



23rd September 2019

▼ **Picato® (ingenol mebutate) – Use with caution in patients with a history of skin cancer**

Dear Healthcare professional,

LEO Pharma in agreement with the European Medicines Agency and the HPRA would like to inform you of the following:

Summary

- **Cases of squamous cell carcinoma have been reported in patients using ingenol mebutate and some clinical studies show an increased incidence of skin cancer**
- **Health care professionals should advise patients to be vigilant for any skin lesions developing and to seek medical advice immediately should any occur**
- **Ingenol mebutate should therefore be used with caution in patients with a history of skin cancer**

Background on the safety concern

Picato (ingenol mebutate) is used for the treatment of actinic keratosis in adults when the outer layer of the skin affected is not thickened or raised.

The potential for Picato to induce skin cancer was considered during the initial marketing authorisation application evaluation. In 2017, as a result of data from LP0105-1020 trial comparing ingenol mebutate gel to vehicle (the gel without the active ingredient), the product information of Picato was updated to reflect an excess of benign skin tumours (keratoacanthoma). In addition, an imbalance in the incidence of squamous cell carcinoma between ingenol mebutate and imiquimod arms was observed in the preliminary results of the ongoing long-term safety study LP0041-63. A meta-analysis of four studies of the related ingenol disoxate (a non-authorised treatment investigated for AK) found an increase in skin cancer at 14 months in the active group compared to vehicle when analysing the incidence for all tumour types together, including basal cell carcinoma, Bowen's disease and squamous cell carcinoma.

The product information for Picato will be revised to include a warning about reports of basal cell carcinoma, Bowen's disease and squamous cell carcinoma, and to advise that Picato should be used with caution in patients with a history of skin cancer.

A review by EMA is ongoing to explore the risk of skin cancer and the implications for the balance of benefits and risks of Picato.



Call for reporting

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie

▼ Picato is subject to additional monitoring to allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Company contact point

Telephone: +353 1 490 8924

Email: medical-info.ie@leo-pharma.com

Post: Medical Information, LEO Pharma, Cashel Road, Dublin 12, Ireland

Yours faithfully,

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