Part VI: Summary of the risk management plan by product

VI.1 Elements for summary tables in the EPAR

VI.1.1 Summary table of Safety concerns

Important Identified Risk:	• Visual disturbance including visual impairment, vision blurred, impaired colour vision • Risk of Thromboembolic events such as deep vein thrombosis (DVT), pulmonary embolism and cerebral thrombosis • Convulsions • Disseminated Intravascular Coagulation (DIC)
Important Potential Risk:	• Renal insufficiency • Drug administration error (administering via other route of administration) • Haematuria
Missing Information:	• Use during first trimester of pregnancy • Effect on fertility • Use in children undergoing cardiac surgery

VI.1.2 Table of on-going and planned studies in the Post-authorisation Pharmacovigilance Development Plan

Not applicable.

VI.1.3 Summary of Post authorisation efficacy development plan

Not applicable.

VI.1.4 Summary table of risk minimisation measures

Safety concern	Routine risk minimisation measures	Additional risk minimisation measures
Important identified risk: Visual disturbance including visual impairment, vision blurred, impaired colour vision	Section 4.4 and 4.8 of Tranexamic acid proposed SmPC and corresponding sections of PIL have information on this safety concern. Other routine risk minimisation measures including the prescription only status of the product.	None proposed
Important identified risk: Risk of thromboembolic events such as deep vein thrombosis (DVT), pulmonary embolism and cerebral thrombosis	Section 4.3, 4.4, 4.5 and 4.8 of Tranexamic acid proposed SmPC and corresponding sections of PIL have information on this safety concern. Other routine risk minimisation measures including the prescription only status of the product.	None proposed.
Important identified risk: Convulsions	Section 4.3, 4.4, 4.8 and 4.9 of Tranexamic acid proposed SmPC and corresponding sections of PIL have information on this safety concern. Other routine risk minimisation measures including the prescription only status of the product.	None proposed.

Safety concern	**Routine risk minimisation measures**	**Additional risk minimisation measures**
Important identified risk: Disseminated Intravascular Coagulation (DIC)	Section 4.3 and 4.4 of Tranexamic acid proposed SmPC and corresponding sections of PIL have information on this safety concern. Other routine risk minimisation measures including the prescription only status of the product.	None proposed.
Important potential risk: Renal insufficiency	Section 4.2 and 4.3 of Tranexamic acid proposed SmPC and corresponding sections of PIL have information on this safety concern. Other routine risk minimisation measures including the prescription only status of the product.	None proposed.
Important potential risk: Drug administration error (administering via other route of administration)	Section 4.4 of tranexamic acid proposed SmPC and corresponding sections of PIL have information on this safety concern. Other routine risk minimisation measures including the prescription only status of the product.	None proposed.
Important potential risk: Haematuria	Section 4.3, 4.4 and 5.3 of tranexamic acid proposed SmPC and corresponding sections of PIL have information on this safety	None proposed.

Safety concern	**Routine risk minimisation measures**	**Additional risk minimisation measures**
	concern. Other routine risk minimisation measures including the prescription only status of the product.	
Missing information: Use during first trimester of pregnancy	Section 4.6 and 5.2 of tranexamic acid proposed SmPC and corresponding sections of PIL have information on this safety concern. Other routine risk minimisation measures including the prescription only status of the product.	None proposed.
Missing information: Effect on fertility	Section 4.6 and 5.3 of tranexamic acid proposed SmPC has information on this safety concern. Other routine risk minimisation measures including the prescription only status of the product.	None proposed.
Missing information: Use in children undergoing cardiac surgery	Section 4.2 of tranexamic acid proposed SmPC has information on this safety concern. Other routine risk minimisation measures including the prescription only status of the product.	None proposed

VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Bleeding is the name commonly used to describe blood loss. It can refer to blood loss inside the body (internal bleeding) or blood loss on surface of the body (external bleeding). Blood loss can occur in almost any area of the body. Typically, internal bleeding occurs when blood leaks out through damage to a blood vessel or organ. External bleeding occurs either when blood exits through a break in the skin, or when blood exits through a natural opening in the body, such as the mouth, vagina, or rectum. Bleeding can occur either due to traumatic injury or underlying medical conditions. Some medicines like blood-thinning medicines can also cause bleeding. Studies indicated that 5% to 32% of women with menorrhagia have bleeding disorders. The incidence of gastrointestinal bleeding is more common in male than females. Around 3% patients have bleeding after tonsillectomy (surgical procedure to remove tonsils).

VI.2.2 Summary of treatment benefits

Tranexamic acid belongs to a group of medicines called antifibrinolytics. Tranexamic acid works by stopping the clots from breaking down and so reduces the unwanted bleeding. It is used to control bleeding in a number of different conditions. It reduces unwanted or heavy bleeding following some surgery (such as surgery on the prostate, bladder, or cervix), nosebleeds, heavy periods (menorrhagia), bleeding inside the eye and tooth extraction in people who bleed more easily than normal, and in a condition called hereditary angio-oedema (genetic blood disorder showing frequent attacks of swelling including face, extremities, genitals, gastrointestinal tract and upper airways). Literature review of 12 efficacy studies in paediatric cardiac surgery shows that tranexamic acid reduced blood loss and blood product requirement in paediatric cardiac surgery under cardiopulmonary bypass (CPB) where there is a high risk of haemorrhage.

VI.2.3 Unknowns relating to treatment benefits

The efficacy of tranexamic acid in children undergoing cardiac surgery has not fully established.

VI.2.4 Summary of safety concerns

Important identified risks:

Risk	What is known	Preventability
Visual disturbance including visual impairment, vision blurred, impaired colour vision	Patient may experience possible visual disturbances including visual impairment, vision blurred and impaired colour vision. Patient may experience vision disturbances including impaired colour vision with unknown frequency	Treatment should be discontinued on problems related to vision disturbance. If patient is on continuous long term use, regular ophthalmologic examinations (eye examinations including visual acuity, colour vision, fundus, visual field etc.) are needed
Risk of events caused due to blocked blood vessels such as blood clot in a leg or lung or brain (thromboembolic events such as deep vein thrombosis	Patient may experience rare but serious side effect like blood clot. Symptoms of blood clot may include swelling or pain in your legs or chest, headache, weakness of the face and limbs on one side of body	Do not take this injection if you are suffering from any disease or conditions leading to blood clot. Tell your doctor if you have a risk of having blood clot. Please tell your doctor or pharmacist if you are taking or have recently taken any medicine

Risk	What is known	Preventability
(DVT), pulmonary embolism and cerebral thrombosis)		that help blood to clot (antifibrinolytic medicines) or prevent blood clotting (thrombolytics medicines)
Fits (Convulsions)	Patient may experience side effect on nervous system like fits (convulsions) with unknown frequency. Fits (convulsions) tend to occur at higher frequency with increasing dose.	Do not take this injection if you have history of fits (convulsions). Doctor must use minimal possible dose to avoid fits (convulsions).
Excessive clotting or bleeding throughout your body (Disseminated Intravascular Coagulation (DIC))	Patient may experience side effect like blood clot with unknown frequency.	Do not take this injections if you have a condition called 'consumption coagulopathy' where blood in whole body start to clot. Tell your doctor if you have excessive clotting or bleeding throughout your body.

Important potential risks

Risk	What is known
Kidney disease (Renal insufficiency)	If you have kidney problem, your doctor may reduced medicine dose according to a test performed on your blood

Risk	What is known
	(serum creatinine level).
Drug administration error (administering via other route of administration)	Intrathecal and intraventricular injection and intracerebral application are not recommended due to the risk of cerebral oedema and convulsions. Patient may experience not known (frequency cannot be estimated from available data) side effect like malaise with hypotension (low blood pressure) if injection is given too quickly. Epileptic activity has been observed in animals with intrathecal administration of tranexamic acid.
Blood in urine (Haematuria)	Blood in urine may lead to urinary tract obstruction.

Missing information

Risk	What is known
Use during first trimester of pregnancy	There is insufficient clinical data on the use of tranexamic acid in pregnant women. Animal studies do not indicate any harmful effect of foetus, as precaution for use, tranexamic acid is not recommended during first trimester of pregnancy. Limited data available for tranexamic acid use in second and third trimester pregnancy. Tranexamic acid should be used throughout pregnancy only if the expected benefit justifies the potential risk.
Effect on fertility	There are no clinical data on the effects of tranexamic acid on

Risk	What is known
	fertility.
Use in children undergoing cardiac surgery	Tranexamic acid in children over one year of age reduced blood loss and reduced blood product requirements in children undergoing cardiac surgery. However, efficacy, posology and safety of tranexamic acid in children undergoing cardiac surgery have not been fully established. Currently available data are limited.

VI.2.5 Summary of additional risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which 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). The measures in these documents are known as routine risk minimisation measures.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

No studies planned.

VI.2.7 Summary of changes to the risk management plan over time

Version	Date	Safety Concerns	Comments
Version 3.0	13 October 2016	No change in safety concerns.	RMP has been updated with revised SmPC and PIL.

Version 2.0	31 March 2016	No change in safety concerns	RMP has been updated with RMS Day 70 Draft Assessment Report, dated 03 December 2015. SmPC and PIL updated