EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

23 February 2017
EMA/312676/2017
Committee for Medicinal Products for Human Use (CHMP)

Scientific conclusions and grounds for the variation to the terms of the marketing authorisation(s)

Active substance(s): ingenol mebutate

Procedure No. EMEA/H/C/PSUSA/00010035/201607

Period covered by the PSUR: 1 February 2016 to 31 July 2016

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Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for ingenol mebutate, the scientific conclusions of CHMP are as follows:

In study LP0105-1020, a double-blind, vehicle controlled study in patients with actinic keratosis on trunk and extremities, ingenol mebutate gel 600 mcg/g was applied once daily for 2, 3 or 4 days to a skin area of 250 cm2 in a group of severely sun-damaged patients. 12 out of 163 subjects in the ingenol mebutate group reported 16 skin tumours inside the treatment area: one squamous cell carcinoma, 1 Bowen's disease and 14 keratoacanthomas following centralised pathology review compared to zero out of 61 subjects in the vehicle group.

In addition, in the post-marketing phase, a total of 42 spontaneous cases of squamous cell carcinoma have been reported including 5 new cases reported during the covering period of this PSUR. 3 out of the 5 new cases were considered as possibly related to treatment with Picato and the time to onset was

quite short (3 weeks to 4 months). In addition 3 cases of keratoacanthoma were reported cumulatively including 1 during the covering period of this PSUR.

Based on the available evidence, the PRAC considered that a new warning should be included in section 4.4 'Special warnings and precautions' of the SmPC on the risk of keratoacanthoma with a recommendation for patients to be vigilant for any lesions developing within the treatment area. As already concluded in December 2016 as part of the LEG, the PRAC also considered that section 5.1 'Pharmacodynamic properties' of the SmPC should also be updated to include information on the high

incidence of keratoacanthoma observed in study LP0105-1020.

Therefore, in view of the data presented in the reviewed PSUR, the PRAC considered that changes to the product information of medicinal products containing ingenol mebutate were warranted.

The CHMP agrees with the scientific conclusions made by the PRAC.

Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions for ingenol mebutate the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing ingenol mebutate is unchanged subject to the proposed changes to the product information

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The CHMP recommends that the terms of the marketing authorisation(s) should be varied.

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