



IMPORTANT MEDICINE SAFETY INFORMATION

30 May 2024

INTRAVENOUS TRANEXAMIC ACID – RISK OF INTRATHECAL ADMINISTRATION ERROR

Dear Healthcare Professional,

In collaboration with the South African Health Products Regulatory Authority (SAHPRA), the companies listed below would like to draw your attention to the important safety information regarding the risk of error in the administration of intravenous (IV) tranexamic acid.

Background on safety concerns

- Tranexamic acid is often used to reduce bleeding in obstetric, orthopaedic, surgical, and trauma patients. It is imperative that healthcare professionals are aware of the potential for errors with harmful consequences if tranexamic acid is administered incorrectly.⁹
- There have been national and international reports of IV tranexamic acid being mistaken for the spinal anaesthetic (bupivacaine) used for caesarean section and other procedures; resulting in inadvertent intrathecal administration.
- Tranexamic acid administered intrathecally is neurotoxic, causing severe neurological sequelae. Neurological toxicity includes refractory seizures, with a risk of 50 % mortality.^{1,2,3,4,9} Patients who have survived often experience long-term neurological adverse effects.⁹
- The World Health Organisation (WHO) has drawn attention to a review of the available data, which showed 21 cases on inadvertent intrathecal injection of tranexamic acid since 1988, of which 20 were life-threatening and 10 were fatal. Of these cases, 16 were reported between 2009 and 2018.⁷
- According to a United States Food and Drug Administration (U.S. FDA) safety alert, intrathecal administration of tranexamic acid injection may result in serious life-threatening injuries, including seizures, cardiac arrhythmias, paraplegia, permanent neurological injury, and death.⁹

Tranexamic acid

- Tranexamic acid is an antifibrinolytic medication and is used in the management of haemorrhagic conditions.
- The injectable formulation is intended only for IV administration.

Bupivacaine

- Bupivacaine is used for the induction of spinal anaesthesia. It is a solution for injection and is injected into the sub-arachnoid space.

An additional warning stating “HIGH ALERT” and “For IV use only”, will be added to the product labels of tranexamic acid medicines listed below:

Advice to Healthcare professionals

- If acute signs and symptoms (myoclonus, status epilepticus, cardiac arrhythmias, paraplegia, neurological symptoms etc.) suggestive of accidental intrathecal injection of the incorrect medicine appear, appropriate treatment, in discussion with a specialist, must be administered.⁹
- Tranexamic acid IV injection, bupivacaine injection and other medication used in the perioperative setting may have similar packaging appearances that may contribute to administration and medication errors. It is therefore important to consider the following:
 - storing of products with similar packaging appearance in different locations and avoiding close proximity,
 - double-checking medication labels before administration.^{5,6,8,9}
- Healthcare professionals are urged to report any adverse drug reactions (ADRs) or product quality issues associated with administration errors of tranexamic acid products listed below to SAHPRA via this eReporting link <https://primaryreporting.who-umc.org/ZA> available on the SAHPRA website (www.sahpra.org.za).
- Alternatively, an ADR reporting form accessible via the SAHPRA website at <https://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/> can be completed and sent to adr@sahpra.org.za.
- Additionally, reporting can be done via the Med Safety App. The App can be downloaded into a smart mobile phone through Google Play or App Store. For more information on Med Safety App, please visit <https://medsafety.sahpra.org.za/>.
- For more information on ADR reporting of products listed below, please contact the SAHPRA Pharmacovigilance unit at pvqueries@sahpra.org.za or alternatively use the contact details indicated below:

Details for the respective companies indicated in the table below:

Company	Product name	Active ingredient	Registration Number	Contact details
Acino Pharma (Pty) Ltd	Transun IV	Tranexamic acid 500 mg/5 ml	49/8.1/0445	Shaistha Sing Responsible Pharmacist Shaistha.Sing@acino.swiss Tanya Huysamen Pharmacovigilance Manager/QPPV DrugSafety_ZA@acino.swiss
Arya Pharma Pty Ltd	Arytrans IV	Each 5 ml ampoule contains 500 mg tranexamic acid	48/8.1/0053	Anju Binoop compliance@pharmacygroup.co.za
Aspen Pharmacare	Fibtin Injection	Tranexamic acid 500 mg / 5 ml	48/8.1/0251	Tel: +27 800 118 088 Fax: +27 11 239 6306 drugsafety@aspenpharma.com
Pharma Dynamics (Pty) Ltd	Klotigo 500 (solution for injection/infusion)	Each 5 mL ampoule contains 500 mg tranexamic acid	52/8.1/0806	Tel: +27 21 707 7000 Petra van Vuuren Pharmacovigilance@pharmadynamics.co.za
	Klotigo 1000 (solution for injection/infusion)	Each 10 mL ampoule contains 500 mg tranexamic acid	52/8.1/0807	
Pharma-Q Holdings (Pty) Ltd	Tranexamic acid PharmaQ injection	Each 10 mL ampoule contains 1000 mg Tranexamic acid	54/8.1/0223	Tel: +27 11 247 1600 pv@pharmaq.co.za Naseera Pickard QPPV / Pharmacovigilance Manager npickard@pharmaq.co.za
Ranbaxy Pharmaceuticals (Pty) Ltd	Cynex 500 mg injection, solution for injection	Each 5 mL ampoule contains 500 mg tranexamic acid	43/8.1/0263	Geeta Ghela Responsible Pharmacist Geeta.Ghela@sunpharma.com Pitchai Pandikumar Pharmacovigilance manager Pitchai.pandikumar@sunpharma.com
Ruby Pharmaceuticals (Pty) Ltd	Immatra	Each 5 mL ampoule contains 500 mg tranexamic acid	55/8.1/0127	adr@rubypharma.co.za

	Rubinx	Each 5 mL ampoule contains 500 mg tranexamic acid	55/8.1/0128	
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Yours faithfully,

Shaistha Sing Responsible Pharmacist Acino Pharma (Pty) Ltd Signature	Anju Binoop Responsible pharmacist Arya Pharma Pty Ltd Signature
Nikola Whelan Responsible Pharmacist Aspen Pharmacare Signature	Celeste Naude Responsible Pharmacist Pharma Dynamics (Pty) Ltd Signature
Fatima Shakoor Responsible Pharmacist Pharma-Q Holdings (Pty) Ltd Signature	Geeta Ghela Responsible Pharmacist Ranbaxy Pharmaceuticals (Pty) Ltd Signature
A.Ghoor Responsible Pharmacist Ruby Pharmaceuticals (Pty) Ltd Signature	

References

1. SAHPRA letter to all applicants: *IV Tranexamic acid – risk of administration error*.
2. *MEDICINE SAFETY ALERT IV Tranexamic acid -Administration error via the intrathecal route (2023)* Org.za. Available at: https://www.sahpra.org.za/wp-content/uploads/2023/12/Urgent-Medicine-Safety-Alert_IV-Tranexamic-acid_21-December-2023.pdf (Accessed: December 28, 2023).
3. Butala, B., Shah, V., Bhosale, G., & Shah, R. (2012). Medication error: Subarachnoid injection of tranexamic acid. *Indian Journal of Anaesthesia*, 56(2), 168. <https://doi.org/10.4103/0019-5049.96335>.
4. Kaabachi, O., Eddhif, M., Rais, K., & Zaabar, M. (2011). Inadvertent intrathecal injection of tranexamic acid. *Saudi Journal of Anaesthesia*, 5(1), 90. <https://doi.org/10.4103/1658-354x.76504>.
5. Patel, S., Robertson, B., & McConachie, I. (2019). Catastrophic drug errors involving tranexamic acid administered during spinal anaesthesia. *Anaesthesia*, 74(7), 904–914. <https://doi.org/10.1111/anae.14662>.
6. Bishop, D. G., Lundgren, A. C., Moran, N. F., Popov, I., & Moodley, J. (2019). Intrathecal tranexamic acid during spinal anaesthesia for caesarean delivery: A lethal drug error. *South African Medical Journal*, 109(11), 841. <https://doi.org/10.7196/samj.2019.v109i11.14242>.
7. *Risk of medication errors with tranexamic acid injection resulting in inadvertent intrathecal injection*. (n.d.). Who.int. Retrieved December 27, 2023, from <https://www.who.int/news/item/16-03-2022-risk-of-medication-errors-with-tranexamic-acid-injection-resulting-in-inadvertent-intrathecal-injection>.
8. *FDA alerts healthcare professionals about the risk of medication errors with tranexamic acid injection resulting in inadvertent intrathecal (spinal) injection (2020)* U.S. Food and Drug Administration. FDA. Available at: <https://www.fda.gov/drugs/drug-safety-and-availability/fda-alerts-healthcare-professionals-about-risk-medication-errors-tranexamic-acid-injection-resulting> (Accessed: December 28, 2023).
9. ISMP Canda Safety *ALERT: Substitution Error with Tranexamic Acid during Spinal Anesthesia Bulletin (2022)*. Available at: <https://ismpcanada.ca/wp-content/uploads/ISMPCSB2022-i6-Tranexamic-Acid-Spinal-Anesthesia.pdf> (Accessed: December 28, 2023).