STRAGEN NORDIC A/S
Helsingørsgade 8 C
3400 Hillerød
DANMARK
tel +45 48 10 88 10
info@stragen.dk
www.stragen.dk
CVR nr. 26717825

RMP section VI.2 Elements for Public Summary

Product: Tranexamic acid Stragen 100 mg/ml solution for injection

RMP: Version 4.0

DLP: 01-09-2012

MAH: Stragen Nordic A/S

VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Bleeding or hemorrhaging is the loss of blood or blood escaping from the circulatory system. Bleeding can occur internally, where blood leaks from blood vessels inside the body, or externally, either through a natural opening such as the mouth, nose, ear, urethra, vagina or anus, or through a break in the skin. Traumatic bleeding is caused by some type of injury. Non-traumatic bleeding denotes hemorrhage as a result of an underlying medical condition (i.e. due to general or local fibrinolysis).

Overview on epidemiology statistics from UK regarding for purpura and other haemorrhagic conditions (Hospital Episode Statistics, Department of Health, England, 2002-03)

0.097% (12,320) of hospital consultant episodes were for purpura and other haemorrhagic conditions

94% of hospital consultant episodes required hospital admission

47% of hospital consultant episodes were for men

53% of hospital consultant episodes were for women

40% of hospital consultant episodes required emergency hospital admission

3.6 days was the mean and 1 days was the median length of stay in hospitals

40 was the mean age of patients hospitalized for purpura and other haemorrhagic conditions

38% of hospital consultant episodes occurred in 15-59 year olds

14% of hospital consultant episodes occurred in people over 75

48% of hospital consultant episodes were single day episodes

VI.2.2 Summary of treatment benefits

Tranexamic acid is indicated for use in the prevention and treatment of haemorrhages due to general or local fibrinolysis in adults and children from one year.

Specific indications include bleeding caused by general or local fibrinolysis such as menorrhagia and metrorrhagia, gastrointestinal bleeding, haemorrhagic urinary disorders, further to prostate surgery or surgical procedures affecting the urinary tract, ear nose throat surgery (adenoidectomy, tonsillectomy, dental extractions), gynecological surgery or disorders of obstetric origin, thoracic and abdominal surgery and other major surgical intervention such as cardiovascular surgery, and management of haemorrhages due to the administration of a fibrinolytic agent.

There are no general gold standards for the treatment of haemorrhages due to general or local fibrinolysis. Guidelines exist for specific conditions like stroke, intracerebral bleeding or gastrointestinal bleeding.

VI.2.3 Unknowns relating to treatment benefits

Experience is limited and whether efficacy is expected to be different in conditions like acute venous or arterial thrombosis, fibrinolytic conditions following consumption coagulopathy, severe renal impairment, patient with a history of convulsions and women of childbearing potential. There is no

evidence to suggest that results would be any different in relation to gender, age, and ethnic origin within the given indication.

In the current medical discussion the benefit in gynecology and traumatic patients is discussed and under investigation.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Blood clotting (Arterial and venous thrombosis)	There is a risk of increased blood clot formation in patients with a history of thromboembolic diseases and/or female patients taking estrogens containing drugs.	Consider risk factors, use of alternative medication or medical devices
Cramps, jerk reaction (Convulsion)	Cases of convulsions have been reported in association with tranexamic acid treatment. In coronary artery bypass graft (CABG) surgery, most of these cases were reported following intravenous (i.v.) injection of tranexamic acid in high doses. With the use of the recommended lower doses of TXA, the incidence of post-operative seizures was the same as that in untreated patients.	Do not use intrathecal and intraventricular injection, intracerebral application. Avoid risk by use of appropriate route of administration. Do not use product in conditions of history of convulsion.
Changes in colour seeing (Visual disturbances)	Attention should be paid to possible visual disturbances including visual impairment, vision blurred, impaired colour vision and if necessary the treatment should be discontinued. With continuous long-term use of TXA solution for injection, regular ophthalmologic examinations (eye examinations including visual acuity, colour vision, fundus, visual field etc.) are indicated. With pathological ophthalmic changes, particularly with diseases of the retina, the physician must decide after consulting a specialist on the necessity for the long-term use of Tranexamic acid solution for injection in each individual case.	Attention should be given on chances in visual capacity and a physician has to be contact in case of any observation. In long-term use, regular ophthalmologic examinations are indicated
Rash to allergic shock	Allergic type of reactions can be	Do not use product if allergic

Risk	What is known	Preventability
(anaphylaxis/severe hypersensitivity reactions)	induced in patient sensible to tranexamic acid or one of the excipients of the product	conditions are known

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Severe changed blood function (Risk of accumulation/ Overdosage in severe renal impairment)	In patient with renal impairment, tranexamic acid may accumulate in the blood inducing severe changes of blood function
Risk of prolonged shock in patients with Disseminated intravascular coagulation	Tranexamic acid is acting on the coagulation pathway. Tranexamic acid exerts an anti haemorrhagic activity by inhibiting the fibrinolytic properties of plasmin. A complex involving tranexamic acid, plasminogen is constituted; the tranexamic acid being linked to plasminogen when transformed into plasmin. The activity of the tranexamic acid-plasmin complex on the activity on fibrin is lower than the activity of free plasmin alone. In vitro studies showed that high tranexamic dosages decreased the activity of complement
Haematuria	In case of haematuria from the upper urinary tract, there is a risk for urethral obstruction.
Thromboembolic events	Tranexamic acid is acting on the coagulation pathway. Tranexamic acid exerts an anti haemorrhagic activity by inhibiting the fibrinolytic properties of plasmin. A complex involving tranexamic acid, plasminogen is constituted; the tranexamic acid being linked to plasminogen when transformed into plasmin. The activity of the tranexamic acid-plasmin complex on the activity on fibrin is lower than the activity of free plasmin alone. In vitro studies showed that high tranexamic dosages decreased the activity of complement
Off-label use (intrathecal, intraventricular or intracerebral application)	Tranexamic acid is not intended to use for intrathecal, intraventricular or intracerebral application, because of risk of cerebral oedema and convulsions.

Missing information

Risk	What is known
A transfer of tranexamic acid on the fetus cannot be excluded, that might be harmful for the fetus.	Insufficient clinical data on the use of tranexamic acid in pregnant women
Unexpected change in the blood clotting system might occur in the combined used with other drug acting on the blood coagulation system.	No interaction studies have been performed. There is a theoretical risk for interaction with estrogens containing contraceptives.

VI.2.5 Summary of risk minimisation measures by safety concern

The Summary of Product Characteristics (SmPC) provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimizing 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 post authorisation developments are planned.

Studies which are a condition of the marketing authorisation

Not applicable.

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

Not applicable.