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 acenocoumarol, the scientific conclusions are as follow:

In view of available data on Anticoagulant related nephropathy from the literature and spontaneous reports including in some cases a close temporal relationship and a positive de-challenge and in view of a plausible mechanism of action the PRAC considers a causal relationship between acenocoumarol, and Anticoagulant related nephropathy is at least a reasonable possibility. The PRAC concluded that the product information of products containing acenocoumarol should be amended accordingly.

In view of available data on Drug interaction in association with concomitant use of acenocoumarol and semaglutide resulting in International normalized ratio decreased from the literature and spontaneous reports, including in some cases a close temporal relationship, a positive de-challenge and re-challenge and in view of a plausible mechanism of action, the PRAC considers a causal relationship between the International normalized ratio decreased and concomitant use of acenocoumarol and semaglutide is at least a reasonable possibility. The PRAC concluded that the product information of products containing acenocoumarol should be amended accordingly.

Having reviewed the PRAC recommendation, the CMDh agrees with the PRAC overall conclusions and grounds for recommendation.

Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions for acenocoumarol the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing acenocoumarol is unchanged subject to the proposed changes to the product information.

The CMDh recommends that the terms of the marketing authorisation(s) should be varied.

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:

Anticoagulant-related nephropathy:

In patients with altered glomerular integrity or with a history of kidney disease, acute kidney injury may occur, possibly in relation to episodes of excessive anticoagulation and hematuria. A few cases have been reported in patients with no pre-existing kidney disease. Close monitoring including renal function evaluation is advised in patients with a supratherapeutic INR and hematuria (including microscopic).

- **Section 4.5**

An interaction should be added under the subheading for substances that diminish the effect of acenocoumarol

Semaglutide may impair acenocoumarol absorption due to its effect to delay gastric emptying.

- **Section 4.8**

The following adverse reaction should be added under the SOC Renal and urinary disorders with a frequency unknown:

SOC: Renal and urinary disorders
Frequency 'not known': Anticoagulant-related nephropathy (see section 4.4)

Package Leaflet

Section 2. What you need to know before you use Acenocoumarol

Subsection Other medicines and acenocoumarol

Medicines that could decrease the efficacy of acenocoumarol:

Semaglutide, a medicine used to lower blood sugar levels

Section 4 – Possible side effects

Adverse effects with no known frequency: **Bleeding in the kidney sometimes with presence of blood in urine leading to inability of the kidneys to work properly (anticoagulant-related nephropathy)**

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	February 2025 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	13 April 2025
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	12 June 2025