MCAZ Medicines Control Authority of Zimbabwe

November 2024

Medicines Information Bulletin

VigiMobile for Medicines

VigiMobile for Vaccines

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MCAZ Pharmacovigilance updates

1 January to 30 September 2024 Individual Case Safety Reports

The Medicines Control Authority of Zimbabwe (MCAZ) is the National Centre for Pharmacovigilance (PV) and PV activities are coordinated by the Pharmacovigilance and Clinical Trials (PVCT) Division. Zimbabwe is a participating member of the World Health Organisation Programme for International Drug Monitoring (WHO PIDM) since 1998 to date, through the MCAZ national PV centre.

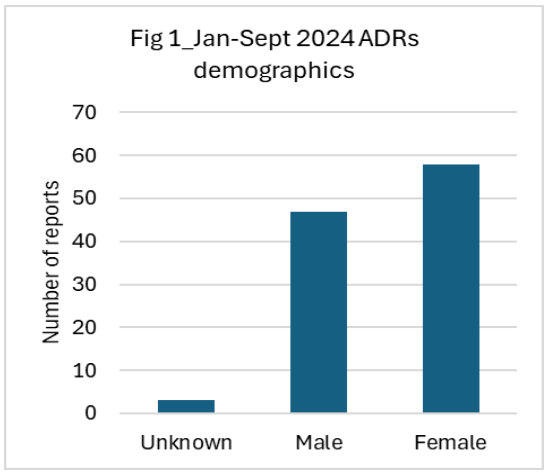
The MCAZ-PVCT conducts spontaneous (voluntary) adverse drug reaction monitoring and active pharmacovigilance programs of all essential medicines, including vaccines, marketed in Zimbabwe for quality, safety, and effectiveness with the aim of promoting patient safety. Special thanks to all the reporters for their continued support in promoting patient safety.

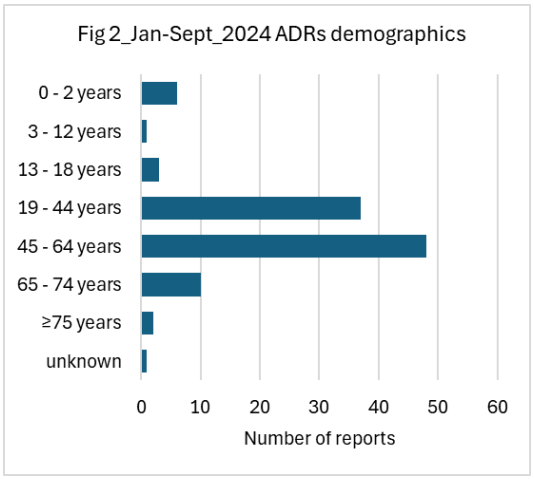
Table 1: Summary of Individual Case Safety Reports (ADRs, AEFIs and SAEs) received at the MCAZ for the period 1 January to 30 September 2024

Type of ICSR reports	ADRs received and processed from January to September 2024
ADRs from pharmaceutical industry (CIOMs, XML/E2B)	**50**
Adverse Events Following Immunization (AEFIs)	**320** (*The VigiMobile app and VigiFlow system for AEFI reporting have greatly improved AEFI reporting timelines*)
ADRs from the TSR of all essential medicines including ARVs and Anti-TBs from public and private sector	**108** *ARVs – 56 (TDF and renal toxicity most reported)* *Anti-TBs – 19* *Other essential medicines – 33*
SAEs from approved clinical trials conducted in Zimbabwe	**59**
Total	**537**

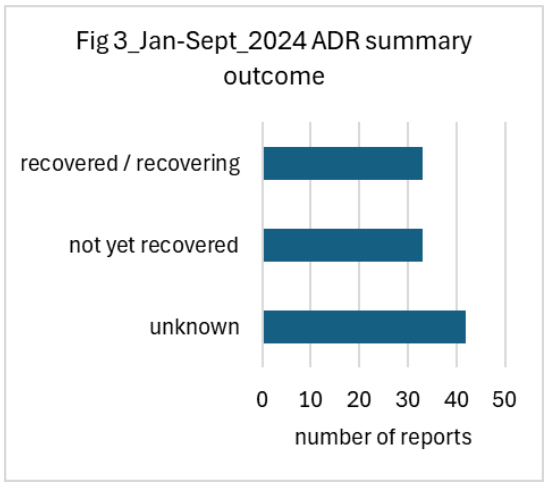
ADR reports summary (Jan-Sept 2024)

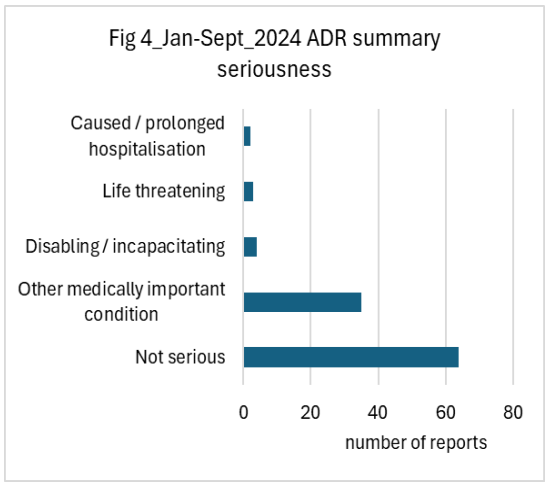
A total of 108 ADR reports were received in from Jan to Sept 2024. Females reported more adverse reactions as compared to males. Individuals aged between 45 to 64 years experienced the most adverse reactions.



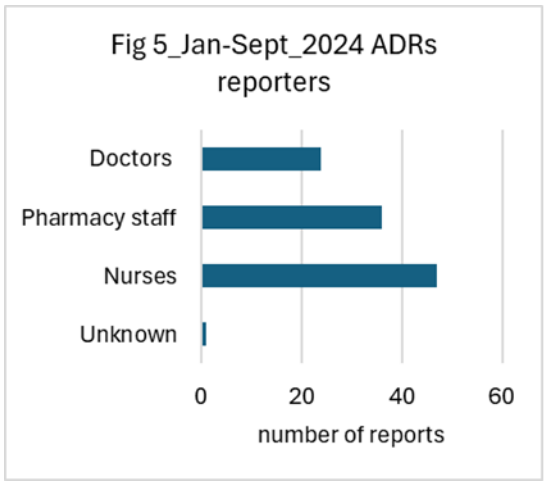


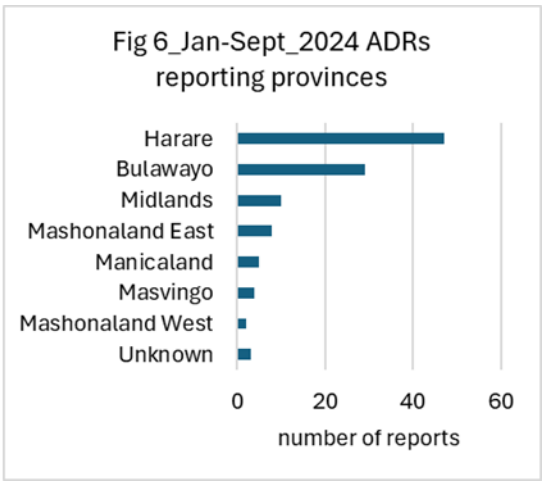
The outcomes of the reactions in the 108 ADR reports were mostly unknown. Most of the reactions were not serious.





Harare province reported the most reports. The health care practitioners who submitted the most reports were nurses.





The most reported adverse reactions were renal and urinary disorders associated with tenofovir disoproxil fumarate. The outcome of the reactions was unknown in 40% of the reports and not yet recovered in 53% and recovered in 7%. Causality assessment in 80% of these reports was possible or probable.

Table 2: Most reported medicines and adverse reactions_ Jan to Sept 2024

Suspected medicine(s)	Adverse reaction/ adverse	Number of reports
Amlodipine	Joint swelling	5
Cabotegravir	Pruritus	2
Ciprofloxacin	Pruritus	2
Dolutegravir	Weight gain	6
	Generalised oedema	1
Dolutegravir; emtricitabine; tenofovir alafenamide	Pruritus	2
Dolutegravir; lamivudine; tenofovir disoproxil fumarate	Weight gain	2
Enalapril	Lip swelling	2
Rifampicin; isoniazid	Rash	2
Rifampicin; isoniazid; pyrazinamide; ethambutol	Diarrhoea	2
	Headache	2
	Rash	2
Tenofovir disoproxil fumarate	Nephropathy toxic	19
	Creatinine renal clearance decreased	5
	Acute kidney injury	1
Tetracycline	Eye swelling	4

VigiMobile - Electronic Adverse Reaction reporting

Substandard and Falsified medicines

A **substandard medical product** is an *authorized product* that does not meet quality standards or specifications, produced by a known manufacturer with *no intent to fool or defraud* the patient.

A **falsified medical product** is one that is *deliberately and fraudulently labelled* in a way that misrepresents its identity, source or composition and is often produced in unsanitary and unregulated conditions by an unknown manufacturer.

Summarized below is a medicinal product alert communicated by the World Health Organization (WHO) Global Surveillance and Monitoring System for Substandard and Falsified Medical Products for the year 2024 *(May to November 2024)*.

Alert No	Alert Summary
WHO Medical Product Alert N°2/2024 – Falsified OZEMPIC (semaglutide) identified in the WHO Regions of Americas and Europe	This WHO Medical Product Alert refers to three falsified batches of OZEMPIC (semaglutide). This falsified product has been detected in Brazil (October 2023), the United Kingdom of Great Britain and Northern Ireland (October 2023), and the United States of America (December 2023), and was supplied in the regulated supply chain. The genuine manufacturer of OZEMPIC confirmed that the three products referenced in this Alert are falsified: the products were not manufactured by Novo Nordisk: • batch number LP6F832 is not recognized. • the combination of batch number NAR0074 with serial number 430834149057 does not correspond to genuine manufacturing records. • batch number MP5E511 is genuine, but the product is falsified. **Ways to identify falsified products** 1. Check the Lot Number and Serial Number: WHO advises not to distribute, use, or sell products labelled with batch numbers listed in Annex. 2. Examine the Pen: Falsified Ozempic pens may have a scale extending out from the pen when setting the dose. 3. Assess the Label Quality: The label might be of poor quality and may not adhere well to the pen. 4. Look for Spelling Mistakes: The carton may have spelling mistakes on the front of the box.
WHO Alert No. 3/2024 – Falsified	This WHO Medical Product Alert refers to one batch of falsified Oxymorphone Hydrochloride 40mg. The falsified product was detected in the unregulated supply chain in Finland and reported to WHO in July 2024 by the Finnish Medicines Agency

(contaminated) Oxymorphone Hydrochloride identified in the Europe	(FIMEA). This product is confirmed as falsified because it deliberately misrepresents its identity, composition, and source. To identify this falsified product check for the following: • The falsified version label does not have a barcode on the bottle. • The falsified version is labelled 40mg. AUROLIFE PHARMA Oxymorphone Hydrochloride is only available as 5mg and 10mg doses. • The falsified versions of the tablets lack embossed letters/numbers. • The falsified product's label is missing the National Drug Code of the United States of America.
WHO Alert No 4/2024 – Falsified USP/EP Propylene Glycol the WHO Eastern Mediterranean Region	This WHO Alert refers to falsified DOW USP/EP PROPYLENE GLYCOL detected in Pakistan in August 2024 and notified to WHO in September 2024. In April 2024, WHO also issued Medical Product Alert No.1/2024 concerning the detection of five batches of falsified and contaminated DOW USP/EP PROPYLENE GLYCOL which had been detected in Pakistan and linked to the manufacture of contaminated oral liquid medicines. The falsified PROPYLENE GLYCOL had been found to be contaminated with ethylene glycol. WHO has now received information concerning three new falsified batches of DOW USP/EP PROPYLENE GLYCOL which were detected in Pakistan in August 2024. WHO shared this information with the Drug Regulatory Authority of Pakistan (DRAP) which issued a national rapid alert on 22 August 2024, detailing these new falsified batches of DOW USP/EP PROPYLENE GLYCOL. (See DRAP ALERT No: I/S/8-24-29 and : I/S/9-24-32.

✓ Suspected substandard and falsified products can be reported to MCAZ using the Report on Medicinal (Pharmaceutical) Product Defect or Problem (LEF 80), available on request and accessible on the MCAZ website.

If you, or someone you know, has or may have used any substandard or falsified medicines and suffered an adverse reaction or unexpected side-effect after use, you are advised to seek immediate medical advice from a healthcare professional and report the adverse event to MCAZ.

✓ Adverse events can be reported to MCAZ using the online consumer reporting form available on the MCAZ website or by completing either the Adverse Drug Reaction reporting form or the consumer reporting form both of which are available on request from MCAZ as hard copies and can be downloaded the MCAZ website.

References

1. www.who.int/news/item/19-06-2024-medical-product-alert-n-2-2024--falsified-ozempic-(semaglutide)
2. https://www.who.int/news/item/05-08-2024-medical-product-alert-n-3-2024--falsified-(contaminated)-oxymorphone-hydrochloride-40mg
3. https://www.who.int/news/item/10-10-2024-medical-product-alert-n-4-2024--falsified-usp-ep-propylene-glycol
4. https://www.who.int/teams/regulation-prequalification/incidents-and-SF/full-list-of-who-medical-product-alerts

Highlights from the WHO Pharmaceuticals Newsletter

The WHO Pharmaceuticals Newsletter provides the latest information on the safety of medicinal products and regulatory actions taken by authorities around the world. Summarised below are highlights from the WHO pharmaceutical newsletter edition No. 2 (2024) and No.3 (2024):

Isotretinoin – Potential risk of mental health and sexual function adverse reactions - United Kingdom (U.K) The Medicines and Healthcare products Regulatory Agency (MHRA) has announced that the product information for isotretinoin has been updated to include new warnings and precautions on potential mental health and sexual function adverse reactions and requirement for two healthcare professionals to agree that there is no other appropriate effective treatment in patients under 18 years of age. Reference: Drug Safety Update, MHRA, 31 October 2023 (link to the source within www.gov.uk/mhra)

Singapore. The Health Sciences Authority (HSA) has re-evaluated whether the existing safety measures on isotretinoin oral forms should be further strengthened Based on the current available information including the newly introduced measures by the MHRA as above, HSA, in consultation with its Product Vigilance Advisory Committee (PVAC), has concluded that the benefit risk profile of isotretinoin remains favourable for its approved indications Patient educational materials for isotretinoin are available on publicly accessible platforms, including the Medication Information Leaflets (MILs) on HealthHub. Reference: Announcements, HSA, 15 December 2023 (link to the source within www.hsa.gov.sg)

Fluoroquinolone antibiotics

Risk of persisting serious adverse reactions – New Zealand. The Medsafe has alerted healthcare professionals on the risks of prolonged, disabling and potentially irreversible serious adverse reactions including tendonitis and tendon rupture, and peripheral neuropathy associated with use of fluoroquinolone antibiotics. Health-care professionals should inform patients about the risks associated with fluoroquinolones and advise them to tell their doctor straight away if symptoms develop. Discontinuing fluoroquinolone treatment may reduce the risk of irreversible adverse reactions. Reference: Prescriber Update, Medsafe, September April 2023 (link to the source within www.medsafe.govt.nz)

Risk of suicidal thoughts and behaviour – United Kingdom. The MHRA has reminded health-care professionals to be alert to the risk of psychiatric reactions, including depression and psychotic reactions, which may potentially lead to thoughts of suicide or suicide attempts. Warnings on the potential for psychiatric adverse drug reactions to occur with ciprofloxacin and other fluoroquinolones are included in the product information. In rare cases, depression or psychosis can progress to suicidal ideation or suicide attempts. If this happens, ciprofloxacin should be discontinued immediately. Reference: Drug Safety Update, MHRA, 26 September 2023 (link to the source within www.gov.uk/mhra)

Valaciclovir and acyclovir - Risk of drug reaction with eosinophilia and systemic symptoms (DRESS) - South Africa. The South African Health Products Regulatory Authority (SAHPRA) has reminded health-care professionals about the risk of DRESS associated with the use of valaciclovir/acyclovir-containing medicines. DRESS is a rare, but serious, and potentially life-threatening fatal drug reaction that includes fever, severe skin rash or peeling of the skin over large areas of the body, swollen face, elevated white blood cell count (including eosinophils), and can affect one or more organs (commonly liver). The SAHPRA has advised health-care professionals that at the time of prescription, patients should be advised of the signs and symptoms of DRESS; and monitored for skin reactions. Reference: Communication to health care professionals, SAHPRA, 19 January 2024 (link to the source within

Proton pump inhibitors (PPIs) - Risk of tubulointerstitial nephritis (TIN) – South Africa. The South African Health Products Regulatory Authority (SAHPRA) has alerted health-care professionals on the risk of acute tubulointerstitial nephritis (TIN) associated with use of Proton Pump Inhibitors. TIN (previously called interstitial nephritis) is characterized by an inflammatory reaction within the tubulointerstitial space of the kidney, and acute TIN can result in acute kidney injury. Symptoms and signs of acute TIN may be nonspecific and are often absent unless symptoms and signs of renal failure develop. Many patients develop polyuria (increased frequency of urination) and nocturia (the need for patients to get up at night on a regular basis to urinate). Health-care professionals are advised that treatment by PPIs must be stopped when TIN is suspected, and patients should be asked to report any alteration in urine volumes or if they suspect that there is blood in their urine while on PPIs. Reference: Safety Information and Updates, SAHPRA, 30 October 2023 (link to the source within www.sahpra.org.za)

Statins – Potential risk of myasthenia gravis and ocular myasthenia gravis – United Kingdom. The MHRA has announced that that the product information for all statins is being updated to list myasthenia gravis and ocular myasthenia gravis as adverse drug reactions. Globally, there has been a very small number of reports of new-onset or aggravation of pre-existing myasthenia gravis with statins. A recent European review recommended new warnings on the risk of new onset or aggravation of pre-existing myasthenia gravis with multiple statins.

Health-care professionals should advise patients taking statins to consult their doctor if they experience weakness in the arms or legs that worsens after periods of activity, double vision or drooping of eyelids, difficulty swallowing, or shortness of breath. Reference: Drug Safety Update, MHRA, 26 September 2023 (link to the source within www.gov.uk/mhra)

Reference

1. https://www.who.int/teams/regulation-prequalification/regulation-and-safety/pharmacovigilance/guidance/reports-and-newsletters

Product Recalls

A **product recall** is a process of withdrawing or removing a medicine, vaccine and/or medical device product from the pharmaceutical distribution chain because of defects in the product, complaints of serious adverse reactions to the product and/ or concerns that the product is or may be counterfeit.

The recall might be initiated by the manufacturer, wholesale dealer, applicant or the MCAZ. Recalls are classified according to the relative health hazard associated with the use of or exposure to the recalled product.

There are three possible classifications: class I, class II and class III.

- ✓ **Class I recalls** occur when products are potentially life-threatening or could cause a serious risk to health, e.g., microbial contamination of sterile injection or ophthalmic product.
- ✓ **Class II recalls** occur when product defects could cause illness or mistreatment, but are not Class I, e.g., non-compliance with specifications such as assay, stability, fill/ weight or dissolution.
- ✓ **Class III recalls** occur when product defects may not pose a significant hazard to health i.e., low risk to health but recall may be initiated for other reasons, due to quality, safety or efficacy, e.g., wrong or missing batch number or expiry date.

As with classification, the level (or depth) of a recall is to be assigned in agreement with the MCAZ. In determining the recall level, the principal factors to be considered are the significance of the hazard (if any), the channels by which the medicine, vaccine or medical device pharmaceutical products have been distributed, and the level to which distribution has taken place. Again, expert opinion may be necessary to determine the significance of the hazard or risk. There are three levels of recall i.e. wholesale, retail and consumer.

Information on product recalls issued by the MCAZ is available on the MCAZ website mcaz@mcaz.co.zw

Healthcare practitioners and consumers are encouraged to report any product defects to MCAZ using the medicinal product problem or defect form which is available on the MCAZ website or on request via email to mcaz@mcaz.co.zw .

Product defects and recalls are handled using the Guidelines for the Notification of Medicinal Product Problem or Defect and Recall Procedure

References

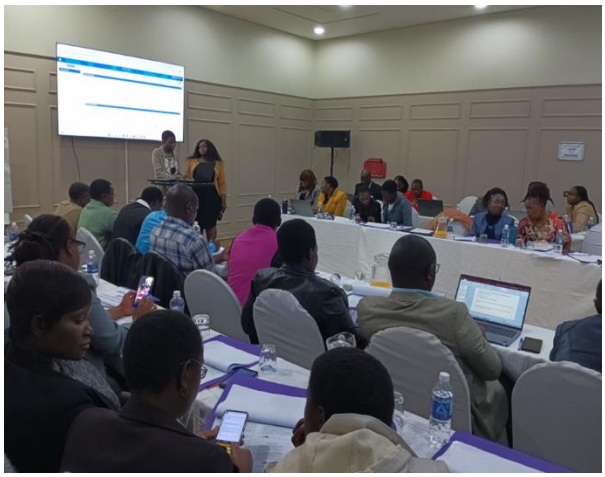
1. https://www.mcaz.co.zw/licensing-and-enforcement/product-defects-recalls
2. https://www.mcaz.co.zw/documents/circulars/
3. Guidelines-for-the-Notification-of-Medicinal-Product-Problem-or-Defect-and-Recall-Procedure.pdf

Pharmacovigilance trainings 2024

Strengthening Patient Safety Across Zimbabwe

Throughout 2024, the MCAZ-PVCT division, sponsored by the Global Fund through UNDP, conducted 8 provincial pharmacovigilance trainings across Zimbabwe. The objective of these trainings was to equip healthcare workers with the crucial skills required to effectively identify, manage, and timeously report Adverse Drug Reactions (ADRs) related to medicines, particularly antiretroviral and anti-tuberculosis medicines, using the electronic reporting tools, VigiMobile for ADR and VigiMobile for AEFI.

By strengthening pharmacovigilance, Zimbabwe is building a more informed, responsive healthcare system that actively monitors and addresses drug safety concerns. We extend our heartfelt appreciation to all healthcare workers, PMDs, provincial pharmacists, PNOs, DMOs, DNOs, health information officers, EPI officers, and district pharmacy managers. Your dedication to monitoring and reporting ADRs is invaluable, and your efforts are directly contributing to a safer healthcare environment.



For healthcare institutions interested in virtual or on-site pharmacovigilance trainings, please send a signed request letter via email to mcaz@mcaz.co.zw . Let's continue to work together to enhance patient safety and improve healthcare quality across Zimbabwe!