



Medicines Control Authority of Zimbabwe

August 2022



Medicines Information Bulletin

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MCAZ Pharmacovigilance updates 2022: AEFI surveillance, ART & TB Programs

The Medicines Control Authority of Zimbabwe (MCAZ) is the national centre for pharmacovigilance; hence Zimbabwe is a participating country for the WHO International Drug Monitoring Program since 1998. As part of the objectives of pharmacovigilance and post marketing surveillance, the MCAZ Pharmacovigilance and Clinical Trials Division (PVCT) is required to integrate pharmacovigilance into private and public health programs by conducting 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.

The MCAZ deployed an E2B compatible e-PV system for submission and processing of Individual Case Safety Reports (ICSR) i.e. ADRs, AEFIs, SAEFIs and SAEs for utilization by all public and private health sectors reporters. The e-PV system can be accessed via computers, iPads, tablets and phone by using mobile and offline desktop applications. The e-PV system is also available online using the link, <https://e-pv.mcaz.co.zw/>

Below is the summary of the ICSRs received at the MCAZ from January to June 2022 from patients and consumers; the pharmaceutical industry, approved clinical trials being conducted in Zimbabwe, public MoHCC sites; and private sector health care facilities including pharmacies, hospitals and clinics. Special thanks to all the reporters for their continued support in promoting patient safety.

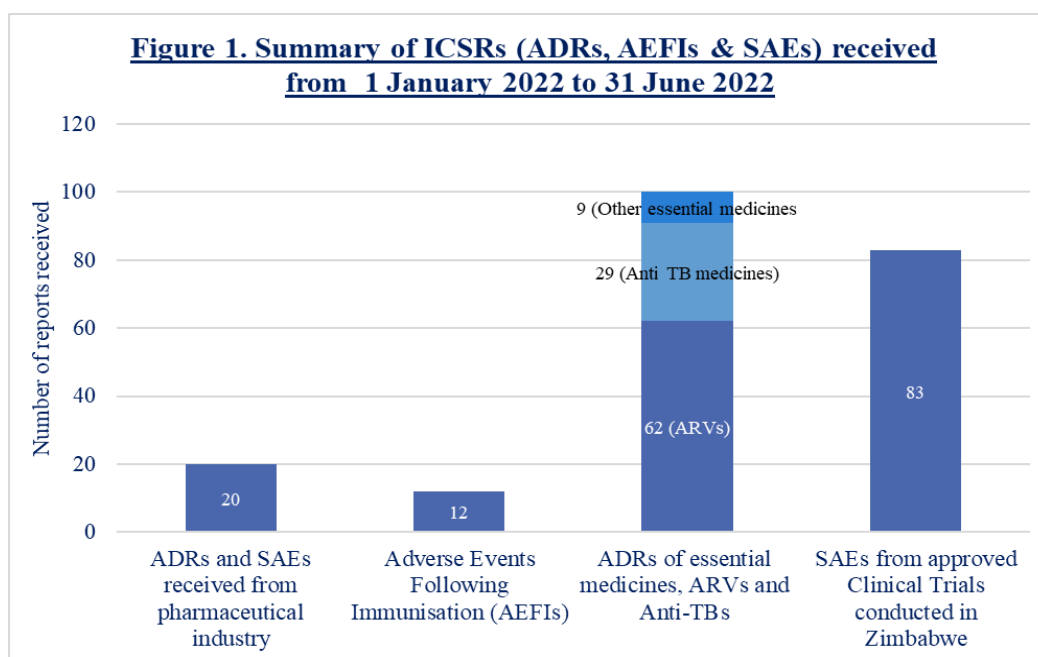
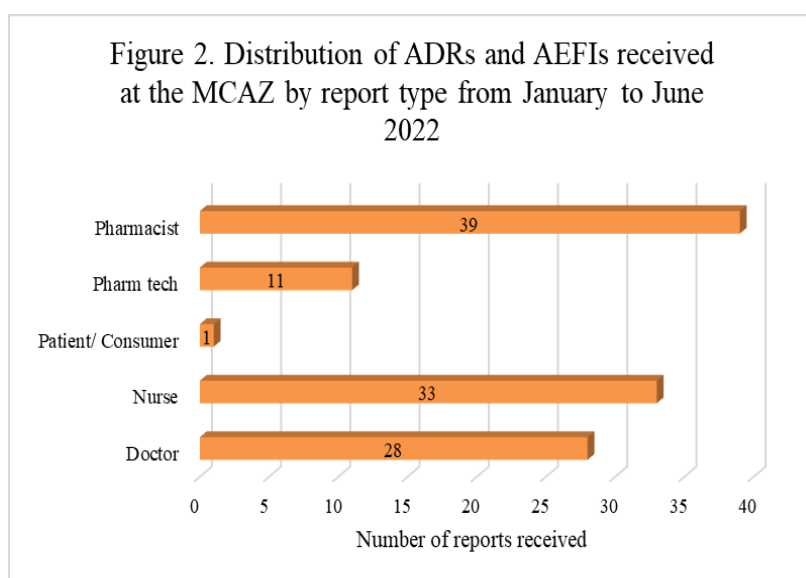
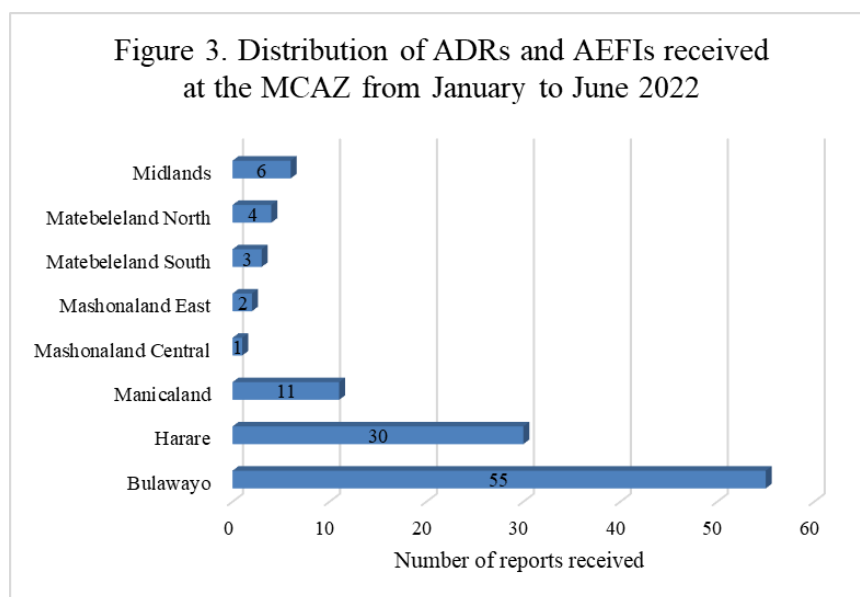


Figure 1 shows that a total of 215 ICSRs were received in the period of January to June 2022. ADRs from the TSR of all essential medicines including ARVs and Anti-TBs from public MoHCC sites and some private sector clinics and doctors (100 reports) and AEFI reports (12) comprised of 47% of the total ICSRs. The majority of the ADR and AEFI reports were from female patients/ consumers (73%). The most commonly suspected medicines were dolutegravir, isoniazid, isoniazid/ rifapentine and tenofovir disoproxil fumarate. Dolutegravir was associated with higher rates of weight gain, isoniazid and isoniazid/rifapentine were associated with higher rates of dermatological reactions and tenofovir disoproxil fumarate was associated with higher rates of renal impairment adverse events. COVID-19 vaccines were the suspected vaccines in all 12 AEFI reports. The most commonly reported adverse reactions included headache, dizziness and rash.



Anyone, including (but not limited to) health care professionals, patients, consumers, guardians and caregivers can report all suspected adverse reactions to medicines (including vaccines, X-ray contrast media, complementary medicines), especially when the reaction is unusual, potentially serious or clinically significant. From January to June 2022, according to figure 2 above;

pharmacists, nurses and doctors reported the majority of ADR reports. Nurses reported all of the AEFI reports received. Figure 3 below shows the provinces that have reported ADR and AEFI reports to the MCAZ from January to June 2022. Bulawayo submitted the majority of reports from January to June 2022. We encourage everyone to continue reporting adverse events hence promoting patient safety. Many thanks to the tenacity and assistance of all our reporters in promoting patient safety.



Medicine Safety Alerts



The Medicines Control Authority of Zimbabwe (MCAZ) regularly reviews medicines safety issues for products that are registered and marketed in Zimbabwe. This information helps in ensuring ongoing safety monitoring by checking for any safety concerns raised by other regulatory agencies or World Health Organization (WHO), particularly for safety issues or adverse drug reactions (ADRs) that would not have been published before, or included in the package inserts for medicines. The WHO publishes regular WHO Pharmaceuticals Newsletters, whose aim is to disseminate regulatory information on the safety of pharmaceutical products, based on communications received from our network of national pharmacovigilance centres and other sources such as specialized bulletins and journals, as well as partners in WHO. Healthcare professionals are sensitized to carefully monitor the below mentioned alerts, ensuring any event related to these drugs is reported to the MCAZ.

| Name of Medicine | Risk Warning |
|----------------------------|------------------------------|
| Methotrexate | Muscle spasm |
| Tocilizumab | Gastric perforation |
| Amiodarone and rivaroxaban | Gastrointestinal haemorrhage |

Sources

1. WHO Pharmaceuticals Newsletter No. 4/2021, <https://apps.who.int/iris/rest/bitstreams/1365342/retrieve>
2. WHO Pharmaceuticals Newsletter No. 1/2022, <https://apps.who.int/iris/rest/bitstreams/1407437/retrieve>





Safety measures for sodium valproate and the risk of congenital malformation in neonates and neurodevelopmental problems in children exposed to sodium valproate during pregnancy

Background of Safety Issue

A recent newspaper article by the Daily mail UK, highlighted concerns around the use of sodium valproate/ valproic acid products by pregnant women and women of child-bearing age. Sodium Valproate is indicated for the treatment of epilepsy (complex partial seizures and /or simple and complex absence seizures, among others), bipolar disorder and rarely in migraines.

Sodium valproate has been known to cause congenital malformations in neonates (approximately 10% of cases), and serious developmental problems among children in

up to 30-40% of cases whose mothers were exposed to sodium valproate during pregnancy (1). Examples of congenital malformations include neural tube defects, facial dysmorphism, cleft lip and palate, and multiple anomalies involving various body systems. Available data showed that children with a history of sodium valproate exposure in utero may experience delays in their early development and had increased risk of developmental disorders compared to the general study population. The product is contraindicated in girls and women of childbearing potential unless other treatments are ineffective or not tolerated.



Advice for Healthcare Professionals

The Authority wishes to advise health care professionals as follows;

1. The product is contraindicated in girls and women of childbearing potential unless other treatments are ineffective or not tolerated.
2. **All female patients who are considering sodium valproate therapy must be informed on the following points:**
 - There is a risk of congenital malformation and neurodevelopmental problems in children whose mothers were exposed to sodium valproate during pregnancy.
 - Pregnancy testing is required before starting sodium valproate and throughout treatment, as necessary.
 - The use of effective contraception during the entire duration of treatment is important.
 - Patients to consult their doctor if they are planning for pregnancy.
3. **If sodium valproate is required for the patient and other treatment options are ineffective or not tolerated, please ensure the following:**
 - Treatment should only be initiated after pregnancy has been excluded (negative pregnancy test).
 - Annual review should be carried out, and ad-hoc treatment review conducted when required. The benefit and risk should be carefully reconsidered during every treatment review.
 - When patient is planning for pregnancy, all efforts should be made to switch to appropriate alternative treatment prior to conception, if possible.
 - In the case where sodium valproate must be used during pregnancy, prenatal monitoring is recommended to detect any malformations.

References

1. Valproate medicines (Epilim ▼, Depakote ▼): contraindicated in women and girls of childbearing potential unless conditions of Pregnancy Prevention Programme are met - GOV.UK (www.gov.uk)
2. <https://www.dailymail.co.uk/news/article-10725253/NHS-faces-thalidomide-style-scandal-doctors-gave-pregnant-women-drug-known-cause-birth-defects.html>





Substandard and Falsified Medicines Alerts

A substandard medical product is an **authorized product** which 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 labeled** in a way that misrepresents its identity, source or composition and is often produced in unsanitary and unregulated conditions by an unknown manufacturer. Suspected substandard and falsified products can be reported to MCAZ using Product Defect Forms (PVF 05), available on request and accessible on the MCAZ website.

Summarized below are medicinal products alerts communicated by World Health Organization (WHO) Global Surveillance and Monitoring system for Substandard and Falsified Medical Products for the year 2022 (as at 31 May 2022).

WHO Medical Product Alert N°2/2022 - Falsified DESREM Remdesivir for Injection 100mg/vial

Two falsified batches of DESREM Remdesivir for Injection 100mg/vial were identified in Guatemala and India and reported to WHO in February 2022. The genuine manufacturer of DESREM, Mylan Laboratories Ltd, confirmed that the products identified in this alert was falsified. Laboratory analysis of these falsified products, conducted by the genuine manufacturer, established that they do not contain any of the stated active pharmaceutical ingredient (remdesivir). The vials of these falsified products may be smaller than genuine DESREM and the labels have multiple spelling errors and use the wrong font styles and colors. Although the identified batch numbers are genuine, the expiry dates listed below are falsified. The falsified products had batch numbers 7605854B and CRM21001MA and expiry dates of 09/2022 and 07/10/2022 respectively.

Source

[https://www.who.int/news/item/09-03-2022-medical-product-alert-n-2-2022-falsified-desrem-\(remdesivir\)](https://www.who.int/news/item/09-03-2022-medical-product-alert-n-2-2022-falsified-desrem-(remdesivir))

WHO Medical Product Alert N°3/2022- Falsified Intratect (Human normal immunoglobulin)

This WHO Medical Product Alert refers to four falsified lots of Intratect reported from Brazil (September 2021), India (February 2022), Bolivia (Plurinational State of) (April 2022) and Egypt (April 2022). The genuine manufacturer of Intratect is Biotest GmbH, who confirmed that all the products referenced in this alert are falsified, including those labelled “Immunoglobulina G Endovenosa Biotest”. Biotest GmbH does not manufacture any products with this name. The stated lot numbers ID 05 G 20050; 3C30000087; C146181P02 and B842961 were also confirmed as falsified.

Source

<https://www.who.int/news/item/27-05-2022-medical-product-alert-n-3-2022-falsified-intratect-human-normal-immunoglobulin>

WHO requests increased vigilance worldwide to prevent the distribution of these falsified medical products. Additional information on these alerts can be obtained on the WHO website on the following link: <https://www.who.int/teams/regulation-prequalification/incidents-and-SF/full-list-of-who-medical-product-alerts>



Pharmacovigilance trainings 2022

The main objectives of pharmacovigilance trainings are to capacitate healthcare workers on reporting and management of adverse drug reactions related to antiretroviral and anti-tuberculosis medicines. These trainings help in strengthening of the national pharmacovigilance system by improving reporting of adverse events and promoting patient safety to prevent drug-related adverse effects.



Clinton Health Access Initiative (CHAI) requested the support of MCAZ in conducting drug safety monitoring and reporting training at 20 CHAI Implementing sites for Tuberculosis Preventative Treatment (TPT), Paediatric Dolutegravir (pDTG) and Advanced HIV

Disease (AHD) management. This was in line with the approved request to resume activities aimed at improving reporting of adverse drug reactions identified in people taking HIV and TB medicines, in line with the pharmacovigilance strategy for CHAI Zimbabwe. The collaborative pharmacovigilance strengthening activities started in 2021, with trainings having been conducted at 24 CHAI implementing sites in the last quarter of 2021.



A special thanks to CHAI, all 20 sites, healthcare workers, PMDs, PP, PNOs, DMOs, DNOs, district pharmacy managers, health information's, and ART & TB -MoHCC, & MCAZ teams for their support and commitment in promoting patient

safety.



RCORE Trainings 2022

The MCAZ was designated by the New Partnership for African Development (NEPAD) and the African Regulatory Harmonization (AMRH) as a Regional Centre of Regulatory Excellence (RCORE) in Clinical Trials.

The MCAZ in partnership with the Medicines Research Council of Zimbabwe (MRCZ) have designed an intensive course to build capacity and equip regulators in Clinical Trials. The course is designed to promote harmonization in regulatory requirements.



Course Objective:

The objective of this course is to train and equip participants with the requisite knowledge and skills to enable them to evaluate and review clinical trial applications and effectively monitor on-going clinical trials. This includes compliance with WHO Global Bench Marking Tools.

Table 1: RCORE Trainings conducted in 2022

| Country | Institution(s) Trained | Name of Course | Training Dates |
|----------|---|--|-----------------|
| Botswana | Botswana Medicines Regulatory Authority (BOMRA) | Clinical Trials Protocol evaluation using the AVAREF templates | 26-28 July 2022 |



Regional collaboration in Pharmacovigilance

The MCAZ National Pharmacovigilance Centre collaborates with local, regional, and international stakeholders to enhance pharmacovigilance activities, and to share relevant strategies and ideas concerning medicines safety. One such collaborative activity is the SPaRCS Project.



SPaRCS is an acronym for **S**trengthening **P**harmacovigilance **a**nd **R**egulatory **C**apacities in four **S**outhern African countries. The project is funded by EDCTP, its aim is to strengthen pharmacovigilance systems and clinical trials oversight of National Regulatory Authorities (NRAs) in Namibia, South Africa, Eswatini and Zimbabwe. The project uses a participatory action learning, and co-creation approach to develop personal and institutional capacities of the NRAs in the four countries. The project will run from 2020 to 2023 and so far participatory workshops, virtual interactive workshops and an exchange visit has been planned for October 2022. The MCAZ through the PVCT division participated in all the training workshops.



Good Pharmacovigilance Practices (GVP) Updates



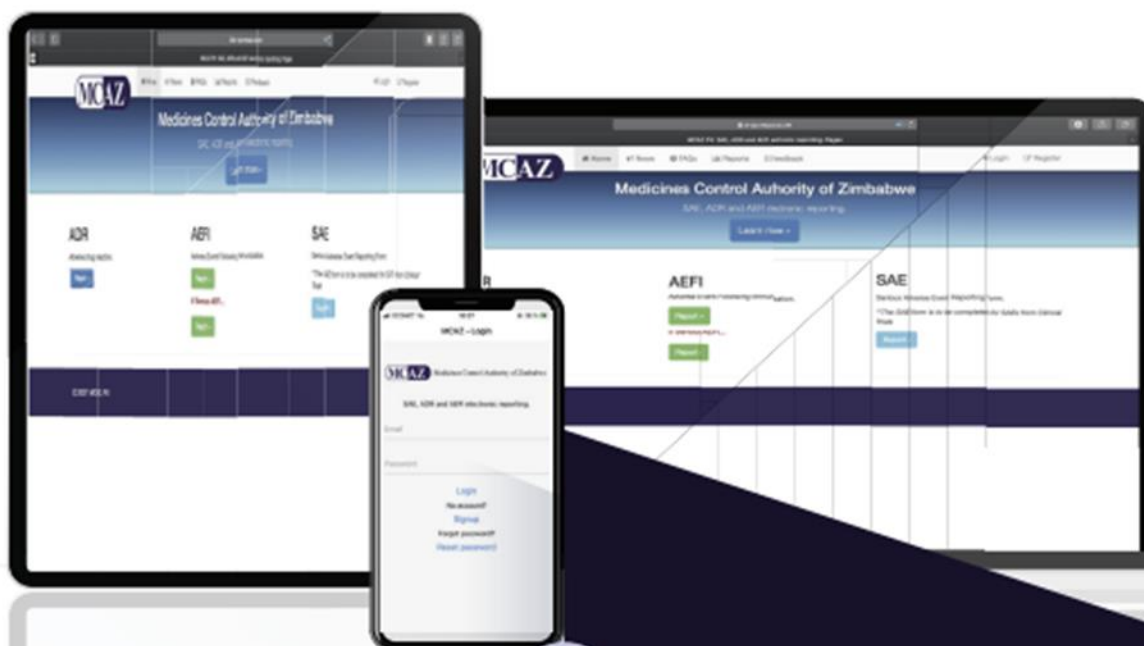
As a follow up to MCAZ Circular 3 of 2022 dated 17 February 2022 (available on the MCAZ website [link](#)), which states that

3. Applicant, manufacturer and/or market authorization holder (MAH) is required to have a functional Pharmacovigilance system in place for their medical products;
4. Applicant, manufacturer and/or market authorization holder (MAH) is required to designate a responsible person for Pharmacovigilance (QPPV) to be in charge of the pharmacovigilance system for the MAH;

an MCAZ Pharmacovigilance virtual meeting with representatives from manufacturing companies and wholesalers in Zimbabwe was held on the 20th of April 2022. The main objective of the meeting was to communicate the MCAZ Pharmacovigilance requirements for Pharmaceutical Industry. A presentation was made by the MCAZ on Good Pharmacovigilance practices (GVP), GVP inspections and structures for the establishment of the Qualified Person Responsible for Pharmacovigilance (QPPV) for Market Authorisation Holders (MAH).

In addition to the meeting, Circular 13 of 2022 dated 22 June 2022 [link](#), was released. The circular served to inform all applicants, manufacturers and market authorisation holders (MAHs) of medicines and vaccines registered and / or granted Emergency Use Authorisation (EUA) that they were required to notify the MCAZ in writing of the Pharmacovigilance system that they had in place and who the qualified person for pharmacovigilance (QPPV) is including the QPPV's curriculum vitae, contact details and their responsibilities by 25 July 2022. The MCAZ has received 31 QPPV notifications as at 22 August 2022.





e-PV Medicines & Vaccines Monitoring

The Medicines Control Authority of Zimbabwe (MCAZ) with support from the Global Fund To Fight AIDS, TB and Malaria, and in partnership with United Nations Development Programme (UNDP) developed an electronic platform for reporting adverse drug reactions (ADR) or side effects, with both online and offline reporting capabilities. This gives healthcare providers and patients a number of reporting options that would allow the Authority to continuously monitor medicines safety.

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Web based reporting

<https://e-pv.mcaz.co.zw>

Android/iOS Mobile Apps

Search "MCAZPV" on Apple App Store or "MCAZ Pharmacovigilance" on Google Play Store

Desktop Applications

Windows, MacOs (MacBook) or Linux based operating systems

Patient/Consumer reporting

<https://primaryreporting.who-umc.org/ZW>



Social Media: [mcazofficial](https://www.facebook.com/mcazofficial)



Medicines Control Authority of Zimbabwe



MCAZ MEDICINES INFORMATION BULLETIN August 2022



Benefits of the ePV electronic reporting system

- Available as an online & offline reporting system
- Automated email response is provided when:
 - the reports/applications are submitted
 - the Committee considers the report/application
 - feedback is given by the Authority
- The system allows users to:
 - View/download submitted reports/applications
 - Track the progress of submissions made to MCAZ
 - Submit feedback to MCAZ
 - View the Pharmacovigilance and Clinical Trials (PVCT) Committee meeting dates
 - View anonymised public statistics/reports
- Using the ePV system assists in ensuring efficient reporting of adverse drug reactions (side effects), thereby protecting your right to safe, effective and good quality medicines.



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