



## IMPORTANT MEDICINE SAFETY INFORMATION

21 June 2021

Dear Healthcare Professional

### **RE: SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIs) AND SEROTONIN–NOREPINEPHRINE REUPTAKE INHIBITORS (SNRIs) ASSOCIATED WITH THE RISK OF POSTPARTUM HAEMORRHAGE**

The below listed companies, as directed by the South African Health Products Regulatory Authority (SAHPRA), would like to inform you of the risk of postpartum haemorrhage (PPH) following the use of selective serotonin reuptake inhibitors (SSRIs) and serotonin–norepinephrine reuptake inhibitors (SNRIs).

The Professional Information (PI) and Patient Information Leaflet (PIL) of SSRI and SNRI containing medicines will be amended to reflect the above safety information.

#### **Background on Safety Concern**

- The safety concern emanated from European Medicines Agency's (EMA's) Pharmacovigilance Risk Assessment Committee (PRAC) report <sup>[1]</sup> based on several observational studies, including an article by Palmsten et al., 2013, titled, "Use of antidepressants near delivery and the risk of postpartum haemorrhage: Cohort study of low-income women in the United States", published in British Medical Journal <sup>[2]</sup>.
- Postpartum haemorrhage (PPH) is defined as blood loss of more than 500 mL following vaginal delivery or more than 1000 mL following caesarean delivery with signs and symptoms of hypovolemia within 24 hours of the birth process <sup>[3]</sup>.

- Appropriate clinical follow-up of PPH includes monitoring for ongoing blood loss and vital signs, assessing for signs of anaemia (fatigue, shortness of breath, chest pain, or lactation problems), and debriefing patients [4].

### **Advice to Healthcare Professionals**

- PPH is a leading cause of maternal mortality. Treatment with SSRIs and SNRIs within one month prior to birth may increase the risk of PPH.
- Observational data indicate an increased risk of PPH following SSRI/SNRI exposure within the month prior to delivery [2].
- Healthcare professionals should be aware of the potential risk of PPH while making treatment decisions for prescribing SSRI/SNRI towards the end of pregnancy.
- Patients should be advised to inform their doctors before taking SSRI/SNRI containing medicines if they have history of bleeding disorders (e.g von Willebrand disease, haemophilia A, deficiency in F VIII, and haemophilia B); and comorbid bleeding disorders (e.g multiple pregnancy, gestational hypertension or preeclampsia).

Healthcare professionals are urged to report any adverse drug reactions (ADRs) or product quality issues to SAHPRA via the eReporting link available on the SAHPRA website ([www.sahpra.org.za](http://www.sahpra.org.za)). Alternatively, please complete the ADR reporting form accessible via the SAHPRA website and email it to [adr@sahpra.org.za](mailto:adr@sahpra.org.za). Healthcare professionals may also use the National Department of Health Mobile Application accessible from the Essential Medicines List (EML) Clinical Guide to report ADRs or product quality issues. For more information on ADR reporting of products listed below, please contact the SAHPRA vigilance unit at [pvqueries@sahpra.org.za](mailto:pvqueries@sahpra.org.za) or alternatively use the contact details indicated below:




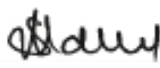



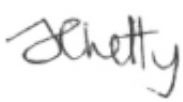
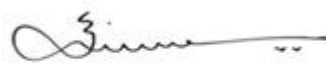





Company	Product Name	Active Ingredient(s)	Registration Number	Contact Details
<b>Xixia Pharmaceuticals (Pty) Ltd</b> [Marketed by Mylan (Pty) Ltd]	<b>Mylan Citalopram 10</b>	Citalopram	A38/1.2/0547	<i>Tel:</i> 071 281 2503 <i>Email:</i> <a href="mailto:medinfos@mylan.co.m">medinfos@mylan.co m</a>
	<b>Mylan Citalopram 20</b>	Citalopram	A38/1.2/0548	
	<b>Mylan Citalopram 40</b>	Citalopram	A38/1.2/0549	
	<b>Mylan Escitalopram 10</b>	Escitalopram	41/1.2/0568	
	<b>Mylan Escitalopram 15</b>	Escitalopram	41/1.2/0569	
	<b>Mylan Escitalopram 20</b>	Escitalopram	41/1.2/0570	
	<b>Mylan Escitalopram 5</b>	Escitalopram	41/1.2/0567	
<b>Macleods Pharmaceuticals SA</b>	<b>Emerdyne 10 mg</b>	Escitalopram	45/1.2/0881	<i>Tel:</i> 083 266 9223 082 450 6204
	<b>Emerdyne 20 mg</b>	Escitalopram	45/1.2/0882	




Company	Product Name	Active Ingredient(s)	Registration Number	Contact Details
				<i>Email:</i> <a href="mailto:vanitar@macleodspharma.com">vanitar@macleodspharma.com</a> <a href="mailto:rgosai@macleodspharma.com">rgosai@macleodspharma.com</a>
Dr. Reddy's Laboratories (Pty) Ltd	Citraz 5	Escitalopram	41/1.2/0843	<i>Tel:</i> 011 324 2100
	Citraz 10	Escitalopram	41/1.2/0844	<i>Email:</i> <a href="mailto:AdverseEvents.SA@drreddys.com">AdverseEvents.SA@drreddys.com</a>
	Citraz 20	Escitalopram	41/1.2/0845	
Austell Pharmaceuticals (Pty) Ltd.	Austell-Citalopram 10 mg	Citalopram	A39/1.2/0337	<i>Tel:</i> 011 611 1400/ 011 611 1603
	Austell-Citalopram 20 mg	Citalopram	A39/1.2/0338	<i>Email:</i> <a href="mailto:medsafety@austell.co.za">medsafety@austell.co.za</a>
	Austell-Citalopram 40 mg	Citalopram	A39/1.2/0339	
Sanofi-Aventis South Africa (Pty) Ltd	Citalopram-Winthrop 20 mg	Citalopram	A40/1.2/0740	<i>Tel:</i> +27 11 256 3700 <i>Email:</i> <a href="mailto:za.drugsafety@sanofi.com">za.drugsafety@sanofi.com</a>
Accord Healthcare (Pty) Ltd	Accord Escitalopram 10	Escitalopram	44/1.2/0851	<i>Email:</i> <a href="mailto:medinfo@accordhealth.co.za">medinfo@accordhealth.co.za</a>
	Accord Escitalopram 20	Escitalopram	44/1.2/0852	
Ranbaxy Pharmaceuticals (Pty) Ltd	Serlife 50	Sertraline	36/1.2/0272	<i>Tel:</i> +27 11 495 0117
	Serlife 100	Sertraline	36/1.2/0273	<i>Fax:</i> +27 11 495 0150
	Efegen XR 75	Venlafaxine	42/1.2/0423	<i>Email:</i> <a href="mailto:Geeta.ghela@sunpharma.com">Geeta.ghela@sunpharma.com</a>
	Efegen XR 150	Venlafaxine	42/1.2/0424	<a href="mailto:Pitchai.Pandikumar@sunpharma.com">Pitchai.Pandikumar@sunpharma.com</a>
	Ranflocs 20 Capsules	Fluoxetine	34/1.2/0129	
	Duzela 30	Duloxetine Hydrochloride	48/1.2/0680	
	Duzela 60	Duloxetine Hydrochloride	48/1.2/0681	
Adcock Ingram Limited	Adco Talomil 20 mg	Citalopram	35/1.2/0272	<i>Tel:</i> 011 635 0134
	Adco Paroxetine 20 mg	Paroxetine	36/1.2/0096	<i>Fax:</i> 086 553 0128
	Venlafaxine XR 37,5 Adco	Venlafaxine hydrochloride	43/1.2/0577	<i>Email:</i> <a href="mailto:Adcock.Aereports@adcock.com">Adcock.Aereports@adcock.com</a>
	Venlafaxine XR 75 Adco	Venlafaxine hydrochloride	43/1.2/0578	
	Venlafaxine XR 150 Adco	Venlafaxine hydrochloride	43/1.2/0579	
Zydus Healthcare SA (Pty) LTD	Odiven 37,5	Venlafaxine IR	A41/1.2/0440	<i>Tel:</i> 012 748 6400
	Odiven 50	Venlafaxine IR	A41/1.2/0441	<i>Email:</i> <a href="mailto:medicinesafety@zydus.co.za">medicinesafety@zydus.co.za</a>
	Odiven 75	Venlafaxine IR	A41/1.2/0442	
	Zydus Fluoxetine 20mg	Fluoxetine	A37/1.2/0265	
	Zylin 50	Sertraline	A39/1.3/0596	
	Xet 20	Paroxetine	A39/1.2/0216	

Company	Product Name	Active Ingredient(s)	Registration Number	Contact Details
Unicorn Pharmaceuticals (Pty) Ltd	Cilate 20	Citalopram	39/1.2/0548	<u>Tel:</u> 021 460 6572 <u>Fax:</u> 021 467 3952 <u>Email:</u> <a href="mailto:enquiries@unicornpharma.co.za">enquiries@unicornpharma.co.za</a>
	Escitalopram Unicorn 5	Escitalopram	46/1.2/0340	
	Escitalopram Unicorn 10	Escitalopram	46/1.2/0341	
	Escitalopram Unicorn 15	Escitalopram	46/1.2/0342	
	Escitalopram Unicorn 20	Escitalopram	46/1.2/0343	
	Paroxetine Unicorn 20	Paroxetine	38/1.2/0072	
Pharma Dynamics (Pty) Ltd	Dulta 30 mg	Duloxetine	A46/1.2/0889	<u>Tel:</u> 021 707 7000 <u>Email:</u> <a href="mailto:pharmacovigilance@pharmadynamics.co.za">pharmacovigilance@pharmadynamics.co.za</a>
	Dulta 60 mg	Duloxetine	A46/1.2/0890	
	Exlov XR 50 mg	Desvenlafaxine	A51/1.2/0009	
	Exlov XR 100 mg	Desvenlafaxine	A51/1.2/0010	
	Dyna Sertraline 50	Sertraline	A43/1.2/0339	
	Dyna Sertraline 100	Sertraline	A43/1.2/0340	
	Serrapress 20	Paroxetine	A38/1.2/0069	
	Zytomil 10 mg	Escitalopram	A42/1.2/0912	
Zytomil 20 mg	Escitalopram	A42/1.2/0914		
Oethmaan Biosims (Pty) Ltd	Citalopram 20 Oethmaan	Citalopram	36/1.2/0469	<u>Tel:</u> 011 433 0602 <u>Email:</u> <a href="mailto:regulatory@oethmaan.co.za">regulatory@oethmaan.co.za</a>
	Citalopram 20 Oethmaan Biosims	Citalopram	38/1.2/0090	
	Citalopram 40 Oethmaan	Citalopram	38/1.2/0091	
	Fluoxetine 20 Oethmaan	Fluoxetine	32/1.2/0040	
	Fluvoxamine 50 Oethmaan	Fluvoxamine	36/1.2/0046	
	Fluvoxamine 100 Oethmaan	Fluvoxamine	36/1.2/0047	
	Paroxetine 20 Oethmaan	Paroxetine	36/1.2/0160	
	Paroxetine 40 Oethmaan	Paroxetine	36/1.2/0161	
GlaxoSmithKline (Pty) Ltd	Aropax 20	Paroxetine	Y/1.2/419	<u>Tel:</u> 011 745 600 082 900 6730 <u>Email:</u> <a href="mailto:Mu.Zinchub@gsk.com">Mu.Zinchub@gsk.com</a>
	Aropax CR 12,5	Paroxetine	A38/1.2/0612	
	Aropax CR 25	Paroxetine	A38/1.2/0613	
Dezzo Trading 392 (Pty) Ltd	Prolax 20mg	Fluoxetine	A38/1.2/0413	<u>Tel:</u> 087 405 9660 <u>Email:</u> <a href="mailto:medsafety@dezzopharm.co.za">medsafety@dezzopharm.co.za</a> <a href="mailto:lsuleman@dezzopharm.co.za">lsuleman@dezzopharm.co.za</a>
Aspen Pharmacare	Cilift 20 mg Tablet	Citalopram	36/1.2/0092	<u>Tel:</u> 0800 118 088 <u>Fax:</u> 011 239 6303
	Deparoc 20 mg Tablet	Paroxetine	37/1.2/0595	
	Espradep 10 mg Tablets	Escitalopram	41/1.2/0897	

Company	Product Name	Active Ingredient(s)	Registration Number	Contact Details
	<b>Lorien Tablets 20 mg</b>	Fluoxetine	34/1.2/0381	<i>Email:</i> <a href="mailto:drugsafety@aspenpharma.com">drugsafety@aspenpharma.com</a>
	<b>Lorien Capsules 20 mg</b>	Fluoxetine	30/1.2/0024	
<b>Cipla Medpro (Pty) Ltd</b>	<b>Depramil 20</b>	Citalopram 20mg	A38/1.2/0489	<i>Tel:</i> 021 943 4200 <i>Email:</i> <a href="mailto:drugsafetysa@cipla.com">drugsafetysa@cipla.com</a>
	<b>Depramil 40</b>	Citalopram 40mg	A38/1.2/0490	
	<b>Lexamil 5</b>	Escitalopram 5mg	41/1.2/0394	
	<b>Lexamil 10</b>	Escitalopram 10mg	41/1.2/0395	
	<b>Lexamil 20</b>	Escitalopram 20mg	41/1.2/0396	
	<b>Nuzak</b>	Fluoxetine 20mg	32/1.2/0384	
	<b>Serdep 50</b>	Sertraline 50mg	38/1.2/0020	
	<b>Serdep 100</b>	Sertraline 100mg	A38/12.2/0617	
	<b>Venlor XR 37.5</b>	Venlafaxine XR 37.5mg	A40/1.2/0032	
	<b>Venlor XR 75</b>	Venlafaxine XR 75mg	A40/1.2/0033	
	<b>Venlor XR 150</b>	Venlafaxine XR 150mg	A40/1.2/0034	
<b>Sandoz SA (Pty) Ltd</b>	<b>Sandoz Venlafaxine XL 75</b>	Venlafaxine	A40/1.2/0494	<i>Tel:</i> +27 11 347 6600 <i>Email:</i> <a href="mailto:patientsafety.sacg@novartis.com">patientsafety.sacg@novartis.com</a> <i>Web:</i> <a href="https://www.report.novartis.com/">https://www.report.novartis.com/</a>
	<b>Sandoz Venlafaxine XL 150</b>	Venlafaxine	A40/1.2/0492	
	<b>ProHexal 20</b>	Fluoxetine	31/1.2/0638	
	<b>ProHexal 20 T</b>	Fluoxetine	32/1.2/0103	
	<b>ProHexal 40 T</b>	Fluoxetine	32/1.2/0104	
	<b>Sertraline Hexal 50</b>	Sertraline	A38/1.2/0398	
<b>Aurobindo Pharma (Pty) Ltd</b>	<b>Recita 20mg</b>	Citalopram	42/1.2/0531	<i>Tel:</i> 078 9323804 <i>Email:</i> <a href="mailto:pv.za@aurobindo.com">pv.za@aurobindo.com</a>
	<b>Dolin 10 mg</b>	Escitalopram	44/1.2/0952	
	<b>Dolin 20 mg</b>	Escitalopram	44/1.2/0953	
	<b>Lenio 20 mg</b>	Paroxetine hydrochloride	42/1.2/0208	

Yours faithfully

<p>Thameshnee Pillay Responsible Pharmacist <b>Xixia Pharmaceuticals (Pty) Ltd</b></p>  <p>Signature:</p>	<p>Vanita Rajool Responsible Pharmacist <b>Macleods Pharmaceuticals SA</b></p>  <p>Signature:</p>	<p>Herman Beyers Responsible Pharmacist <b>Dr Reddy's Laboratories (Pty) Ltd</b></p>  <p>Signature:</p>
<p>Shehnaz Mahomed Responsible Pharmacist <b>Austell Pharmaceuticals (Pty) Ltd.</b></p>  <p>Signature:</p>	<p>Graeme James Head of Regulatory/ Responsible Pharmacist <b>Sanofi-Aventis South Africa (Pty) Ltd.</b></p>  <p>Signature:</p>	<p>Reshlan Nagoor Responsible Pharmacist &amp; CEO <b>Accord Healthcare (Pty) Ltd</b></p>  <p>Signature:</p>
<p>Geeta Ghela Responsible Pharmacist and QA Head <b>Ranbaxy Pharmaceuticals (Pty) Ltd</b></p>  <p>Signature:</p>	<p>Tammy Chetty Responsible Pharmacist <b>Adcock Ingram Limited</b></p>  <p>Signature:</p>	<p>Madhu B Swarna Responsible Pharmacist <b>Zydus Healthcare SA (Pty) LTD</b></p>  <p>Signature:</p>
<p>Haroun Geyer Responsible Pharmacist <b>Unicorn Pharmaceuticals (Pty) Ltd</b></p>  <p>Signature:</p>	<p>Petra van Vuuren Deputy Responsible Pharmacist <b>Pharma Dynamics (Pty) Ltd</b></p> <p><i>P van Vuuren</i></p> <p>Signature:</p>	<p>Shahaboodeen Charfaray Deputy Responsible Pharmacist <b>Oethmaan Biosims (Pty) Ltd</b></p>  <p>Signature:</p>
<p>Dr Santoshni Govindasamy Country Medical Director <b>GlaxoSmithKline (Pty) Ltd</b></p>  <p>Signature:</p>	<p>Lutfiyya Suleman Responsible Pharmacist <b>Dezzo Trading 392 (Pty) Ltd</b></p>  <p>Signature:</p>	<p>Lorraine Hill Group Operating Officer and Responsible Pharmacist <b>Aspen Pharmacare</b></p>  <p>Signature:</p>

<p>Ralph Banks Vice President – Head of Quality SAGA and Responsible Pharmacist <b>Cipla Medpro (Pty) Ltd</b></p>  <p>Signature:</p>	<p>Lindiwe Ngcanga Regulatory Affairs Manager and Responsible Pharmacist <b>Sandoz SA (Pty) Ltd</b></p>  <p>Signature:</p>	<p>Kudzai Chiumburu Responsible Person for Pharmacovigilance <b>Aurobindo Pharma (Pty) Ltd</b></p>  <p>Signature:</p>
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## References:

1. 26 October 20201 EMA/PRAC/513083/2020 Pharmacovigilance Risk Assessment Committee (PRAC) PRAC recommendations on signals Adopted at the 28 September-1 October 2020 PRAC meeting
2. Palmsten K, Hernández-Díaz S, Huybrechts KF, Williams PL, Michels KB, Achtyes ED, Mogun H, Setoguchi S. Use of antidepressants near delivery and risk of postpartum hemorrhage: cohort study of low income women in the United States. *BMJ*. 2013 Aug 21;347:f4877. doi: 10.1136/bmj.f4877. PMID: 23965506; PMCID: PMC3748906
3. Wormer KC, Jamil RT, Bryant SB. Acute Postpartum Hemorrhage. 2020 Nov 30. In: *StatPearls [Internet]*. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. PMID: 29763164.
4. Evensen A, Anderson JM, Fontaine P. Postpartum Hemorrhage: Prevention and Treatment. *Am Fam Physician*. 2017 Apr 1;95(7):442-449. PMID: 28409600.