

Ref. N°: DD/PVCT/2766/FDA /2025

SAFETY INFORMATION COMMUNICATION

| [Medical Product category] | Title |
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| Phenobarbital | Warning on potential risk of Drug Rash with Eosinophilia & Systemic Syndrome (DRESS) |

1. Introduction

Reference is made to the law No 003/20218 of 09/02/2018 establishing the Rwanda FDA, and to the regulations governing pharmaceutical products and medical devices, in especially Articles 23 on safety information and communication. Rwanda FDA warns about the Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) associated with the use of phenobarbital.

Referring to the safety information published in WHO Pharmaceuticals Newsletters, further reference is also made to the National Co-ordination Centre for Pharmacovigilance programme of India, which has forwarded their recommendations based on adverse drug events reports on the risk of Drug Rash with Eosinophilia & Systemic Symptoms (DRESS) by using Phenobarbital (1).

2. Description

Phenobarbital is a barbiturate, non-selective central nervous system depressant that is used as a sedative anticonvulsant in various dosage forms with side effects of Drug Rash with Eosinophilia and systemic symptoms (DRESS) syndrome. DRESS is a rare and severe hypersensitivity reaction that is an immune-mediated reaction involving macrophage and T-lymphocyte activation and cytokine release, although no consensus has been reached as to its aetiology (2)(3). It is characterized by fever, a diffuse cutaneous rash, angioedema and anaphylaxis, lymphadenopathy, hematologic abnormalities (eosinophilia, leukopenia, or atypical lymphocytosis), and some internal organ involvement usually two to eight weeks after the initiation of drug therapy, with a possibility of persistence or even worsening of symptoms despite the discontinuation of the drug. Most aromatic anticonvulsants, such as phenytoin, phenobarbital, and carbamazepine can cause DRESS (4).

The Summary of Product Characteristics (SmPC) states that Phenobarbital can cause life-threatening cutaneous reactions such as Stevens-Johnson syndrome and toxic epidermal necrolysis. Therefore, it is advised that a patient on the medication monitor the signs and symptoms for skin reactions(5).

The study shows that the exact mechanism of DRESS related to anticonvulsant drugs involves three components: (i) deficiency or abnormality of the epoxide hydroxylase enzyme that detoxifies the metabolites of aromatic amine anticonvulsants (metabolic pathway); (ii) reactivation of herpesvirus family; and (iii) ethnic predisposition linked to certain human leukocyte antigen (HLA) alleles (immune response) (6). Therefore, Rwanda FDA recommends the following:

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3. *Information to the Patients and Caregivers*

- Patients should be aware of rare side effects of phenobarbital, like DRESS syndrome.
- Patients should immediately report to their healthcare professionals when they experience a skin eruption while taking Phenobarbital.
- Patients should follow instructions: Use as directed by a healthcare professional or according to the product label.

4. *Information to Healthcare Professionals*

Healthcare professionals are therefore required to:

- Closely monitor the possibility of adverse events mentioned above while prescribing Phenobarbital.
- Be aware that DRESS syndrome is a rare but potentially life-threatening drug-induced hypersensitivity reaction.
- Immediately discontinue the suspected causative drug.
- Encouraged to report suspected DRESS cases to Rwanda FDA.
- Educate patients on warning signs and advise them to seek immediate medical attention if symptoms occur.
- Avoid re-challenge with the same drug or chemically related compounds.
- Look beyond the skin eruption to assess the severity and decide on the cessation of suspected medicine if DRESS syndrome is suspected.

5. *Information for the Marketing Authorization Holders/Manufacturers*

Rwanda FDA is requesting Marketing Authorization Holders to submit an updated SmPC for Phenobarbital to include the risk of Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) as an adverse drug reaction. The product label and/or box warning should also be updated to remind healthcare professionals of the potential effects of phenobarbital.

6. *Reporting channel*

Patients and Healthcare Professionals are urged to report any suspected adverse drug event/reaction associated with Phenobarbital medicine or any other medical product to the Rwanda FDA by using an online reporting tool called VigiMobile for medicines, which is available on the Rwanda FDA website at <https://vigiflow-eforms.who-umc.org/rw/adr> or using online reporting system (PViMS) accessible on <https://pvims.rwandafda.gov.rw/security/landing>

Sincerely,



Prof. Emile BIENVENU
Director General

7. References

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