

## **Retinoids (Isotretinoin) – update on teratogenicity and neuropsychiatric disorders**

### **Direct Healthcare Professional Communication**

12.08.2020

Dear Healthcare professional,

**Pharmathen S.A., Marketing Authorization Holder of A-cnotren (isotretinoin), soft caps 10, 20 mg**, in agreement with the European Medicines Agency and the Scientific Centre of Drug and Medical Technology Expertise after Academician E. Gabrielyan CJSC would like to inform you of the following:

#### **Summary**

##### **Teratogenicity**

- Oral retinoids are highly teratogenic and must not be used during pregnancy.
- The oral retinoid isotretinoin must be used in accordance with the conditions of a Pregnancy Prevention Programme (PPP) for all women of childbearing potential.
- Discuss the risks of oral retinoid-containing medicines with women before prescribing isotretinoin, using the revised and streamlined educational materials.

##### **Neuropsychiatric disorders**

- Cases of depression, depression-aggravated anxiety, and mood alterations have been reported rarely in patients taking oral retinoids.
- Advise patients taking oral retinoids that they may experience changes in their mood and/or behaviour and that they and their families should be alert to this and should speak to their doctor if this occurs.
- Monitor all patients treated with oral retinoids for signs and symptoms of depression and refer for appropriate treatment, if necessary. Special care should be taken in patients with history of depression.

#### **Background on the safety concern**

Retinoid-containing medicinal products are available in oral and topical forms and are widely used to treat various forms of acne, severe chronic hand eczema unresponsive to corticosteroids, severe forms of psoriasis and keratinisation disorders. Following a recent in-depth review of all relevant data, the Pharmacovigilance Risk Assessment Committee has strengthened information provided to patients and healthcare professionals (through the product information and educational materials) on teratogenicity and neuropsychiatric disorders.

##### **Teratogenic risk**

Oral retinoids (isotretinoin) are highly teratogenic.

Use of isotretinoin in women of childbearing potential must be in accordance with the conditions of a Pregnancy Prevention Programme (PPP).

##### **Neuropsychiatric disorders**

Depression, depression-aggravated anxiety, and mood alterations have been reported in patients treated with oral retinoids. The available evidence from published literature and individual case reports shows conflicting study results and the published studies suffer from a number of limitations. Therefore, it has not been possible to identify a clear increase in risk of psychiatric disorders in people who take oral retinoids compared to those that do not. Furthermore, it is recognised that patients with severe skin disorders are themselves at an increased risk of psychiatric disorders. It is recommended that patients who are taking oral retinoids are advised of the possibility that they may experience changes in their mood and behaviour and that they should speak to their doctor if this happens. Any

patient who shows signs of depression should be referred for appropriate treatment, as necessary. Special attention should be given to patients treated with oral retinoids with a history of depression and all patients should be monitored for signs of depression. The product information will be updated to include the results of this review.

**Call for reporting**

Please report any adverse events that occur to your patients receiving retinoids. When reporting, please provide as much information as possible, including information on medical history, any co-administration of another drug, and dates of onset and treatment. Please be reminded that adverse events associated with the use of retinoids may be reported to the Scientific Centre of Drug and Medical Technology Expertise after Academician E. Gabrielyan with the following ways:

- E-mail: [vigilance@pharm.am](mailto:vigilance@pharm.am)
- Phone: (+374 60)83-00-73, (+374 10)23-08-96, (+374 10)23-16-82
- Hot Line: (+374 10) 20-05-05, (+374 96) 22-05-05

▼Oral retinoid isotretinoin is under additional monitoring. This will allow new safety information to be quickly identified. Healthcare professionals are requested to report any possible adverse events.

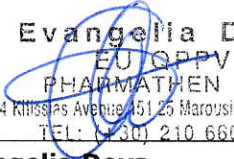
Alternatively, you can report or request more information by the Marketing Authorization Holder or Distributor in Armenia for **A-cnotren (isotretinoin) soft caps 10, 20 mg**, using the information in the table below:

<b>Marketing Authorization Holder</b>	<b>Distributor</b>
Pharmathen S.A.	Innovapharm LLC
E-mail: <a href="mailto:pharmacovigilance@pharmathen.com">pharmacovigilance@pharmathen.com</a> Telephone: +30 2106604300 (ext 9) Fax: +30 210 66 04 588	E-mail: <a href="mailto:info@innovapharm.am">info@innovapharm.am</a> Telephone: +374 11 55 15 53 Fax: n/a

**Annex – Conditions of the PPP for the oral retinoids isotretinoin**

- The Pregnancy Prevention Programme for oral retinoids has been streamlined and harmonised to provide clear and concise information for both healthcare professionals and patients. Any use of isotretinoin in female patients at risk of pregnancy should be in the context of a Pregnancy Prevention Programme. The conditions of the Pregnancy Prevention Programme require prescribers to ensure that every female patient understands that: oral retinoids pose a risk to an unborn baby and should not be taken during pregnancy;
- she must use effective contraception without interruption for at least one month before initiating therapy, throughout treatment and for 1 month after stopping treatment;
- she understands the need and accepts to undergo regular follow-up and pregnancy testing before, ideally monthly during treatment and 1 month after stopping treatment
- she must stop taking isotretinoin immediately and consult a doctor urgently if she becomes pregnant or thinks she may be pregnant.

**On behalf of Pharmathen S.A.**

  
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**On behalf of Innovapharm LLC**



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