Tranexamic acid
Newborn Use Only

2024

Alert	Dosing regimen for neonates undergoing cardiopulmonary bypass is beyond the scope of this guideline. Clinical experience in patients < 2 years old is limited and tranexamic acid should only be used if the benefit outweighs the risk.
Indication	Reduction of bleeding during significant haemorrhage (e.g. subgaleal, pulmonary, gastrointestinal haemorrhage or surgery)
Action	Synthetic lysine-analogue antifibrinolytic that competitively inhibits the activation of plasminogen to plasmin. At high concentrations it non-competitively blocks plasmin, thus inhibits the dissolution and degradation of fibrin clots by plasmin.[1] Inhibits plasmin-induced platelet activation during extracorporeal circulation, such as cardiopulmonary bypass (CPB) used in cardiac surgery.[1]
Drug Type	Antifibrinolytic and haemostatic agent.
Trade Name	Zamic solution for injection Tranexamic-AFT solution for injection Tranexamic Acid LumaCina solution for injection Tranexamic Acid LU solution for injection Tranexamic Acid Juno solution for injection
Presentation	500mg/5mL vial Protect from light
Dose	Loading dose[2] 10-15 mg/kg/dose, followed by Maintenance infusion (optional)[2] If surgical bleeding: Can consider ongoing infusion of 1-5 mg/kg/hour intraoperatively or until haemostasis achieved. Consider discussion with haematologist. If non-surgical bleeding: Not enough evidence/guidance to support maintenance infusion currently. Consider discussion with haematologist. Dosing regimen for neonates undergoing cardiopulmonary bypass is beyond the scope of this guideline.
Dose adjustment	Therapeutic hypothermia – No information. ECMO – Beyond the scope of this guideline. Refer to evidence section. Hepatic impairment – No dose adjustment Renal impairment – Avoid in severe impairment. Reduce dose in mild to moderate impairment. No specific dose adjustment is available.
Route	IV
Preparation	Prepare loading dose and maintenance infusion separately. **Loading dose:** Draw up 1mL of Tranexamic acid (100mg) and add to 9mL of sodium chloride 0.9% to make a final volume of 10mL with a final concentration of 10mg/mL solution. **Maintenance dose for continuous infusion:** Draw up 5mL of Tranexamic acid (500mg) and add to 45mL of sodium chloride 0.9% to make a final volume of 50mL with a final concentration of 10mg/mL.
Administration	Loading dose: Over 15 minutes
Monitoring	Blood pressure, renal function
Contraindications	Hypersensitivity to tranexamic acid. Active clotting disease Active or history of thrombosis/thromboembolism (e.g. cerebral thrombosis, renal vein thrombosis
Precautions	Renal impairment Upper urinary tract bleeding – ureteral obstruction due to clot formation is a possibility. Disseminated Intravascular Coagulation (DIC) – Extreme caution is necessary in DIC requiring antifibrinolytic therapy

Drug Interactions	Do not administer concomitantly with factor complex concentrates or coagulant concentrates due to increased risk of thrombosis.
Adverse Reactions	Hypotension (with rapid IV injection) Seizures Diarrhea, vomiting Life threatening allergic reactions - Rare Dermatitis Cerebral thrombosis Deep vein thrombosis, retinal artery/vein thrombosis, pulmonary embolism Renal cortical necrosis, ureteral obstruction with clot formation.
Overdose	Overdose data are limited. There is no known antidote for tranexamic acid overdose. For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).
Compatibility	Fluids: Glucose 5%, sodium chloride 0.9%. Others not tested. (3) Y site: Heparin sodium.
Incompatibility	Fluids: No information. Y site[3]: Ampicillin sodium, benzylpenicillin, potassium, piperacillin, piperacillin/tazobactam, ticarcillin/clavulanate. Do not mix with blood products
Stability	Diluted solution is stable for 24 hours at room temperature for continuous infusion.
Storage	Store below 25°C. Do not freeze. Protect from light. Discard any unused product.
Special Comments	
Evidence	**Background** Fibrinolysis plays a major role in coagulopathy in trauma, cardiac surgery and other bleeding conditions. Fibrinolysis is the process wherein the fibrin clot is broken down into its degradation products. Plasmin is the central enzyme of the fibrinolytic system.[4] Antifibrinolytics can be used to reduce blood loss in major surgical procedures as well as non-surgical diseases. TXA is antifibrinolytic. TXA competitively inhibits the activation of plasminogen to plasmin; at high concentrations it non-competitively blocks plasmin, thus TXA inhibits the dissolution and degradation of fibrin clots by plasmin. In addition, TXA inhibits plasmin-induced platelet activation during cardiopulmonary bypass (CPB) used in cardiac surgery. TXA possibly also attenuates the inflammatory response and related hemodynamic instability in patients undergoing CPB.[1,5] **Efficacy** Meta analysis and Cochrane reviews of adult studies found a clear evidence of TXA reducing peri-operative bleeding and transfusion requirements during cardiac and non-cardiac surgeries.[6,7] Prior systematic reviews from paediatric population undergoing cardiac or non-cardiac surgery or paediatric trauma reported variable findings.[8-11] The more recent systematic review by Hovgesen et al, 2021 evaluated efficacy and safety of antifibrinolytic drugs in paediatric surgery and trauma to determine the optimal dosing regimen. They included randomized controlled studies investigating the effect of tranexamic acid (TXA), aprotinin, and epsilon-aminocaproic acid, in terms of reducing blood loss, blood transfusions, reoperations, and rebleeds in paediatric patients aged 0 to 18 years undergoing cardiac surgery, noncardiac surgery, or trauma. Fifty randomized controlled trials (RCTs) were included; 28 RCTs investigated cardiac surgery and 22 investigated noncardiac surgery. No RCTs regarding trauma met the inclusion criteria. All antifibrinolytic drugs reduced postoperative blood loss and transfusions when used in paediatric surgery. The dosing regimen varied between studies, but similar effect sizes were found in terms of reduced blood loss regardless of the cumulative dose used. Few studies found adverse events, and no difference in incidence or type of adverse events was seen between the antifibrinolytic and the placebo group. The review concluded that the use of antifibrinolytics is efficient and safe in children undergoing surgery. The authors proposed TXA as the drug of choice based on its level of evidence and safety profile; they recommended a dosing regimen composed of a loading dose of 10 to 15 mg/kg prior to surgery followed by 1 to 5 mg/kg/hour as continuous infusion throughout surgery.[2] **TXA dosing regimen for cardiac surgery:** Pharmacokinetics and the suggested plasma concentration of TXA required for neonates undergoing cardiac surgery/cardiopulmonary bypass (CBP) are different to non-CBP procedures. A PK study by Wesley et al, 2015 suggested low to high dosing regimens for 0-2 month old infants based on the desired/targeted TXA plasma concentrations from 20 to 150 µg/mL. Low dose regimen proposed by Wesley et al to achieve plasma TXA concentration of 20 µg/mL was a loading dose of

	15 mg/kg, followed by 2.5 mg/kg/hour as maintenance infusion with CPB prime dose of 20 µg per mL of prime volume. Suggested high dose regimen to achieve plasma TXA concentration of 150 µg/mL was a loading dose of 120 mg/kg, followed by 17 mg/kg/hour as maintenance infusion with CPB prime dose of 150 µg per mL of prime volume.[12] However, adult cardiac surgery data suggest an association between high TXA concentration and seizures. Gertler et al 2017 suggested a modified regimen for infants less than 12 months of age to prohibit the potential risk of seizures. They suggested a target TXA plasma concentration of 20 µg/mL, that can be achieved with 10 mg/kg loading dose, followed by 10 mg/kg/hr, then a 4 mg/kg bolus into the prime and a reduced infusion of 4 mg/kg/hr after the start of CPB.[13] **ANMF consensus:** While definitive evidence is not available in neonates, dosing regimen suggested by Hovgesen et al[2] can be extrapolated to neonatal population. Dosing regimen for infants undergoing cardiac surgery is beyond the scope of this guideline. TXA for other neonatal conditions such as subgaleal haemorrhage (SGH) and pulmonary haemorrhage has been limited to case reports. Thomas et al reported a neonate with severe SGH treated with recombinant activated factor VII and TXA. TXA was initially given at 10 mg/kg/dose 3 times a day and reduced to 10 mg/kg/day on day 3 and was continued for 10 days.[14] TXA was used in a 5-day old neonate with neonatal encephalopathy and severe pulmonary haemorrhage. The dosing regimen was ill defined in this case report.[15] **Pharmacokinetics** Bioavailability after IV is 100%. Time to peak serum concentration after IV dose is 5 minutes. Mostly excreted unchanged in urine. **Safety** High plasma TXA concentration has been associated with seizures in adults.[16-18]
Practice points	
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