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SAFETY INFORMATION COMMUNICATION

Medicine	Safety information
Oral Retinoid Medicines	**Warning on pregnancy prevention in women of childbearing potential and the potential risk of psychiatric adverse events in patients using oral retinoid medicines.**

1. Introduction

Reference is made to the new safety information on oral retinoid medicines published in the WHO Pharmaceuticals Newsletter - N° 04/2021 warning on the potential risk of psychiatric adverse events and pregnancy prevention [1].

Reference is also made to the Drug Safety Update published by the Medicines and Healthcare products Regulatory Agency (MHRA) providing guidance about the use of remote consultations for pregnancy prevention in women of childbearing potential and monitoring for signs of psychiatric reactions, especially depression, and other safety risks in all patients taking oral retinoid medicines [2,3]; and the Drug Safety Update on risk of neuropsychiatric symptoms associated with oral retinoids published by the National Pharmaceutical Regulatory Agency of Malaysia [4].

Further reference is made to the complete review of retinoid medicines by the European Medicines Agency recommending the updated prescribing information for oral retinoid medicines by including possible risks such as neuropsychiatric disorders (depression, anxiety, and mood changes) and fetal harm [5].

2. Description of the safety information

Retinoids are a class of compounds that are chemically derived from Vitamin A which are taken by mouth or applied as creams or gels to treat severe skin conditions such as severe acne and psoriasis, and certain forms of cancer. Retinoids act at a cellular level where they activate genes involved in the physiology of keratinocytes by binding to specific nuclear receptors, retinoic acid receptor (RAR) and retinoid X receptor (RXR) [6]. Retinoids can be classified into four generations: 1) 1st generation (non-aromatic retinoids): Isotretinoin, tretinoin, and Alitretinoin; 2) 2nd generation (mono-aromatic retinoids): Acitretin; 3) 3rd generation (poly-aromatic retinoids): Adapalene, Tazarotene, and Bexarotene; and 4) 4th generation (retinoid): Trifarotene[7].

Oral retinoid medicines Isotretinoin, Alitretinoin and Acitretin are used to treat severe dermatological diseases that are resistant or unresponsive to standard therapies [4].

The use of oral retinoid medicines during pregnancy causes significant harm to an unborn baby including congenital malformations and a high incidence of spontaneous abortion [3]. Oral retinoid medicines (acitretin, alitretinoin, bexarotene, isotretinoin and tretinoin) are highly teratogenic and are contraindicated in women of childbearing potential [8].

In addition, there is a risk of hepatobiliary and lipid metabolism disorders as well as the risk of depression [3]. It has also been reported that the users of oral retinoid medicines can face neuropshychiatric disorders including

depression, depression-aggravated anxiety and mood and/or behaviour alterations [4].

3. *Information to Consumers/Patients/Caregivers*

- Patients are warned about the potential risk of psychiatric adverse events associated with the use of oral retinoid medicines.
- Women and women planning to have a baby should not use oral retinoid medicines due to their harmfulness to the unborn child.
- Patients are encouraged to inform close family members and/or friends and family that they are taking an oral retinoid medicine so that they can be alerted for any psychiatric disorders including changes in mood.
- Patients are advised to report any adverse reaction induced by the use of oral retinoid medicines to health professionals or to Rwanda FDA.

4. *Information to Healthcare Professionals*

- Healthcare providers are reminded to undertake pregnancy tests before/during/after treatment to identify any potentially exposed pregnancy, and the need for at least one effective method of contraception during and after treatment with oral retinoid medicines.
- Healthcare providers are advised to inform their patients about the possible risk of psychiatric disorders associated with the use of oral retinoid medicines.
- Healthcare providers are advised to ensure adequate monitoring of mental health and other potential adverse events.
- Healthcare providers are advised to recognize drug reactions early for further therapeutic actions.
- Pharmacists are encouraged to provide detailed medicine information and related-potential risks to patients and encourage them to report any adverse reaction encountered.

5. *Information to Manufacturers/Marketing Authorization Holders*

- Marketing Authorization Holders are advised to update the safety information for oral retinoid medicines to include the potential risk of psychiatric disorders and prevention of their use in women of childbearing potential.

6. *Reporting Channel*

Patients and Healthcare Professionals are urged to report any suspected serious adverse drug reactions associated with oral retinoid medicines and other medicines to Rwanda FDA by completing ADR/AEFI reporting form accessible on Rwanda FDA website via the link http://www.rwandafda.gov.rw/web/fileadmin/adr_aefi__reporting_form.pdf and the filled form should be sent to the email: pv-sm@rwandafda.gov.rw

Sincerely,

01/09/2022

Dr. Emile BIENVENU
Director General

7. *References*

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