

Topical calcineurin inhibitors factsheet

What are topical calcineurin inhibitors?

Topical calcineurin inhibitors are treatments that alter the immune system and have been developed for controlling eczema. There are two types available: **Tacrolimus ointment (Protopic®) for moderate to severe eczema** and **Pimecrolimus cream (Elidel®) for mild to moderate eczema**. They are sometimes referred to as 'TCIs'. 'Topical' means that it is applied to the skin. 'Calcineurin inhibitor' means that it works with the immune system by blocking one of the chemicals that can contribute to the flaring of atopic eczema. It is important to understand that TCIs are not a cure for atopic eczema – rather, they are a way of controlling flares.

When can TCIs be used?

The National Institute for Clinical Excellence (NICE) recommends that TCIs can be used for adults and children over the age of 2 who have not responded adequately to topical steroid treatments – i.e. they are an option if, in your prescribing doctor's opinion, topical steroids of the appropriate potency and properly applied have failed to work on your atopic eczema. TCIs are particularly suitable for delicate areas of skin (e.g. face, neck, eyelids, skin folds and genitals) where prolonged treatment with topical steroids may be inappropriate. Both **Tacrolimus** and **Pimecrolimus** can be used short-term to treat flares and also longer-term to prevent them.

TCIs are only available on prescription and can be prescribed by a GP.

How do they work?

Atopic eczema is a skin condition in which the body reacts to things in the environment. The immune system may be triggered by allergens such as house dust mite droppings, some foods and pollen, but often the eczema flares up with no obvious allergen being identified. In

atopic eczema, the immune system is overactive (particularly the T-cells) – hence the inflammation (redness and itch) in the skin. Calcineurin inhibitors can help to suppress this overactivity by acting on the T-cells to dampen down the immune system. This helps to reduce inflammation and makes the skin less itchy and red.

How are they used?

TCIs need to be applied thinly to the affected skin, twice a day. They should only be applied to areas of active eczema (where there is redness) and used until the skin is clear (when the redness has gone). They should not be applied to mucous membranes (the nose, mouth and internal genital areas).

A mild burning sensation may be experienced after the first few applications but this tends to settle down after a week.

Tacrolimus (Protopic®) comes in two strengths (0.1% is stronger and 0.03% is weaker). Adults normally start with the stronger 0.1% and apply it twice a day. Once the flare of eczema is better, the weaker 0.03% can be prescribed for application just twice a week (e.g. Monday and Thursday nights) to try to prevent (or lessen the number of) flares of eczema. Studies showed this to be effective over a 1-year period. Children normally use the weaker 0.03% ointment twice a day from the start of treatment for 3 weeks and then reduce to once a day until the atopic eczema is clear. However, if there is no improvement after 6 weeks, Tacrolimus should be stopped.

Pimecrolimus (Elidel®) should be applied twice daily at the first appearance of redness or itching or to treat established eczema. It should be used for as short a period as possible (i.e. until the eczema is under control). When prescribed for maintenance (i.e. in the long-term

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for the prevention of progression to flares), it should be applied just twice a week (e.g. Monday and Thursday nights). As with **Tacrolimus**, if there is no improvement after 6 weeks, **Pimecrolimus** cream should be stopped.

If in any doubt about the usage of either treatment, please discuss with your doctor, nurse or pharmacist.

Can TCIs be used alongside other treatments?

Yes, TCIs can be used alongside other treatments (on the advice and instruction of your healthcare professional) and always in addition to emollients (wash products and moisturisers). However, *there are some important rules to follow when using TCIs with emollients.*

Emollients are a very important part of atopic eczema treatment and need to be used every day. Apply liberally as often as possible to keep the skin smooth, supple and well moisturised. The recommendations from the manufacturer are that emollients should not be used within 2 hours of applying **Tacrolimus**. In practice, this means *you should use emollient bath/wash products and moisturisers and then leaving a 2-hour gap before **Tacrolimus** is applied.*

In the case of **Pimecrolimus**, apply to dry skin and leave a short gap before putting on your emollient.

TCIs and topical steroids should not be used at the same time on the same areas of the body. However, it is likely that your doctor will tell you to use TCIs alongside topical steroids on different parts of the body – for example, TCIs may be prescribed for unresponsive facial atopic eczema while you continue to use a topical steroid on your body.

As TCIs work by damping down the immune system, they could worsen skin infections by reducing the skin's natural resistance. For this reason, *TCIs should not be applied to skin that is infected either with bacteria (e.g. impetigo) or viruses (e.g. chickenpox, cold sores or warts).* In addition, *TCIs are not suitable for use under wet wraps.*

Oral antibiotics may be used alongside TCIs for infected atopic eczema.

Vaccinations

It is wise to avoid treatment with topical **Tacrolimus** for 3 weeks after vaccination. In the case of live vaccines, treatment with topical Tacrolimus is best avoided for 28 days before and after vaccinations, to avoid the additional theoretical possibility of an abnormal vaccine infection.

As far as **Pimecrolimus** is concerned, in patients with extensive disease, it is recommended to administer vaccinations during treatment-free intervals.

What else do I need to be aware of?

The main precaution for TCIs is *avoidance of excessive/strong sun exposure and ultraviolet light.* This is because when similar treatments are taken by mouth over very many years there is an increased risk of skin cancer occurring, although there is no evidence of this happening in any patients using TCIs. It is very important that you do not use sun beds or have any other exposure or treatment such as phototherapy with ultraviolet light. A sunscreen (at least factor 15) should be used to protect your skin. Direct sunlight, particularly in the hottest part of the day (11.00am to 3.00pm) should be avoided. This is general sun-care advice and children's sun exposure should always be limited anyway.

Do they work?

There have been a number of clinical trials using TCIs to treat atopic eczema.

Tacrolimus has been measured against a placebo (a dummy drug) and to 1% hydrocortisone (a weak topical steroid) and the results look very good in its favour. More recently, it has been measured against hydrocortisone butyrate, which is a potent topical steroid. The results of this study suggest that the stronger strength of **Tacrolimus** (0.1%) is as effective in treating atopic eczema as hydrocortisone butyrate. However, hydrocortisone butyrate was more effective than the 0.03% **Tacrolimus** in that study. It should be noted that even though **Tacrolimus** is often prescribed for those for whom conventional treatment has not worked, none of

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the trials to date have tested Tacrolimus with this particular group of people, so it is difficult to say how well it will work on them.

Pimecrolimus has been shown to work in people with mild to moderate atopic eczema when compared against placebo cream, both in terms of treating active eczema and in reducing the number of flare-ups. What is unclear is how **Pimecrolimus** compares with mild to moderate topical steroids.

What are the side effects?

Clinical trials involving TCIs have looked into potential side effects, and research is ongoing to assess the long-term side effects of this relatively new treatment.

The main short-term side effects identified are an irritating, burning and itching feeling on the skin where TCIs are applied – this is estimated to occur in half of all people using them. As a patient you should be prepared to put up with this for a day or two as these symptoms seem to disappear within a week of use.

Other side effects include some increased skin redness, a sensation of warmth on the area of application and ‘pins and needles’. A few people also experienced blocked skin pores (folliculitis), an increase in spots (acne) and viral skin infections such as cold sores and warts.

Although drinking alcohol is allowed, some people experience increased skin irritation and facial flushing during **Tacrolimus** treatment.

Tests have also been performed to see whether TCIs can pass into the bloodstream, and the risk of this happening to a significant degree appears to be very small. Tests conducted to see whether TCIs can cause the skin to become thinner show that this does not happen.

At present it is impossible to know what the long-term side effects of using TCIs for many years might be, as this treatment has only been available in the UK since 2002.

Can TCIs be used for other types of eczema?

At present TCIs have only been licensed to treat adults and children (over 2 years of age) with atopic eczema. However, if necessary, dermatologists may use their professional judgement and prescribe them to patients who fall outside of these categories.

Further information

As well as reading the patient information leaflet contained in the box with your treatment, you may wish to find out more by visiting the electronic Medicines Compendium (eMC) and the NICE websites.

The eMC is continually updated and contains information about all prescription medicines. If you search for **Tacrolimus** and **Pimecrolimus**, you will find a full summary of the product characteristics (SPC) and patient information leaflet (PIL). These documents are written and updated by the pharmaceutical companies, based on their research trials and product knowledge, and approved by the UK product licensing authority, the Medicines and Healthcare products Regulatory Agency (MHRA). The website address for the eMC is www.medicines.org.uk.

NICE is the independent organisation responsible for providing national guidance on the promotion of good health and the prevention and treatment of ill-health. The NICE guidance on topical calcineurin inhibitors can be accessed at

<http://guidance.nice.org.uk/TA82/Guidance>.

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