

IMPORTANT MEDICINE SAFETY INFORMATION

10 January 2024

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

Dear Healthcare Professional,

Aspen Pharmacare, Adcock Ingram Limited, Pharma Dynamics and Sandoz SA (Pty) Ltd, in collaboration with the South African Health Products Regulatory Authority (SAHPRA), would like to draw your attention to the following important safety information associated with the use of valaciclovir/aciclovir-containing medicines registered in South Africa.

Background on safety concern

- The safety concern is regarding the risk of drug reaction with eosinophilia and systemic symptoms (DRESS) associated with the use of valaciclovir/aciclovir-containing medicines.
- DRESS is classified among the severe cutaneous adverse reactions (SCARs) which are unpredictable and present a serious risk to patients that can be life-threatening or fatal.
- DRESS has been reported in association with valaciclovir/aciclovir treatment. DRESS is a serious skin reaction that may affect one or more organs (commonly liver).
- Valaciclovir is a prodrug of aciclovir. The metabolism of valaciclovir occurs within the gut lumen and in the liver. After uptake of valaciclovir, hydrolysis of the molecule rapidly yields aciclovir, resulting in significantly greater systemic aciclovir levels with oral valaciclovir compared with oral aciclovir.

Therapeutic indications: Valaciclovir

- 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 ano-genital area.
- Prophylaxis of cytomegalovirus (CMV) infection, CMV disease and other herpes virus infections following organ transplantation, where a special risk exists.

Therapeutic indications: Aciclovir

- Treatment of initial and recurrent simplex infections of the skin and mucous membranes including initial and recurrent genital herpes simplex virus infections.
- Suppression of recurrent genital herpes simplex infections in immuno-competent patients.
- Prophylaxis of herpes simplex and varicella zoster infections in immuno-compromised patients.
- Treatment of herpes simplex and varicella zoster infections in immuno-compromised patients.
- Treatment of herpes zoster infections if the lesions are not older than 72 hours.

- Treatment of varicella zoster (chickenpox) within 24 hours after appearance of the typical chickenpox rash.
- Treatment of herpes simplex infections in neonates.
- Treatment of herpes simplex encephalitis.
- Prevention of reactivation of CMV infection in seropositive patients following bone marrow transplantation.
- Topical Aciclovir:
 - Aciclovir is effective in the treatment of viral infections due to herpes simplex type 1 and type 2 of the skin and genitalia in the initial and recurrent situations.
 - Application to the lips in the early treatment of recurrent herpes simplex virus infections.

Advice to Healthcare professionals

- At the time of prescription, patients should be alerted about signs and symptoms of DRESS, which include fever, severe rash, peeling skin, facial oedema, lymphadenopathy, flu-like feeling, jaundice, dyspnoea, dry cough, chest pain or discomfort, dehydration, and eosinophilia.
- Furthermore, patients should be monitored for skin reactions and if signs and symptoms suggestive of DRESS appear, valaciclovir/aciclovir should be withdrawn immediately and an alternative treatment considered (as appropriate); and in discussion with a specialist.
- If a patient has developed DRESS with the use of valaciclovir/aciclovir, 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 issues associated with valaciclovir/aciclovir-containing medicines listed below to SAHPRA via the eReporting link available on the SAHPRA website (www.sahpra.org.za).
- Alternatively, an ADR reporting form accessible via the SAHPRA website at <https://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/> can be completed and sent 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:


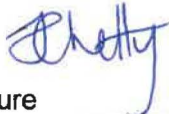
The Professional Information (PI) and Patient Information Leaflets (PILs) for valaciclovir/aciclovir-containing medicines will be updated accordingly.

Table 1: Company Products

Company	Product name	Registration Number	Contact details
Aspen Pharmacare	Aspen Acyclovir 250 mg Cyclivex 400 mg Tablets Cyclivex 200 mg Tablets Vavirex 500 Aspen Valaciclovir 250 mg Aspen Valaciclovir 500 mg	32/20.2.8/0257 31/20.2.8/0298 28/20.2.8/0715 43/20.2.8/0388 43/20.2.8/0748 43/20.2.8/0749	Tel: +27 800 118 088 Fax: +27 11 239 6303 drugsafety@aspenpharma.com
Adcock Ingram Limited	Adco-Acyclovir 200 mg Tablets Adco-Acyclovir Topical Cream Beta-Vira Topical Cream	28/20.2.8/0552 28/20.2.8/0369 31/20.2.8/0549	Tel:+27 11 635 0134 Safety number:+27 73 540 7052 Adcock.Aereports@adcock.com
Pharma Dynamics	Acyrax I.V.	48/20.2.8/0387	Tel: +27 21 707 7000 Pharmacovigilance@pharmadynamics.co.za

Sandoz SA (Pty) Ltd	Valatrex 250	42/20.2.8/0340	Tel: +27 11 347 6600 patient.safety.sac@sandoz.com
	Valatrex 500	42/20.2.8/0341	
	Varizost 250	42/20.2.8/0342	
	Varizost 500	42/20.2.8/0343	
	Aciclovir Sandoz 200	32/20.2.8/0378	
	Aciclovir Sandoz 400	32/20.2.8/0379	

Yours faithfully,

Nikola Whelan Responsible Pharmacist Aspen Pharmacare  Nikola Whelan <small>Digitally signed by Nikola Whelan Date: 2024.01.10 14:51:35 +02'00'</small> Signature	Celeste Naude Responsible Pharmacist Pharma Dynamics Signature
Tammy Chetty Responsible Pharmacist Adcock Ingram Limited  Signature	Indirani Govender Responsible Pharmacist Sandoz SA (Pty) Ltd Signature

References

1. SAHPRA Letter dated 22 November 2023 Re: Valacyclovir/acyclovir-containing medicines – risk of drug reaction with eosinophilia and systemic symptoms (DRESS)
2. S. Ingen-Housz-Oro, C. Bernier, G. Gener, F. Fichel, A. Barbaud, B. Lebrun-Vignes, H. Assier, Valaciclovir: a culprit drug for drug reaction with eosinophilia and systemic symptoms not to be neglected. Three cases, British Journal of Dermatology, Volume 180, Issue 3, 1 March 2019, Pages 666–667, <https://doi.org/10.1111/bjd.17207>
3. Conan MacDougall, B. Joseph Guglielmo, Pharmacokinetics of valaciclovir, Journal of Antimicrobial Chemotherapy, Volume 53, Issue 6, June 2004, Pages 899–901, <https://doi.org/10.1093/jac/dkh244>

