astellas
Leading Light for Life

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DIRECT HEALTHCARE PROFESSIONAL COMMUNICATION

Important recommendations for appropriate use of PROTOPIC (tacrolimus) (0.03% and 0.1%) ointment to minimise risks.

11th May 2012

Dear Healthcare Professional,

Astellas Pharma Europe wishes to remind healthcare professionals of important risk minimisation measures for the treatment of moderate to severe atopic dermatitis with tacrolimus ointment.

The content of this letter has been approved by the European Medicines Agency and the Irish Medicines Board.

Summary

- Cases of malignancies, including lymphomas and skin cancers have been reported in patients using tacrolimus ointment.
- Since approval in 1999 an estimated 2.5 million patient years of exposure to Protopic have been accumulated.
- Some epidemiological studies have suggested an increased risk of lymphoma in patients treated with topical calcineurin inhibitors (TCI), including tacrolimus ointment[1-3].

Healthcare Professionals are reminded of the following risk minimisation measures:

- Protopic should be used in patients with moderate to severe atopic dermatitis who failed to respond adequately or were intolerant to conventional therapies such as topical corticosteroids
- Protopic should not be prescribed to patients younger than 2 years of age. The effect of treatment with Protopic on the developing immune system of children aged below 2 years has not been established.
- Use of Protopic in children aged 2 to 16 years of age is restricted to the lower strength only i.e. Protopic 0.03% ointment.
- Protopic ointment should not be applied to lesions that are considered to be potentially malignant or pre-malignant

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Further information on the safety concern

Prolonged systemic exposure to intensive immunosuppression following systemic administration of calcineurin inhibitors (in combination with other systemic imunosuppressants) has been associated with an increased risk of developing lymphomas and skin malignancies.

In patients using Protopic, cases of malignancies, including cutaneous and other types of lymphomas and skin cancers have been reported.

Recent published epidemiological studies have suggested a potentially increased risk for cutaneous T-cell lymphoma in patients treated with topical calcineurin inhibitors, including tacrolimus ointment[1-3]. One study agreed with the EMA is planned to investigate this risk.

Healthcare professionals are reminded of the following recommendations:

- When used to treat active flares (twice daily), treatment should not be continuous on a long-term basis. If no signs of improvement are seen after two weeks of treatment, alternative treatment options should be considered.
- During maintenance use (twice weekly), patients should be monitored for response to therapy and the need for continued treatment should be evaluated. After 12 months treatment, a review of the patient's condition should be conducted and a decision taken whether to continue maintenance treatment based on an individual benefit-risk-assessment. In children 2 to 16 years old, Protopic therapy should be stopped after 12 months to assess the need to continue this regimen and to evaluate the course of the disease.
- Lymphadenopathy present at initiation of therapy should be investigated and kept under review. Patients who receive Protopic and who develop lymphadenopathy should be monitored to ensure that the lymphadenopathy resolves. In case of persistent lymphadenopathy, the aetiology of the lymphadenopathy needs to be investigated. In the absence of a clear aetiology for the lymphadenopathy or in the presence of acute infectious mononucleosis, discontinuation of Protopic should be considered.
- Protopic should not be used in patients with congenital or acquired immunodeficiencies or in patients on therapy that cause immunosuppression. Exposure of the skin to sunlight should be minimised and the use of ultraviolet (UV) light (solarium, therapy with UVB or PUVA) should be avoided. You should advise your patients on appropriate sun protection methods while under treatment with Protopic.

Further information is contained in the Summary of Product Characteristics (SmPC) for Protopic ointment which will be updated to clarify the available information. When prescribing or dispensing Protopic, both at the time of first prescription and each time a prescription is refilled, please advise patients to read and understand the package leaflet.

Reporting Adverse Drug Reactions:

Please remember to report any adverse reaction suspected to be associated with the use of Protopic to the Irish Medicines Board. Suspected adverse reactions should be reported to the IMB using a Yellow Card obtained either from the IMB, or electronically via the website at www.imb.ie

Should you have any questions or require additional information regarding the use of Protopic or if you would like to report a suspected adverse drug reaction to the company, please contact Astellas at the following phone number:+353 1 467 1555.

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