Medicines Information Bulletin

July 2020
Edition

MCAZ Medicines Control Authority of Zimbabwe

Dear readers,

Dear readers, working coherently together is more effective than the same number of people working separately. With that principle we can fight together as one the COVID-19

The coronavirus pandemic poses an unprecedented collective challenge to the right to life and to health for people in the world. May the souls claimed by this pandemic rest in peace. Given the speed with which the pandemic and policy responses have unfolded, the bulletin does not present in-depth measures and their impact. However, I concur with Michael O'Flaherty's assertion above.

Inside this bulletin we have provided some insights into the issues surrounding substandard and falsified medicines (SF). Low-to-middle-income countries (LMICs) have become targets of substandard and falsified antimicrobials, essential for the treatment of life-threatening diseases, such as malaria, tuberculosis, HIV and AIDS.

We continue to underscore the importance of reporting Adverse Drug Reactions (ADRs) via the platforms provided in this read. This is important so as to ensure patient safety and to record the frequency with which the ADRs are reported and evaluate factors that may increase risk and provide information to prescribers with a view to preventing future ADRs.

In closing let me emphasize the importance of social distancing and following other basic preventive measures so that we can collectively manage the COVID-19 pandemic. Either we meld up or we melt down. The choice is resident in us.

Do enjoy the read.

Priscilla Nyambayo

Head, Pharmacovigilance & Clinical Trials

"We clearly need strong public health responses to protect life during the pandemic…the more we respect human rights, the better will be our public health strategies"

As asserted by Michael O'Flaherty

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COVID-19

WHAT YOU NEED TO KNOW

The world is currently facing an outbreak of a respiratory disease caused by a novel coronavirus that was first detected in Wuhan City, Hubei Province, China, in December 2019. The virus has since been named "SARS-CoV-2" and the disease it causes has been named "Coronavirus Disease 2019" (COVID-19). The novel coronavirus (2019-nCoV) is a new strain of coronavirus that had not previously been identified in humans. The coronavirus family is known to cause illness in humans, from the common cold to more severe or even fatal diseases such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) (1). The virus has been detected in many locations internationally, including cases in Zimbabwe. The outbreak of COVID-19 was declared a Public Health Emergency of International Concern on 30 January 2020 by the World Health Organization (WHO). Current epidemiologic information suggests that human-to-human transmission of COVID-19 can occur when an individual is in close contact with a symptomatic case. Current studies are investigating if the virus can be transmitted to others if someone is not showing symptoms (2).

Human coronaviruses are most commonly spread from an infected person through: respiratory droplets; close, prolonged personal contact and touching an infected area, then touching your mouth, nose or eyes before washing hands (3).

Those who are infected with COVID-19 may have little to no symptoms. Symptoms, similar to a cold or flu, may take up to 14 days to appear after exposure to COVID-19. Symptoms include: cough, fever, difficulty breathing, pneumonia in both lungs. In severe cases, infection can lead to death. While most people with COVID-19 develop only mild or uncomplicated illness, approximately 14% develop severe disease that requires hospitalization and oxygen support. 5% of those infected require admission to an intensive care unit. In severe cases, COVID-19 can be complicated by acute respiratory distress syndrome (ARDS), sepsis, septic shock, multiorgan failure, including acute kidney injury and cardiac injury. Older age and co-morbidities have been reported as risk factors for death (4). There is currently no vaccine against or specific treatment for COVID-19. Treatment is supportive and should be tailored to the patient's condition. At present, clinical management includes infection prevention and control measures; supportive care, including supplementary oxygen and mechanical ventilatory support when indicated. An array of medicines approved for other indications as well as several investigational drugs are being studied in several hundreds of clinical trials that are underway across the globe, including agents such as hydroxychloroquine/chloroquine, remdesvir, lopinavir/ritonavir and many others. (5).

In recent months there has been considerable focus on the potential for HCQ and CQ. As a result of conflicting findings from different clinical trial settings across the globe, this has led to the need for additional robust clinical data to guide decision-making regarding the clinical use of these therapies for the treatment of COVID-19.

It is of utmost importance that patients and healthcare professionals only use chloroquine and hydroxychloroquine for their authorised uses or as part of clinical trials or as advised as per national emergency use guidelines. All clinical trials must be approved by the MCAZ before they are conducted. Chloroquine and hydroxychloroquine are vital medicines for patients with autoimmune conditions such as lupus. It is important that such patients are still able to access them and do not face shortages caused by stockpiling for their use outside the authorised indications. In some countries, prescribing of the medicines has been restricted to reduce the risk of shortages.

There are clinical trials currently under way to generate the robust data needed to establish the efficacy and safety of chloroquine and hydroxychloroquine in the treatment of COVID-19. The WHO is conducting a multi-centre clinical trial (Solidarity trial) to assess the safety and efficacy hydroxychloroquine and chloroquine, remdesvir, Lopinavir/ritonavir, Interferon beta-1a and standard of care in adult hospitalised patients diagnosed with COVID-19 (6). Similar trials are being conducted in Europe i.e. DISCOVERY AND RECOVERY trials.

MCAZ will be closely monitoring progress and outcomes of these trials to guide local treatment and management. Further to this, any other potential therapies, would need to go through rigorous clinical trials, to ensure evidence-based clinical data is obtained ethically.

For more information on COVID-19 you can click on the links below:

https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance

https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov

References

1. EMA, March 2020, Coronavirus disease (COVID, https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19
2. WHO, 2 April 2020, Coronavirus disease 2019 (COVID-19) Situation Report –73 https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200402-sitrep-73- covid-19.pdf?sfvrsn=5ae25bc7_2
3. Health Canada, April 2020, Coronavirus disease (COVID-19): For health professionals, https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/health-professionals.html
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5. CDC, Information for Clinicians on Therapeutic Options for COVID-19 Patients, https://www.cdc.gov/coronavirus/2019-ncov/hcp/therapeutic-options.html#r1
6. WHO, April 2020, "Solidarity" clinical trial for COVID-19 treatments https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments

MCAZ Core Values

Customer Focus

Integrity

Accountability

Continuous Improvement

Substandard & Falsified Medicines

Substandard and falsified medical products (including medicines, vaccines, biologics, and diagnostics) represent a significant and growing threat to public health. According to the WHO, a substandard medicine, also referred to as "out of specification", is an authorized medical product that fails to meet either quality standards or specifications, or both. Whilst a falsified medical product is one that deliberately/fraudulently misrepresents the identity, composition or source. Falsified medical products are often disguised as authentic medicines but may contain incorrect quantities of the active pharmaceutical ingredient (API) or excipients and dangerous contaminants.

Substandard and falsified medicines commonly reported in high-income countries (HICs) include novel medicines, such as hormones, steroids, and supplements, while low-to-middle-income countries (LMICs) have become targets of substandard and falsified antimicrobials, essential for the treatment of life-threatening diseases, such as malaria, tuberculosis, HIV and AIDS. According to the WHO Global Surveillance and Monitoring System for Substandard and Falsified Medicines, antibiotics and antimalarials were the most commonly reported substandard and falsified medical products reported between 2013 and 2017, representing around 36% of all the products reported by member states. It is important to note that substandard production and falsification affects all types of medical products and the WHO Global Surveillance and Monitoring System for substandard and falsified medical products has reports for lifesaving to so-called lifestyle products for cosmetic use, body-building and weight loss.

On an individual level, falsified medicines can lead to treatment failure with prolonged or more severe sickness and death. At a public health level, delivery of subtherapeutic antimicrobial drug concentrations may increase the incidence of resistance. Ineffective treatment translates to depletion of healthcare resources as well as loss of confidence in medical products, healthcare professionals and health systems In a study by Bassat Q et al (2016), falsified artemisinin was observed to contain only paracetamol, there- by exerting an antipyretic effect but with disease progression and even death.

Medical devices are also prone to counterfieting. Although the primary action of these devices is not pharmacological, they are however not exempt from counterfeiting, with WHO reporting an increase in circulation of counterfeit medical devices

The solution to the global problem of substandard and falsified products is to prevent the manufacture, sale and consumption of substandard medical products, implement systems to detect substandard or falsified products already in the supply chain and respond quickly and proportionately to any incidents that are detected. For more information, visit

https://www.who.int/news-room/fact-sheets/detail/substandard-and-falsified-medical-products

Suspected substandard and falsified products can be reported using Product Defect Forms, available on request and accessible via the MCAZ website via the following link:
https://www.mcaz.co.zw/index.php/downloads/category/16-forms?download=107:product-defect-form

Product Safety Alerts

Falsified Quinine sulphate 300mg presented in six different combinations of batch numbers, expiry and manu- factured dates with fraudulent use of the outdated WHO Essential Drugs Programme logo circulating in West and Central Africa. Analysed samples did not contain any of the expected active ingredients. For more : https://www.who.int/news-room/detail/09-03-2020-medical-product-alert-n-1-2020- english-version

Falsified Uni-Gold™ HIV rapid diagnostic tests displaying falsified expiry date. The genuine manufacturer, Trinity Biotech confirmed that they did not manufacture the falsified products. Genuine lot numbers HIV7120026 and HIV6120030 were made by Trinity Biotech plc but expiry dates are incorrect and do not correspond with their batch manufacturing records. Additional details and pictures available here: https://www.who.int/news-room/ detail/27-03-2020-medical-product-alert-n-2-2020

Falsified in vitro diagnostics (IVDs) and laboratory reagents for the detection of SARS-CoV-2 and falsified medicines and vaccines for the treatment and prevention of COVID-19. Due diligence is required from all actors in the procurement, use and administration of medical products, in particular those affected by the current crisis of, or related to, COVID-19. Please refer to WHO's Emergency Use Listing for a list of diagnostics approved for clinical use by WHO.

Nine different falsified chloroquine products in 100mg and 250mg tablet presentations circulating in three countries in Africa. On analysis, the products either did not contain the correct amount of active pharmaceutical ingredients and/or had falsified/non-existent manufacturer details. Please refer to the WHO Medical Product Alert website for photographs and additional information on the falsified chloroquine products.

Reporting Adverse Drug Reactions (ADRs)

What is an ADR?

An adverse drug reaction (ADR) is a response to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease, or for modification of physiological function

Why report ADRs?

- To ensure patient safety
- To identify new reactions
- To record the frequency with which the ADRs are reported and evaluate factors that may increase risk and provide information to prescribers with a view to preventing future ADRs.
- Reduce risks associated with the use of medicines
- To help regulatory authorities to make vital decisions regarding the safe use of medicines

What to report?

- All healthcare professionals
- All types of suspected ADRs (Known or unknown, serious or non-serious, frequent or rare) regardless of an established causal relationship.
- Adverse Drug Reactions (ADRs) associated with medicines, vaccines, complementary medicines, contrast media and other pharmaceuticals
- Inefficacy of medicines

Who can report ADRs?

- All healthcare professionals
- Pharmaceutical industry
- Consumers/patients

How to report?

Adverse Drug Reaction Form

All suspected ADRs can be reported using the ADR form which the MCAZ distributes or can be downloaded from the MCAZ website. The completed forms should be forwarded to the MCAZ. This can be done physically or can be sent to the email: mcaz@mcaz.co.zw

Online reporting

- Browser-based application https://e-pv.mcaz.co.zw
- Android mobile application (MCAZ Pharmacovigilance)
- iOs mobile application (iphone, ipad) - (MCAZ Pharmacovigilance)
- Windows desktop application
- Mac Os desktop application
- Linux desktop application

The mobile and desktop applications have offline functionality and reports can be completed offline then sent later when internet is available.

Visit www.mcaz.co.zw > Online Services > ADR E-Reporting > Choose "Consumer reporting" or "Healthcare Professional Reporting" > Complete the form

MedSafety Week

Look out for yet another exciting opportunity to learn more about why it is important to report ADRs and issues around Medicine Safety. MCAZ will be taking part in the global campaign coordinated by Uppsala Monitoring Centre.

More details to follow.

How to report ADRs

Browser-based Web application

E-PV: https://e-pv.mcaz.co.zw

E-CT: https://e-ctr.mcaz.co.zw

Mobile phone application - MCAZ Pharmacovigilance

Android - Play Store

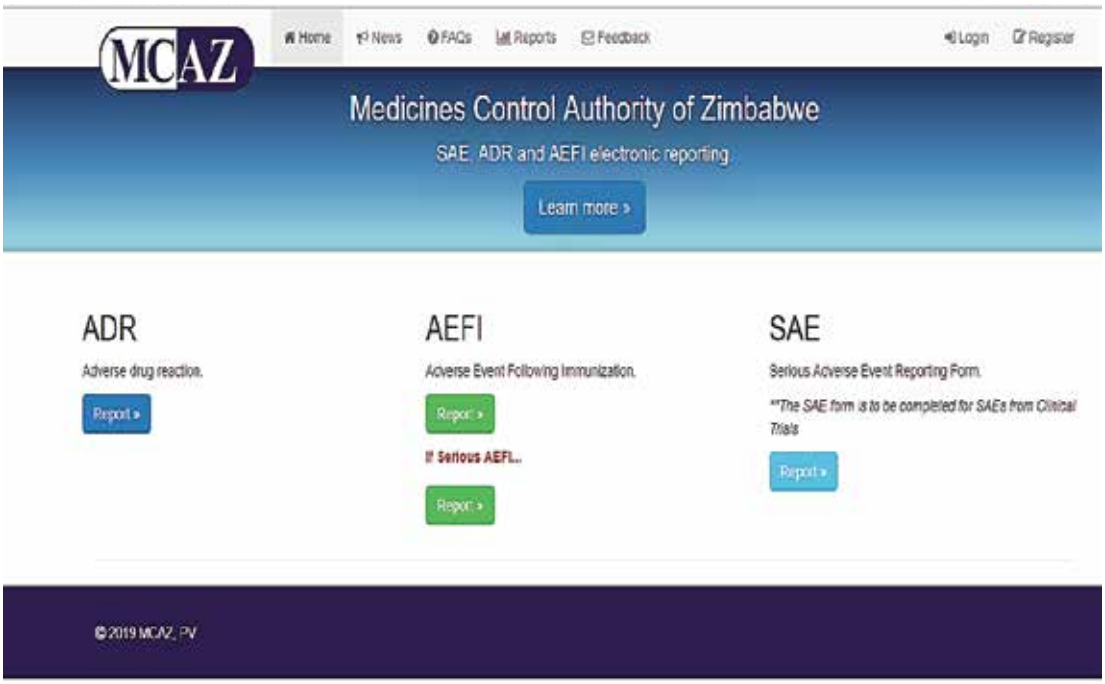
iOs - App Store

Desktop applications

Windows

Mac Os

Linux



ADRs Case Series Benefit/risk analysis

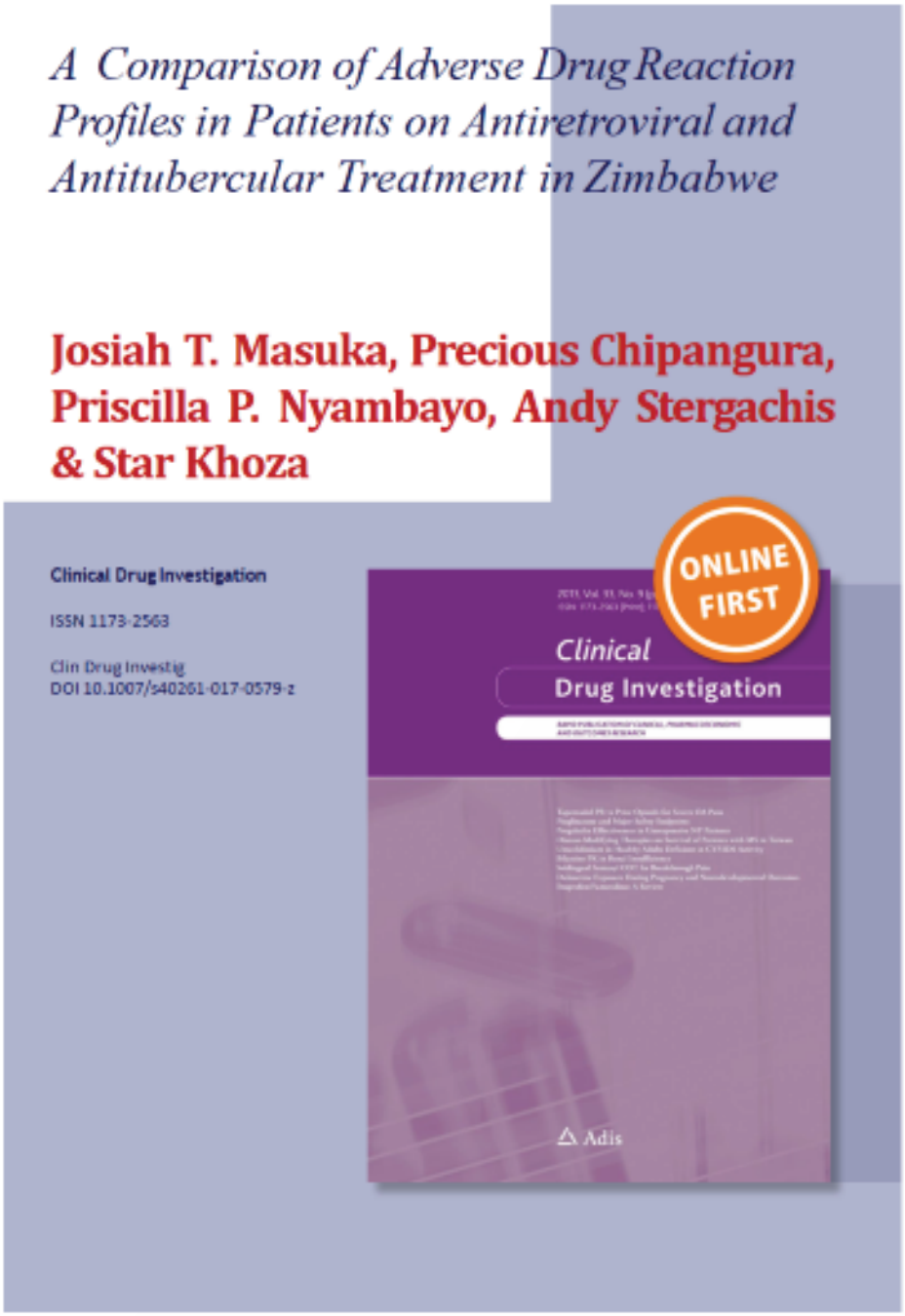
Summary

ART was associated with a higher frequency of Stevens-Johnson Syndrome, gynaecomastia, and lipodystrophy. Co-administration of ART and Ant-TBs was associated with a higher frequency of medicines-induced liver injury and peripheral neuropathy.

Similarly, co-administration of isoniazid preventive therapy (IPT) and ARVs was associated with a higher risk for psychosis. There is a need to carefully manage TB/HIV co-infected patients, due to the higher risk of ADRs which may lead to poor treatment adherence and outcomes.

Click link below to access the publication:

https://link.springer.com/article/10.1007/s40261-017-0579-z



Highlights from 2019

Targeted Spontaneous Reporting (TSR) Trainings

Every year the MCAZ Pharmacovigilance and Clinical trials division conducts pharmacovigilance trainings for healthcare professionals in all provinces of the country. The trainings are aimed to educate, encourage and remind all health care professionals to continuously participate effectively in the reporting of Adverse Drug Reactions (ADRs). Amongst the health care professionals trained were District Medical Officers (DMO), District Health Information Officers (DHIO), nurses, doctors and pharmacy personnel.

In the year 2019 a total of 101 healthcare professionals were trained in 4 provinces. The provinces trained were Harare, Matebeleland South, Manicaland and Mashonaland central with 25, 28, 28 and 20 healthcare professionals trained respectively.

Clinical Trials ReCORE Training

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 other regulators in Clinical Trials. The course is designed to promote harmonization in regulatory requirements. 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 ongoing clinical trials.

The Pharmacovigilance and Clinical trials division conducted a 2 week benchmarking and best practice learning training in clinical trials from the 25th of November to the 6th of December 2019. Five participants from the Namibia Medicines Regulatory Council (NMRC) and the Namibia ministry of health and social services attended the training. The participants were exposed to different aspects of clinical trials being done by the Authority and the MRCZ.

2020 Events

Formalisation of Provincial and District Pharmacovigilance Sentinel Sites

The Medicines Control Authority of Zimbabwe (MCAZ) in collaboration with the Ministry of Health and the Directorate of Pharmacy Services (DPS), has been running the Targeted Spontaneous Reporting of Essential Medicines (TSR) programme to monitor all ADRs from ARVs, Anti-TB medication and other Essential Medicines from 2012 to 2020. The main objective was integration of pharmacovigilance into public health programs and identification of provincial and district sentinel sites. ADR reporting from ART and TB clinics countrywide increased significantly and many sites started reporting. Signal detection and causality data analysis of the reports was published (Masuka JT et al 2017). Newlands clinic, Parirenyatwa, Harare Central , Chitungwiza and Mpilo hospitals were identified as some of the highest reporting sites. Thanks to all reporters!

The program will be coordinated by the MCAZ as the National Pharmacovigilance center and the DPS as the pharmacovigilance focal team. The formalization of the pharmacovigilance public health regional centers will be done for all provincial and district centers as the focal centers in respective provinces. Consultative pharmacovigilance meetings were held that assisted in drafting the Term of Reference (TOR) of Formalization of provincial and district Pharmacovigilance sentinel sites. Central hospitals, private hospitals and clinics are also welcome. The next bulletin issue will provide the list of PV sentinel sites and reporting rates.

Pharmacovigilance trainings

Increasing awareness about the pharmacovigilance program through training appears to be necessary to enhance reporting of ADRs. This year MCAZ will be revising the Pharmacovigilance training model to include online trainings. The unprecedented COVID-19 pandemic has presented an opportunity for MCAZ to explore virtual pharmacovigilance trainings and workshops, as well as making the most of remote/online tools to enhance pharmacovigilance in Zimbabwe.

Training of healthcare providers on pharmacovigilance

MCAZ Regional Centre of Regulatory Excellence (RCORE) clinical trials regulation benchmarking visit for five cadres from Namibia Ministry of Health

Recategorization of medicines

What is recategorization of medicines?

The sale and supply of medicines in Zimbabwe is governed by the Medicines and Allied Substances Control Act [Chapter 15:03]. Currently, Section 39 (Sixth schedule) of Medicines and Allied Substances Control Regulations (SI 150 of 1991) prescribes the categorization of medicines for human use into:

Special Restricted preparations or ("S. R.")
Prescription Preparations or ("P. P.")
Prescription Preparations ("P.P 10")
Pharmacist Initiated Medicines or ("P. I. M."). - These non-prescription medicines may only be supplied on the recommendation of a pharmacist and proper records need to be maintained.
Pharmacy Medicines or ('P.")
Household Remedies or ("H. R.") are medicines suitable for self-medication.

Application can therefore be made to the MCAZ to change the category for distribution of medicines. This procedure is referred to as 'recategorisation'. Below are some of the medicines that were recategorised.

Pantoprazole 20mg Oral Dosage Forms

What is it used for? - Gastroesophageal Reflux Disease
Pharmacological Classifications - Proton Pump Inhibitors
Previous Category For Distribution - Prescription Preparation (P.P)
New Category For Distribution - Pharmacist Initiated Medicines (P.I.M)

Esomeprazole 20mg Oral Dosage Forms

What is it used for? - Reduces stomach acid, Gastroesophageal Reflux Disease, peptic ulcers
Pharmacological Classifications - Proton Pump Inhibitors
Previous Category For Distribution - Prescription Preparation (P.P)
New Category For Distribution - Pharmacist Initiated Medicines (P.I.M)

Lansoprazole 20mg Oral Dosage Forms

What is it used for? - Reduces stomach acid, Gastroesophageal Reflux Disease, peptic ulcers
Pharmacological Classifications - Proton Pump Inhibitors
Previous Category For Distribution - Prescription Preparation (P.P)
New Category For Distribution - Pharmacist Initiated Medicines (P.I.M)

Rabeprazole 20mg Oral Dosage Forms

What is it used for? - Reduces stomach acid, Gastroesophageal Reflux Disease, peptic ulcers
Pharmacological Classifications - Proton Pump Inhibitors
Previous Category For Distribution - Prescription Preparation (P.P)
New Category For Distribution - Pharmacist Initiated Medicines (P.I.M)

Medicines Safety Alerts

Name of drug:	Propofol
Risk Warning:	Priapism
Information source:	Summary Safety Review, Health Canada, 12 July 2019 https://www.hc-sc.gc.ca

Name of drug:	Febuxostat
Risk Warning:	Potential risk of cardiovascular death
Information source:	WHO Pharmaceuticals Newsletter No.4, 2019 https://www.who.int/medicines/publications/PharmaNewsletter4-19/en/

Name of drug:	Iron Sucrose
Risk Warning:	Kounis Syndrome
Information source:	European Medicine Agency (2019). PRAC recommendations on signals. EMA/PRAC/580132/2019.
Retrieved from:	https://www.ema.europa.eu/en/documents/prac-recommendation/prac-recommendations-signals-adopted-28-31-october-2019-prac-meeting_en.pdf

Healthcare professionals are sensitized to carefully monitor the above mentioned alerts, ensuring any event related to these drugs is reported to the MCAZ

Editorial Note

Dear Reader

We would like to thank you for taking an interest in reading our first volume of the bulletin for 2020 and your continued support in reporting ADRs and AEFIs to the MCAZ National Pharmacovigilance Centre. We cherish your reports and will continue the publication of the Medicines information bulletin as one of the ways of disseminating Medicines Safety information to Healthcare professionals. Please note that the reporting of a seemingly insignificant or common adverse reaction or side effect may help pinpoint a more widespread adverse effect or prescribing problem. If you have ques- tions on any area of concern, please write to us on 106 Baines Avenue, Harare or call us on 708225/792165, Cell: 0772145191-3.

Thank you for reading.

Acknowledgement

MCAZ is grateful for the support from the Ministry of Health Child Care (MoHCC), Health Development Fund (HDF) supported by UNICEF, Global Fund and United Nations Development Programme (UNDP), Drug and Toxicology Information Service (DaTIS) and other partners who made the publication of this bulletin possible.

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