VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Haemorrhage and fibrinolysis

Haemorrhage (profuse bleeding from ruptured blood vessels) is a common complication of surgical procedures and traumatic injury. According to a global study of the burden of disease, 30-40% of trauma-related death is attributable to haemorrhage **[Grottke, 2007].** Fibrinolysis is a condition in which the body's natural ability to dissolve blood clots is enhanced. This condition is present in 2-8% of all trauma patients, resulting in an increased risk of haemorrhage growth and higher mortality **[Wikkels, 2011; Perel, 2012].**

VI.2.2 Summary of treatment benefits

Since Tranexamic acid 100 mg/ml, solution for injection is a generic medicinal product, clinical studies were not conducted for the evaluation of effective and safe use . The available medical literature is considered to be sufficient to evaluate the safety of Tranexamic acid in the proposed therapeutic indications.

VI.2.3 Unknowns relating to treatment benefits

Tranexamic acid passes into breast milk. Hence, lactation is discouraged. However, if Tranexamic acid is required by a mother, medical supervision and follow-up of the breastfed infant is recommended.

There is insufficient clinical data on the use of Tranexamic acid in pregnant women. As a result, although studies in animals do not indicate teratogenic effects (fetal developmental abnormalities), as precaution for use, tranexamic acid is not recommended during the first trimester of pregnancy. Tranexamic acid should only be used throughout pregnancy if the expected benefits outweigh the risks.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Arterial and venous thrombosis (abnormal blood clotting in arteries and veins).	The use of tranexamic acid increases the risk of abnormal blood clotting. There is a theoretical risk of increased blood clot	Yes, tranexamic acid should not be used in patients with acute venous or arterial blood clots. Risk factors for blood clotting disorders should be

Risk	What is known	Preventability
	formation with oestrogens (e.g. the contraceptive pill). Tranexamic acid prevents severe bleeding by inhibiting the fibrinolytic (blood clot dissolving) properties of plasmin. The antifibrinolytic action of the tranexamic acid (preventing the dissolution of blood clots) may be reduced when taken with thrombolytic (blood clot dissolving) drugs. The use of tranexamic acid can also lead to retinal vein thrombosis (retinal veins blocked by a blood clot), which causes visual disturbances.	considered before using tranexamic acid. In patients with a history of blood clotting disorders, or an increased incidence of blood clotting disorders in their family history, tranexamic acid solution for injection should only be used if there is a strong medical benefit after consultation with a physician experienced in blood disorders and under strict medical supervision. Tranexamic acid should be administered with care in patients receiving oral contraceptives. Yes, tranexamic acid should not be used in patients with bleeding disorders following consumption coagulopathy (the activation of blood clotting mechanisms leading to the formation of small blood clots inside blood vessels), except in those with activation of the fibrinolytic system with short-term severe bleeding.
Use in patients with severe renal impairment (kidney damage).	There is a risk of drug accumulation in patients with severe kidney damage.	Yes, tranexamic acid should not be used in patients with severe kidney damage.
Use in patients with disseminated intravascular coagulation (a blood clotting disorder leading to the	The use of tranexamic acid may alter various elements of blood composition or state in patients with	Yes, the use of tranexamic acid in patients with disseminated intravascular coagulation must be

Risk	What is known	Preventability
formation of small blood clots inside blood vessels).	underlying blood clotting disorders.	restricted to those with predominant activation of the fibrinolytic system with acute severe bleeding. In acute cases, a single dose of 1g tranexamic acid is frequently sufficient to control bleeding. The use of tranexamic acid in patients with disseminated intravascular coagulation should be considered only when appropriate medical facilities and expertise are available.
Haematuria (the presence of blood in urine).	In case of the presence of blood in the urine from the upper urinary tract, there is a risk for urethral obstruction.	Yes, patients are warned of this adverse event.
Visual disturbances	Retinal lesions have been described at in animals, and have demonstrated to be dose-related. At lower doses, some of them appear to be reversible. No retinal changes have been reported or noted in eye examinations in patients treated with tranexamic acid for weeks to months in clinical trials.	In case of long-term treatment, an ophthalmological examination, including visual acuity, color vision, eye-ground and visual fields, is advised, before commencing and at regular intervals during the course of treatment. The treatment should be stopped if changes in examination results are found.
Concomitant use with anticoagulants	In case of concomitant use of anticoagulants, there is an increased risk of thrombosis	Concomitant treatment with anticoagulants should be performed under close

Risk	What is known	Preventability
	(formation of a blood clot inside a blood vessel)	supervision of a physician experienced in the field.
Use during lactation	Tranexamic acid is excreted in human milk (even if in small quantity).	Lactation is discouraged. If tranexamic acid is required by a mother, medical supervision and follow-up of the breastfed infant is recommended.
Use in pregnancy	There is insufficient clinical data on the use of tranexamic acid in pregnant women. As a result, although studies in animals do not indicate teratogenic effects (fetal developmental abnormalities), as precaution for use, tranexamic acid is not recommended during the first trimester of pregnancy. Limited clinical data of the use of tranexamic acid during the second and third trimesters did not identify a harmful effect for the fetus.	Tranexamic acid should only be used throughout pregnancy if the expected benefit justifies the risk.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Seizures (convulsions and proconvulsive behaviours following an episode of abnormal electrical activity in the brain)	Misuse and high dose of tranexamic acid can induce convulsive seizures. The frequency of this phenomenon is unknown, but it appears to be dose-related.
Malaise with hypotension with or without loss of consciousness	Hypotension has been observed when the intravenous injection is too rapid. The frequency of this risk is unknown.
Anaphylaxia (severe allergic reaction to the injection of a drug, resulting from a previous contact)	Hypersensitivity reactions including anaphylaxis have been reported in the literature. The frequency of this risk is unknown.

VI.2.5 Summary of risk minimization measures by safety concern

Summary of Product Characteristics (SmPC) of tranexamic acid provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). All these risk minimization measures are given in SmPC and PL of tranexamic acid.

This medicine has no additional risk minimization measures.

VI.2.6 Planned post authorisation development plan

No post authorisation study is planned for this product.

VI.2.7 Summary of changes to the Risk Management Plan over time

This section is not applicable as this is version 01 of RMP.