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 hydrochlorothiazide / quinapril, the scientific conclusions are as follows:

In view of available data on hyponatremia/Syndrome of inappropriate antidiuretic hormone secretion (SIADH) from the literature and spontaneous reports including in some cases with a close temporal relationship and a positive de-challenge and in view of a plausible mechanism of action, the PRAC Lead Member State considers a causal relationship between Quinapril/hydrochlorothiazide (HCTZ) and hyponatremia/SIADH is at least a reasonable possibility. The PRAC Lead Member State concluded that the product information of products containing Quinapril/HCTZ 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 hydrochlorothiazide / quinapril the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing hydrochlorothiazide / quinapril 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 hydrochlorothiazide / quinapril 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:
Hyponatremia and syndrome of inappropriate antidiuretic hormone secretion (SIADH)
Syndrome of inappropriate antidiuretic hormone secretion (SIADH) and subsequent hyponatraemia has been observed in some patients treated with quinapril and other ACE inhibitors. It is recommended that serum sodium levels are monitored regularly in the elderly and in other patients at risk of hyponatremia.

- Section 4.8

The following adverse reaction(s) should be added under the SOC Metabolism and nutrition disorders with a frequency 'common':

Hyponatremia

The following adverse reaction(s) should be added under the SOC Endocrine disorders with a frequency 'unknown':
Syndrome of inappropriate antidiuretic hormone secretion (SIADH)

Package Leaflet

Section 4

The following side-effects have also been reported in patients with high blood pressure being treated with quinapril:
Common: May affect more than 1 in 100 people
decreased sodium concentrations in the blood

Not known: the frequency cannot be estimated from available data

- **Dark urine, nausea, vomiting, muscle cramps, confusion and seizures. These may be symptoms of a condition called SIADH (inappropriate antidiuretic hormone secretion).**

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	December 2021 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	31 January 2022
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	31 March 2022