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Tanzania Medicines & Medical Devices Authority

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Editorial Note

Dear readers,

I am pleased to present the Fifth Edition, Issue 3, of the 2026 Drug Safety Bulletin. This issue highlights significant updates to the safety profiles of several medicines of critical public importance.

As an Executive Agency under the Ministry of Health, the TMDA is responsible for ensuring that all medicines, medical devices, and diagnostics meet the highest standards of safety, efficacy and quality.

As a Maturity Level 3 Authority, TMDA remains dedicated to strengthening the safety and quality monitoring of regulated products through robust pharmacovigilance and post-marketing surveillance. This includes the continuous collection and assessment of Adverse Drug Reactions (ADRs) and Adverse Events Following Immunization (AEFIs).

A vital component of this mission is the timely dissemination of this safety data to healthcare professionals, stakeholders, and the public.

I encourage you to review the critical information contained in this issue. We welcome your constructive feedback particularly regarding content and design to help us refine future publications.

I trust that you will find this Bulletin informative and valuable.

Happy reading,

Dr. Adam Fimbo
Editor-in-Chief

VISION

To be the leading regulatory authority in ensuring safe, quality, and effective medicines, medical devices, diagnostics, and other health-related products for all.

MISSION

To protect and promote public health by ensuring the quality, safety, and effectiveness of medicines, medical devices, diagnostics, and other health-related products.

PHILOSOPHY

TMDA strives to offer quality regulatory services in the pursuit of protecting public health and the environment by using competent and dedicated staff.

Safety Updates:

Linezolid, Sildenafil citrate, Atorvastatin calcium trihydrate, Alprazolam, Vitamin B6, Azathioprine, and oral anticoagulants (Rivaroxaban, Dabigatran, Apixaban, Edoxaban, and Warfarin)

Dear Marketing Authorization Holders (MAHs), Local Technical Representatives, Health Professionals and the General Public.

TMDA has operationalized a data-driven pharmacovigilance system designed to support timely and evidence-based decision-making. This system enhances our ability to efficiently assess safety concerns reported by healthcare workers, patients and (MAHs).

Following the recent evaluation of safety data for *Linezolid, Sildenafil citrate, Atorvastatin calcium trihydrate, Alprazolam, Vitamin B6, Azathioprine, Rivaroxaban, Dabigatran, Apixaban, Edoxaban and Warfarin*, significant updates to their safety profiles have been identified. Consequently, the labelling and product information for these medicines must be revised.

All MAHs of the products listed in **Table 1** are hereby required to submit applications for variation of product information in accordance with the TMDA Guidelines on Variations for Registered Medicinal Products (March 2020).

Table 1: Newly identified safety concerns related to the medicine

SN	Product	Newly identified Safety concern	Regulatory recommendations
	Linezolid	Hypoglycaemia induced adverse reactions	Revision of Section 4.8 of the Summary of Product Characteristics (SmPC) to add the adverse reactions "hypoglycemia" (frequency: uncommon) and "black hairy tongue" (frequency: rare). The Patient Information Leaflet (PIL) should be updated as well.
	Sildenafil citrate	Central serous chorioretinopathy (CSCR) with phosphodiesterase-5 inhibitors	Revision of Sections 4.4 and 4.8 of the data sheets to incorporate information on central serous chorioretinopathy (CSCR). In addition, corresponding updates should be made to sections 4.4, 4.5, and 4.8 of the SmPC, as well as sections 2 and 4 of the PIL.
	Atorvastatin calcium trihydrate	Photosensitivity reaction	Revision of Section 4.8 of SmPC and Section 4 of PIL.
	Alprazolam	Increased risk of miscarriage	Revision of warnings and precautions in the SmPC and PIL to include information on an increased risk of miscarriage.
	Vitamin B6-containing products with a daily dose of 10mg or higher of vitamin B6.	Link to peripheral neuropathy	Revision of the monograph to include the risk of peripheral neuropathy.

SN	Product	Newly identified Safety concern	Regulatory recommendations
	Azathioprine	hypersensitivity reaction and pellagra/ Nicotinic acid deficiency, posterior reversible encephalopathy syndrome and tremor	Revise SmPC sections 4.4, 4.6, and 4.8, as well as sections 2 and 4 of the PIL. To incorporate information on cardiac dysfunction due to hypersensitivity reactions, posterior reversible encephalopathy syndrome (PRES), tremor, and pellagra (nicotinic acid deficiency), and remove the warning regarding cholestasis of pregnancy.
	Rivaroxaban, Dabigatran, Apixaban, Edoxaban and Warfarin-containing products	Atraumatic splenic rupture	Revision of the monograph for all oral anticoagulants to include the risk of atraumatic splenic rupture.

Propofol Reported Safety Concerns:

3 -Year Insits from Spontaneous Adverse Events Reporting system in Tanzania Mainland

Propofol is a short-acting intravenous anaesthetic agent widely used for the induction and maintenance of general anaesthesia, as well as for procedural sedation in clinical settings. It has a rapid onset of action, typically within 30 seconds and a short recovery duration of 30 to 45 minutes once administration is discontinued (Allampati et al., 2019).

Propofol is generally considered safe when administered appropriately by trained healthcare professionals; However safety monitoring remains vital as there is no medicine which is 100% safe. Over the last three (3) years, TMDA received a total of 1,439 adverse event reports from healthcare workers and the public: 26 reports in fiscal year 2022/23, 772 in 2023/24, and 641 in 2024/25.

The clinical presentations of these reported adverse events varied significantly. Cardiovascular effects predominated, with **hypotension** representing the vast majority of cases (79%), followed by **bradycardia** (6%). A complete breakdown of the top ten frequently reported adverse events is detailed in **Table 2** below.

Table 2: List of frequently reported adverse events associated with Propofol

Adverse Event	Number of Reports (N=1,439)	Percentage (%)
Hypotension	1,132	79.0
Bradycardia	92	6.0
Rash	25	1.7
Nausea	20	1.4
Confusional State	20	1.4
Dizziness	14	1.0
Chills	12	0.8
Somnolence	10	0.7
Hypertension	8	0.5
Vomiting	8	0.5

The majority of reported adverse events align with the official Propofol Summary of Product Characteristics (SmPC) published by TMDA (link: https://www.tmda.go.tz/uploads/1708943173-T17H0418%20SmPCV1.pdf). However, **rash, confusional state, somnolence and anxiety** are currently unlisted. The emergence of these unlisted adverse drug reactions (ADRs) highlights less common or under-recognized effects and necessitates continued surveillance to further to better characterize their association with propofol.

Neurocognitive Effects (Confusion and Anxiety)

Recent literature indicates that propofol administration may be associated with an increased incidence of postoperative confusion, anxiety, neurocognitive disorders, and delirium (Cao et al., 2023; Evered et al., 2023; Sun et al., 2026).

These adverse neurocognitive outcomes are particularly pronounced among physiologically vulnerable populations, such as older adults undergoing cardiovascular surgery and patients with underlying systemic inflammation.

The heightened susceptibility likely reflects reduced physiological reserve and increased sensitivity to anaesthetic-related neurotoxicity and inflammatory responses. Collectively, these findings underscore anaesthetic selection as a critical, modifiable factor influencing perioperative neurological integrity and overall survival outcomes in high-risk older patients.

Cutaneous Reactions (Rash)

Although propofol is a widely used anaesthetic agent with a well-established safety profile, skin reactions remain poorly documented. Rare propofol-induced cutaneous events include cutaneous and subcutaneous anaphylaxis, subacute cutaneous lupus erythematosus and pruritic rashes (occasionally accompanied by low-grade fever).

These events are typically uncommon, transient and self-limiting (Baldo, 2023; Mertes & Laxenaire, 2002; Schoenfeldt et al., 2023). While symptoms are generally mild, careful, critical evaluation is crucial to distinguish benign cutaneous reactions from early signs of severe perioperative allergic or anaphylactoid responses, especially when multiple anaesthetic agents are administered simultaneously.

Prolonged Somnolence

While somnolence is an anticipated pharmacodynamic effect of sedative agents, it is classified as an ADR when it is excessive in intensity, prolonged in duration, or accompanied by additional central nervous system depressant effects that compromise recovery or functional capacity. Evidence from an outpatient endoscopy study highlights this variance: while the majority of patients (86.6%) experienced a resolution of somnolence before discharge, a clinically significant proportion (2.7%) exhibited persistent drowsiness extending into the evening or the following morning (Kanno et al., 2021).

These observations highlight distinct interindividual variabilities in recovery trajectories. They emphasize the need for rigorous post-procedural monitoring and patient counselling, particularly within ambulatory care settings, like in Tanzania, where early discharge is routinely practiced.

Conclusion

The occurrence of unlisted events including specifically pruritic rashes, neurocognitive disorders, and prolonged somnolence that warrants close follow-up, evaluation, and validation. This requires a coordinated effort between the Authority (TMDA), Marketing Authorization Holders (MAHs), and healthcare professionals involved in administering propofol.

Post Marketing Surveillance of selected Medicines and In Vitro Diagnostics under BREEDIME Project:

A Joint activity between TMDA, ZFDA and Rwanda FDA

Post-Marketing Surveillance (PMS) studies are critical to pharmacovigilance, providing real-world evidence on the safety, effectiveness, and utilization of medicines and vaccines post approval.

Beginning June, 2023 TMDA in collaboration with other eight (8) institutions namely Zanzibar Food and Drug agency (ZFDA), Muhimbili University of Health and Allied Sciences (MUHAS), Zanzibar Health Research Institute (ZAHRI), Kilimanjaro Clinical Research Institute (KCRI), Rwanda Food and Drugs Authority (Rwanda FDA), National Institute for Medical Research (NIMR), The University Curt of The University of St. Andrew (UStAn) and Karolinska Institute (KI) implemented the "**B**uilding **R**esilient **R**esearch **E**thics, **D**iagnostics and **M**edicines regulatory capacity during routine and public health Emergency periods" (**BREEDIME)** project.

This initiative, funded by the European and Developing Countries Clinical Trial Partnership (EDCTP3 Global Health), aimed at strengthening clinical trials oversight, ethical review processes, and PMS of therapeutics, vaccines, diagnostics, and critical medical devices.

Under the **BREEDIME** project, three National regulatory authorities (NRAs)-Rwanda FDA, TMDA and ZFDA-implemented a collaborative PMS programme. Using harmonized tools, the program surveyed the quality of selected antibiotics and in vitro diagnostics.

This cross-sectional, multicountry PMS study was conducted across selected regions of Tanzania Mainland, Zanzibar and Rwanda. Samples of essential medicines (Amoxicillin, Azithromycin and Co-trimoxazole of different formulations) and IVDs, primarily Malaria Rapid Diagnostic Tests (mRDT), Urine Pregnancy Tests (UPTs) and Hepatitis B surface antigen Rapid Diagnostic Tests (HBsAg RDT) were collected from the supply chain.

...products circulating within these markets are generally of high-quality despite the notable administrative non-conformances found during PIR.

Standardized forms were used to record product characteristics. Initial product information review (PIR) and screenings were conducted using Global Pharma Health Fund (GPHF) minilab kits, followed by confirmatory testing at the TMDA WHO pre-qualified laboratory according to Pharmacopeial methods.

Screening (n=347), and confirmatory testing (n=40). While all samples passed the Minilab screening, 68% to 70% failed the PIR, primarily due to missing or incomplete product information. However, confirmatory testing identified three Co-trimoxazole samples that failed assay and dissolution tests; two originated from domestic manufacturers and one from a foreign facility outside the BREEDIME consortium countries.

A total of 1,018 samples were collected (655 medicines and 363 IVDs) and evaluated through a tiered approach of PIR, screening 68% to 70% failed the PIR, primarily due to missing or incomplete product information. However, confirmatory testing identified three Co-trimoxazole samples that failed assay and dissolution tests; two originated from domestic manufacturers and one from a foreign facility outside the BREEDIME consortium countries.

The study indicates that products circulating within these markets are generally of high-quality despite the notable administrative non-conformances found during PIR. Nonetheless, the sub-standard Co-trimoxazole samples necessitate immediate regulatory action to safeguard public health. Ultimately, this multi-country approach underscores the power of regional collaboration in strengthening regulatory systems, optimizing resources, and generating data-driven evidence for future risk-based surveillance efforts.

Improving Adverse Events Data Quality: The contribution of Saving Lives and Livelihood Project.

The Tanzania Medicines and Medical Devices Authority (TMDA) play a central role in safeguarding public health by ensuring that Adverse Drug Reactions (ADRs) and Adverse Events Following Immunization (AEFIs) are reported, assessed, and acted upon. These safety reports are collected from patients, healthcare professionals, public health programs, and the general public.

To maximize reporting rates, TMDA utilizes a diverse range of channels including paper-based forms (yellow forms for healthcare workers and green forms for patients and the general public) and digital platforms such as the Unstructured Supplementary Services Data (USSD) code **(152*00#)**, the Safety and Quality Reporting Tool (SQRT) mobile and web-applications (sqrt.tmda.go.tz), the VigiMobile app (for AEFIs), a toll-free hotline (0800 1100 84), and direct email to TMDA offices. Validated reports are entered into the Vigiflow database to share vital safety data with the World Health Organization (WHO) and the global community.

Despite these robust systems, TMDA efforts are frequently impeded by poor quality, incomplete ADR and AEFI reports. This critical data quality gap highlighted the need for targeted training of pharmacovigilance focal persons stationed across TMDA Zone offices and regional centres.

To address this and align with international ICH E2B standards for electronic transmission of safety reports, TMDA, under the Saving Lives and Livelihoods (SLL) Project funded by the Mastercard Foundation, in collaboration with Africa CDC through AKROS Research Initiative, conducted a specialized training on data quality. The initiative brought 16 pharmacovigilance focal persons from TMDA Zone offices and pharmacovigilance centres to improve reporting accuracy and generate high quality reports. To ensure long-term impact, continuous monthly monitoring is currently underway to track how effectively this training translates into higher-quality adverse event reporting.

Training Qualified Personnel for Pharmacovigilance (QPPV): Success from MUHAS - TMDA Joint Training Programme

Section 11(a) of the Tanzania Medicines and Medical Devices (Pharmacovigilance) Regulations, 2018 requires Marketing Authorization Holders (MAHs) to maintain a robust pharmacovigilance quality system, including designating a Qualified Personnel responsible for Pharmacovigilance (QPPV) . Furthermore, Section 12(1) mandates that MAHs or manufacturer provide both initial and ongoing training to all personnel involved in pharmacovigilance activities.

Under these Regulations, MAHs are legally required to report all domestic and foreign adverse events to TMDA. If no adverse drug reactions are recorded, they must submit "null" reports. Additionally, MAHs must notify TMDA of significant safety concerns or regulatory actions taken by foreign authorities including the underlying rationale while routinely submitting Periodic Safety Update Reports (PSURs) and Risk Management Plans (RMPs) to the Authority.

To address the demand for certified expertise, TMDA and MUHAS launched a joint training initiative in 2020 to qualify healthcare professionals holding a medical degree as QPPVs. This partnership has successfully trained and certified 258 QPPVs as of March 2025 **(Figure 2).** By equipping participants with the necessary technical competencies and practical expertise, this initiative has significantly strengthened medicine safety surveillance and reinforced the broader regulatory framework. Consequently, MAHs are now better positioned to recruit qualified personnel, strengthen their internal safety systems, and ensure full compliance with national pharmacovigilance regulations.

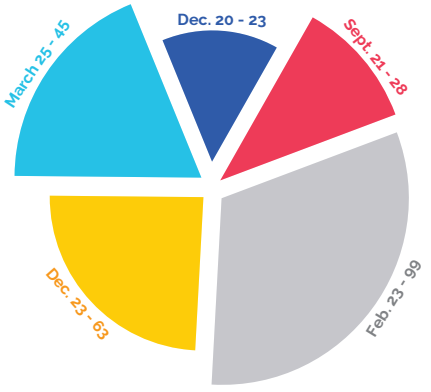
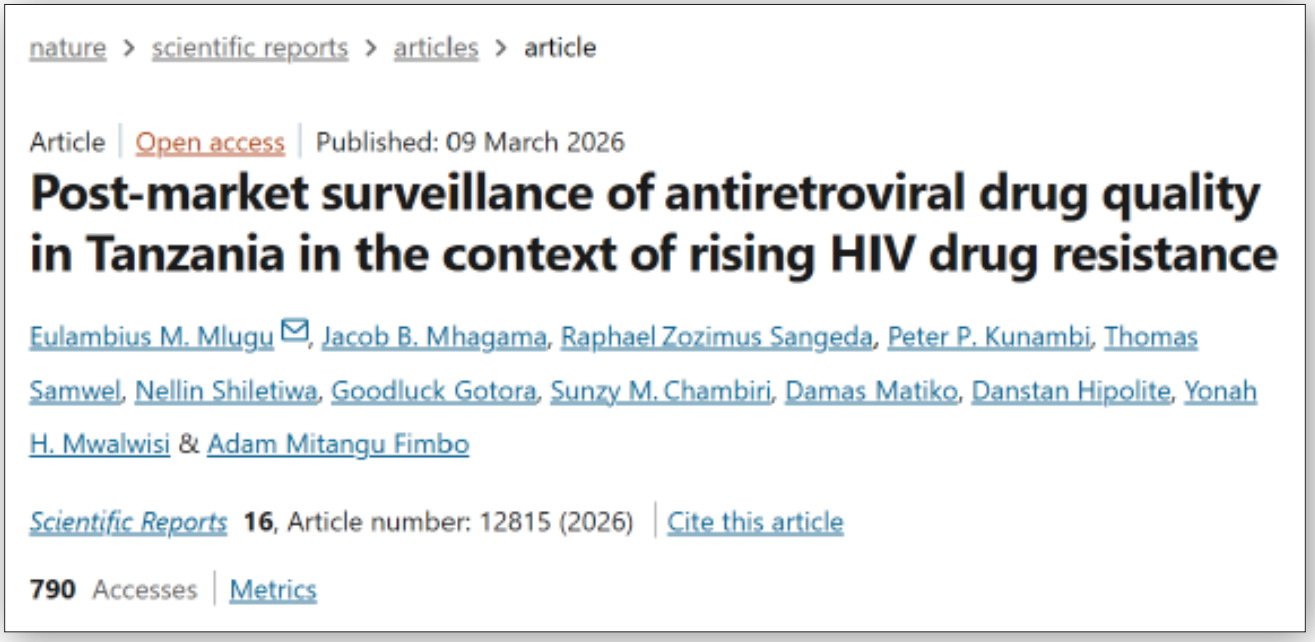


Figure 2: Indicating the number of trained Qualified Personnel responsible for Pharmacovigilance (QPPV) from December 2020 to March 2025

Publications

One (1) publication on Post Market Surveillance of Antiretroviral Drug Quality in Tanzania in the Context of Rising HIV Drug Resistance has been made in spring nature available via the link. https://www.nature.com/articles/s41598-026-43655-w


nature > scientific reports > articles > article

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Post-market surveillance of antiretroviral drug quality in Tanzania in the context of rising HIV drug resistance

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Summary of the Publication

HIV/AIDS remains a major global public health issue, with about 40.8 million people living with HIV as of 2024. The majority of cases are in Africa, especially Sub-Saharan Africa. In Tanzania, around 1.7 million people live with HIV, with a prevalence of 4.7% (2022). Antiretroviral therapy (ART) plays a pivotal role in the global battle against HIV/AIDS, both for prevention and treatment.

To drive the fight against HIV/AIDS, the Joint United Nations Program instituted the 95-95-95 AIDS program targeting to achieve 95% of all people living with HIV know their status, 95% of those diagnosed receive ART and 95% of those receiving ART have viral loads suppressed by the end of 2030

ART effectiveness relies on the wide availability and accessibility of high-quality antiretroviral drugs. As access to ARV improves, ongoing monitoring of drug quality is essential to guide public awareness and policy decisions. Ensuring ARV quality requires coordinated efforts from regulators, healthcare providers, pharmaceutical companies, and international partners.

TMDA conducted a post-marketing surveillance study in 15 of Tanzania mainland's 26 regions whereby a total of 1,432 ARV samples were collected from July 2019 to December 2023. The regions from which samples were collected included Arusha, Dar es Salaam, Dodoma, Coast, Iringa, Kagera, Katavi, Kilimanjaro, Mara, Mbeya, Morogoro, Mwanza, Mtwara, Njombe and Tanga. Selection of these regions was based on prescribed criteria such as high population, border location, high HIV prevalence, and reports of medicine quality issues

About half of the samples from distribution outlets failed Product Information Review (PIR) requirements under TMDA guidelines, with most failures occurring in 2023/24. This suggests a rising trend of non-compliance among manufacturers that cannot be explained by sampling differences alone. The main issues included incorrect labeling language and deviations in packaging artwork from approved standards, signifying some weaknesses in regulatory compliance.

All sampled ARVs met both screening and confirmatory quality standards, aligning with recent findings from Cameroon that suggest improved drug quality in the region. This contrasts with earlier studies in Tanzania and the DRC that found substandard ARVs, likely reflecting progress from stronger surveillance and regulation. However, concerns about HIV drug resistance (HIVDR) remain, highlighting the need for ongoing monitoring and improved adherence to ART.

Conclusion

This study demonstrates that antiretroviral drugs circulating in Tanzania meet established quality standards. It highlights the importance of integrating post-marketing surveillance findings into national HIV program quality assurance systems to sustain quality of service across the HIV care continuum. Observed deviations in labeling pose potential public health risks, underscoring the need for strengthened regulatory enforcement. The study further emphasizes the necessity of continuous monitoring of medicine quality, including ARVs

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