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 vancomycin, the scientific conclusions for haemolytic anaemia are as follows:

In view of available data on haemolytic anaemia from the literature, and spontaneous reports including in some cases a close temporal relationship, a positive de-challenge and/or re-challenge and in view of a plausible mechanism of action, the PRAC considers a causal relationship between vancomycin and haemolytic anaemia is at least a reasonable possibility. The PRAC concluded that the product information of products containing vancomycin 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 vancomycin the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing vancomycin 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 4.8

The following adverse reaction should be added under the SOC Blood and lymphatic system disorders with frequency 'not known': **haemolytic anaemia**

Package Leaflet

Section 4 – Possible side effects

[…]

Not known (frequency cannot be estimated from the available data):

[…]

Excessive breakdown of red blood cells causing tiredness and pale skin (haemolytic anaemia).

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	October 2025 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	30 November 2025
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	29 January 2026

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 vancomycin, the scientific conclusions for drug-induced liver injury (DILI) are as follows:

In view of available data on increased hepatic enzymes from the literature, and spontaneous reports including in some cases a close temporal relationship, a positive de-challenge and/or re-challenge and in view of a plausible mechanism of action, the PRAC considers that a causal relationship between vancomycin and increased hepatic enzymes is at least a reasonable possibility. The PRAC concluded that the product information of products containing vancomycin 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 vancomycin the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing vancomycin 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 4.8

The following adverse reaction(s) should be added under the SOC hepatobiliary disorders with a frequency 'common': **alanine aminotransferase increased, aspartate aminotransferase increased**

Package Leaflet

Section 4 - Possible side effects

Common side effects (may affect up to 1 in 10 people):

[…]

- **Increase of liver enzymes**

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	October 2025 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	30 November 2025
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	29 January 2026

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 vancomycin, the scientific conclusions Kounis syndrome are as follows:

In view of available data on Kounis syndrome from the literature, and spontaneous reports including in all a close temporal relationship, a positive de-challenge and/or re-challenge and in view of a plausible mechanism of action, the PRAC considers that a causal relationship between vancomycin and Kounis syndrome is at least a reasonable possibility. The PRAC concluded that the product information of products containing vancomycin 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 vancomycin the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing vancomycin 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:

Cardiovascular and cerebrovascular effects

Cases of Kounis syndrome have been reported in patients treated with vancomycin. Kounis syndrome has been defined as cardiovascular symptoms secondary to an allergic or hypersensitive reaction associated with constriction of coronary arteries and potentially leading to myocardial infarction.

- Section 4.8

The following adverse reaction(s) should be added under the SOC Cardiac disorders with frequency 'not known': **Kounis syndrome**

Package Leaflet

Section 2 – What you need to know before you use vancomycin

Warnings and precautions

[…]

- Signs of an allergic reaction to this medicine, including breathing problems and chest pain, have been reported with [product name]. Stop immediately [product name] and contact immediately your doctor or medical emergencies if you notice any of these signs.

Section 4 – Possible side effects

Vancomycin may cause allergic reactions, although severe allergic reactions (anaphylactic shock) are rare. Tell your doctor right away if you suddenly get wheezing, difficulty breathing, redness in the upper part of the body, rash or itching.

Stop taking vancomycin and tell your doctor or nurse immediately, if you experience any of the following symptoms:

[…]

- Chest pain, which can be a sign of a potentially serious allergic reaction called Kounis syndrome.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	October 2025 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	30 November 2025
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	29 January 2026