Coventry & Warwickshire Area Prescribing Committee

Guidance on the use of pimecrolimus cream and tacrolimus ointment in moderate to severe atopic dermatitis

This should be read in conjunction with the Summary of Product Characteristics (SPC)[1] and the patient's clinical letters which will detail diagnosis and previous therapies.

PIMECROLIMUS and TACROLIMUS GUIDELINES SUMMARY

- Treatment can be initiated by physicians with a special interest and experience in dermatology and by GPs[8,9]
- **Dosing Tacrolimus**
  Adults aged 16 years and above: 0.1% twice daily for 3 weeks, then 0.03% twice daily and stop as eczema clears

  Children aged 2 years and above: 0.03% twice daily for 3 weeks then once daily and stop as eczema clears
- **Dosing Pimecrolimus**
  Children aged 2-16 years with moderate to severe eczema affecting the face and neck: 1% cream to be applied twice daily for up to 6 weeks then once daily and stop as eczema clears
- Attempt should be made to reduce the frequency of application as the clinical condition allows
- For short term use rather than continuous treatment
- Treatment should continue until the lesions are cleared. If no signs of improvement are seen after 2 weeks (tacrolimus) or 6 weeks (pimecrolimus) of ointment/cream this should be discontinued
- **Precautions**
  - Sun protection. Avoid UV treatment while on treatment with tacrolimus or pimecrolimus
  - Do not apply other preparations within 2 hours of application of tacrolimus or pimecrolimus
  - Treat infection first
  - Vaccines should be given pre-treatment or 14 days (28 days for live vaccines) after treatment finishes
- **Contraindications**
  - Child less than 2 years of age (tacrolimus and pimecrolimus)
  - Child less than 16 years of age (0.1% tacrolimus)
  - Pregnancy/ breast feeding
  - Not to be applied under occlusion
  - Immunocompromised patients
  - Not to be applied on mucous membranes
  - Not to be applied to malignant/ potentially malignant skin lesions e.g. cutaneous lymphoma
  - Hypersensitivity to tacrolimus, pimecrolimus, macrolides or excipients
  - Genetic epidermal barrier defects *e.g.* Netherton's syndrome

Coventry & Warwickshire APC – Approved Guideline [G001]
Responsible organisation: South Warwickshire General Hospitals NHS Trust
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Background Information

Atopic dermatitis (AD) is a chronic, relapsing, highly pruritic, inflammatory skin disease, which is often associated with a personal or family history of asthma and/or allergic rhinitis.

Patients with AD can have their condition complicated by an increased number of bacterial, fungal and viral skin infections. *Staphylococcus aureus* and *β-haemolytic streptococci* commonly colonise or secondarily infect the skin[2].

The prevalence of AD has increased two to three fold over the past 30 years, affecting 15-20% of children aged 7-18 years in the UK[3] and 2.3% of adults in the USA[4]. Most affected individuals (~85%) develop AD before the age of 5 years[2].

In adults topical steroids are the mainstay of therapy. Oral antihistamines may decrease scratching in some patients. Second line treatments include allergen avoidance, dietary intervention and treatment with ultraviolet light under specialist care. Third line treatments include short courses of systemic corticosteroids for severe acute flares and ciclosporin A.

In children, mild corticosteroids such as 1% hydrocortisone ointment are widely used for the treatment of AD. The more potent corticosteroids should be avoided if possible and are contraindicated in infants less than one year old. For children over one year a potent or moderately potent corticosteroid may be appropriate for AD on the limbs for 1-2 weeks only, followed by a weaker preparation as the condition improves.

Prescribed indications for tacrolimus ointment

0.03% strength
Treatment of moderate to severe AD in adults and children (aged 2 years and older) that has not been controlled by topical corticosteroids, where there is serious risk of adverse effects from further corticosteroid use, particularly skin atrophy.

0.1% strength
Treatment of moderate to severe AD in adults (16 years and above) that has not been controlled by topical corticosteroids, where there is serious risk of adverse effects from further corticosteroid use, particularly skin atrophy.

Prescribed indications for pimecrolimus 1% cream

Treatment of moderate to severe AD affecting the face and neck in children aged 2-16 years that has not been controlled by topical corticosteroids, where there is serious risk of adverse effects from further corticosteroid use, particularly skin atrophy.

Dosage and administration

Tacrolimus ointment or pimecrolimus cream should be applied as a thin layer to affected areas of the skin until the lesions are cleared. The preparations may be used on any part of the body including the face, neck and flexure areas with the exception of the mucous membranes. They should not be applied under occlusion[1].

Treatment should be started twice a day for up to 3 weeks (6 weeks for pimecrolimus). The frequency of application should then be reduced to once a day for children. For adults and adolescents aged 16 years and above the strength of the ointment should be reduced from 0.1% to 0.03% and the frequency of application should be reduced to once a day.

Duration of treatment

Treatment should continue until the lesions are cleared[1]. If no signs of improvement are seen after 2 weeks (six weeks for pimecrolimus cream) of initiating therapy the ointment should be discontinued.

Adverse effects

Over 2,000 patients have been exposed to tacrolimus ointment in clinical trials. Site-specific adverse events such as erythema, burning sensation and pruritus were common with approximately 50% of patients experiencing some kind of skin irritation. These sensations decreased with time and duration of treatment[1,5]. Increased risk of folliculitis, acne, and herpes virus infections. Similar problems are seen with pimecrolimus cream.

Non application site events included flu-like symptoms, alcohol intolerance (flushing), headache and fever[1,2].

Longer term open label studies reported minimal systemic exposure to tacrolimus. The incidence of adverse events did not change with the cumulative amounts of tacrolimus used or the duration of treatment[6,7].

Special precautions

Tacrolimus ointment, or pimecrolimus cream, should not be used if the patient is pregnant[1]. Human data shows that following systemic administration tacrolimus is excreted in breast milk. Although systemic exposure from application of tacrolimus ointment is low, breast feeding during treatment with tacrolimus ointment or pimecrolimus cream is not recommended.

Exposure of the skin to sunlight should be minimised during treatment. 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.

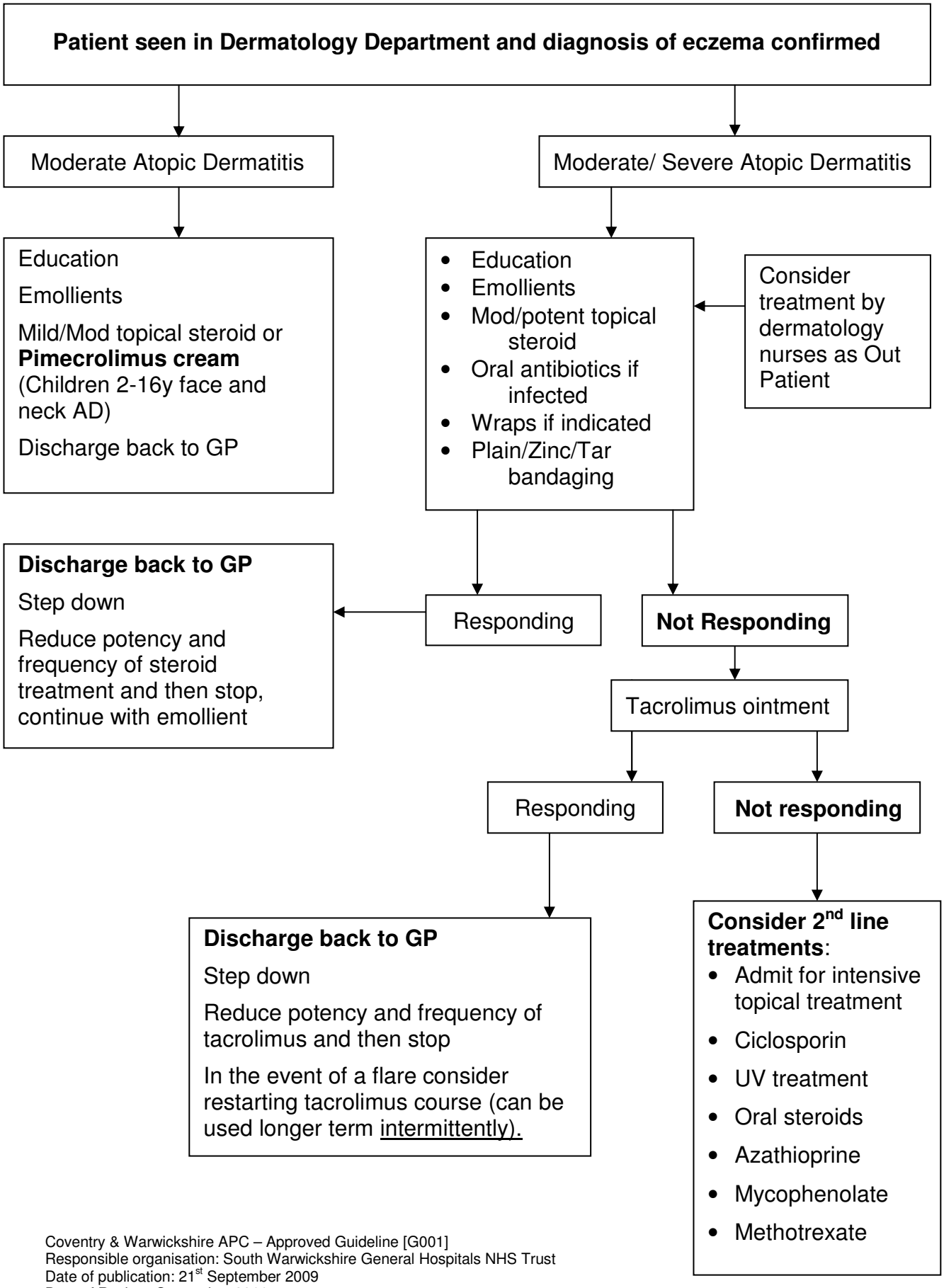
Clinically relevant drug interactions

Because of the potential risk of vaccination failure vaccinations should be administered prior to commencement of treatment or during a treatment free interval with a period of 14 days (28 days for live vaccines) between the last application of tacrolimus ointment or pimecrolimus cream and the vaccination.

References

1. Astellas Pharma Ltd Protopic Summary of Product Characteristics 2008. Electronic Medicines Compendium see www.emc.medicines.org.uk.
2. Rudikoff D et al. Atopic dermatitis. Lancet 1998; **351**: 1715-21.
3. Eedy DJ. Topical Review-what's new in atopic dermatitis. Br J Dermatol 2001; **145**: 380-384.
4. Smethurst D. Atopic eczema. Clinical evidence 2001; **6**: 1266-1279.
5. Cheer SM. Tacrolimus ointment-A review of its therapeutic potential as a topical therapy in atopic dermatitis. Am J Clin Dermatol 2001; **2**(6): 389-406.
6. Reitamo S et al. Safety and efficacy of tacroliumus ointment monotherapy in adults with atopic dermatitis. Arch Dermatol 2002; **136**: 999-1066.
7. Kang S et al. Long term safety and efficacy of tacrolimus ointment for the treatment of atopic dermatitis in children. J Am Acad Dermatol 2001; **44**(1):S58-64.
8. MTRAC Pimecrolimus Verdict and Summary; January 2005 see http://www.keele.ac.uk/schools/pharm/MTRAC/ProductInfo/prdrecm.htm
9. MTRAC Tacrolimus Verdict and Summary; January 2005 see http://www.keele.ac.uk/schools/pharm/MTRAC/ProductInfo/prdrecm.htm

Simple algorithm for the use of tacrolimus ointment and pimecrolimus cream in the management of atopic dermatitis



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