

## Picato – Use with caution in patients with a history of skin cancer

The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) has commenced a review of data on skin cancer in patients using Picato\* (ingenol mebutate) and will assess the impact of the available data on the benefit-risk balance of Picato. This review was triggered by data from some clinical studies which indicated a higher number of skin cancer cases, including cases of squamous cell carcinoma, in patients using ingenol mebutate or a related investigational medicinal product containing ingenol disoxate.

Picato is indicated for the cutaneous treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis in adults and has been authorised for use throughout the European Union since 2012. Picato is available in two strengths, 0.015% and 0.05% ingenol mebutate.

In 2017, as a result of data from a randomised, double-blind, vehicle-controlled study conducted with an investigational product of ingenol mebutate 0.06% in patients with actinic keratosis on trunk and extremities (study LP0105-1020), the product information for Picato was updated to reflect the potential for development of benign skin tumours (keratoacanthoma) in those treated with ingenol mebutate and this information was highlighted in the HPRAs Drug Safety Newsletter at that

time (79th edition). In addition, an increased incidence of squamous cell carcinoma in those treated with ingenol mebutate compared to imiquimod was observed in the preliminary results of the ongoing randomised long-term safety study LP0041-63. A meta-analysis of four randomised, double-blind, vehicle-controlled studies of the related ester ingenol disoxate (a non-authorised treatment investigated for actinic keratosis) found an increased incidence of skin cancer at 14 months in those treated with ingenol disoxate. An imbalance in tumour incidence was noted for a number of tumour types including basal cell carcinoma, Bowen's disease and squamous cell carcinoma.

The product information for Picato will be updated to include a warning regarding 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.

### Advice to Healthcare Professionals

- Picato should be used with caution in patients with a history of skin cancer.
- Continue to advise patients to be vigilant for any skin lesions developing within the treatment area and to seek medical advice immediately should any occur.

### Key Message

- Cases of squamous cell carcinoma have been reported in patients using ingenol mebutate and some clinical studies have indicated an increased incidence of skin cancer.
- The product information (Summary of Product Characteristics (SmPC) and Package Leaflet (PL)) for Picato will be updated to include a warning regarding 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.
- Patients should be advised to be vigilant for any skin lesions and to inform their doctor immediately should any occur.
- A Direct Healthcare Professional Communication (DHPC) was circulated by the MAH, following approval by the HPRAs, in September 2019.
- All reports of suspected adverse reactions should be reported to the HPRAs via the available methods ([www.hpra.ie](http://www.hpra.ie)).

*\*Further details on Picato are available at [www.hpra.ie](http://www.hpra.ie) and [www.ema.europa.eu](http://www.ema.europa.eu).*

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