Protopic®

(tacrolimus 0.03%, 0.1% ointment)

Now also indicated for twice weekly long-term eczema control

REFERENCES: 1. Wollenberg A et al. *Allergy* 2008; 63: 742-750. 2. Leung DYM et al. *J Clin Invest* 2004; 113(5): 651-657. 3. White MI et al. *Br J Dermatol* 1987; 116: 525-530. 4. Lee Y & Hwang K. *Surg Radiol Anat* 2002; 24: 183-189. 5. Cork M. *J Derm* Treat 1997; 8: S7-S13. 6. Wollenberg A & Bieber T. *Allergy* 2009; 64: 276-278. 7. Protopic Summary of Product Characteristics, 2013. 8. Kang S et al. *J Am Acad Dermatol* 2001; 44: S58-64. 9. Koo J et al. *J Am Acad Dermatol* 2005; 53: S195-205. 10. Thaçi D et al. *Br J Dermatol* 2008; 159: 1348-1356. 11. Astellas Pharma: Data on file..

ABBREVIATED PRESCRIBING INFORMATION

(Please refer to full Summary of Product Characteristics before prescribing.)

PRESCRIBING INFORMATION: Protopic™ 0.03% ointment (tacrolimus monohydrate) Protopic™ 0.1% ointment (tacrolimus monohydrate) **ACTIVE INGREDIENT** Protopic™ 0.03% ointment (1g) contains 0.3mg of tacrolimus as tacrolimus monohydrate (0.03%). Protopic™ 0.1% ointment (1g) contains 1.0mg of tacrolimus as tacrolimus monohydrate (0.1%). **THERAPEUTIC INDICATIONS** Protopic™ 0.03%: - treatment of moderate to severe atopic dermatitis in children (2 years of age and above) who failed to respond adequately to conventional therapies such as topical corticosteroids. - treatment of moderate to severe atopic dermatitis in adults who are not adequately responsive to or are intolerant of conventional therapies such as topical corticosteroids. Protopic™ 0.1%: - treatment of moderate to severe atopic dermatitis in adults who are not adequately responsive to or are intolerant of conventional therapies such as topical corticosteroids. Protopic™ 0.03%, 0.1%: - maintenance treatment of moderate to severe atopic dermatitis for prevention of flares and 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). **DOSAGE AND METHOD OF USE** Protopic™ should be initiated by physicians with experience in the diagnosis and treatment of atopic dermatitis. Protopic™ can be used for short-term and intermittent long-term treatment. Treatment should not be continuous. Protopic™ should be applied as a thin layer to affected or commonly affected areas of the skin and may be used on any part of the body, including face, neck and flexure areas (except eyes and mucous membranes). Protopic™ should not be applied under occlusion. Protopic™ is not recommended for use in children below the age of 2 years until further data are available. Specific studies have not been conducted in elderly patients. However clinical experience has not shown the necessity for any dosage adjustment. Treatment of flares: Protopic™ treatment should begin at the first appearance of signs and symptoms. Each affected region of the skin should be treated with Protopic™ until lesions are cleared, almost cleared or mildly affected. Thereafter, patients are considered suitable for maintenance treatment (see below). At the first signs of recurrence (flares) of the disease symptoms, treatment should be re-initiated. *General considerations for treatment of flares*: Use in children (2 years of age and above) Protopic™ 0.1% is not indicated for use in children. Treatment with Protopic™ 0.03% should be started twice a day for up to three weeks. Afterwards the frequency of application should be reduced to once a day until clearance of the lesion. Use in adults (16 years of age and above) Treatment should be started with Protopic™ 0.1% twice a day and continued until clearance of the lesion. If symptoms recur, twice daily treatment with Protopic™ 0.1% should be restarted. An attempt should be made to reduce the frequency of application or use the lower strength if the clinical condition allows. Generally, improvement is seen within one week of starting treatment. If no signs of improvement are seen after two weeks of treatment, further treatment options should be considered. Maintenance of flare-free intervals: Protopic™ should be applied once a day twice weekly (e.g. Monday and Thursday) to commonly affected areas to prevent progression to flares. Between applications there should be 2-3 days without Protopic™ treatment. Adult patients (16 years of age and above) should use Protopic™ 0.1%; children (2 years of age and above) should use the lower strength Protopic™ 0.03%. If signs of a flare reoccur, twice daily treatment should be reinitiated. After 12 months, a review of the patient's condition should be conducted by the physician and a decision taken whether to continue maintenance treatment. In children, this review should include suspension of treatment to assess the need to continue this regimen and to evaluate the course of the disease. **UNDESIRABLE EFFECTS** Very common: Burning sensation (which tends to resolve within one week of starting treatment), pruritus. Common: Sensation of warmth, erythema, pain, irritation, paraesthesia and rash at site of application. Alcohol intolerance (facial flushing or skin irritation after consumption of an alcoholic beverage). Patients may be at an increased risk of herpes viral infections (herpes simplex [cold sores], eczema herpeticum, Kaposi's varicelliform eruption) and folliculitis. Uncommon: acne. During post-marketing experience: Rosacea. Also, cases of malignancies, including cutaneous and other types of lymphoma, and skin cancers, have been reported in patients using tacrolimus ointment. Application site impetigo and application site infections occurred more frequently in a study of maintenance treatment in adults and children. Prescribers should consult the summary of product characteristics in relation to other side effects. **PRECAUTIONS FOR USE** Protopic™ should not be used in patients with congenital or acquired immunodeficiencies or in patients on therapy that causes immunosuppression. The effect of treatment with Protopic™ 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. Exposure of the skin to sunlight should be minimised and the use of ultraviolet (UV) light from a solarium, therapy with UVB or UVA in combination with psoralens (PUVA) should be avoided during use of Protopic™. Patients should be advised on appropriate sun protection methods, such as minimisation of the time in the sun, use of a sunscreen product and covering of the skin with appropriate clothing. Protopic™ ointment should not be applied to lesions that are considered to be potentially malignant or pre-malignant. Emollients should not be applied to the same area within 2 hours of applying Protopic™. Concomitant use of other topical preparations has not been assessed. There is no experience with concomitant use of systemic steroids or immunosuppressive agents. Before commencing treatment with Protopic™, clinical infections at treatment sites should be cleared. The potential for local immunosuppression (possibly resulting in infections or cutaneous malignancies) in the long term (i.e. over a period of years) is unknown. Protopic™ contains the active substance tacrolimus, a calcineurin inhibitor. 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 tacrolimus ointment, 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. Lymphadenopathy was uncommonly (0.8%) reported in clinical trials. The majority of these cases related to infections (skin, respiratory tract, tooth) and resolved with appropriate antibiotic therapy. Patients who receive Protopic™ and who develop lymphadenopathy should be monitored to ensure that the lymphadenopathy resolves. Lymphadenopathy present at initiation of therapy should be investigated and kept under review. In case of persistent lymphadenopathy, the aetiology of the lymphadenopathy should 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 be used with caution in patients with hepatic failure. Protopic™ should not be used in patients with Netherton's syndrome. Care should be exercised if applying Protopic™ to patients with extensive skin involvement over an extended period of time, especially in children. The development of any new change different from previous eczema within a treated area should be reviewed by the physician. Protopic™ should not be used during pregnancy unless clearly necessary and is not recommended when breast-feeding. The safety of Protopic™ has not been established in patients with generalised erythroderma. Protopic™ is unlikely to have an effect on the ability to drive or use machines. **CONTRAINDICATIONS** Hypersensitivity to macrolides in general, to tacrolimus or to any of the excipients. **INTERACTIONS** An interaction study with protein-conjugated vaccine against Neisseria menigitidis serogroup C has been investigated in children aged 2-11 years. No effect on immediate response to vaccination, the generation of immune memory, or humoral and cell-mediated immunity has been observed (for more data see summary of product characteristics). Systemically available tacrolimus is metabolised via the hepatic Cytochrome P450 3A4. The possibility of interactions cannot be ruled out and the concomitant systemic administration of known CYP3A4 inhibitors in patients with widespread and/or erythrodermic disease should be done with caution. **PACKAGE SIZES** Protopic™ 0.03% ointment 30g tube; Protopic™ 0.1% ointment 30g tube **LEGAL CATEGORY**: POM. **MARKETING AUTHORISATION NUMBERS** Protopic™ 0.03% ointment EU/1/02/201/001-2 Protopic™ 0.1% ointment EU/1/02/201/003-4. **FURTHER INFORMATION AVAILABLE FROM**: Astellas Pharma Europe B.V., Sylviusweg 61, P.O. Box 344, 2300AH Leiden, the Netherlands. **DATE OF REVISION**: June 2013. **FOR FULL PRESCRIBING INFORMATION REFER TO THE SUMMARY OF PRODUCT CHARACTERISTICS.**

Adverse events should be reported. Please check local requirements. Adverse events should also be reported to your local Astellas office or representative.

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