ARABIAN OASIS
واحـــة العـــرب

Aminocaproic Acid (Epsicaprom 25 mg/mL, Solution for Injection)
Notification to Healthcare Professionals Regarding Packaging and Leaflet Deficiency

Date: 9/4/2025

Dear Healthcare Professionals,
Greetings,

With reference to the report received from one of the healthcare institutions regarding a packaging defect in Epsicaprom 25 (Batch No. 3091), we would like to inform you of the following after reviewing the batch release data:
This information is being communicated in agreement with the Saudi Food and Drug Authority (SFDA).

Nature of the Issue:

It has been found that the outer packaging and patient information leaflet of the affected batch are written in a foreign language other than English or Arabic, and no versions in Arabic or English were provided. This is non-compliant with SFDA requirements for ensuring clarity of information for users.

Actions Taken:

- Coordination is ongoing with NUPCO to implement the necessary corrective actions.
- The patient information leaflet has been printed in English.
- Label stickers have been printed to provide the required information on the outer packaging.

Recommendations:

- All healthcare professionals are kindly requested to refer to the English version of the Patient Information Leaflet for this batch to ensure that all necessary information is clearly communicated for safe and effective use.
- If you require more details regarding this batch, please contact the company at 0562442566 or via email at **Regulatory@aodci.com.sa**.
- If you notice any packaging with unclear information for any other batch, please report it immediately to the SFDA reporting system: https://ade.sfda.gov.sa/Home/Report.

Attachments:

- For full details, please refer to the Patient Information Leaflet provided in Annex 1.

Adverse Event Reporting:

If you experience any adverse events or have concerns related to the use of *Epsicaprom 25 (Aminocaproic Acid) 2500 mg/10 mL, Solution for Injection/Infusion*, please report through the following channels:

- **Marketing Authorisation Holder (MAH):**
  BIAL – Aristegui, Produtos Farmacêuticos, S.A.
  À Av. da Siderurgia Nacional, 4745-457 S. Mamede do Coronado, Portugal
  Tel: +351 229 866 100
  Email (PV): pharmacovigilance@bial.com.
- **National Pharmacovigilance Center (NPC) – SFDA:**
  Call Center: **19999**
  Email: **npc.drug@sfda.gov.sa**
  Website: **ade.sfda.gov.sa**.

We appreciate your commitment to patient safety and quality care, and we thank you for your continued cooperation.

Sincerely,
Arabian Oasis for Development and Commercial Investment Company

ARABIAN OASIS
واحـــة العـــرب

ANNEX 1

SUMMARY OF PRODUCT CHARACTERISTICS

1. MEDICINE NAME

EPSICAPROM 25, 2500 mg/10 ml, solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Aminocaproic acid 2.50 g per 10 ml ampoule. Full list
of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for infusion.
Clear, colorless and odorless solution, contained in amber glass ampoules. 4. CLINICAL

INFORMATION

4.1 Therapeutic indications

Aminocaproic acid is indicated for use in patients of all ages in bleeding caused by local or generalised fibrinolysis, including:
Post-surgical hemorrhages in:
Urology (bladder and prostate surgery)
Gynaecology (cervical surgery), in patients when tranexamic acid is not available or tolerated
Obstetrics (postpartum and postabortion hemorrhages) after correction of the coagulation defect Cardiac surgery (with or without bypass placement)
Gastroenterology
Odontostomatology (extractions Dental in Hemophiliacs sick undergoing anticoagulant therapy)
Life-threatening bleeding induced by thrombolytics (streptokinase, etc.). Hemorrhages associated with thrombocytopenia, thrombopenic purpura, leukemia.
Non-surgical haematuria of the lower urinary tract (secondary to cystitis, etc.). Heavy menstruation, menorrhagia and hemorrhagic metropathies.
Angioneurotic edema.

4.2 Dosage and method of

administration Dosage

Adults
Intravenously: The desired blood level is reached with an initial dose of 4 to 5 g by slow intravenous infusion (over one hour), followed by a continuous infusion of 1 g/hour. If it is necessary to prolong treatment, the maximum dose in the 24-hour period should normally not exceed 24 g.

Paediatric population

The safety and efficacy of EACA in children aged 0 to 17 years have not yet been established. However, the following doses have been used in patients under 18 years of age:

Intravenously: 100 mg/kg or 3 g/m^2 by slow intravenous infusion during the first hour, followed by a continuous infusion at a rate of 33.3 mg/kg per hour or 1 g/m^2 per hour. The total dose should not exceed 18 g/m^2 (600 mg/kg) in 24 hours.

Elderly patients

No dose decreases are required except in cases of renal failure.

Renal impairment

A more moderate dose of aminocaproic acid is indicated in patients with renal impairment, along with frequent monitoring.

Method of administration

Intravenously: EPSICAPROM 25 should be administered as a slow intravenous injection with glycosylated serum, glucosaline or dextrose.
EPSICAPROM 25 should not be administered intramuscularly under any circumstances as it is a highly hypertonic solution.

4.3 Contraindications

Hypersensitivity to the active substance or any of the excipients listed in section 6.1.
Aminocaproic acid should not be used when there is evidence of an active intravascular coagulation process (see section 4.4).

4.4 Special warnings and precautions for use

Thrombogenic effect

Numerous clinical studies indicate that aminocaproic acid has no effect thrombogenic. However, it should be administered with caution in cases where thrombosis or embolism is suspected, and in renal failure.

Inhibition of fibrinolysis by aminocaproic acid can theoretically result in coagulation or thrombosis. However, there is no clear evidence that the administration of aminocaproic acid was responsible for the few cases of intravascular coagulation after treatment. Instead, it seems that the said intravascular coagulation was probably due to a pre-existing clinical situation, i.e., the presence of disseminated intravascular coagulation (DIC). It has been suggested that extravascular clots formed in vivo may not undergo spontaneous lysis like normal clots.

Establishing the cause of bleeding
In cases where there is doubt, it should be clarified whether the aetiology of the control haemorrhage for which EPSICAPROM 25 is being used is primary fibrinolysis or disseminated intravascular coagulation (DIC) prior to aminocaproic acid being administered. The following tests may be performed to differentiate between the two conditions:

Platelet count: this is usually decreased in DIC but not in primary fibrinolysis.
Protamine paracoagulation test: positive in ICD; A precipitate is formed when a drop of protamine sulfate is added to the "citrate" plasma. This test is negative in primary fibrinolysis.
Euglobulin clot test: abnormal in primary fibrinolysis and normal in DIC.
Aminocaproic acid should not be used in DIC without concomitant administration of heparin.

Upper urinary tract hemorrhage
In patients with upper urinary tract haemorrhage, administration of aminocaproic acid produced intrarenal obstruction in the form of glomerular capillary thrombosis or clots in the bacinet or ureters. Therefore, aminocaproic acid should not be administered in the case of haematuria originating in the upper urinary tract unless the anticipated benefits outweigh the risks.

Effects on skeletal muscle
In rare cases, skeletal muscle weakness with necrosis of muscle fibres has been described after prolonged administration. The clinical manifestation can range from mild myalgia with weakness and fatigue to severe proximal myopathy with rhabdomyolysis, myoglobinuria, and acute renal failure. Muscle enzymes, especially creatine phosphokinase (CPK), are elevated. CPK should be monitored in patients undergoing long-term treatment. Administration of aminocaproic acid should be discontinued if an increase in CPK is observed. The condition suffers remission after suspension of administration; however, the syndrome may recur if aminocaproic acid administration is restarted.

When skeletal myopathy occurs, the possibility of heart muscle injury should also be considered. A case of cardiac and hepatic injury in humans has been described. The patient received 2 g of aminocaproic acid at 6-hour intervals until a total dose of 26 g was reached. The patient died from prolonged cerebrovascular bleeding. Necrotic changes of the heart and liver were observed at autopsy.

Inhibition of plasmin activity
Aminocaproic acid inhibits the effect of plasminogen activators and, to a lesser extent, plasmin activity. This medicinal product should not be administered without a definitive diagnosis and/or laboratory results indicating hyperfibrinolysis (hyperplasminaemia).

Rapid infusion
Rapid intravenous administration should be avoided because it may cause hypotension, bradycardia, and/or arrhythmias.

Neurological effects
The literature contains publications on an increased incidence of certain neurological deficiencies such as hydrocephalus, cerebral ischemia, and cerebral vasospasm, associated with the use of antifibrinolytics in the treatment of subarachnoid hemorrhage (SAH). All these events have also been described as part of the natural evolution of SAH, as a result of diagnostic procedures such as angiography.

Thrombophlebitis
Thrombophlebitis, a possibility with all intravenous treatments, should be avoided, paying particular attention to proper needle insertion and fixation.

Administration with Factor IX complex concentrate or with anti-inhibitor coagulant concentrates
Aminocaproic acid should not be administered with Factor IX complex concentrate or with anti-inhibitor coagulant concentrates, because this administration may increase the risk of thrombosis.

4.5 Drug interactions and other forms of interaction

Concomitant administration of coagulation factors (Factor IX) and oestrogens may increase the risk of thrombosis.
Laboratory tests: administration of aminocaproic acid may alter platelet function test results.

4.6 Fertility, pregnancy and lactation

Pregnancy
The amount of data on the use of epsilon-aminocaproic acid in women pregnant women, is limited or non-existent. Animal studies have shown reproductive toxicity (see section 5.3). Aminocaproic acid is not recommended during pregnancy.

Women of childbearing potential
Aminocaproic acid is not recommended in women of childbearing potential who do not use contraception.

Breastfeeding
It is not known whether epsilon-aminocaproic acid is excreted in human milk. A decision must be made on discontinuation of breastfeeding or discontinuation/abstention of aminocaproic acid therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman.

Fertility

There are no clinical data in humans on the effect of EPSICAPROM 25 on fertility.

Administration of a dose equivalent to the maximum human therapeutic dose in the diet of rats caused fertility disturbances in both sexes. The clinical relevance of these observations is unknown (see section 5.3).

4.7 Effects on ability to drive and use machines

The effects on the ability to drive and use machines have not been studied.
In case of dizziness or drowsiness, driving a vehicle and using machines is not recommended.

4.8 Undesirable effects

a. Security Profile Summary

The most frequently reported adverse reactions during treatment are dizziness, hypotension, and headache; Hypotension is more likely to occur with rapid infusion. Serious cases of myopathy and rhabdomyolysis have been reported; these are usually reversible upon discontinuation of treatment, but CPK should be monitored in patients undergoing long-term treatment, and treatment discontinued if CPK elevations occur.

b. Tabulated list of adverse reactions

The following adverse reactions have been reported based on clinical trials, post-authorisation safety studies, and spontaneous case reports, with the following frequencies: very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1,000, <1/100), rare (≥1/10,000, <1/1,000); very rare (<1/10,000), not known:

Class of Systems Organs	Common (≥1/100, <1/10)	Uncommon (≥1/1,000 to <1/100)	Rare (≥1/10,000, <1/1,000)	Very much rare (<1/10,000)	Unknown*
Blood of diseases th a e nd system lymphatic		Agranulocytes and, coagulation diseases			Leucopenia, thrombocytope nes a
Immune of system the disorders		Allergic reactions a nd anaphylactoids, anaphylaxis			Eritema maculopapular
Nervous of system the diseases	Dizziness			Confusion, convulsions , delirium,	

				hallucinations, intracranial hypertension, stroke cerebral, syncope	
Affections Eye			Vision Decreased eyes Crimeans		

Class of Systems Organs	Common (≥1/100, <1/10)	Uncommon (≥1/1,000 to <1/100)	Rare (≥ 1/10,000, <1/1,000)	Very much rare (<1/10,000)	Unknown*
Ear and the disorders maze	Tinnitus				
Heart	Hypotension	Bradycardia	Peripheral ischemia		Thrombosis
Respiratory, thoracic and respiratory diseases mediastinum	Nasal congestion	Dyspnoea	Pulmonary embolism		
Gastrointestinal disorders	Abdominal pain, diarrhea, nausea, Vomiting				
Affections of skin tissues and Subcutaneous		Pruritus, rash			
Musculoskeletal disorders and Of connective tissues		Muscle weakness, myalgia	Elevation from CPK, myositis		Acute myopathy, rhabdomyolysis

Renal and urinary disorders					Renal failure, increased nitrogen of blood urea, nephritic colic and disturbances of renal function
Diseases of the genitals And from the breast					Dry ejaculation
General disorders and Changes On-site from administration	Headaches, malaise; pain, necrosis and reactions in local from injection	Oedema			

* frequency not known (cannot be calculated from the available data)

4.9 Overdose

Aminocaproic acid is not very toxic, so intoxication can only occur in very exceptional cases, such as cases of relative overdose with renal failure. In this case, the drug should be adjusted to the degree of renal impairment or, possibly, it should be discontinued.

A few cases of acute overdose following intravenous administration of aminocaproic acid have been described. The consequences ranged from no effects and transient hypotension to acute renal failure that resulted in death. A patient with a history of brain tumour and seizures had seizures after being given a bolus injection of 8 g of aminocaproic acid. It is not known which single dose of aminocaproic acid produces symptoms of overdose or is considered to be potentially fatal. Some patients tolerated doses up to 100 g, while cases of acute renal failure have been reported following a 12 g dose.

There is no known treatment for overdose, although there is evidence that aminocaproic acid is eliminated by hemodialysis and can be eliminated by peritoneal dialysis. Pharmacokinetic studies show that total body clearance of aminocaproic acid is greatly decreased in patients with acute renal failure.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Therapeutic subgroup: Antihemorrhagic
Pharmacotherapeutic group: Antifibrinolytics
ATC code: B02AA01.

Aminocaproic acid is an amino acid that is structurally similar to other physiological amino acids, especially to two fundamental amino acids, lysine and arginine. Most of its effects are probably due to this structural similarity.

Aminocaproic acid has several pharmacological effects. The most important affects the fibrinolytic enzyme system, which is the mechanism responsible for dissolving fibrin networks and, therefore, clots. Aminocaproic acid has an inhibitory effect on this system, which takes place on two levels: on the one hand, at relatively low concentrations, it inhibits the action of plasminogen activators through a competitive mechanism; On the other hand, in higher concentrations it inhibits plasmin activity. While the two effects do indeed have the same results, the first is the most important.

As a result of these effects, aminocaproic acid prevents the destruction of the clot by plasmin, thus preventing the appearance of bleeding due to excessive activity of the fibrinolytic system. However, the anti-haemorrhagic effect of aminocaproic acid is not necessarily linked to the presence of fibrinolysis in the blood, as demonstrated by the respective tests. In fact, the appearance or persistence of bleeding may be and in many cases is due to local hyperfibrinolysis, especially when the bleeding occurs in organs rich in plasminogen activators, such as the uterus, prostate, lungs, urinary tract, etc. On the other hand, aminocaproic acid has been shown to have a beneficial effect on general bleeding, such as haematological bleeding, in which hyperfibrinolysis is not detected in the circulating blood.

Plasmin can act on other components of the coagulation system such as factors V and VIII and, in particular, on fibrinogen. It has been shown that there are clear relationships between the proteolytic activity of plasmin and the system that forms kinins, polypeptides with different biological effects basically related to inflammation and allergy.

5.2 Pharmacokinetic properties

Aminocaproic acid is rapidly absorbed when administered orally and its peak plasma concentrations are reached after two hours. It distributes widely (spreads readily through tissues, appearing in semen, synovial fluid, and fetal tissue) and is excreted in the urine, mostly in unchanged form, with a terminal elimination half-life of approximately 2 hours.

5.3 Preclinical safety data

The median (50) oral and intravenous lethal dose of aminocaproic acid was 3 and 12 g/kg in mice and 3.2 and 16.4 g/kg in rats, respectively. An intravenous dose of 2.3 g/kg was fatal in dogs. Following intravenous administration, tonic-clonic seizures have been observed in dogs and mice.

Aminocaproic acid has been observed to enhance teratogenic effects in rats.

Carcinogenesis, mutagenesis and fertility disorders: No long-term studies in animals have been conducted to evaluate the carcinogenic or mutagenic potential of aminocaproic acid. Administration of a dose equivalent to the maximum human therapeutic dose in the diet of rats caused fertility disturbances in both sexes.

6. PHARMACEUTICAL INFORMATION

6.1 List of excipients

Sodium hydroxide (for pH adjustment).
Water for injections.

6.2 Incompatibilities

EPSICAPROM 25 should not be used with levulose solutions, penicillin-containing solutions or with blood.

Aminocaproic acid is incompatible with fructose by infusion.

6.3 Shelf life 5 years.

6.4 Special precautions for storage Store

at a temperature below 25ºC.

6.5 Nature and contents of the container

Each pack contains 6 amber type I glass ampoules of 10 ml packed in a plastic tray.

6.6 Special precautions for disposal and handling There

are no special requirements.
Unused products or waste should be disposed of in accordance with the
Local requirements

7. MARKETING AUTHORISATION HOLDER

BIAL - Aristegui, Produtos Farmacêuticos, S.A.
À Avenida da Siderurgia Nacional
4745-457 S. Mamede do Coronado
Portugal

8. MARKETING AUTHORISATION NUMBER(S)

Registration number: 9108803 – 6 units, solution for infusion, 2500 mg/10 ml, amber type I glass ampoules.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF MARKETING AUTHORISATION

Date of first authorization: 29 September 1964 Date of last renewal: 15 November 2002

10. DATE OF REVISION OF THE TEXT