elderly diabetic patients receiving concomitant treatment with oral antidiabetic medicines that lower blood sugar (e.g. glibenclamide) or with insulin. Loss of consciousness due to severe reduction in blood sugar~~ (hypoglycaemic coma) **in severe cases (see section 4)**~~has been reported~~. **This is important for people who have diabetes.** If you suffer from diabetes, your blood sugar should be carefully monitored.

- Section 4 Side effects:
  - **Syndrome associated with impaired water excretion and low levels of sodium (SIADH)**

    Frequency: Not known.
  - **Loss of consciousness due to severe decrease in blood sugar levels (hypoglycaemic coma). See section 2.**

    Frequency: Not known.

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:	20 September 2019
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	19 November 2019