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DEAR HEALTH CARE PROFESSIONAL LETTER

Important safety reminder on PROTOPIC ointment[1] and recommendations for monitoring with maintenance treatment.

Dear Health Care Professional,

As part of our commitment to EMEA/CHMP during the recent licensing procedure, Astellas Pharma Europe wishes to remind health care professionals of the safety messages required for the use of Protopic for maintenance treatment of moderate to severe atopic dermatitis for the prevention of flares and the prolongation of flare-free intervals in patients experiencing a high frequency of disease exacerbations (i.e. occurring 4 or more times per year) who have had an initial response to a maximum of 6 weeks treatment of twice daily tacrolimus ointment (lesions cleared, almost cleared or mildly affected).

The content of this letter has been approved by the Irish Medicines Board (IMB) and the CHMP.

It is important to adhere to the following recommendations both when initially prescribing Protopic for maintenance therapy and during subsequent monitoring of treatment. Particular care should be exercised when treating children:

Initial therapy

- Protopic should be initiated by physicians with experience in the diagnosis and treatment of atopic dermatitis.
  Protopic should initially only be prescribed for short term and intermittent long-term (twice daily) therapy for patients with active moderate to severe flares who are not adequately responsive to or are intolerant of conventional therapies, such as topical corticosteroids. If no signs of improvement are seen after 2 weeks of treatment, further therapeutic options may be considered.

Maintenance therapy

- Patients who have been prescribed maintenance therapy should be advised to apply Protopic once a day, twice weekly to the areas commonly affected by atopic dermatitis to prevent occurrence of flares and prolong flare-free intervals. Between the applications there should be 2-3 days without Protopic treatment. If signs of a flare reoccur, twice daily treatment with Protopic should be reinitiated.
- In studies of maintenance treatment of atopic dermatitis with twice weekly Protopic, application site infections (6.4% in children and 6.3% in adults) and application site impetigo (7.7% in children) were noted to occur more frequently than in the control (ointment without tacrolimus) group.
- Long-term safety of maintenance treatment with twice weekly Protopic beyond 12 months has not been established. After 12 months treatment, you should reassess the need to continue maintenance therapy with your patients. In children this reassessment should include suspension of twice-weekly treatment to assess the need to continue this regimen and evaluate the course of the disease.

[1] Containing 0.03% tacrolimus or 0.1% tacrolimus

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The following cautions for initial treatment also apply to the use of Protopic as maintenance therapy and should be taken into consideration when prescribing and during monitoring:

- Protopic 0.1% is not recommended for use in children below 16 years of age. In children above 2 years of age only Protopic 0.03% may be used.
- Treatment with Protopic may be associated with an increased risk of herpes viral infections (herpes simplex dermatitis [eczema herpeticum], herpes simplex [cold sores], Kaposi's varicelliform eruption). In the presence of these infections, the balance of risks and benefits associated with Protopic use should be evaluated.
- 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 during use of Protopic ointment. Physicians should advise patients on appropriate sun protection methods i.e. to minimise time in the sun, use sunscreen products and covering of the skin with appropriate clothing.
- The effect of treatment with Protopic ointment on the developing immune system of children, especially the young, has not yet been established and this should be taken into account when prescribing to this age group.
- In transplant patients, prolonged systemic exposure to intense immunosuppression following systemic administration of calcineurin inhibitors 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 lymphoma, and skin cancers have been reported. Patients with atopic dermatitis treated with Protopic have not been found to have significant systemic tacrolimus levels.
- Protopic ointment should not be applied to lesions that are considered to be potentially malignant or pre-malignant.
- Protopic ointment should not be used during pregnancy unless clearly necessary; breastfeeding during treatment with Protopic ointment is not recommended.

It is important that patients are aware of and adhere to the approved recommendations for safe and effective use of Protopic. Patients should always be advised to read and understand the package leaflet.

Call for reporting
Healthcare professionals should report any adverse event suspected to be associated with the use of Protopic to the IMB. Suspected adverse reactions may also be reported to Astellas Pharma Co. Ltd.

Should you have any questions or require additional information regarding the use of Protopic please contact our Medical Department on 01 4671555.

Yours faithfully,

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European Qualified Person for Pharmacovigilance
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Signature:

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