AUROBINDO
Committed to Healthier Life

IMPORTANT SAFETY INFORMATION

8 October 2018

Dear Healthcare Professional

Lamotrigine containing medicines: Risk of Hemophagocytic Lymphohistiocytosis

In agreement with the South African Health Products Regulatory Authority (SAHPRA), Aurobindo Pharma (Pty) Ltd would like to inform you of the following important information regarding the risk of Hemophagocytic Lymphohistiocytosis (HLH) associated with the use of lamotrigine containing medicines.

Lamotrigine containing medicines are indicated in the management of epilepsy and bipolar mood disorder.

Summary

Lamotrigine can cause a very serious cutaneous reaction called Hemophagocytic Lymphohistiocytosis (HLH). This can cause severe inflammation throughout the body and lead to hospitalization and death, especially in cases where the condition is not diagnosed and treated quickly. HLH is an immune system reaction that typically presents as a persistent fever, usually greater than 38 °C which can lead to blood, liver, kidney, and lung dysfunction. HLH may also be confused with other serious immune-related adverse reactions such as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS).

Recommendations for Healthcare Professionals:

Patients who develop fever or rash should be promptly evaluated and lamotrigine should be discontinued if HLH or another serious immune-related adverse reaction is suspected and an alternative etiology for the signs and symptoms cannot be established. Advise patients to seek immediate medical attention if they experience symptoms of HLH during lamotrigine treatment. A diagnosis of HLH can be established if a patient has at least five of the following eight signs or symptoms:

- fever and rash
- enlarged spleen (Splenomegaly)

- cytopenias
- elevated levels of triglycerides or low blood levels of fibrinogen
- high levels of ferritin
- hemophagocytosis identified through bone marrow, spleen, or lymph node biopsy
- decreased or absent Natural Killer (NK) Cell activity
- elevated blood levels of CD25 showing prolonged immune cell activation.

Aurobindo is in the process of updating the Professional Information and Patient Information leaflet to include HLH in the Warnings and Special Precautions and Side effects sections of the medicines stated in table 1 below:

Table 1: Lamotrigine containing medicines marketed by Aurobindo Pharma (Pty) Ltd

Product	Registration Numbers
GIROTEC 50 mg Each uncoated tablet contains 50 mg lamotrigine	43/2.5/0048
GIROTEC 100 mg Each uncoated tablet contains 100 mg lamotrigine	43/2.5/0049
GIROTEC 200 mg Each uncoated tablet contains 200 mg lamotrigine	43/2.5/0050

Healthcare Professionals should report all suspected adverse events associated with Lamotrigine to:

SAHPRA Pretoria Office

Telephone: 012 395 9133

Fax: 086 620 7253

Email: adr@health.gov.za

OR

National Adverse Drug Monitoring Centre (NADEMC)

Telephone: 021 447 1618

Fax: 021 448 6181

For further information regarding the use of Lamotrigine containing medicines stated in Table 1 kindly contact:

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Yours Sincerely,

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