Medicines Control Authority of Zimbabwe

Medicines Information Bulletin

August 2023

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MCAZ Medicines Control Authority of Zimbabwe

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P.O. Box 10559
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REF:B/279/35/9/2023

Date: 5th of May 2023

CIRCULAR 9 of 2023

To: All PMDs, PP, PNOs, DMOs, DNOs, DPM, PHIOs, HIOs, EPI provincial officers, doctors, nurses, pharmacists, pharmacy technician and all healthcare professionals in both public and private clinics and hospitals, ZMA, PSZ, NAZ, Pharmacy Technician Association, Retail Pharmacist Association, and Pharmaceutical Wholesaler Association.

RE: Deployment of VigiMobile and VigiFlow vaccine safety Adverse Events Following Immunisation (AEFI) reporting tools for use by only healthcare professionals to report AEFIs.

The Medicines Control Authority of Zimbabwe (MCAZ) in collaboration with the Zimbabwe Expanded Program on Immunization (ZEPI) – Ministy of Health and Childcare(MoHCC) launched a new mobile application for vaccine safety AEFI reporting form known as VigiMobile. Healthcare professionals are encourged to use this user friendly reporting form. VigiMobile and VigiFlow electronic reporting tools are aimed for ease of reporting, early AEFI detection, risk minimisation and promotion of vaccinees/patient safety.

1. The Zimbabwe "**live**" VigiFlow for vaccines safety AEFI report form for use by healthcare professional as can be accessed using the following link: https://vigiflow.who-umc.org
2. The Zimbabwe "**live**" VigiMobile for vaccines safety AEFI report form for use by healthcare professionals can be accessed using the following link: https://vaccine-primaryereporting.who-umc.org/zw_aefi

The Vigimobile application can also be downloaded using the QR codes below: whose scan code below is downloadable and usable on mobile phone, tablet, iPad and laptop/computer

OR:

Once you send the report via VigiMobile or VigiFlow reporting reporting tools, the MCAZ will process the report for causality assessment by the National AEFI Committee and signed feedback will be sent to the reporters. Please note in the event that you are not able to report using

VigiMobile and VigiFlow due to internet challenges, please complete and send a hard copy AEFI report to ZEPI-MoHCC and MCAZ so that we continue to account for all AEFIs countrywide and promote public safety.

Any questions or comments for further clarification may be directed to the Director General, MCAZ 106 Baines Avenue, Email address mcaz@mcaz.co.zw; Telephone 0242708255/0242792165 or mobile phone 0772145191/3

We look forward to your participation in AEFI reporting and promoting vaccinees/patient safety.

Your faithfully

MEDICINES CONTROL AUTHORITY OF ZIMBABWE

R. T. Rukwata (Mr.)
DIRECTOR-GENERAL

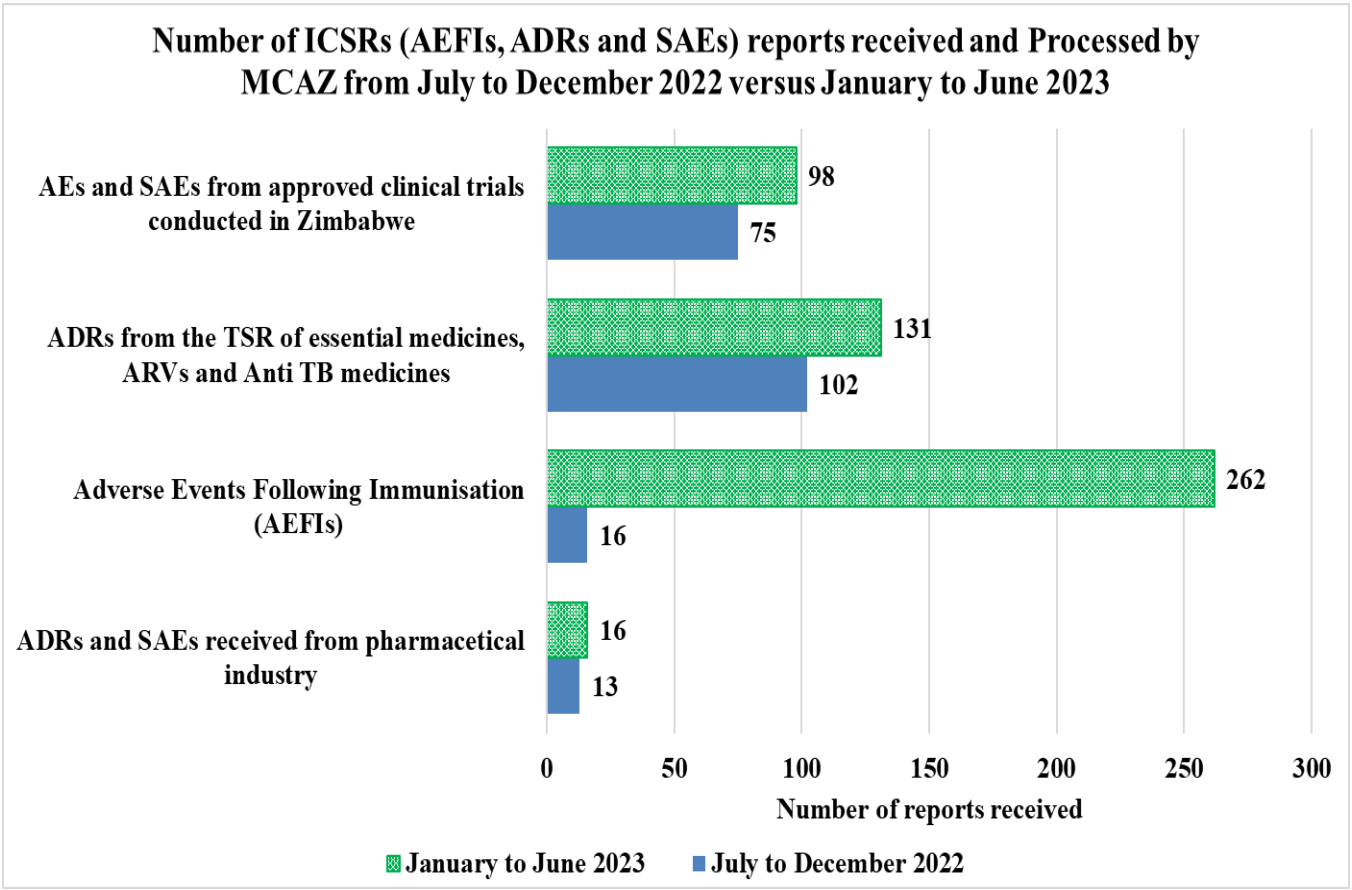
MCAZ Pharmacovigilance Updates

The Medicines Control Authority of Zimbabwe (MCAZ) is the National Centre for Pharmacovigilance (PV) implemented 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.

Figure 1 below is the summary of the Individual Case Safety Reports (ICSRs) received and analysed at the MCAZ from January to 30 June 2023 compared to the period July to December 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.

A total of 507 ICSRs were received and processed during the period January to June 2023 compared to 206 ICSRs that were received and processed during the period July to December 2022.

This increase in the number of ICSRs is mainly attributed to the VigiMobile app and VigiFlow system for AEFI reporting that was deployed for use by all provinces, districts and health facilities in Zimbabwe in April 2023.



Anti-Retroviral medicines

A total of 70 reports associated with ARVs were received and processed during the reporting period (January to June 2023) compared to 67 reports received and processed during the period (July to December 2022).

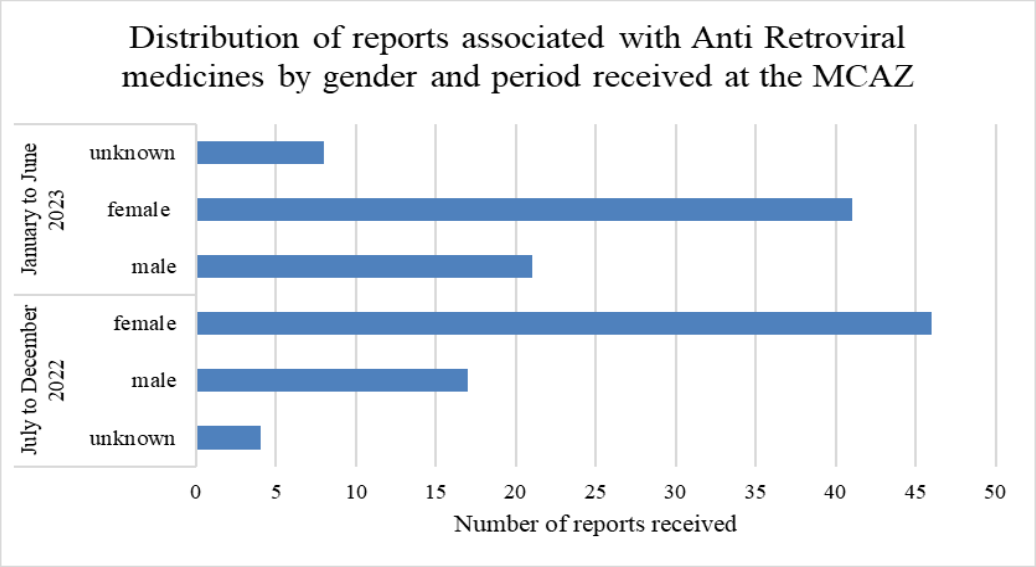


Figure 2 above shows the reports received from January to June 2023 and July to December 2022 by gender. It shows that in both periods, female patients experienced more adverse reactions associated with antiretroviral medicines. This is probably because women generally have better health seeking behaviour than men, and it is beyond the scope of the MCAZ to change this demographic characteristic.

Table 1: Most common Adverse Drug Reactions to Anti-Retroviral medicines from reports received in the period January to June 2023

Suspected medicines	Common ADRs	PVCT Committee Causality Assessment using WHO algorithm criteria
Dolutegravir	Itchiness of the body Pustules-pimples Insomnia Swollen limbs	Possible and Probable
Tenofovir, Lamivudine, Dolutegravir	Cough Rash Itchy skin Eye itchiness Dermatitis Chest pain Epigastric pain	Possible

Tenofovir disoproxil fumarate	Renal impairment (reduced eGFR, increases serum creatinine, nephrotoxicity, etc)	Possible

Table 1 above shows the PVCT Committee causality assessment of the most common ADRs, the suspected medicines and the adverse reactions from reports received in the period January to June 2023. Renal impairment was the commonly reported ADR due to tenofovir.

Anti TB medicines

A total of 34 reports associated with Anti TB medicines were received and processed during the reporting period (January to June 2023) compared to 25 reports received in the period (July to December 2022).

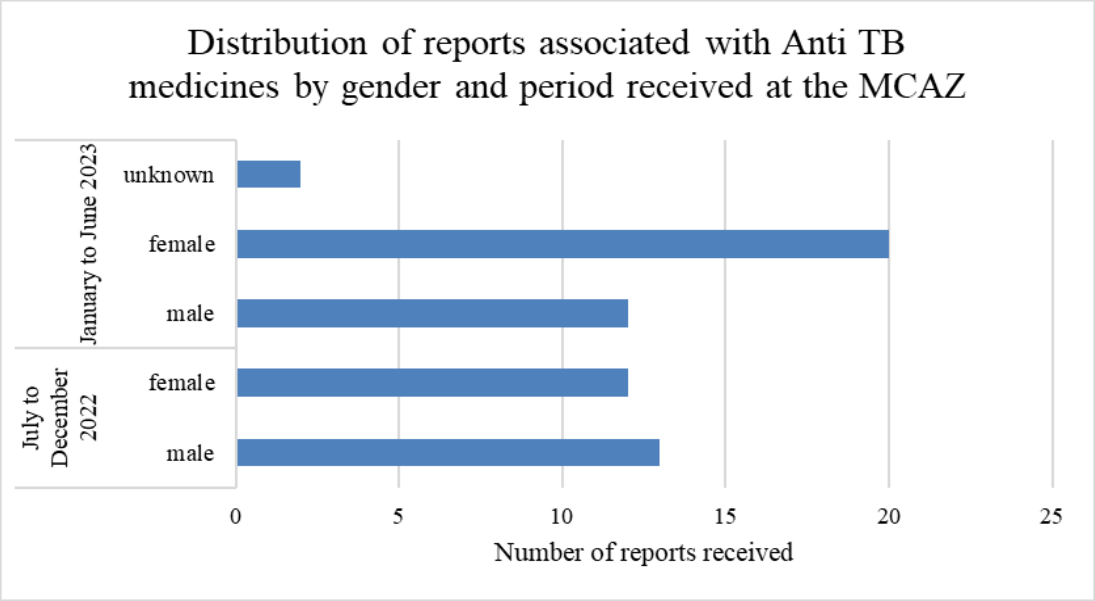


Figure 3 above shows the reports received from January to June 2023 and July to December 2022 by gender.

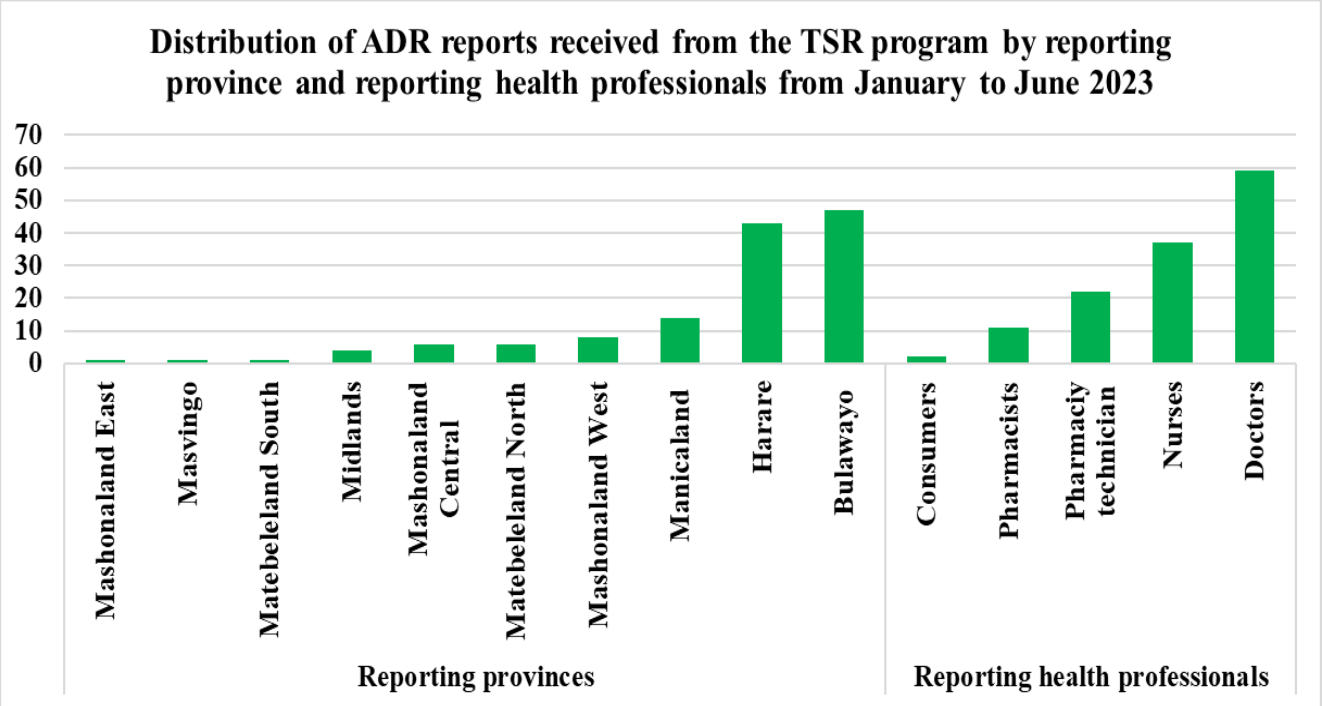
Table 2: Most common Adverse Drug Reactions to Anti-Tuberculosis medicines from reports received in the period January to June 2023

Suspected medicines	Common ADRs	PVCT Committee Causality Assessment using WHO algorithm criteria
Clofazimine	Rash Sores Hyperpigmentation	Possible
Isoniazid	Headache Rash Anaemia Dizziness Dermatitis Peripheral neuropathy Skin peeling Heartburn	Probable Possible

Isoniazid/ rifapentine	Rash Dizziness Headache Shortness of breath Fever Diarrhea Loss of appetite General body malaise Jaundice Vomiting	Probable Possible
Isoniazid/ Rifampicin/ Pyrazinamide/ Ethambutol	Cough Headache Shortness of breath Muscle pain Joint pain	Possible

Table 2 above shows the PVCT Committee causality assessment of the most common ADRs, the suspected medicines and the adverse reactions from reports received in the period January to June 2023. Isoniazid and isoniazid/ rifapentine were the most commonly reported medicine.

According to figure 4 below; nurses, doctors and pharmacy technicians reported the majority of ADR reports. Bulawayo and Harare province submitted the majority of ADR reports in the period January to June 2023. Many thanks to the tenacity and assistance of all our reporters in promoting patient safety.



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.

ADR reports can be submitted as hardcopies to the MCAZ or electronically via the Consumer Reporting platform available on the MCAZ website under Online Services .

Safety Monitoring Of Medicines

1. National Pharmacovigilance centre

MCAZ, through the Pharmacovigilance and Clinical Trials (PVCT) Division, is the National Pharmacovigilance Centre. This means that it is responsible for safety monitoring of medicines, particularly adverse drug reactions or side effects monitoring.

2. Side Effects

Side effects, sometimes referred to Adverse Drug Reactions (ADRs), are usually secondary undesirable effects that happen when the body reacts to medicines, even when the medicines have been taken correctly. Side effects can also be exeperienced after taking other medicines such as herbal and traditional medicines.

3. Why report side effects

Reporting helps:

1. to ensure patient safety;
2. to identify new reactions;
3. to record the frequency with which ADRs are reported;
4. to evaluate factors that may increase risk and provide information to prescribers with a view to prevent future ADRs;
5. to reduce risks associated with the use of medicines;
6. regulatory authorities to make vital decisions regarding safe use of medicines

How to report

There are a number of avenues that you can use to submit reports to us:

ADR Form. Can be accessed by visiting your nearest healthcare provider who will assist you to complete one

Online Consumer reporting or Healthcare reporting form

Online reporting via E-PV: e-pv.mcaz.co.zw

Via MCAZ Official Whatsapp

Contact us:

(+263242) 708225 | mcazofficial | mcazofficial | mcazofficial | +263718855934 | mcaz@mcaz.co.zw

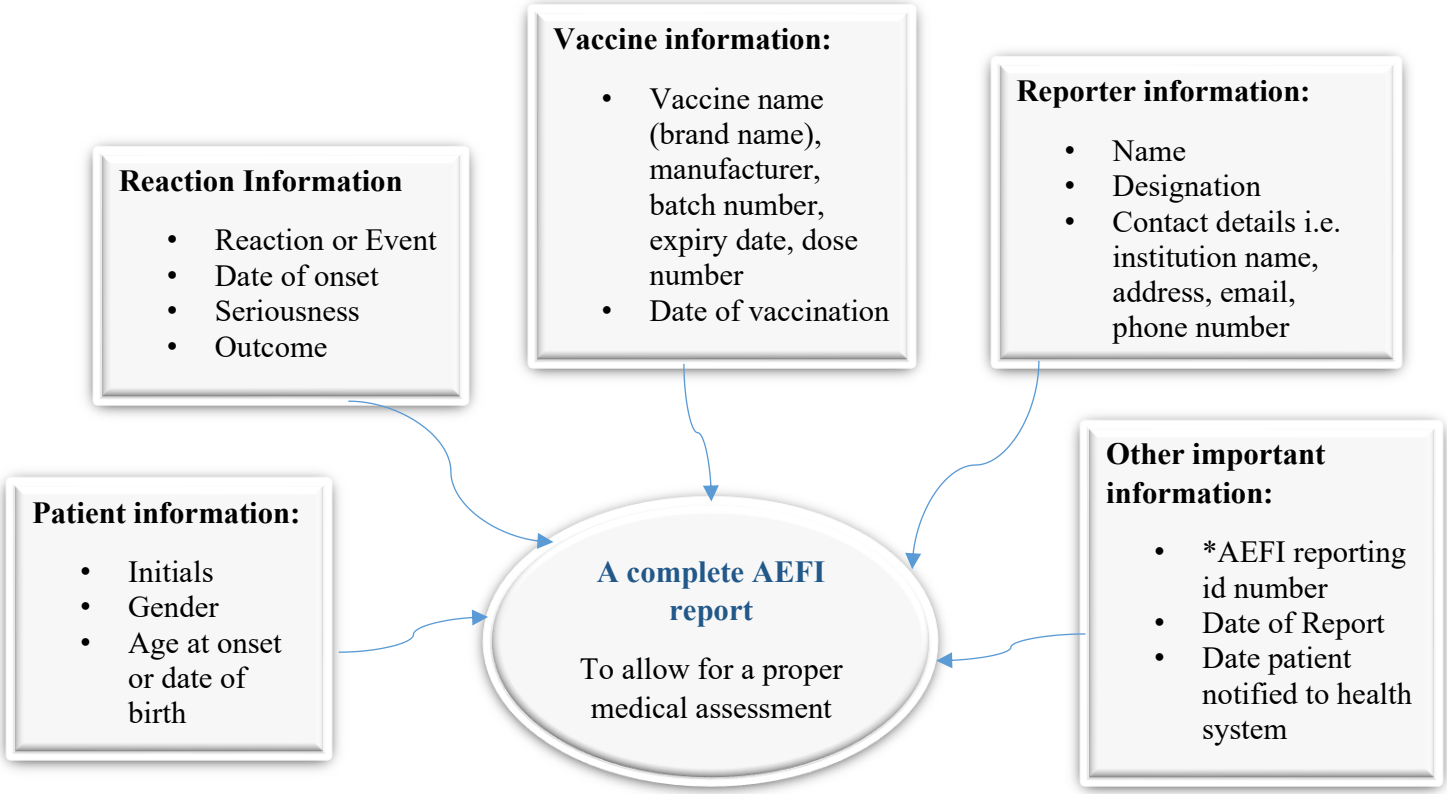
Protecting your right to quality Medicines and Medical devices

MCAZ Medicines Control Authority of Zimbabwe

Submitting complete AEFI reports to the MCAZ using VigiMobile and VigiFlow for AEFI

Adverse Events Following Immunisation (AEFI) reports constitute a key resource for the early identification of patient safety issues in relation to vaccines. The quality of data in the AEFI databases is crucial; the consequence of poor-quality data is the risk of drawing wrong or delayed conclusions about a vaccine or a safety signal, which in turn could lead to patients being harmed unnecessarily. It is therefore important to submit complete, high-quality reports.

Fig 1. Components of a complete AEFI report



*For reports sent using VigiMobile, it is important to enter **any unique** number in the section 'AEFI reporting id number' for example; *reporter name-date-time* so that the reports are seamlessly integrated and accepted by the VigiFlow server.

Below are the links to access the VigiFlow and VigiMobile for AEFI reporting platforms:

- VigiFlow for AEFI URL: https://vigiflow.who-umc.org
- VigiMobile for AEFI URL: https://vaccine-primaryereporting.who-umc.org/zw_aefi

We thank all the health care professionals for their continuous support of the national AEFI surveillance program and for promoting patient safety. We look forward to receiving more reports using VigiMobile and VigiFlow for AEFI.

Pharmacovigilance Regulatory Safety Updates

Package inserts (PI) and Patient Information Leaflets (PIL) are routinely updated by market authorization holders (MAHs) based on information obtained during safety monitoring of marketed products. The following updates have been made to the package inserts of listed products from January to June 2023.

Product	Package Insert Safety Update
Ibuprofen tablets	People taking high dose ibuprofen (more than 2400mg per day) for long-term therapy are at higher risk of thrombotic events (heart attack, stroke). Long-term daily use of ibuprofen may reduce the cardio-protective effect of low-dose aspirin.
Tamoxifen citrate	Women of child-bearing age must not become pregnant during treatment with tamoxifen and for nine months after the end of treatment.
Latanoprost/ timolol eye drops	Cases of corneal calcification have been reported very rarely in association with the use of phosphate containing eye drops in some patients with significantly damaged corneas.
Indomethacin capsules	NSAIDS cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at an increased risk for serious gastrointestinal events. NSAIDS can cause an increase in the risk of serious cardiovascular thrombotic events, including myocardial infarction and stroke, which can be fatal.
Spironolactone tablets	The concomitant use of spironolactone with angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARB) increases the risk of severe hyperkalaemia, particularly in patients with marked renal impairment. The "Interaction with other medicines and other forms of interaction" section was updated to include that – spironolactone binds to the androgen receptor and may increase prostate specific antigen (PSA) levels in abiraterone-treated prostate cancer patients. Use with abiraterone is not recommended.
Brinzolamide/ timolol maleate eye drops	Addition of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) related warnings and precautions under hypersensitivity reactions with unknown frequency.
Sevoflurane 100% solution	Inclusion of the information on bradycardia seen in children with down syndrome.

Product	Package Insert Safety Update
Paracetamol/ Ibuprofen/ Codeine phosphate capsules	Avoid use of NSAIDs in women around 30 weeks gestation and later in pregnancy due to the risks of oligohydramnios/ foetal renal dysfunction and premature closure of the foetal ductus arteriosus.
Bimatoprost/ timolol eye drops	Due to its negative effect on conduction time, the product should only be given with caution to patients with first-degree heart block. "There is a potential for hair growth to occur in areas where the solution comes repeatedly in contact with the skin surface. Thus, it is important to apply the product as instructed and avoid it running onto the cheek or other skin areas. Benzalkonium chloride has been reported to cause punctate keratopathy and/or toxic ulcerative keratopathy. Therefore, monitoring is required with frequent or prolonged use of the product in dry eye patients or where the cornea is compromised.
Diclofenac	If an NSAID is necessary from the 20th week gestation to the end of the 2nd trimester, limit the use to the lowest effective dose and shortest duration possible.
Midazolam injection	Under warnings and special precautions, the following text was added: Midazolam is not recommended for the primary treatment of psychotic illness. Midazolam may precipitate or exacerbate encephalopathy in patients with severe hepatic impairment. Midazolam should be used with extreme caution in patients with sleep apnoea syndrome and patients should be regularly monitored.
Latanoprost solution	Update to the listed adverse events including addition of the following documented adverse drug reactions: Angina, pruritus, photophobia, periorbital and lid changes resulting in deepening of the eyelid sulcus, localised skin reaction on eyelids, darkening of palpebral skin of the eyelids, iris cyst, pseudopemphigoid of ocular conjunctiva. A statement regarding rare reports of corneal calcification associated with use of eye drops containing phosphate in patients with significantly damaged corneas was also added.
Brinzolamide eye drops	Update to include Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) under hypersensitivity reactions and under the adverse drug reactions from spontaneous reports and literature with unknown frequency.
Quetiapine	The package insert has been updated to include the addition of ADR "confusional state" under undesirable effects and frequency 'Uncommon'
Darunavir tablets	Update to add 'crystal nephropathy' to the list of adverse drug reactions (ADRs) with a rare frequency based on recent post-marketing data.
Somatropin subcutaneous injection	Updates to include acute pancreatitis and gynaecomastia under the undesirable effects section.

Long term treatment with metformin and the potential for reduced vitamin B12 levels

Metformin is a medicine indicated for the treatment of type 2 diabetes mellitus and it is the most frequently prescribed first line therapy. Decreased vitamin B12 levels are a known consequence of long-term treatment with metformin. The mechanism is currently thought to be multifactorial, comprising altered intestinal motility, bacterial overgrowth, and reduced uptake of vitamin B12 within the small intestine (or a combination of these factors). Available data also show that higher daily and cumulative doses of metformin were strongly associated with lower cobalamin and holotranscobalamin concentrations, and that the decrease in vitamin B12 levels is progressive.[1],[2] The product information for metformin from marketing authorisation holders for healthcare professionals and patients has now been updated to state that vitamin B12 deficiency is a common adverse drug reaction.

Vitamin B12 (cobalamin) is required for the development, myelination, and function of the central nervous system; healthy red blood cell formation; and DNA synthesis. It is found in foods of animal origin including; milk, cheese, yoghurt, and eggs. It is also added to some fortified foods such as breakfast cereals.

Vitamin B12 deficiency is more common especially in those receiving a higher dose of metformin or longer treatment duration and in those with existing risk factors. Common causes of vitamin B12 deficiency include infections, malabsorption, medical conditions (Crohn's disease, pernicious anaemia), gastric resection, and inadequate dietary intake. [3]

Symptoms of vitamin B12 deficiency – Patients with a vitamin B12 deficiency can be asymptomatic or they can present with symptoms of megaloblastic anaemia or neuropathy or both. Other symptoms of low vitamin B12 levels may include mental disturbance (depression, irritability, cognitive impairment), glossitis (swollen and inflamed tongue), mouth ulcers, and visual and motor disturbances. It is important for patients with anaemia or neuropathy caused by vitamin B12 deficiency to be diagnosed and treated as soon as possible to avoid the development of permanent symptoms.

Risk factors for vitamin B12 deficiency

Risk factors for vitamin B12 deficiency are wide ranging. They include:

1. Baseline vitamin B12 levels at the lower end of the normal range
2. Conditions associated with reduced vitamin B12 absorption (such as elderly people and those with gastrointestinal disorders such as total or partial gastrectomy, Crohn's disease and other bowel inflammatory disorders, or autoimmune conditions)
3. Diets with reduced sources of vitamin B12 (such as strict vegan and some vegetarian diets)
4. Concomitant medication known to impair vitamin B12 absorption (including proton pump inhibitors or colchicine)

5. Genetic predisposition to vitamin B12 deficiency, such as intrinsic factor receptor deficiency (Imerslund-Gräsbeck syndrome) and transcobalamin II deficiency.

Advice for healthcare professionals:

- Test vitamin B12 serum levels if deficiency is suspected (for example, in patients presenting with megaloblastic anaemia or new-onset neuropathy) and follow current clinical guidelines on investigation and management of vitamin B12 deficiency.
- Consider periodic vitamin B12 monitoring in patients with risk factors for vitamin B12 deficiency.
- Administer corrective treatment for vitamin B12 deficiency in line with current clinical guidelines; continue metformin therapy for as long as it is tolerated and not contraindicated
- Report suspected adverse drug reactions associated with metformin on MCAZ consumer reporting form online, e-PV platform or ADR reporting forms.

Advice for healthcare professionals to give to patients and carers:

- If you are taking metformin, seek medical advice if you develop new or worsening symptoms of extreme tiredness, a sore and red tongue, pins and needles, or pale/yellow skin – these can be signs of low vitamin B12 levels
- You may need blood tests to find out the cause of your symptoms; these symptoms can also be caused by diabetes or other unrelated health issues
- You can keep taking metformin while vitamin B12 levels are being corrected
- Do not stop your treatment without first discussing this with your doctor

References

1. Metformin and reduced vitamin B12 levels: new advice for monitoring patients at risk (Webpage). Available at: https://www.gov.uk/drug-safety-update/metformin-and-reduced-vitamin-b12-levels-new-advice-for-monitoring-patients-at-risk. [Accessed on 24/07/2023]
2. Metformin Hydrochloride Extended-Release tablets USP500/1000mg. Package insert: Revision date: June 2015. MSN Laboratories Private Limited.
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6. de Jager J and others. Long term treatment with metformin in patients with type 2 diabetes and risk of vitamin B-12 deficiency: randomised placebo-controlled trial. British Medical Journal 2010; volume 340: c2181 (viewed on 24 June 2022).
7. Miller JW. Proton Pump Inhibitors, H2-Receptor Antagonists, Metformin, and Vitamin B-12 Deficiency: Clinical Implications. Advances in Nutrition 2018; volume 9: pages 511S to 518S (viewed on 24 June 2022).
8. Viaphage 500mg Tablets. Package insert: Publish date: February 2021. Varichem Pharmaceuticals (Pvt) Ltd.

Substandard and Falsified Medicines Alerts

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 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 the Report on Medicinal (Pharmaceutical) Product Defect or Problem (LEF 80), available on request from MCAZ 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 2023 (as at 27 July 2023).

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

Alert No	Alert Summary
WHO Medical Product Alert N°1/2023 **Substandard AMBRONOL syrup and DOK-1 Max syrup in the WHO European Region and Western Pacific Region**	The stated manufacturer of both products is MARION BIOTECH PVT. LTD, (Uttar Pradesh, India). Laboratory analysis of samples of both products found ***unacceptable amounts*** of ***diethylene glycol*** and /or ***ethylene glycol*** as contaminants. Diethylene glycol and ethylene glycol are toxic to humans when consumed and can prove fatal. These substandard products are unsafe and their use, especially in children, may result in serious injury or death. Both of these products are not registered in Zimbabwe but may have marketing authorizations in other countries in the region.
WHO Medical Product Alert N°2/2023 **Tetracycline hydrochloride**	The manufacturer, Galentic Pharma (India) Pvt Ltd initiated a voluntary recall for several batches (AF20011, AF21160, AF21161, AF22031, AF22032, AF22093, AF22100, AF22101, AF22107, AF20097, AF22021, AF22105, AF20060A, AF22025, AF22026 & AF22061) due to a range of quality issues. **Circular 5 of 2023**, an instruction to quarantine tetracycline hydrochloride ophthalmic

Alert No	Alert Summary
ophthalmic ointment USP 1%	ointment the above mentioned batches was issued by MCAZ on 23 February 2023.
WHO Medical Product Alert N°3/2023 **Falsified DEFITELIO (defibrotide sodium) in the WHO Regions of Europe and the Eastern Mediterranean**	A falsified batch, batch number **19G19A** of DEFITELIO (defibrotide sodium) was identified in the United Arab Emirates. Defibrotide is an antithrombotic agent used to treat severe veno-occlusive disease (VOD) in adult and paediatric patients undergoing haematopoietic (blood) stem cell transplantation. The stated batch number is not a genuine DEFITELIO batch number and the expiry dates are falsified..Laboratory analysis of a sample of the falsified product found it did not contain any of the stated active ingredient
Medical Product Alert N°4/2023 **Substandard (contaminated) Guaifenesin Syrup TG syrup in WHO Region of the Western Pacific**	Samples of this product from the Marshall Islands analysed by the Therapeutic Goods Administration (TGA) of Australia and were found to contain unacceptable ***amounts*** of ***diethylene glycol*** and ***ethylene glycol*** as contaminants. The stated manufacturer of the affected product is QP PHARMACHEM LTD (Punjab, India) and the stated marketer is TRILLIUM PHARMA (Haryana, India). Neither the stated manufacturer nor the marketer provided guarantees to WHO on the safety and quality of these products. This product is not registered in Zimbabwe but may have been distributed through informal markets.
Medical Product Alert N°5/2023 **Substandard (contaminated) Naturcold syrup identified in WHO Region of Africa**	Samples of the NATURCOLD syrup from Cameroon were analyzed by WHO and found to contain ***unacceptable amounts*** of ***diethylene glycol*** as contaminants. Diethylene glycol was detected in samples of NATURCOLD as much as **28.6%.** The acceptable limit for Diethylene Glycol is **no more than 0.10%.** The stated marketer of the affected product is listed on the product packaging as FRAKEN INTERNATIONAL (England). The United Kingdom national regulatory authority, the MHRA, has confirmed that **no such manufacturer exists in the UK**. This product referenced is not registered in Zimbabwe but may also have been distributed through informal channels.

WHO requests increased vigilance worldwide to prevent the distribution of these falsified medical products. If you have any of the affected products, WHO recommends that you do not use them Substandard or falsified medicines can be reported to MCAZ using the Report on Medicinal (Pharmaceutical) Product Defect or Problem (LEF 80), which is available on request from MCAZ and can be downloaded from the MCAZ website. If you, or someone you know, has or may have used the affected product, or 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. https://www.who.int/teams/regulation-prequalification/incidents-and-SF/full-list-of-who-medical-product-alerts
2. https://www.mcaz.co.zw/circulars/

Toxic epidermal Necrosis (TEN) associated with Sulphadoxine and Pyrimethamine tablets

Sulphadoxine and Pyrimethamine (SP) tablets are indicated for the treatment of acute, uncomplicated P. falciparum malaria for those patients in whom chloroquine resistance is suspected and for intermittent prevention of malaria in pregnant women in the malaria-endemic Sub-Saharan region. According to the EDLIZ (2020), 3 tablets of SP (each tablet containing 500mg of Sulphadoxine and 25mg of pyrimethamine) are given at booking (after quickening) and at each scheduled antenatal care visit up to the time of delivery in pregnant women in regions of moderate to high malaria transmission. Chemoprophylaxis in this group is based on the assumption that every pregnant woman in a malaria-endemic area is infected with malaria and has malaria parasites in the blood or in the placenta.

Registered products in the country

Generic Name	Brand Name	Registration Number	Category for Distribution	Manufacturer
Pyrimethamine; Sulphadoxine	AMALAR	2000/7.5/3802	Pharmacist Initiated Medicines (P.I.M.)	Brown & Burk Pharm Pvt Ltd; Micro Labs Ltd;
Pyrimethamine; Sulphadoxine	MALACURE	2022/7.5/6222	Pharmacist Initiated Medicines (P.I.M.)	S Kant Healthcare Ltd;

Safety Issues of concern

Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, toxic epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis are documented adverse events with SP. The following adverse events in the SOC of “infections and infestations," and “skin and subcutaneous disorders” were received by MCAZ from 1999 to 2023 (as at 25 July 2023).

Safety report ID	Year reported	Sex	Age (years)	Serious	Action taken with drug	MedDRA preferred term	Outcome	Committee Causality
ZW-MCAZ-ADR330/2020	2020	Female	32	No	Unknown	Dermatitis allergic	Unknown	Possible
ZW-MCAZ-2019-00017	2019	Female	34	Yes	Drug withdrawn Drug withdrawn	Septic rash	Recovered	Probable
ZW-MCAZ-2018-00686	2018	Female	27	Yes	Drug withdrawn	Rash maculo-papular Pruritus	Not recovered Not recovered	Possible
REP2098	2001	Female	8		Drug withdrawn	Blister Pruritus	Recovered Recovered	Probable
REP3697	1999	Male	45		Drug withdrawn	Rash erythematous	Recovered	Certain

According to literature, the use of sulphadoxine-pyrimethamine, like other sulphonamides, is sometimes associated with the development of some forms of drug hypersensitivity reaction. It has been reported to cause a spectrum of SJS, TEN or SJS/TEN overlap although these serious cutaneous reactions occur rarely. Fatalities associated with the administration of sulphadoxine and pyrimethamine have occurred due to severe reactions, including Stevens-Johnson syndrome (SJS) and TEN.

Advise for health professionals

- SP must be discontinued at the first appearance of skin rash or an urticarial reaction.
- SP should **not** be administered to women receiving cotrimoxazole prophylaxis due to an increased risk of adverse effects.
- The best approach to management includes high suspicion for this syndrome, early clinical diagnosis, immediate cessation of suspected culprit medication, supportive therapy, and close monitoring for and treatment of complications with high morbidity, such as infection and ophthalmologic sequelae.
- Malaria in pregnancy is associated with increased risk for both maternal and neonatal adverse outcomes, notably low birthweight and neonatal mortality.
- Intermittent preventive treatment in pregnancy with sulphadoxine/pyrimethamine (IPTp-SP) has been one of the most effective approaches to reduce the burden of malaria during pregnancy.

References

1. https://www.nafdac.gov.ng/wpcontent/uploads/Files/Resources/Pharmacovigilance_Newsletter/Sulfadoxine-and-Pyrimethamine-Newsletter.pdf
2. https://www.clinical-medicine.panafrican-med-journal.com/content/article/8/9/full/
3. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7122590/

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.

The following product recalls were conducted from January to June 2023 due to reported product defects:

	Name of product & batch number	Manufacturer	Nature of defect or problem	Type/class of recall
1.	Metronidazole 200mg tablets, Batch number 220185	Datlabs (Pvt) Ltd, Bulawayo	Discoloured tablets	**Class II** recall up to retail level
2.	Roxithromycin 150mg tablets, Batch number ABZ021001	IPCA Laboratories, India	Observed out-of-specification result (OOS) at the 18-month time point in ongoing stability studies on the water content test. High water content can result in degradation of the active ingredient.	**Class III** recall up to retail level

	Name of product & batch number	Manufacturer	Nature of defect or problem	Type/class of recall
3.	Povidone iodine (Betacleanse) 10% solution, Batches 5220031, 5220033 and 5220034	Cospharm Pharmaceuticals, Harare	Product defect indicated that the product in question was showing perceived low effectiveness due to low assay and change in consistency and potential to cause causing burns to patients	**Class II** recall up to retail level
4.	Paracetamol (Parapaed) 120mg/5ml suspension; Batch number 072203 & 072205	Gulf Drug Company, Harare	The product defect report indicated that the product in question is a suspension that was caking	**Class II** recall up to retail level

Healthcare practitioners and consumers are encouraged to report any product defects to MCAZ using the Medicine, Vaccine or Medical Device Product Problem/Defect Form (LEF 63) which is available on the MCAZ website or on request via email to mcaz@mcaz.co.zw .

Information on product defects and recalls initiated in Zimbabwe can be found on the MCAZ website under the Regulatory Functions – Licensing and Enforcement tab.

References

1. https://www.mcaz.co.zw/licensing-and-enforcement/product-defects-recalls/
2. https://www.mcaz.co.zw/circulars/
3. http://www.mcaz.co.zw/Guidelines%20for%20%20the%20Notification%20of%20Medicinal%20Product%20Problem%20or%20Defect%20and%20Recall%20Procedure

Pharmacovigilance Trainings 2023

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.

Gweru Provincial hospital submitted a request for an on-site pharmacovigilance training for their opportunistic infections (O.I) department staff. The MCAZ – PVCT division therefore conducted a Pharmacovigilance – medicines and vaccines AEFI VigiFlow and VigiMobile training at Gweru Provincial hospital on 8 June 2023. The training was a success and a total of 23 healthcare professionals were trained.

We also received another request from Mpilo Central hospital for an on-site two day pharmacovigilance training for their health care professionals. Two MCAZ-PVCT division travelled to Bulawayo, and conducted the Pharmacovigilance – medicines and vaccines AEFI VigiFlow and VigiMobile training on the 5th and 6th of July 2023. A total of 73 health care workers were trained.

We look forward to continue receiving adverse reaction/ event reports from both Gweru Provincial hospital and Mpilo Central hospital and we appreciate their continued support of the national pharmacovigilance program.

The MCAZ-PVCT division usually conducts annual provincial pharmacovigilance trainings of health care workers in Zimbabwe. In the event that any health care institution requires either virtual or on-site pharmacovigilance training, they are encouraged to submit a signed request letter via email to mcaz@mcaz.co.zw.

A special thank you to all the healthcare workers, PMDs, provincial pharmacists, PNOs, DMOs, DNOs and district pharmacy managers for their support and commitment in promoting patient safety through adverse drug reaction monitoring and reporting.

Regional collaboration in Pharmacovigilance

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

SPaRCS
Strengthening Pharmacovigilance and Regulatory Capacities in four Southern African countries

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 MCAZ through the PVCT division participated in a 2 day workshop in Windhoek, Namibia in July 2023. The objectives of the workshop were to share the experiences of the PV system strengthening activities within the SADC region (outside of SPaRCS project), to provide an update/share experiences regarding the PV system strengthening initiatives implemented as part of SPaRCS project and to discuss future PV/clinical trials projects based on the experiences of the SPaRCS project.

MCAZ Medicines Control Authority of Zimbabwe

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Press Statement

21 July 2023

RE: Substandard (contaminated) syrup medicines identified in WHO Region of Africa

Harare – The Medicines Control Authority of Zimbabwe (MCAZ), would like to alert Health professionals and members of the public of the existence of substandard syrup medicines identified in WHO Region of Africa. Like other regulators globally, MCAZ has been notified by the World Health Organization (WHO) through Medical Product Alert Number 5/2023 of the circulation of substandard products identified in Cameroon and reported to WHO on 13 March 2023.

The product known as NATURCOLD Syrup whose stated manufacturer is listed on the product packaging as FRAKEN INTERNATIONAL (England). The United Kingdom national regulatory authority, the MHRA, has confirmed to the WHO that no such manufacturer exists in the UK. Therefore, the stated manufacturer has not provided guarantees to WHO on the safety and quality of these products.

The stated active ingredients of NATURCOLD syrup are listed as paracetamol, phenylephrine hydrochloride & chlorpheniramine maleate. The combination of these three ingredients is used to relieve symptoms associated with the common cold, flu, and allergic rhinitis.

This product is reported to contain unacceptable amounts of diethylene glycol as contaminants. To date, this product has been identified in Cameroon, but may have been distributed, through informal markets, to other countries or regions. Toxic effects can include abdominal pain, vomiting, diarrhoea, inability to pass urine, headache, altered mental state, and acute kidney injury which may lead to death.

The Authority wishes to inform Health professionals and members of the public that these products are not registered in Zimbabwe. Furthermore, the manufacturer is not registered in Zimbabwe and the Authority has not authorized any importation of any products from this manufacturer. However, through illegal means, these products may find their way into the local market. As a precautionary measure, the Authority will intensify its market surveillance activities through strict premises inspection and public awareness to ensure that these products are not circulated.

In the unlikely event that members of the public are in possession of and/or come across these products, please notify the Authority and/or healthcare provider immediately and desist from administering them to children.

The mandate of the Medicines Control Authority of Zimbabwe (MCAZ) is to protect public health by ensuring that medicines and medical devices on the market are safe, effective, and of good quality and will continue to monitor the situation through the WHO guidelines. The Authority also urges members of the public to access medicines from licenced persons and premises for easier monitoring. The Authority and law enforcement agencies continue to work together to eradicate any substandard and falsified health products.

For further clarification, please do not hesitate to contact the Authority.

MEDICINES CONTROL AUTHORITY OF ZIMBABWE

pp. .....
R. T Rukwata (Mr.)
DIRECTOR-GENERAL

Zimbabwe CEO's Network Awards

Zimbabwe CEO's Network awards are a significant event in the Zimbabwe business community as they are a great way to celebrate that achievements of the country's top business leaders and to inspire others to achieve greatness.

The Medicines Control Authority of Zimbabwe (MCAZ) has been recognized as the centre of excellence by the Zimbabwe CEO Network, being the Platinum Award recipient!

As a distinguished stellar medical fraternity leader of repute, our Director-General, Mr R.T. Rukwata received the Platinum award for being and Outstanding Leader In Medical and Health.

Congratulations Makorokoto!

Paediatric Antiretroviral Treatment

Paediatric antiretroviral treatment goal

The goal of antiretroviral treatment (ART) for children is to increase survival and decrease HIV related morbidity and mortality. Regimens and dosage should be adjusted appropriately based on age and weight.

Drug-drug interactions

Drug-drug interactions can reduce or increase the efficacy of ARV therapy. Healthcare providers should be aware of all medicines being used by the patient, including alternative medicinal products such as herbal remedies, vitamins and dietary supplements that may interact with ARV medicines.

Adverse events monitoring

Always check for possible adverse effects of the medicines. The Guidelines for Antiretroviral Therapy for the Prevention and Treatment of HIV in Zimbabwe highlight the importance of watching out for common side effects such as anaemia, renal impairment, CNS symptoms and peripheral neuropathy

Reporting of Adverse Drug Reactions (ADRs)

MCAZ is the National Centre for Pharmacovigilance (PV) in Zimbabwe. PV is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems. ADR reports should be completed and submitted to MCAZ.

Hard copy ADR forms are available on request from the Medicines Control Authority of Zimbabwe (MCAZ) at 106 Baines Avenue Harare and electronic copies can be downloaded from this link: https://www.mcaz.co.zw/?smd_process_download=1&download_id=2500

• The (MCAZ) also has an electronic platform for reporting ADRs/ side effects, called the Electronic Pharmacovigilance (e-PV) system which has:

*web-based reporting available via the following link: https://e-pv.mcaz.co.zw/

Android/iOS mobile applications which can be downloaded from Google play store (MCAZ Pharmacovigilance) and Apple store (MCAZ PV) respectively

* Desktop applications for Windows/ MacOs/ Linux -based operating systems

The mobile and desktop apps have both online and offline reporting capabilities.

Patient/ Consumer reporting can also be done via the following link https://primaryreporting.who-umc.org/ZW

Who should report?

Anyone can report including health professionals, health and community workers, patients or patient's family members and the general public.

MCAZ Medicines Control Authority of Zimbabwe

Contact: 263772145191-2/ +263(242)736981-7

Email: mcaz@mcaz.co.zw

Website: www.mcaz.co.zw

Telephone +263-242-798537-61

*All correspondences should be addressed to the **Permanent Secretary for Health and Child Care***

ZIMBABWE

Reference:
Ministry of Health And Child Care
P.O. Box CY1122
Causeway
Zimbabwe

24 May 2023

All Provincial Medical Directors

HEALTH ALERT ON JOHNSON AND JOHNSON BABY POWDER

The above matter refers.

On 18 April 2023, an American television channel, Consumer News and Business Channel (CNBC) reported that Johnson and Johnson, an American multinational corporation, had assumed the liability to pay eight point nine billion United States Dollars (US$8.9 billion) to the medical industry in compensation over allegations that the company's baby powder was causing cancer. Research by the American Academy of Paediatrics unearthed that the talc used in the production of the baby powder was highly toxic due to contamination with carcinogen asbestos.

Tanzania Bureau of Standards on the 19th of April 2023, banned the importation and distribution and sale of Johnson and Johnson's baby powder containing the talc ingredient. The product is still popular in South Africa amid indications that most consumers are unaware of its potential risks. Given the significant importation of health products by Zimbabwe from South Africa, there is a high risk that the contaminated baby powder could still be finding its way into the Zimbabwean market.

Ministry of Health and Child Care is banning the importation and distribution and sale of Johnson and Johnson's baby powder containing the talc ingredient with immediate effect. Environmental Health Officers and Technicians are advised to remove all Johnson and Johnson's baby powder containing the talc ingredient from the market. Inspectors are advised to document their findings and the products must be destroyed or recalled to the manufacturers.

Air Commodore (Dr) J Chimedza
Secretary for Health and Child Care

SECRETARY FOR HEALTH AND CHILD CARE
24 MAY 2023