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Risks of Picato for actinic keratosis outweigh benefits

On 30 April 2020, EMA completed its review of Picato (ingenol mebutate), a gel for treating the skin condition actinic keratosis, and concluded that the medicine may increase the risk of skin cancer and that its risks outweigh its benefits.

The review looked at results of a study comparing Picato with imiquimod (another medicine for actinic keratosis). After 3 years, 6.3% of patients treated with Picato (15 out of 240 patients) developed skin cancer, particularly squamous cell carcinoma, in the treated skin area compared with 2% of patients treated with imiquimod (5 out of 244 patients).

Data from other studies with ingenol mebutate or a similar medicine ingenol disoxate, laboratory studies and reports received since the medicine has been on the market were also assessed in the review.

It was noted that recent data from a study on the effectiveness of actinic keratosis treatments supported the previous observation, detailed in the medicine's product information, that Picato's effectiveness decreases over time.

Picato is no longer authorised in the EU as the marketing authorisation was withdrawn on 11 February 2020 at the request of LEO Laboratories Ltd, the company that marketed the medicine.

Information for patients

- Picato, a gel used on the skin to treat actinic keratosis, may increase the risk of skin cancer.
- A study showed that patients treated with Picato had a higher number of cases of skin cancer in the area of skin where the medicine was applied than patients using another treatment, imiquimod.
- The medicine has been taken off the market.
- Patients who have been treated with Picato should look out for unusual skin changes or growths, which could occur from weeks to months after use, and seek medical advice if any occur.
- Patients who have questions or concerns about their treatment should consult their doctor or pharmacist.

[1] 14 October 2020: correction of the date of the European Commission decision.

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Information for healthcare professionals

- Studies have found a higher incidence of skin tumours, especially squamous cell carcinoma, in the treatment area in patients treated with Picato (ingenol mebutate) or ingenol disoxate (a related ester not currently authorised and no longer in development) than with a comparator or vehicle (gel not containing any active substance).
- In the final results of a 3-year safety study in 484 patients, skin tumours were observed inside the treatment area in 6.3% of patients treated with ingenol mebutate compared with 2% of those treated with imiquimod. The difference was driven by squamous cell carcinoma (3.3% versus 0.4% of patients) and Bowen's disease (2.5% versus 1.2%).
- In a pooled analysis of four 14-month trials involving 1234 patients, higher incidence of tumours, including basal cell carcinoma, Bowen's disease and squamous cell carcinoma, was seen with the related ester ingenol disoxate than with vehicle (7.7% versus 2.9% of patients).
- Picato has already been taken off the market and is therefore no longer a treatment option for actinic keratosis.
- Other treatment options for actinic keratosis include topical diclofenac, fluorouracil and imiquimod, as well as photodynamic therapy, cryotherapy, curettage or excisional surgery.
- Healthcare professionals should advise patients who have been treated with Picato to be vigilant for any skin lesions developing and to seek medical advice promptly should any occur. Time to onset can range from weeks to months following treatment.

More about the medicine

Picato was available as a gel which was applied to skin areas affected by actinic keratosis. It was used when the outer layer of the affected skin was not thickened or raised. Actinic keratosis is caused by too much sunlight exposure and can turn into skin cancer.

Picato was authorised for use in the EU in November 2012.

More about the procedure

The review of Picato was initiated on 3 September 2019 at the request of the European Commission, under Article 20 of Regulation (EC) No 726/2004.

The review was first carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines. On 17 January 2020, the marketing authorisation of Picato was suspended as an interim measure while the review was ongoing.

On 11 February 2020, the European Commission withdrew the marketing authorisation of the medicine at the request of the marketing authorisation holder, LEO Laboratories Ltd.

The PRAC concluded its review, and its recommendation was sent to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which adopted the Agency's opinion. The CHMP opinion was forwarded to the European Commission, which issued a final legally binding decision applicable in all EU Member States on 6 July 2020.