



31 May 2018

**Dear Healthcare Professional Communication**

**CLOZAPINE containing products – clozapine induced gastrointestinal hypomotility**

Dear Healthcare Professional,

**In collaboration with the South African Health Products Regulatory Authority (SAHPRA)  
Novartis, Litha Pharma and Aspen Pharmacare,**

would like to remind you of the following labelled safety information regarding the safe use of clozapine as contained in:

- LEPONEX 25 mg (F/2.6/70) and 100 mg (F/2.6/71) tablets
- CLOMENT 25 mg (35/2.6.5/ 0373) and 100 mg (35/2.6.5/0374) tablets
- ASPEN CLOZAPINE 25 mg (38/2.6.5/0167) and 100 mg (38/2.6.5/0168) tablets

**Summary:**

Dose dependent clozapine induced GIT hypomotility may be severe or life-threatening and sometimes fatal. Severe life threatening hypomotility may lead to:

- severe ileus constipation
- bowel obstruction
- faecal impaction
- faecaloma
- megacolon
- bowel perforation and
- gut ischaemia

**Background on the safety concern and next steps**

Clozapine as contained in LEPONEX, CLOMENT and ASPEN CLOZAPINE; has potent anticholinergic activity. Due to these anticholinergic properties, LEPONEX, CLOMENT and ASPEN CLOZAPINE have been associated with varying degrees of impairment of intestinal peristalsis, ranging from constipation, faecal impaction, faecaloma, megacolon, paralytic ileus, intestinal obstruction, bowel perforation, and gut ischaemia which may be fatal.

When prescribing clozapine, care should be taken in patients at risk of constipation, including those:

- receiving medications known to cause constipation (especially those with anticholinergic properties such as some antipsychotics, antidepressants and antiparkinsonian treatments; as well as opioids.)
- with a history of colonic disease or a history of lower abdominal surgery
- aged 60 years and older

It is vital that constipation is recognised early and actively treated.

Healthcare professionals should encourage adequate hydration, physical activity, and a high-fiber diet. Review all medications (especially anti-cholinergics and opiates) and re-assess need. Strongly encourage monitoring of bowel function by patient, family and health care providers. Most importantly, constipation should be actively managed. Patients should be urgently advised to inform their healthcare professionals if they develop constipation. The prevention and the treatment of these ADRs should be based on the best medical judgment of the attending physician. Please refer to the professional information of clozapine for a complete list of contraindications, warnings and special precautions and other recommendations regarding clozapine use.

Healthcare professionals should report all suspected adverse events associated with the use of clozapine products to:

SAHPRA Pretoria Office: Telephone: 012 395 9133, Fax: 086 620 7253, Email: [adr@health.gov.za](mailto:adr@health.gov.za)

National Adverse Event Monitoring Centre (NADEMC)

Telephone: 021 447 1618, Fax: 021 448 6181,

OR

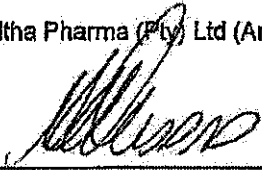
Product	Company	Registration Number	Contact Details
<b>CLOMENT 25mg tablets</b> <b>CLOMENT 100mg tablets</b>	Litha Pharma (Pty) Ltd	35/ 2.6.5/0373  35/ 2.6.5/0374	<b>Tel:</b> 060 998 7896  <b>Email:</b> <a href="mailto:drugsafety_ZA@acino.swiss">drugsafety_ZA@acino.swiss</a>
<b>ASPEN CLOZAPINE 25 mg tablets</b> <b>ASPEN CLOZAPINE 100 mg tablets</b>	Aspen Pharmacare	38/2.6.5/0167  38/2.6.5/0168	<b>Tel:</b> 0800 118 088,  <b>Fax:</b> 011 239 6306,  <b>Email:</b> <a href="mailto:drugsafety@aspenpharma.com">drugsafety@aspenpharma.com</a>
<b>LEPONEX 25 mg tablets</b> <b>LEPONEX 100 mg tablets</b>	<b>Novartis SA (Pty) Ltd</b> Magwa Crescent West, Waterfall City, Jukskei View, 2090	F/2.6/70  F/2.6/71	<b>Tel:</b> +27 11 347 6000,  <b>Fax:</b> +27 11 929 2262,  <b>Email:</b> <a href="mailto:patientsafety.sacq@novartis.com">patientsafety.sacq@novartis.com</a>

Yours sincerely,  
Novartis South Africa (Pty) Limited



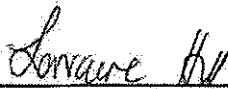
Mrs. Kumeshnie Padayachee  
Head RA, GDD – South Africa & Southern Africa  
Responsible Pharmacist

Litha Pharma (Pty) Ltd (An Acino company)



Nerine du Plessis  
Regulatory Affairs Executive and Responsible Pharmacist

Aspen Pharmacare



Lorraine Hill  
Group Operating Officer and Responsible Pharmacist