IMPORTANT MEDICINE SAFETY INFORMATION

20 May 2025

ANVIRO® (VALACICLOVIR - CONTAINING MEDICINE) — RISK OF DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (DRESS)

Dear Healthcare Professional,

In collaboration with the South African Health Products Regulatory Authority (SAHPRA), Zydus would like to inform you about the risk of drug reaction with eosinophilia and systemic symptoms (DRESS) associated with the use of Anviro® (valaciclovir) tablets.

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- containing medicines.
- The symptoms of DRESS typically appear within 2 weeks to 2 months after starting valaciclovir-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.

The Professional Information (PI) and Patient Information Leaflet (PIL) of Anviro® (valaciclovir) 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 associated with the use of Anviro®; and monitored for skin reactions.

- If signs and symptoms suggestive of DRESS appear, Anviro®, should be withdrawn immediately and an alternative treatment considered (as appropriate), in discussion with a specialist.

- If the patient has developed DRESS with the use of Anviro® tablets, treatment with this product 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 Anviro® tablets, to Zydus using contact details indicated below, or to SAHPRA via this eReporting link https://primaryreporting.who-umc.org/ZA 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-problemreporting-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 the 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 Anviro® tablets please contact the SAHPRA Pharmacovigilance unit at pvqueries@sahpra.org.za or alternatively use the contact details indicated below:

Product	Active ingredient	Registration Number	Contact details
Anviro 500 Tablets	Valaciclovir	42/20.2.8/0820	Responsible Pharmacist: Madhu Babu Swarna Email: medicinesafety@zydus.co.za 012 748 6400

Yours Sincerely,

Madhu Babu Swarna, Responsible Pharmacist,
Zydus Healthcare SA (Pty) LTD.

References:

1. Bouvresse S. et al. Toxic epidermal necrolysis, DRESS, AGEP: do overlap cases exist? Orphanet J Rare Dis. 2012 Sep 25; 7:72.
2. S Ingen-Housz-Oro, et al. Valaciclovir: a culprit drug for drug reaction with eosinophilia and systemic symptoms not to be neglected. Three cases. Br J Dermatol. 2019 Mar;180(3):666-667.
3. Shohei Kitayama, et al. Valacyclovir-induced drug reaction with eosinophilia and systemic symptoms. Eur J Dermatol. 2022 Jul 1;32(4):538-539.
4. WHO Pharmaceuticals Newsletter No. 3, 2022 5. WHO Pharmaceuticals Newsletter No. 4, 2020.
6. Health Canada: Summary Safety Review, Health Canada, 24 May 2022. Available from:https://hpr-rps.hres.ca/reg-content/summary-safety-reviewresult.php?lang=en&term=. Accessed on: 10 Apr 2023.
7. Drug office department of health (Hong Kong). Available from: https://www.drugoffice.gov.hk/eps/upload/eps_news/46992/ZH/1/Valacyclovir.pdf . Accessed on: 11 Apr 2023.
8. EMA: CZ/H/PSUFU/00003086/201812. Minutes of PRAC meeting on 13–16 January 2020. Accessed on: 11 Apr 2023. Available from: https://www.ema.europa.eu/en/documents/minutes/minutes-prac-meeting-13-16january- 2020_en.pdf .