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 quinapril, the scientific conclusions are as follows:

Syndrome of inappropriate antidiuretic hormone secretion (SIADH)
In view of available data on syndrome of inappropriate antidiuretic hormone secretion (SIADH) from the literature, spontaneous reports and in view of a plausible mechanism of action, the PRAC Lead Member State considers a causal relationship between quinapril and SIADH is at least a reasonable possibility. The PRAC Lead Member State concluded that the product information of products containing quinapril should be amended accordingly.

Hyponatremia
In view of available data on hyponatremia from clinical trials, the literature, spontaneous reports including in some cases a positive de-challenge and/or re-challenge and in view of a plausible mechanism of action, the PRAC Lead Member State considers a causal relationship between quinapril and hyponatremia is at least a reasonable possibility. The PRAC Lead Member State concluded that the product information of products containing quinapril should be amended accordingly.

Psoriasis and Psoriasis aggravated
In view of available data on psoriasis and psoriasis aggravated from the literature, spontaneous reports and in view of a plausible mechanism of action, the PRAC Lead Member State considers a causal relationship between quinapril and psoriasis and psoriasis aggravated is at least a reasonable possibility. The PRAC Lead Member State concluded that the product information of products containing quinapril 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 quinapril the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing 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 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

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 'Endocrine disorders' with a frequency 'Not known':

Syndrome of inappropriate antidiuretic hormone secretion (SIADH)
~~Syndrome of Inappropriate Anti-diuretic Hormone (SIADH) and subsequent hyponatremia has been observed in some patients treated with other ACE inhibitors (see section 4.4).~~

The following adverse reaction(s) should be added under the SOC 'Skin and subcutaneous tissue disorders' with a frequency 'not known'.

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

Hyponatremia
MAHs who already have hyponatremia listed in Section 4.8 of the SmPC with another frequency should change the frequency to 'common'.

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
MAHs who already have 'decreased sodium concentrations in the blood' listed in Section 4 of the package leaflet with another frequency should change the frequency to 'common'.

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).**
- **Psoriasis or worsening of existing psoriasis (skin disease characterised by reddened patches covered with silvery scales).**

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