IMPORTANT MEDICINE SAFETY INFORMATION

06 May 2024

THE RISK OF INTRATHECAL ADMINISTRATION ERROR ASSOCIATED WITH INTRAVENOUS TRANEXAMIC ACID INJECTION.

Dear Healthcare Professional,

The pharmaceutical companies listed below, in collaboration with the South African Health Products Regulatory Authority (SAHPRA), would like to inform you about the risk of error in the administration of intravenous (IV) tranexamic acid.

Summary:

- Tranexamic acid is for INTRAVENOUS USE ONLY.
- Intrathecal, epidural, intraventricular and intracerebral administration of tranexamic acid is contraindicated.
- Care should be exercised to ensure the correct route of administration for IV tranexamic acid injection.
- Healthcare professionals should be aware of the potential for confusion of tranexamic acid with other injectables which could result in inadvertent intrathecal administration of tranexamic acid. This includes intrathecally administered injectables (e.g., bupivacaine and other anaesthetics) that may be used during the same procedure (e.g., caesarean section) as tranexamic acid.
- The confusion is due to visual similarity in product ampoules, labelling and packaging.

Background on the Safety Concern:

Tranexamic acid is indicated for intravenous administration only, for the following medical conditions:

- Short-term use for haemorrhage or risk of haemorrhage in increased fibrinolysis or fibrinogenolysis. Local fibrinolysis occurs in the following conditions:
  - Prostatectomy and bladder surgery.
  - Epistaxis.
  - Conisation of the cervix.
  - Traumatic hyphaema.
- Management of dental extraction in haemophiliacs.
- Hereditary angioedema.
- Menorrhagia.

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

There have been cases reported globally in which IV tranexamic acid injection has been erroneously administered intrathecally due to a confusion and mix-up with the intrathecally administered spinal anaesthetic agents, bupivacaine used for caesarean section and other procedures. Tranexamic acid administered intrathecally is neurotoxic, causing severe neurological sequelae. Neurological toxicity includes refractory seizures, with a 50 % of mortality. Patients who have survived; often experience long-term neurological adverse effects.

The World Health Organisation (WHO) has drawn attention to a review of the available data, which showed 21 cases of 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.

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.

Updates will be made on the tranexamic acid product labelling to prominently add “HIGH ALERT” and “For IV Use Only”.

Advice to healthcare professionals:

- Healthcare professionals are advised to store tranexamic acid injection ampoules separately from other medicines, in a way to avoid reliance on identifying products by the ampoule shape, size, colour, and/or label colour.

- Healthcare professionals should always check the packaging and ampoule label to ensure the correct product is selected and administered only by a proper route.

- Healthcare professionals must promptly and visibly label all syringes before use, with the correct product name and route of administration. This is especially important for those circumstances where multiple products are drawn into syringes and/or stored together in preparation for use.

- It is recommended for healthcare professionals to utilise barcode scanning or a second person to double-check the product label when stocking medication cabinets and preparing medication for injection and before administration.

- If acute signs and symptoms (myoclonus, status epilepticus, cardiac arrhythmias, paraplegia, neurological symptoms, etc.) suggestive of accidental intrathecal injection of the incorrect medicine occur, appropriate treatment, in discussion with a specialist, must be administered.

- It is also recommended that healthcare facilities take measures to ensure that staff ~~are~~ is adequately trained and qualified to handle, dispense, prepare, or administer in a safe and rational manner.

- Healthcare professionals are urged to report any adverse drug reactions (ADRs) or product quality issues associated with the below listed products to the applicants or to SAHPRA via this eReporting link https://primaryreporting.who-umc.org/ZA available on the SAHPRA website (www.sahpra.org.za).

- Alternatively, healthcare professionals may complete the ADR reporting form accessible via the SAHPRA website at https://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/ and send it to adr@sahpra.org.za.
- Additionally, reporting can be done via Med Safety App. The App can be downloaded into a smart mobile phone through Google Play or Apple App Store. For more information on Med Safety App, please visit https://medsafety.sahpra.org.za/.

- For more information on ADR reporting of the product listed below, please contact the SAHPRA Pharmacovigilance unit at pvqueries@sahpra.org.za or alternatively use the contact details indicated below:

Company Point of Contact

For further information, please find the contact details below:

Company	Product	Active ingredient	Registration Number	Contact details
Pfizer Laboratories (PTY) Ltd	Cyklokapron IV 500, 500 mg/5 ml Injection (Ampoules)	Tranexamic acid	H/8.1/806	Tel: 0860 PFIZER (0860 734937) E-mail: ZAF.AEReporting@pfizer.com
Kahma Biotech (Pty) Ltd	Cykloclot 100 mg/ ml Injection (Ampoules)	Tranexamic acid	54/8.1/0886	Tel: (010) 045 2500 Email: drugsafety@kahmagroup.co.za
Abex Pharmaceutica (Pty) Ltd	Hemopron 500, 500 mg/5 ml solution for injection (ampoules)	Tranexamic acid	52/8.1/0808	Tel: 012 997 6974 Email: vigilance@abexpharm.com
Dr. Reddy's Laboratories (Pty) Ltd	MORWAK IV 500, 500 mg/ 5 ml solution for injection (Ampoules)	Tranexamic acid	48/8.1/1017	Tel: +27 11 324 2100 Email: AdverseEvents.SA@drreddys.com
Pharmacorp (Pty) Ltd	Tranexamic Acid 100 mg/ml PharmC	Tranexamic acid	48/8.1/1085	Tel: 012 881 1980 Email: info@pharmacorp.co.za

Yours sincerely,

Lawrene Makamu Cluster Safety Lead **Pfizer South Africa (Pty) Ltd**	DocuSigned by: Lawrene Makamu Signer Name: Lawrene Makamu Signing Reason: I approve this document Signing Time: 06-May-2024 | 2:24:29 AM EDT 2FF17577AA8F42F98422A7A3C4A53225
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Lindie Marx Responsible Pharmacist **Abex Pharmaceutica (Pty) Ltd**	Digitally signed by Lindie Marx Date: 2024.05.06 09:34:59 +02'00'
Herman Beyers Responsible Pharmacist **Dr. Reddy's Laboratories (Pty) Ltd**	DocuSigned by: Herman Beyers Signer Name: Herman Beyers Signing Reason: I approve this document Signing Time: 06-May-24 | 1:55:33 PM IST F9F767D5B4B54FED98B66A1ED3C8D5FF
René Meyer Responsible Pharmacist **Pharmacorp (Pty) Ltd**	