IMPORTANT MEDICINE SAFETY INFORMATION

19 Dec 2023

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

Dear Healthcare Professional,

In collaboration with the South African Health Products Regulatory Authority (SAHPRA), the below listed companies (logo's above) would like to inform you about the risk of drug reaction with eosinophilia and systemic symptoms (DRESS) associated with the use of valaciclovir/aciclovir-containing medicines:

Summary

DRESS is a rare, but serious, and potentially life threatening fatal drug reaction that includes fever, severe skin rash or peeling of the skin over large areas of the body, swollen face, elevated white blood cell count (Including eosinophils), and can affect one or more organs (commonly liver).

- DRESS has been reported in association with the use of valaciclovir/aciclovir- containing medicines.
- The symptoms of DRESS typically appear within 2 weeks to 2 months after starting valaciclovir/aciclovir- containing medicines.

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 the 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.

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.

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/mm^3 including patients with acquired immunodeficiency syndrome (AIDS) or AIDS related complex (ARC)or following bone marrow transplantation.

The professional information (PI) and Patient Information Leaflet (PIL) of valaciclovir/aciclovir-containing medicines will be updated to appropriately 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 for skin reactions.
- If signs and symptoms suggestive of DRESS appear, valaciclovir/aciclovir-containing medicines should be withdrawn immediately and an alternative treatment considered (as appropriate); and in discussion with a specialist.
- If the patient has developed DRESS with the use of valaciclovir/aciclovir-containing medicines, treatment with these medicines 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 the listed products to the companies below, or to SAHPRA via the eReporting link available on the SAHPRA website (www.sahpra.org.za).
- Alternatively, please complete the ADR reporting form accessible via the SAHPRA website at https://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/ and email it to adr@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 SAHPRA website. For more information on ADR reporting of products listed below, please contact the SAHPRA Vigilance unit at pvqueries@sahpra.org.za or alternatively use the contact details indicated below:

Company contact points

Company	Product	Active ingredient	Registration Number	Contact details
Ranbaxy Pharmaceuticals (Pty) Ltd	Zelivire 500 (Tablets)	Valaciclovir	42/20.2.8/0476	Responsible Pharmacist: Geeta Ghela Email: Geeta.Ghela@sunpharma.com 011 495 0181
	Lovire 200 Tablets	Aciclovir	32/20.2.8/0017	
	Lovire 400 Tablets	Aciclovir	32/20.2.8/0018	
Biotech Laboratories (Pty) Ltd	Acyclovir 200 Biotech	Aciclovir	31/20.2.8/0430	Responsible Pharmacist: Motshabi Kgantsi motshabi@biotechlabs.co.za 011 848 3050
Aurogen South Africa (Pty) Ltd	Shilova 500 mg tablets	Valaciclovir	45/20.2.8/0590	Responsible Pharmacist: Samantha Pillay Chengiah samantha.Chengiah@aurogensa.co.za
	Shilova 1 g tablets	Valaciclovir	45/20.2.8/0591	
Cipla Medpro (Pty) Ltd	Acitab-200 DT	Aciclovir	38/20.2.8/0129	Responsible Pharmacist: Praba Thandrind Praba.Thandrind@Cipla.com & drugsafetysa@cipla.com Tel: 021 943 4200
	Acitab-400 DT	Aciclovir	38/20.2.8/0128	
	Acitop Cream 2 g	Aciclovir	32/20.2.8/0719	
Novagen Pharma (Pty) Ltd.	Valzost 500 mg	Valaciclovir	45/20.2.8/0588	Responsible Pharmacist gawie@novagenpharma.co.za Pharmacovigilance elizma@novagenpharma.co.za
	Valzost 1000 mg	Valaciclovir	45/20.2.8/0589	
Hetero Drugs SA (Pty) Ltd.	Vorior	Valaciclovir 500 mg	44/20.2.8/0016	Responsible Pharmacist / RA/QA Head Nokuthula Dube Nokuthula.n@hetero.com +27 12 644 1220
Viatris Healthcare (Pty) Ltd	Mylan Valaciclovir 500 mg	Valaciclovir	45/20.2.8/0605	Responsible Pharmacist: Ansie Savrda ansie.savrda@viatris.com (+27) 11 451 1300
Viatris South Africa (Pty) Ltd	Acyclovir 250 Viatris	Aciclovir	42/20.2.8/0069	Responsible Pharmacist: Pranesh Ramadene pranesh.ramadene@viatris.com (+27) 11 451 1300

Yours Sincerely,

Geeta Ghela Responsible Pharmacist/QA Head **Ranbaxy Pharmaceuticals (Pty) Ltd** **Signature:** Geeta Ghela Digitally signed by Geeta Ghela DN: cn=Geeta Ghela, o=Responsible Pharmacist, ou=Ranbaxy Pharmaceuticals(pty)ltd, email=Geeta.Ghela@sunpharma.com, c=ZA Date: 2023.12.19 10:25:09 +02'00'	Nokuthula Dube Responsible Pharmacist / RA/QA Head **Hetero Drugs SA (Pty) Ltd.** **Signature** Mmakgomo Uoane Digitally signed by Mmakgomo Uoane Date: 2023.12.21 09:22:42 +02'00'	Motshabi Kgantsi Responsible Pharmacist **Biotech Laboratories (Pty) Ltd** **Signature:** Digitally signed by Motshabi Kgantsi Date: 2023.12.19 13:04:22 +02'00'
Samantha Pillay Chengiah Responsible Pharmacist **Aurogen South Africa (Pty) Ltd.** **Signature:** Digitally signed by sam DN: C=SA, CN=sam, E=samantha.chengiah@aurobindo.com Reason: I am the author of this document Location: C:\Users\samantha\Pictures\Saved Pictures Date: 2023-12-19 13:30:17 Foxit PhantomPDF Version: 9.7.1	Praba Thandrind Responsible Pharmacist: **Cipla Medpro (Pty) Ltd** **Signature** Praba Thandrind Digitally signed by Praba Thandrind Date: 2023.12.19 14:58:38 +02'00'	Gabriël Erwee Responsible Pharmacist **Novagen Pharma (Pty) Ltd** **Signature** Elizma van Biljon Digitally signed by Elizma van Biljon Date: 2023.12.19 15:35:44 +02'00'
Ansie Savrda Responsible Pharmacist **Viatris Healthcare (Pty) Ltd** **Signature:** Ansie Savrda-M535563 Digitally signed by Ansie Savrda-M535563 Date: 2023.12.20 11:15:23 +02'00'	Pranesh Ramadene Responsible Pharmacist **Viatris South Africa (Pty) Ltd** **Signature** Digitally signed by Pranesh Ramadene-M529584 Date: 2023.12.20 10:19:58 +02'00'	

References

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