VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Hyperfibrinolysis
Fibrinolysis is a normal body process that prevents blood clots from growing and causing problems. Fibrinolysis is an essential factor in the process of stoppage of bleeding.
Markedly increased fibrinolysis is called hyperfibrinolysis and if uncontrolled, can result in catastrophic bleeding. Hyperfibrinolysis can be inherited or acquired as a result of liver disease or severe trauma. The precise incidence of hyperfibrinolysis remains unclear due to differences in diagnostic techniques and a lack of consensus on definitions.

Hereditary angioedema
Hereditary angioedema is a hereditary blood disorder that causes episodic attacks of swelling that may affect the face, extremities, genitals, gastrointestinal tract and upper airways. The most serious form affects the upper airways and involves swelling of the larynx and pharynx. Trauma and stress are the most commonly reported triggers but in many cases however, there is no obvious trigger (Davis 2008). The exact prevalence of hereditary angioedema is unknown, however it has been estimated that the condition affects between 1:50,000 and 1:10,000 people. Although no clear bias for sex or race has been observed for hereditary angioedema, it appears to affect women more severely due to fluctuating estrogen levels (Davis 2008, Eidelman 2010).

VI.2.2 Summary of treatment benefits

Tranexamic acid is a synthetic analog of the aminoacid lysine. It is used to treat or prevent excessive blood loss during surgery and in various medical conditions or disorders (helping hemostasis). It is also used in the prophylaxis of hereditary angioedema (Ng, Jerath et al. 2015).

Antifibrinolytics are used to control haemorrhage that is considered to be caused by excessive fibrinolysis. Antifibrinolytic therapy may also be indicated in the prevention of rebleeding in some haemorrhagic conditions. In haemorrhage caused by a congenital or acquired deficiency of blood coagulation factors, haemostatic drugs have a secondary role and may be useful in reducing requirements of factor concentrates (Davis 2008).

Tranexamic acid appears to be well tolerated, having low acute toxicity. Clear benefits arise from the mortality-morbidity perspective, regarding its use in reduction of perioperative bleeding and transfusion requirements, in both cardiac and non-cardiac surgery. Its efficacy and safety profile is also supported in orthopedic surgery, menorrhagia and in trauma. Tranexamic acid has been suggested to control bleeding also in many other conditions including haemorrhage after surgical or other procedures including prostatectomy, bladder surgery and cervical conisation (Nilsson 1980, Ng, Jerath et al. 2015).

VI.2.3 Unknowns relating to treatment benefits

There are no unknowns relating to treatment benefits that the MAH is aware of.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Thrombotic and embolic events inc., pulmonary embolism and stroke	Tranexamic acid is contra-indicated for patients with active thromboembolic diseases, with a previous thromboembolic event or with a family history of thromboembolic disease.	Patients with high risk of thrombosis must not take Tranexamic acid or should only use it if there is a strong medical indication and under close medical supervision.
Convulsions	Cases of convulsions associated with treatment with tranexamic acid have been reported. The majority of cases have been reported with the use of intravenous injection of tranexamic acid in high doses.	Tranexamic acid is contra-indicated in patients who have previously experienced convulsions. Reports and other safety information should be closely monitored.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Drug-drug interactions	No significant interactions have been observed with tranexamic acid. Simultaneous treatment with anticoagulants should therefore be undertaken under strict supervision.

Missing information

Risk	What is known
Use in adolescents with menorrhagia below 15 years (heavy menstrual bleeding)	No clinical data are available with adolescents with menorrhagia below 15 years.
Use during pregnancy and lactation	Non-clinical studies are insufficient to assess safety with respect to reproduction, embryonal/foetal development, course of gestation and peri-/postnatal development and no clinical studies with tranexamic acid have been conducted on pregnant women. Therefore it is not recommended in pregnancy unless absolutely necessary. No clinical studies have been conducted on the excretion

Risk	What is known
	tranexamic acid in breast milk. Therefore it is not recommended in lactation unless absolutely necessary.

VI.2.5 Summary of 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.

The Summary of Product Characteristics and the Package leaflet for Tranexamic acid can be found in the Tranexamic acid's EPAR page

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

Not applicable.

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

Not applicable.