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 tranexamic acid, the scientific conclusions are as follows:

Risk of medication errors with intravenous formulations of tranexamic acid associated with incorrect route of product administration.

In view of the available data on adverse reactions, including fatal adverse reactions, following incorrect route of product administration via the intrathecal route, the PRAC considers that the product information of intravenous formulations of tranexamic acid should inform healthcare professionals and raise awareness of the nature of medication errors that have occurred in the post-marketing setting with tranexamic acid and the resulting harms particularly in relation to intrathecal administration. It is also considered that recommendations on measures to minimise the risk of incorrect route of product administration should be provided to healthcare professionals. Furthermore, there is also more limited evidence of inadvertent epidural administration. Given the potential for serious morbidity and mortality when non-epidural medicines are administered by this route, it is also considered that a contraindication should be added to the existing contraindications included in the product information regarding epidural administration. In addition, given the role of the product packaging in communicating essential safety information, updates to the particulars of the outer packaging are recommended to reinforce information on the correct route of administration.

Acute renal cortical necrosis

In view of available data on acute renal cortical necrosis from the literature, and spontaneous reports, including in some cases a close temporal relationship, and in view of a plausible mechanism of action, the PRAC considers a causal relationship between tranexamic acid and acute renal cortical necrosis is at least a reasonable possibility. The PRAC concluded that the product information of products containing tranexamic acid should be amended accordingly.

Fixed drug eruption

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

The PRAC concluded that the product information of products containing intravenous formulations of tranexamic acid 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 tranexamic acid the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing tranexamic acid 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~~)>

Intravenous formulations of tranexamic acid

Summary of Product Characteristics

- Section 4.2

A warning and precaution should be added as follows:

Method of administration

[…]
TRANEXAMIC ACID MUST ONLY BE ADMINISTERED INTRAVENOUSLY and must not be administered intrathecally or epidurally* (see sections 4.3 and 4.4).

IN ORDER TO REDUCE THE RISK OF FATAL MEDICATION ERRORS DUE TO INCORRECT ROUTE OF ADMINISTRATION OF TRANEXAMIC ACID, IT IS STRONGLY RECOMMENDED TO LABEL THE SYRINGES CONTAINING TRANEXAMIC ACID (see sections 4.3, 4.4 and 6.6).

*This sentence should be in bold

- Section 4.3

The contraindications should be amended as follows:
[…]
Intrathecal**, epidural,** ~~and~~ intraventricular injection~~,~~ **and** intracerebral application (risk of cerebral oedema and convulsions **and death**)

- Section 4.4

A warning should be added as follows:
[…]
Risk of medication errors due to incorrect route of administration

<Product name> is for intravenous use only. Intrathecal, epidural, intraventricular and intracerebral use of <Product name> is contraindicated (see section 4.3). Serious adverse reactions including fatal events have been reported when tranexamic acid was inadvertently administered intrathecally. These include severe back, gluteal and lower limb pain, myoclonus and generalised seizures, and cardiac arrhythmias.

Care should be exercised to ensure the correct route of administration of <Product name> . Healthcare professionals should be aware of the potential for confusion of <Product name> with other injectables which could result in inadvertent intrathecal administration of <Product name>. This includes in particular intrathecally administered injectables that may be used during the same procedure as tranexamic acid.

Syringes containing <Product name> should be clearly labelled with the intravenous route of administration.

- Section 6.6

A precaution should be added as follows:
Healthcare professionals are strongly advised to label the <Product name> syringes during the withdrawal of the product from the <X> for clear identification and proper route of administration, to help prevent inadvertent medication errors during administration to the patient.

Package Leaflet

- Section 2

Existing wording should be amended as follows:

Do not use <Product name>:
[…]
Due to the risk of ~~cerebral oedema and convulsions, intrathecal and intraventricular injection and intracerebral application are not recommended.~~ **seizures and brain swelling, <Product name> must not be given into the spine, epidurally (around the spinal cord) or into the brain.**
[…]

Warnings and precautions
This medicine is ONLY to be given to you through a vein either by intravenous infusion (IV) or intravenous injection (IV push). This medicine must not be given into the spine, epidurally (around the spinal cord) or into the brain. Serious harms have been reported when this medicine was given into the spine (intrathecal use). If you notice any pain in your back or legs during, or soon after this medicine is given, tell your doctor or nurse immediately.
[…]

- Section 3

Existing wording should be amended as follows:
[…]

Method of administration
[…]
<Product name> must not be injected into a muscle, **into the spine, epidurally (around the spinal cord) or into the brain.**
[…]

Particulars to appear on the Outer Packaging

The following wording should be added, if no such wording or equivalent currently exists (place, lay-out and text colour to be agreed with the national competent authorities):
[…]
For intravenous use only. NOT for intrathecal/epidural use.
[…]

- Section 4.8

If the ADR "Acute renal cortical necrosis" is already included in section 4.8 with another frequency, the existing frequency should be maintained.
The following adverse reaction should be added under the SOC *"Renal and urinary disorders"* with a frequency *"Not known"*, if no such wording or equivalent currently exists

Acute renal cortical necrosis

Package Leaflet

- Section 4. Possible side effects

Not known (frequency cannot be estimated from the available data)
Sudden onset kidney problems due to death of the tissue in the outer part of the kidney (acute renal cortical necrosis)

- Section 4.8

If the ADR "Fixed drug eruption" is already included in section 4.8 with another frequency, the existing frequency should be maintained.
The following adverse reaction should be added under the SOC *"Skin and subcutaneous tissue*

disorders" with a frequency *"Not known"*:

Fixed drug eruption

Package Leaflet

- Section 4. Possible side effects
  Not known (frequency cannot be estimated from the available data)
  An allergic reaction that usually recurs at the same site(s) on re-exposure to the medication and may include round or oval patches of redness and swelling of the skin, blistering, and itching (fixed drug eruption). Darkening of the skin in affected areas, which might persist after healing, may also occur.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	November 2025 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	28 December 2025
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	26 February 2026