IMPORTANT MEDICINE SAFETY INFORMATION

30 October 2023

Dear Healthcare Professional,

Re: The risk of acute tubulointerstitial nephritis (TIN) associated with proton pump inhibitors (PPIs)

The Pharmaceutical Companies listed above, as directed by the South African Health Products Regulatory Authority (SAHPRA), would like to update you on the safety information regarding acute tubulointerstitial nephritis (TIN) that has been observed with the use of Pantoloc® / Topzole® (Pantoprazole), Dexilant® (Dexlansoprazole), Nexiam® / Axiago® (esomeprazole) and Pariet® (rabeprazole). TIN is a recognized adverse drug reaction for these drugs (see Side Effects section of respective Professional Information).

The Professional Information (PI) and Patient Information Leaflet (PIL) of Pantoloc® / Topzole® (Pantoprazole), Dexilant® (Dexlansoprazole), Nexiam® / Axiago® (esomeprazole) and Pariet® (rabeprazole) will be amended to reflect the updated safety information.

Safety concern

Acute interstitial nephritis (AIN), which will now be updated to the current Medical Dictionary for Regulatory Activities (MedDRA) terminology of acute tubulointerstitial nephritis (TIN), has been observed in patients taking PPIs and may occur at any point during PPI therapy.

- TIN is characterized by an inflammatory reaction within the tubulointerstitial space of the kidney.
- Acute TIN can result in acute kidney injury. A delay in diagnosis and continued use of PPIs can impair recovery from the acute kidney injury and may lead to chronic renal failure.

Background on the safety concern

- TIN 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).

Advice to healthcare professionals

- Treatment with Pantoloc® / Topzole®, Dexilant®, Nexiam® / Axiago® and Pariet® must be stopped when TIN is suspected.
- Pantoloc® / Topzole®, Dexilant®, Nexiam® / Axiago® and Pariet® are contraindicated in patients who previously experienced TIN while on treatment 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.
- Healthcare professionals are urged to report any adverse drug reactions (ADRs) or product quality issues to SAHPRA via the Med Safety App. The App can be downloaded onto smart phone via Google Play or App store.
- Reporting of ADRs may be done via the eReporting link available on the SAHPRA website (www.sahpra.org.za). Alternatively, please complete the ADR reporting form accessible via the SAHPRA website and email it to adr@sahpra.org.za. For more information on ADR reporting of products listed below, please contact the SAHPRA Vigilance unit at pvqueries@sahpra.org.za or alternatively use the contact details below:

Product	API	Company	Reg. Nos:	Contact Details
PANTOLOC 20 **PANTOLOC 40** **PANTOLOC IV** **TOPZOLE OTC** **TOPZOLE 20** **TOPZOLE 40**	Pantoprazole	Takeda (Pty) Ltd	34/11.4.3/0005 28/11.4.3/0407 33/11.4.3/0041 43/11.4.3//1001 38/11.4.3/0061 38/11.4.3/0060	Tel: 082 525 3040 Fax: 086 558 7816 Email: AE.SouthAfricaSSA@takeda.com
DEXILANT 30 **DEXILANT 60**	Dexlansoprazole		48/11.4.3/0695 48/11.4.3/0696	
AXIAGO 40 mg IV **NEXIAM 2,5 mg SACHETS** **NEXIAM 5 mg SACHETS** **NEXIAM 10 mg SACHETS** **NEXIAM 20 mg** **NEXIAM 40 mg** **NEXIAM 40 mg IV**	Esomeprazole	AstraZeneca Pharmaceuticals (Pty) Ltd	45/11.4.3/0779 44/11.4.3/0208 44/11.4.3/0209 42/11.4.3/1003 35/11.4.3/0263 35/11.4.3/0264 A38/11.4.3/0384	Tel. (0) 11 797 6000 Fax: (0) 11 797 6133 Email: SA.MEAMedInfo@astrazeneca.com
PARIET 10 mg TABLETS **PARIET 20 mg TABLETS**	Rabeprazole	Janssen Pharmaceutica (Pty)Ltd	33/11.4.3/0206 32/11.4.3/0614	**Tel:** +27 (0)11 518 7100 Fax: +2786 687 8942 or +2711 518 7108 **Email:** AdverseEventZA@its.jnj.com

Responsible Pharmacist	**Company**	**Applicant & RP Details**	**Signatures**
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Pratibha Sobrun	AstraZeneca Pharmaceuticals (Pty) Ltd	(Reg.No.:1992/005854/07) Physical Address: 17 Georgian Crescent West, Building 2, Northdowns Office Park, Bryanston, 2191 Tel : 011 797 6078 Email: pratibha.sobrun1@astrazeneca.com	DocuSigned by: Pratibha Sobrun E1C0899742B745D...
Sara Cowie	Janssen Pharmaceutica (Pty)Ltd	(Reg. No. 1980/011122/07) Physical Address: 2 Medical Road, Halfway House, Midrand, 1685 Tel : 011 518 7179 Email : scowie@its.jnj.com	Sara Cowie S Digitally signed by Sara Cowie S DN: c=US, o=JNJ, ou=Subscribers, cn=Sara Cowie S, 0.9.2342.19200300.100.1.1=27500097 Reason: I have reviewed this document Date: 2023.10.30 17:52:53 +02'00' Adobe Acrobat Reader version: 2020.013.20064