IMPORTANT MEDICINE SAFETY INFORMATION

LEVETIRACETAM – RISK OF DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (DRESS)

09 March 2026

Dear Healthcare Professional,

The following pharmaceutical companies, GlaxoSmithKline (GSK) South Africa, Ranbaxy Pharmaceuticals (Pty) Ltd South Africa, Pharma Dynamics (Pty) Ltd, Unicorn Pharmaceuticals (Pty) Ltd, Cipla Medpro (Pty) Ltd, Hetero Drugs South Africa (Pty) Ltd, Dr Reddy's Laboratories (Pty) Ltd, in collaboration with the South African Health Products Regulatory Authority (SAHPRA), would like to inform you about the potential risk of drug reaction with eosinophilia and systemic symptoms (DRESS) associated with the use of levetiracetam containing medicines.

Summary

- DRESS, also known as drug induced hypersensitivity syndrome (DIHS), is a rare, but serious, and potentially life-threatening fatal drug reaction, characterised by symptoms which include widespread rash, high body temperature, liver enzyme elevations, elevated white blood cell count (including eosinophils), enlarged lymph nodes and possibly other body organs (commonly liver).
- DRESS has been reported in association with the use of levetiracetam- containing medicines, with symptoms appearing within 2 weeks to 2 months after initiating treatment.
- Early recognition of this risk, discontinuation of treatment, and supportive care are crucial.

Background on the safety concern

Levetiracetam is an antiepileptic medicine indicated as monotherapy in the treatment of partial onset seizures with or without secondary generalisation in patients from 16 years of age with newly diagnosed epilepsy. It is also indicated as adjunctive therapy in the treatment of:

- Partial onset seizures with or without secondary generalisation in adults and children over 16 years of age with epilepsy.

- Myoclonic seizures in adults and adolescents from 12 years of age with Juvenile Myoclonic Epilepsy.
- Primary generalised tonic-clonic seizures in adults and children from 16 years of age with idiopathic generalised epilepsy

DRESS is classified among the severe cutaneous adverse reactions (SCARs) (1), which are rare but potentially life-threatening reactions of delayed hypersensitivity. The mechanism and classification of SCARs are described as delayed T-cell mediated type IV hypersensitivity reactions in Gell and Coombs classification in which drug-specific T cells can be identified in the peripheral blood or skin infiltrates (2). The variation in clinical conditions has resulted in type IV reactions being further sub-classified according to different cytokine production patterns by T cell subsets and to the contribution of certain subpopulations of leukocytes to the inflammation and tissue damage. DRESS is considered a type IVb (T helper type 2) Th2-driven reaction (3).

The professional information (PI) and patient information leaflet (PIL) of products listed below will be updated to reflect the above safety information.

Advice for Patients

- Healthcare professionals should inform patients about the risk of DRESS associated with the use of levetiracetam-containing medicines.
- Patients should be warned about the associated signs and symptoms which include fever, rash, and organ-related issues which may occur 2 to 8 weeks post treatment.
- Patients should be advised to seek immediate medical attention if signs and symptoms suggestive of DRESS appear. Healthcare professionals should alert patients that DRESS may lead to hospitalisation or death if untreated.
- Patients are to be informed not to stop the medication abruptly and to consult their healthcare professionals if necessary.

Advice to Healthcare professionals

- At the time of prescription, patients should be advised of the signs and symptoms of DRESS and monitored closely for skin reactions. If signs and symptoms suggestive of DRESS appear, levetiracetam -containing medicines should be withdrawn immediately (3), and an alternative treatment should be considered (as appropriate); and in discussion with a specialist.
- If the patient has developed DRESS with the use of levetiracetam-containing medicines, treatment with the medicine must not be restarted in this patient at any time.
- Healthcare professionals are urged to report any adverse drug reactions (ADRs), or product quality problems associated with the use of products listed below to

SAHPRA via the ADR reporting form accessible at https://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/ and email it to adr@sahpra.org.za.

- Healthcare professionals may report ADRs via the e-Reporting link https://vigiflow-eforms.who-umc.org/za/ereporting.
- Additionally, reporting can be done via the Med Safety App. The App can be downloaded into a smart mobile phone through Google Play or App Store. For more information on Med Safety App, please visit https://medsafety.sahpra.org.za/.
- For more information on ADR reporting of products listed below, please contact the SAHPRA Pharmacovigilance unit at pvqueries@sahpra.org.za, or alternatively use the contact details indicated below:

Table 1: Company Products

Company	Product name	Active ingredient	Registration Number	Contact details
GlaxoSmithKline (Pty) Ltd	Keppra 100 mg/ml	Each 1.0ml solution contains 100 mg of levetiracetam	A40/2.5/0587	Email: Aereporting.za@gsk.com Tel: +27 10 300 1000
	Keppra 250 mg	Each film-coated tablet contains 250 mg of levetiracetam	36/2.5/0088	
	Keppra 500 mg	Each film-coated tablet contains 500 mg of levetiracetam	36/2.5/0089	
	Keppra 750 mg	Each film-coated tablet contains 750 mg of levetiracetam	36/2.5/0090	
Ranbaxy Pharmaceuticals (Pty) Ltd	Leveseize XR 500	Each extended-release tablet contains 500 mg levetiracetam	52/2.5/0256	Email: Geeta.Ghela@sunpharma.com Tel: +27 11 495 0100
	Leveseize XR 750	Each extended-release tablet contains 750 mg levetiracetam	52/2.5/0257	
	Leveseize XR 1000	Each extended-release tablet contains 1000 mg levetiracetam	52/2.5/0258	
	Leveseize XR 1500	Each extended-release tablet contains 1 500 mg levetiracetam	52/2.5/0259	
	Rassetom 250 mg	Each tablet contains 250 mg levetiracetam	44/2.5/0368	

Pharma Dynamics (Pty) Ltd	Rassetom 500 mg	Each tablet contains 500 mg levetiracetam	44/2.5/0369	Email: pharmacovigilance@pharmadynamics.co.za Tel: +27 21 707 7000
	Rassetom 750 mg	Each tablet contains 750 mg levetiracetam	44/2.5/0370	
Hetero Drugs South Africa (Pty) Ltd	Levetiracetam 250 Hetero	Each film coated tablet contains 250 mg of levetiracetam	50/2.5/0379	Email: Nokuthula.N@hetero.com Tel: +27 12 644 1220
	Levetiracetam 500 Hetero	Each film coated tablet contains 500 mg of levetiracetam	50/2.5/0380	
	Levetiracetam 750 Hetero	Each film coated tablet contains 750 mg of levetiracetam	50/2.5/0381	
	Levetiracetam 1000 Hetero	Each film coated tablet contains 1000 mg of levetiracetam	50/2.5/0382	
	Civter	Each ml contains 100 mg of levetiracetam	51/2.5/0094	
	Redilev Oral Solution	Each ml contains 100 mg of levetiracetam	51/2.5/0095.094	
Unicorn Pharmaceuticals (Pty) Ltd	Levetiracetam Unicorn 250	Each film-coated tablet contains 250 mg of levetiracetam	46/2.5/0338	Email: vigilance@unicornpharma.co.za Tel: +27 21 300 6907
	Levetiracetam Unicorn 750	Each film-coated tablet contains 750 mg of levetiracetam	46/2.5/0339	
Cipla Medpro (Pty) Ltd	Epikepp 250	Each film-coated tablet contains 250 mg levetiracetam	43/2.5/1164	Email: Nicole.Carter@Cipla.com drugsafetysa@cipla.com Tel: +27 21 943 4200
	Epikepp 500	Each film-coated tablet contains 500 mg levetiracetam	43/2.5/1165	
	Epikepp 750	Each film-coated tablet contains 750 mg levetiracetam	43/2.5/1166	
Dr Reddy's Laboratories (Pty) Ltd	Redilev 250	Each tablet contains 250 mg levetiracetam	41/2.5/0460	Email: AdverseEvents.SA@drreddys.com Tel: +27 11 324 2100
	Redilev 500	Each tablet contains 500 mg levetiracetam	41/2.5/0461	
	Redilev 750	Each tablet contains 750 mg levetiracetam	41/2.5/0462	

Yours faithfully,

Dr Nawal Alila Country Medical Director South Africa GlaxoSmithKline (Pty) Ltd Signature *Electronically signed by: Nawal Alila* *Reason: I am signing for the reasons as stated in the document.* *Date: Mar 14, 2026 12:16:49 GMT*	Celeste Naude Responsible Pharmacist Pharma Dynamics (Pty) Ltd Signature *Electronically signed by: Celeste Naude* *Reason: I am signing this document as reviewer and attest that the content is accurate and complete.* *Date: Mar 18, 2026 17:58:39 GMT+2*	Nokuthula Dube Responsible Pharmacist Hetero Drugs South Africa (Pty) Ltd Signature *Electronically signed by: Mmakgomo Uoane* *Reason: I am signing for the reasons as stated in the document.* *Date: Mar 18, 2026 14:22:32 GMT+2*
Jeanine Janse Van Rensburg Responsible Pharmacist Unicorn Pharmaceuticals (Pty) Ltd Signature *Electronically signed by: Jeanine Janse Van Rensburg* *Reason: I am signing for the reasons as stated in the document.* *Date: Mar 18, 2026 07:29:50 GMT+2*	Nicole Carter Responsible Pharmacist Cipla Medpro (Pty) Ltd Signature *Electronically signed by: Nicole Carter* *Reason: I am signing for the reasons as stated in the document.* *Date: Mar 17, 2026 10:00:25 GMT+2*	Herman Beyers Responsible Pharmacist Dr Reddy's Laboratories (Pty) Ltd Signature *Electronically signed by: Herman Beyers* *Reason: I am signing this document for the reasons specifically noted on the approval page of the document.* *Date: Mar 16, 2026 10:39:59 GMT+2*
Geeta Ghela Responsible Pharmacist Ranbaxy Pharmaceuticals (Pty) Ltd Signature *Electronically signed by: Geeta Ghela* *Reason: I am signing for the reasons as stated in the document.* *Date: Mar 19, 2026 09:23:48 GMT+2*		

References

(1) Roujeau J.C. Clinical heterogeneity of drug hypersensitivity. Toxicology. 2005;209:123–129. doi: 10.1016/j.tox.2004.12.022.

(2) Coombs, R.R.A., Gell, P.G.H., 1968. Classification of allergic reactions responsible for drug hypersensitivity reactions. In: Coombs, R.R.A., Gells, P.G.H. (Eds.), Clinical Aspects of Immunology, second ed. Davis, Philadelphia, PA, pp.575–596.

(3) Marwa K, Goldin J, Kondamudi NP. Type IV Hypersensitivity Reaction. [Updated 2025 May 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK562228/