



IMPORTANT MEDICINE SAFETY INFORMATION

ACICLOVIR/VALACICLOVIR-CONTAINING MEDICINES – RISK OF DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (DRESS)

01 July 2024

Dear Healthcare Professional,

GlaxoSmithKline (GSK) South Africa, in collaboration with the South African Health Products Regulatory Authority (SAHPRA), would like to inform you about the risk of drug reaction with eosinophilia and systemic symptoms (DRESS) associated with the use of aciclovir- and valaciclovir-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 involvement.
- The symptoms of DRESS typically appear within 2 weeks to 2 months after starting treatment with aciclovir- or valaciclovir-containing medicines.
- The available data from literature and post marketing reports provide sufficient evidence that corroborates the association of aciclovir- and valaciclovir-containing medicines, and the risk of DRESS.

Background on the safety concern

DRESS is classified among the severe cutaneous adverse reactions (SCARs), 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. 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.

Aciclovir is indicated for:

- Treatment of initial and recurrent herpes simplex infections of the skin and mucous membranes including initial and recurrent genital herpes simplex virus infections in both immunocompetent and immunocompromised patients.
- Treatment of herpes zoster (shingles) infections if the lesions are not older than 72 hours.
- Treatment of varicella zoster (chicken pox) infection within 24 hours after appearance of the typical chicken pox lesions.
- Reduction of mortality and risk of developing herpes virus infections in certain severely immunocompromised patients, namely those with advanced HIV disease [(CD4+ counts <200/mm³ including patients with acquired immunodeficiency syndrome (AIDS) or AIDS related complex (ARC)] or following bone marrow transplantation.

Valaciclovir is the L-valine ester of aciclovir and indicated for:

- Treatment of herpes zoster (shingles).
- Episodic treatment of recurrent genital herpes in immunocompetent adult patients.
- Prevention (suppression) of recurrent herpes simplex infection of the skin and mucous membrane of the anogenital area.
- Prophylaxis of cytomegalovirus (CMV) infection, CMV disease and other herpes virus infections following organ transplantation, where a special risk exists.

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

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, aciclovir- or valaciclovir-containing medicines should be withdrawn immediately, 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 aciclovir- or valaciclovir- 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://primaryreporting.who-umc.org/ZA> available on the SAHPRA website (<http://www.sahpra.org.za/>).
- 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	Zovirax iv	Each vial contains aciclovir sodium equivalent to aciclovir 250 mg	Q/20.2.8/164	Email: Aereporting.za@gsk.com Tel: +27 10 300 1000
	Zovirax cream	Each gram contains aciclovir 50 mg	R/20.2.8/271	
	Zovirax suspension	Each 5 ml suspension contains aciclovir 200 mg	S/20.2.8/236	

Yours faithfully,



Electronically signed by: Dr Santoshni Govindasamy
Reason: I am signing for the reasons as stated in the document.
Date: Jul 2, 2024 12:17 GMT+2

Dr Santoshni Govindasamy

Country Medical Director, GSK South Africa