THE SHEFFIELD AREA PRESCRIBING COMMITTEE

Shared Care Protocol

Prescribing Topical Tacrolimus or Pimecrolimus to Adults and Children with Eczema

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Shared Care Protocol for Prescribing Topical Tacrolimus or Pimecrolimus to Adults and Children with Eczema

Statement of Purpose

The aim of this shared care protocol is to support the continuation of care by primary care prescribers of adults and children initiated on topical tacrolimus ointment (Protopic®) or topical pimecrolimus cream (Elidel®) by the dermatology services at the Royal Hallamshire Hospital and Sheffield Children’s Hospital. Primary care will only be asked to take over prescribing within the licensed indication.

Introduction

Tacrolimus and pimecrolimus are topical immunomodulators and belong to the class of immunosuppressant drugs known as calcineurin inhibitors. They work by reducing inflammation through the suppression of T-lymphocyte responses, a different mechanism of action from topical corticosteroids. Although tacrolimus and pimecrolimus have similar mechanisms of action, they have different licensed indications.

NICE has made the following recommendations for the place of tacrolimus and pimecrolimus in management of atopic eczema (http://guidance.nice.org.uk/TA82/Guidance):

Topical tacrolimus is considered, within its licensed indications, as an option for the second-line treatment of moderate or severe atopic eczema in adults and children aged 2 years and over in the following circumstances:
- the individual’s atopic eczema has not been controlled by topical corticosteroids and
- there is a serious risk of important adverse effects from further topical corticosteroid use, particularly irreversible skin atrophy

Pimecrolimus is considered, within its licensed indications, as an option for the second-line treatment of moderate atopic eczema on the face or neck in children aged 2 to 16 years in the following circumstances:
- the child’s facial atopic eczema has not been controlled by topical corticosteroids and
- there is a serious risk of important adverse effects from further topical corticosteroid use, particularly irreversible skin atrophy

Treatment with topical tacrolimus or pimecrolimus is initiated only by a physician (including general practitioners) with a special interest and experience in dermatology.

Treatment with tacrolimus or pimecrolimus is initiated only after careful discussion between the prescribing physician and the patient of the potential risks and benefits of all appropriate second-line treatment options.

Indication for Tacrolimus Ointment (See SPC for full prescribing information)

Tacrolimus (Protopic®) ointment is available in strengths of 0.1% for use in adults over 16 years and 0.03% for adults and children over 2 years old.

It is to be used for the maintenance and treatment of moderate to severe atopic eczema where the individual’s atopic eczema has not been controlled by topical corticosteroids and there is a serious risk of important adverse effects from further topical corticosteroid use, particularly irreversible skin atrophy.
Dosage

Treatment

Adults and children 16 years and above: Each affected region of the skin should be treated with tacrolimus 0.1% twice a day for up to 6 weeks until lesions are cleared, almost cleared or mildly affected. If symptoms recur, twice daily should be restarted. An attempt should be made to reduce the frequency of application or to use the lower strength 0.03% ointment if the clinical condition allows. Children (2 years to 16 years): Each affected region of the skin should be treated with tacrolimus 0.03% twice a day for up to 3 weeks Afterwards the frequency of application should be reduced to once a day until clearance of the lesion.

If there is no improvement or worsening of eczema after two weeks of treatment with topical tacrolimus other treatment options should be considered. It is likely that such patients will be under secondary care. If the patient is being managed in primary care referral to the dermatology service may be needed.

Patients are considered suitable for maintenance treatment (see below) to prolong the flare free intervals provided the initial treatment is effective and the patient has been experiencing 4 or more exacerbations a year. At the first signs of recurrence (flares) of the disease symptoms, daily treatment should be re-initiated.

Maintenance treatment

Adult patients (16 years of age and above) should use tacrolimus 0.1% ointment and children (2 to 16 years) 0.03% strength.

Tacrolimus ointment should be applied once a day twice weekly (e.g. Monday and Thursday) to areas commonly affected by atopic dermatitis to prevent progression to flares. Between applications there should be 2–3 days without tacrolimus treatment. At the first signs of recurrence (flares) of the disease symptoms, daily treatment should be re-initiated. After 12 months, a review of the patient`s condition should be conducted and a decision taken whether to continue maintenance treatment in the absence of safety data for maintenance treatment beyond 12 months

Contra-indications

Hypersensitivity to macrolides, to tacrolimus or to any of the excipients.

Warnings and precautions

Topical tacrolimus should be avoided in:

- Patients with congenital or acquired immunodeficiencies, including those on immunosuppressant treatment
- Patients with potential skin malignancies or pre-malignancies
- Patients with skin infections including herpes virus infections
- Erythrodermic patients
- Pregnancy and breastfeeding

Exposure to sunlight should be minimised and high protection sunscreen used if exposure is unavoidable. Sunbeds should not be used.

Do not apply emollients to the same area within 2 hours of applying tacrolimus ointment.

Avoid contact with eyes and mucous membranes

Not to be used under occlusion.

Vaccines should be administered either before treatment or in the following manner: there should be an interval of 14 days from last application; in case of live attenuated vaccines the interval should be 28 days from last application.

Not to be used on large areas of skin for long periods.
Side-effects

Common reactions:
- Skin irritation (50%): burning sensation; pruritus and erythema; sensation of warmth; pain; parasthesia and rash on application site
- Flushing or skin irritation after consuming alcohol
- Folliculitis, acne and herpes infections possible

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. In patients using tacrolimus ointment, cases of malignancies, including cutaneous and other types of lymphoma, and skin cancers have been reported.

The above details are not a complete list and the current BNF and the SPC remain authoritative.

Monitoring

Patients should be reviewed 12 monthly or sooner if required. The 12 month review should include:
- reinforcing the use of all treatments (including emollient use) as laid out in the patient’s treatment plan
- asking about development of any new change different from previous eczema within a treated area and examining these areas if necessary
- considering the suspension of tacrolimus treatment to assess the need to continue this regimen and to evaluate the course of the disease
- liaising with the dermatologist regarding any areas of concern e.g. side effects, increase in skin infections, need for vaccination, persistent lymphadenopathy or changes in the patient’s condition that may impact on treatments such as development of hepatic failure

Stop topical tacrolimus and contact the secondary care provider if:
- Hypersensitivity/allergic reaction occurs
- Serious infection e.g. eczema herpeticum
- Erythroderma
- Persistent lymphadenopathy
- Malignancy suspected

Indication for Pimecrolimus Cream (See SPC for full prescribing information)

Pimecrolimus is available as 1% cream (Elidel®) and is indicated in line with NICE guidance (TA82) for second-line treatment of moderate atopic eczema on the face and neck in children aged 2-16 years that has not been controlled by topical corticosteroids and where there is a serious risk of important adverse effects from further topical corticosteroid use, particularly irreversible skin atrophy.

Dosage

Pimecrolimus is applied thinly to the affected areas twice daily in the short term for the treatment of the signs and symptoms of atopic eczema and intermittently in the long term for the prevention of progression to flares.

Treatment should be for as short a period as possible during flares and should be stopped when symptoms resolve. If pimecrolimus has failed to control the flare after 6 weeks, treatment should be stopped and if patient is being managed in primary care, referral to dermatology service may be needed.
In long term intermittent treatment, treatment should begin at twice daily dosage at first sign of atopic dermatitis. Data from clinical studies supports intermittent treatment for up to 12 months. After 12 months, a review of the patient’s condition should be conducted and a decision taken whether to continue intermittent treatment.

**Contra-indications**

Hypersensitivity to pimecrolimus, other macrolactams or to any of the excipients.

**Warnings and precautions**

Topical pimecrolimus should be avoided in:

- Patients with congenital or acquired immunodeficiencies, including immunosuppressant treatment
- Patients with potential skin malignancies or pre-malignancies
- Patients with skin infections including herpes virus infections
- Erythrodermic patients
- Patients with Netherton’s syndrome
- Pregnancy. Breastfeeding mothers should avoid applying pimecrolimus to the breast.

Exposure to sunlight should be minimised and high protection sunscreen used if exposure is unavoidable. Sunbeds should not be used.

Avoid contact with eyes and mucous membranes

Not to be used under occlusion.

Emollients may be applied immediately after pimecrolimus.

Vaccinations should be administered during treatment free intervals.

**Side-effects**

Common reactions:

- Skin irritation, burning sensation; pruritus and erythema;
- Folliculitis.

The potential for local immunosuppression in the long term is unknown. In patients using pimecrolimus ointment, cases of malignancies, including cutaneous and other types of lymphoma, and skin cancers have been reported.

The above details are not a complete list and the current BNF and the SPC remain authoritative.

**Monitoring**

Patients should be reviewed 12 monthly or sooner if required. The 12 month review should include:

- reinforcing the use of all treatments (including emollient use) as laid out in the patients treatment plan
- asking about development of any new change different from previous eczema within a treated area and examining these areas if necessary
- assessing the need to continue this regimen beyond 12 months.
- liaising with the dermatologist regarding any areas of concern e.g. side effects, increase in skin infections, persistent lymphadenopathy.
For both topical Tacrolimus and Pimecrolimus:

Responsibilities of the secondary care clinician

- To discuss benefits and side effects of treatment with the patient and his/her patient/carer as appropriate and obtain informed consent
- To initiate treatment with topical tacrolimus/pimecrolimus
- To review initial treatment and ensure patient is responding to initial treatment
- To prescribe at least a month’s supply once a decision has been made to transfer to primary care
- To contact patient’s GP to request prescribing under shared care and send a link to or copy of the shared care protocol
- To advise the GP regarding continuation of treatment, including the length of treatment
- To inform the GP about any specific information regarding the patient

Responsibilities of the primary care clinician

- To refer appropriate patients to secondary care for assessment
- To agree to prescribe for patients in line with the shared care agreement
- To report any adverse reaction to the CHM and the referring consultant
- To inform the consultant if the patient discontinues treatment for any reason
- To seek the advice of the consultant if any concerns with the patient’s therapy
- To conduct an annual medication review

Financial implications

Cost of tacrolimus ointment exclusive of VAT (MIMS August 10)

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Cost of pimecrolimus cream exclusive of VAT (MIMS August 10)

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Support, education and information

Dermatology helpline number: (24-hour answering machine) 0114-2712018
On call specialist via RHH switchboard 0114-2711900

Stop topical pimecrolimus and contact the secondary care provider if:

- Hypersensitivity/ allergic reaction occurs
- Serious infection e.g. eczema herpeticum
- Erythroderma
- Persistent lymphadenopathy
- Malignancy suspected
References

- SPC (summary product characteristics) from eMC (Electronic Medicines Compendium) available at: [www.medicines.org.uk](http://www.medicines.org.uk) <<accessed 10/08/10>>
- Protopic Safety reminder letter from MHRA 8th Feb 2010 [link](#)

Clinicians are reminded that the prescriber is responsible for monitoring the patient on the medication prescribed.