



CALCINEURIN INHIBITORS

What are the aims of this leaflet?

This leaflet has been written to help you understand more about topical (applied to the skin) calcineurin inhibitors. It tells you what they are, how they work, how they are used to treat skin conditions, and where you can find out more about them.

What are calcineurin inhibitors?

There are two types of topical calcineurin inhibitors called tacrolimus ointment (Protopic 0.03% and 0.1%) and pimecrolimus cream (Elidel). They are classified as immunomodulating agents. This means that they act on the immune system to reduce skin inflammation. Both tacrolimus and pimecrolimus block a chemical called calcineurin which activates inflammation in the skin and causes redness and itching of the skin.

What skin conditions are treated with calcineurin inhibitors?

Tacrolimus ointment and pimecrolimus cream are licensed in the UK for the treatment of atopic eczema (atopic dermatitis) in adults, and children over the age of 2 years. Tacrolimus comes in two strengths; 0.03% (weaker) and 0.1% (stronger); the weaker preparation is licensed to be used in children between the ages of 2 and 16, and the stronger preparation in adults over the age of 16. Tacrolimus ointment is also licensed for the prevention of flares of atopic eczema in adults. These topical treatments can also be prescribed for a number of other inflammatory skin conditions such as [psoriasis](#) (particularly on the face), seborrhoeic eczema ([seborrhoeic dermatitis](#)), [lichen planus](#), [lichen sclerosus](#), [vitiligo](#), cutaneous lupus erythematosus and pityriasis alba but the calcineurin inhibitors are not officially licensed for these skin conditions.

Will calcineurin inhibitors cure my skin condition?

No, but they may control inflammation and help settle flares. You should expect to see some improvement within one week.

If you have eczema that is tending to flare frequently other treatments may be recommended. Your doctor or dermatologist will be able to discuss the options with you.

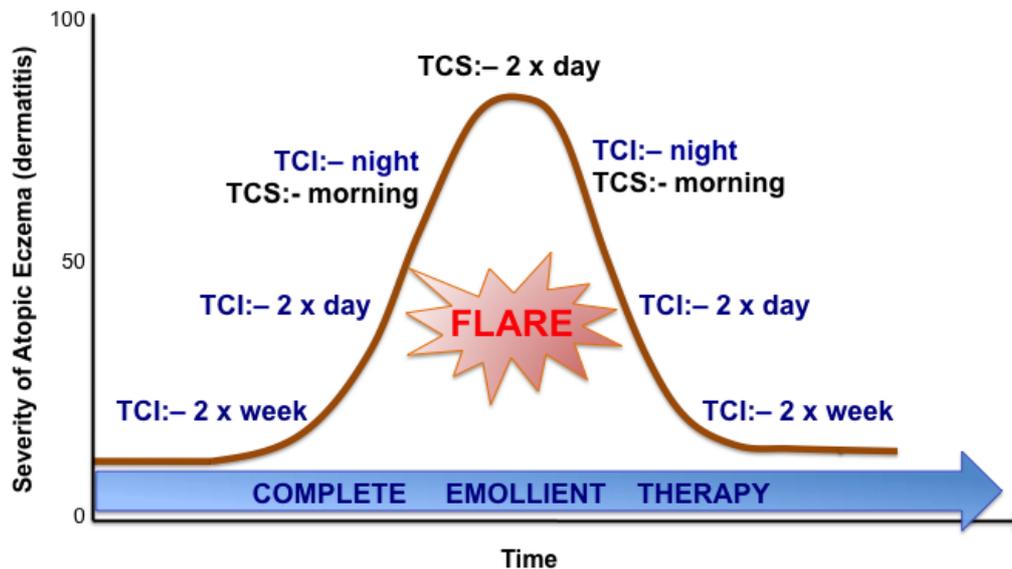
How often should I use calcineurin inhibitors?

Topical application is usually twice daily, but you should use calcineurin inhibitors as instructed by your doctor as it may be decided that you need a different regime depending on your clinical circumstances.

If preventative treatment is recommended you should apply the treatment twice weekly to help keep the skin clear. However, if the condition flares during this maintenance phase the treatment should be applied twice daily. Once the condition comes under control, twice weekly maintenance regime could be restarted. It may also be necessary to use a topical steroid cream to bring flares under control, before reverting to using the calcineurin inhibitor for maintenance. Your doctor will discuss the frequency of treatment with you. The requirement for maintenance treatment should be reviewed at least annually.

Topical corticosteroid and topical calcineurin inhibitor treatment can be combined with an emollient to produce optimal control of flares of atopic dermatitis (see diagram below). Tacrolimus ointment should not be applied to skin within two hours of the application of an emollient cream.

Combination therapy for preventing and treating flares of Atopic Eczema (Atopic Dermatitis)



The diagram illustrates the severity of Atopic Dermatitis (AD) against time. The peak is the most severe time of a flare of AD. When AD is most severe the ideal treatment is to use a topical corticosteroid (TCS) twice daily until the severity of the AD improves. The strength (potency) of the topical corticosteroid is determined by many factors including the body site and age of the patient.

As the flare improves a topical calcineurin inhibitor (TCI) can be used at one end of the day and topical corticosteroid at the other. As improvement continues the amount of topical corticosteroid can be reduced by using on alternate days. As the flare continues to improve the calcineurin inhibitor can be used twice per day. This can subsequently be reduced to once a day. Once there are no signs of any active atopic dermatitis, the use of the calcineurin inhibitor can be reduced to alternate days and eventually to twice per week. This has been shown to reduce the chance of a flare recurring in large clinical trials.

Some dermatologists may prefer to alternate between using the calcineurin inhibitor and topical steroid, switching between these two types of topical treatment if flares are not controlled and/or prevented by the calcineurin inhibitor alone.

What time of day should I apply calcineurin inhibitors?

If you are prescribed tacrolimus ointment or pimecrolimus cream once a day, you should apply it in the evening or at night; if twice daily, then morning and evening/night. If you have eczema or psoriasis you should ensure that you continue to use an emollient (moisturisers) whilst you are using the calcineurin inhibitor.

How much topical calcineurin inhibitor should be applied?

In order to determine the amount of treatment to be applied it is recommended that an adult fingertip unit length (the length of ointment squeezed out of a tube that reaches from the crease overlying the joint at the end of the index finger to the end of the finger) should be applied to twice the area of a handprint (adult palm plus fingers). This amount is about 0.5 grams; therefore for an adult arm up to 3 grams may be needed if the whole arm is affected. Your doctor should give an estimate of the amount of treatment required on a daily basis.

When should I not apply calcineurin inhibitors?

Calcineurin inhibitors should not be applied if the affected area of your skin is infected e.g. if the skin has sore, weeping or crusted areas because it can cause infection to spread.

Clinical trials have demonstrated that neither tacrolimus nor pimecrolimus have any effect on the development of responses to vaccinations.

It is recommended that calcineurin inhibitors should **not** be used if you are pregnant, breastfeeding or have a weakened immune system.

Exposure of the skin to sunlight should be minimised and the use of ultraviolet light treatments or sun beds should be avoided. You should inform the prescribing doctor if you have had a previous skin cancer.

What are the common side effects of calcineurin inhibitors?

About 50% of patients develop some local skin irritation or a burning or itching sensation when these treatments are started, particularly with tacrolimus ointment. However, these side-effects are usually temporary and not a reason to discontinue the treatment because they usually settle within a week. It is important to persevere with treatment during this time. It is also possible to experience redness, tingling, or a feeling of warmth on the skin where the

treatment is applied. Occasionally folliculitis (inflamed or infected hair follicles) may occur. Irritation is much more likely to occur if tacrolimus is applied to an area of severe atopic eczema. As illustrated in the diagram, topical calcineurin inhibitors should not be used when the atopic dermatitis is at its most severe but can be gradually introduced as the severity reduces. It is a good idea to use a calcineurin inhibitor on a test area of active atopic dermatitis to see if any irritation occurs before applying it to larger areas.

There is a small increased risk of developing cold sores (herpes simplex infection) on the treated skin during the first few weeks of treatment.

Calcineurin inhibitors do not cause skin atrophy (thinning or stretch marks) or some of other side-effects associated with using strong topical steroids for a long period, such as fragility of the skin, telangiectasia (dilated blood vessels) or, if used on and around the eyelids, glaucoma (increased pressure within the eye). As a result, they can be particularly useful on the face and neck and in the flexures, particularly if the atopic eczema is very persistent at these sites.

What is known about the long-term effects of calcineurin inhibitors?

When a drug such as a calcineurin inhibitor is taken by mouth it can lead to adverse effects because it suppresses the immune system. One possible consequence of immune suppression is an increased risk of non-melanoma skin cancer and lymphoma. When calcineurin inhibitors are applied topically the amount that is absorbed into the body is very much less than occurs after taking the drug by mouth. The amount of topical calcineurin inhibitor absorbed is less than 0.1 % of the applied dose. As a result, calcineurin inhibitors applied topically do not cause significant suppression of the immune system. There is no evidence from large epidemiological studies that topical calcineurin inhibitors are associated with an increased risk of lymphoma or non-melanoma skin cancer.

Do calcineurin inhibitors affect fertility or pregnancy?

It is not known whether topical calcineurin inhibitors will harm an unborn baby. You should tell your dermatologist or GP if you are pregnant or plan to become pregnant whilst using tacrolimus or pimecrolimus.

Can I drink alcohol while using calcineurin inhibitors?

Yes, but you may find that your face may become red and flushed.

Where can I get more information about calcineurin inhibitors?

http://www.eczema.org/elidel_protopic.pdf

http://www.eczema.org/Factsheet_Pimecrolimus_Cream.pdf

http://www.eczema.org/Factsheet_Tacrolimus_Ointment.pdf

<http://www.nlm.nih.gov/medlineplus/druginfo/meds/a602020.html>

For details of source materials used please contact the Clinical Standards Unit (clinicalstandards@bad.org.uk).

This leaflet aims to provide accurate information about the subject and is a consensus of the views held by representatives of the British Association of Dermatologists; individual patient circumstances may differ, which might alter both the advice and course of therapy given to you by your doctor.

This leaflet has been assessed for readability by the British Association of Dermatologists' Patient Information Lay Review Panel

**BRITISH ASSOCIATION OF
DERMATOLOGISTS
PATIENT INFORMATION LEAFLET
PRODUCED AUGUST 2012
UPDATED JULY 2016
REVIEW DATE JULY 2019**

