Tranexamic acid

Section: 10. Medicines affecting the blood > 10.2. Medicines affecting coagulation

ATC codes: B02AA02

Indication	Haemorrhage, not elsewhere classified ICD11 code: MG27
INN	Tranexamic acid
Medicine type	Chemical agent
List type	Core
Formulations	**Parenteral > General injections > IV:** 100 mg per mL in 10 mL ampoule
EML status history	First added in 2011 (TRS 965)
Sex	All
Age	Adolescents and adults
Therapeutic alternatives	The recommendation is for this specific medicine
Patent information	Patents have expired in most jurisdictions Read more about patents.
Wikipedia	Tranexamic acid
DrugBank	Tranexamic acid

Summary of evidence and Expert Committee recommendations

Tranexamic acid injection for the treatment of adult patients with trauma and significant risk of ongoing haemorrhage was added to the core list of the EML. On the basis of the results of a very large trial of the use of tranexamic acid specifically for trauma patients — including those who have been in road traffic accidents, the Committee concluded that there is sufficient evidence to support the proposal that listing tranexamic acid may contribute to a reduction in this cause of death. In 2009, the Committee considered an application for the addition of tranexamic acid to the EML, but rejected it because the major indication proposed was for use to reduce blood loss in cardiac surgery. This indication was considered to be of uncertain public health relevance. In 2010, the report of a large RCT (1) comparing tranexamic acid to placebo in the treatment of adult patients with trauma and at significant risk of ongoing haemorrhage was published. One of the authors of the trial, Professor Ian Roberts, has resubmitted the application based on the results of the study. The revised application now targets the use of tranexamic acid for trauma patients. As noted in the application, road traffic accidents are the ninth leading cause of death globally. It is proposed that listing tranexamic acid will contribute to a reduction in this cause of death, as well as reduce the need for blood transfusion for the management of trauma patients. Many letters of support for the inclusion of tranexamic acid have been submitted, including many from trial contributors. The WHO Department of Violence and Injury Prevention supported the inclusion of tranexamic acid. The Committee noted that intravenous tranexamic acid is licensed in a number of countries for short-term use as prophylaxis and treatment in surgery; for the treatment of haemorrhagic complications associated with thrombolytic therapy; disseminated intravascular coagulation; and hereditary angioneurotic oedema, but it has not yet been approved for use in trauma. As noted above, the main additional evidence in this application is the CRASH-2 trial. This large (n=20211) double blind multi centre RCT (40 countries) is described in detail in the application. The results for the primary outcome, in-hospital mortality within four weeks of injury were that patients treated with tranexamic acid

had a reduced risk of death (all-cause mortality) (RR 0.91; 95% CI 0.85–0.97) as well as reduced risk of death due to bleeding (RR 0.85; 95% CI 0.76–0.96). Vascular occlusive events were not different between the two groups. There was no difference in transfusion requirements between the two groups, either in terms of number of patients receiving transfusions or the amount of blood products actually used. The Committee considered that the quality of the trial is high. The Committee noted that it is not clear from the trial what degree of specialist monitoring is required for safe use of tranexamic acid. European trauma guidelines recommend monitoring of fibrinolysis in all trauma patients to guide treatment. The Committee noted that the use of tranexamic acid should not replace appropriate provision of blood transfusions. There are no data to establish efficacy and safety in children. The Committee evaluated the information provided about comparative cost and cost–effectiveness. The application provides a sample of prices for tranexamic acid, ranging from US$ 2.57 per gram to US$ 22.83 per gram. The application presents the summary of a (yet unpublished) cost–effectiveness analysis based on the trial, adjusted for estimated survival gains in different settings and the age distribution of trauma patients in each setting. The assumptions are not provided in sufficient detail to independently verify them. Overall, the Committee noted that use of tranexamic acid is likely to be cost effective in settings where the baseline mortality from trauma is at least that in the trial (15%) and where there are facilities for administration of tranexamic acid early following injury, especially if the product can be purchased at prices lower than US$ 10/g. If the baseline risk of mortality is lower, with a resultant NNT between 100 and 200, it is important that the price paid for the product is kept as low as possible to ensure cost–effectiveness and affordability. The Committee therefore recommended addition to the Core List. The Committee recommended that an evidence summary be provided on the web site including the cost–effectiveness data to allow countries to make procurement decisions considering best available prices for products of adequate quality. References: 1. CRASH-2 trial collaborators. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised placebo controlled trial. The Lancet, 2010, 376(9734):23–32.

