BoMRA
MEDICINES REGULATORY AUTHORITY

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Dear Healthcare Professionals

The Botswana Medicines Regulatory Authority (BoMRA) wishes to bring to your attention a safety concern associated with the use of Proton Pump Inhibitors (PPIs), specifically their potential to trigger acute interstitial nephritis, a serious adverse event linked to acute kidney injury.

Background of safety concern

Proton pump inhibitors (PPIs) bind to enzyme H+/K+-ATPase and inhibit its activity in the stomach, thus decreasing the secretion of gastric acid. PPIs are widely used for the treatment of gastro-esophageal reflux disease and other acid-related disorders of the gastrointestinal tract. As a class, PPIs have demonstrated a favorable safety profile. However, PPIs may trigger acute interstitial nephritis, a potentially severe adverse event commonly associated with acute kidney injury. Acute interstitial nephritis is characterized by an inflammatory reaction within the tubulointerstitial space of the kidney. Acute interstitial nephritis can result in acute kidney injury. Further, delayed diagnosis and continual use of PPIs can impair recovery from acute kidney injury and may lead to chronic renal failure.

As of 20th February 2024, globally, there are 6,131 safety case reports or adverse drug reactions related to tubulointerstitial nephritis associated with PPIs use. Notably, the majority of these reports (*n=1,537* cases) were observed in individuals aged 45–64, with females being the most affected. It is important to note that BoMRA has not received any reports of tubulointerstitial nephritis associated with PPIs in Botswana to date. It must be noted that the current benefit-risk balance for PPIs remains favorable based on available data.

Advice to healthcare professionals

- Studies have shown that the elderly with autoimmune diseases and sarcoidosis present an increased susceptibility to drug-induced acute interstitial nephritis.
- Acute interstitial nephritis is a serious adverse event observed in patients taking PPIs and may occur at any point during therapy.
- Patients may present with varying signs and symptoms from symptomatic hypersensitivity reactions (e.g., fever, rash, or arthralgia), to non-specific symptoms of decreased renal function (e.g., malaise, nausea, or anorexia).
- Treatment with PPIs must be stopped when acute interstitial nephritis is suspected.
- PPIs are contraindicated in patients who previously experienced acute interstitial nephritis while on treatment with PPIs.

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- Caution should be taken when other nephrotoxic medicines such as aminoglycosides, non-steroidal anti-inflammatory drugs, antineoplastic agents are co-administered with PPIs.
- Patients should be asked to report any decrease in urine volumes or if they suspect that there is blood in their urine while on PPIs.

BoMRA has requested all Market Authorization Holders of all PPIs to amend Professional Information (PI) and Patient Information Leaflet (PIL) to reflect the updated safety information.

How to report Adverse Drug reactions

Report any suspected ADRs or any discomfort experienced by a patient to BoMRA using any of the following BoMRA platforms:

1. **ADR reporting forms** :You may download the forms from the BoMRA website www.bomra.co.bw and email the completed for to reportadr@bomra.co.bw.
2. **E-reporting:** Follow the Primary eReporting (who-umc.org) link available on BoMRA website_and complete the form online. BoMRA Regulatory Information Management System (BRIMS) Portal (bomra.co.bw) https://brims.bomra.co.bw/#/public/app-home.
3. **MedSafety App**: Use the ADRs reporting App, available on apple store or google store for smart phones.
4. **Phone reporting:** Call BoMRA at 373 1727/ 20.
5. **Information and Support:** For more information on medicine/vaccine safety, contact BoMRA **National Medicines Information Centre** at 373 1788/71 or via nmic@bomra.co.bw.

Dr. Seima Dijeng

Acting Chief Executive Officer

Visit the BoMRA website for additional medicine safety publications.