

Topical calcineurin inhibitors factsheet

What are topical calcineurin inhibitors?

Topical calcineurin inhibitors (TCIs) work by altering the immune system and have been developed for treating atopic eczema. There are two types available:

tacrolimus ointment (Protopic) for moderate to severe eczema and **pimecrolimus cream (Elidel) for mild to moderate eczema**. 'Topical' means applied to the skin. 'Calcineurin inhibitor' means that they work with the immune system by blocking one of the chemicals that can contribute to the flaring of atopic eczema. TCIs are used to treat atopic eczema in adults and children over 2 years of age who are not responding adequately to or who cannot tolerate conventional therapies such as topical steroids. They can be used for both treating and preventing flares.

When can TCIs be used?

The guidance of the National Institute for Health and Care Excellence (NICE) for atopic eczema recommends that TCIs are used for adults and children over the age of 2 as a 'second-line' option. TCIs are particularly suitable for delicate areas of skin, such as the face, neck, eyelids, skin folds and outer genital skin, 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, by prolonging flare-free intervals.

TCIs are only available on prescription and should be prescribed by a specialist, including GPs with a special interest in dermatology.

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 (red or darker patches, depending on the colour of your skin) 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 make the skin less itchy.

How are they used?

For flare treatment, TCIs need to be applied thinly to the areas of skin with eczema twice a day. Treatment should begin at the first sign of active inflamed eczema. In lighter skin, this will manifest as red and itchy skin. In darker skin, redness may not be apparent; the skin will have darker patches and be itchy. Treatment should be used until the eczema has cleared (when the red or darker patches have subsided). TCIs should not be applied to mucous membranes (that is, inside the nose or mouth, eyes, or moist genital skin). After initial treatment of up to 6 weeks, the TCI can be used as maintenance treatment.

Tacrolimus (Protopic) comes in two strengths: 0.1%, which is stronger, and 0.03%, which is weaker. Adults and young people (16 years and above) should start with the stronger 0.1% and apply it twice a day. After an initial treatment period of up to 6 weeks, 0.1% tacrolimus can continue to be prescribed for application just twice a week (for example, on Monday and Thursday nights) to try to prevent or lessen the number of eczema flares. Studies showed this to be effective over a 1-year period. If eczema flares recur, 0.1% tacrolimus can be restarted, but it is recommended to reduce to the 0.03% dose if flares are frequent. Children aged 2-15 years should 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.

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Generally, improvement is seen with **tacrolimus** within a week of starting treatment. If no sign of improvement is seen within 2 weeks, other treatment options should be considered.

Pimecrolimus (Elidel) should be applied twice daily at the first appearance of inflammation or itching, or to treat established eczema. It should be used for as short a period as possible (until the eczema is under control). When prescribed for maintenance (that is, in the long-term for the prevention of progression to flares), it should be applied just twice a week (for example, on Monday and Thursday nights). 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 it 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 (moisturisers and wash products). 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 them liberally and as often as possible to keep the skin smooth, supple and well-moisturised. The manufacturer of **tacrolimus** recommends that emollients should not be used within 2 hours of applying **tacrolimus**. In practice, this means *you should use emollient moisturisers and bath/wash products and then leave a 2-hour gap before applying tacrolimus.*

In the case of **pimecrolimus**, apply it 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 (for example, impetigo) or viruses (for example, 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.

What else do I need to be aware of?

You may experience a mild burning sensation after the first few applications of a TCI, but this tends to settle down within a week.

The main precaution for TCIs is *avoidance of excessive/strong sun exposure and ultraviolet light.* This is because TCIs can make you more sensitive to sunlight. Avoid exposing the skin to sunlight for long periods of time. Also avoid tanning beds and phototherapy treatment with ultraviolet light. A sunscreen (SPF 30-50) should be used to protect adults' and children's skin. Direct sunlight, particularly in the hottest part of the day (11.00am to 3.00pm), should be avoided and sun protective clothing (including sun hats) should be worn.

TCIs should not be used in people with atopic eczema who are susceptible to developing superficial (local) skin infections, including but not limited to: inflamed or infected hair follicles, cold sores, and generalised herpes simplex infections.

TCIs should not be used on mucous membranes (that is, inside the nose or mouth, eyes, or moist genital skin).

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 mild 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.

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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 people for whom conventional treatment has not worked, none of the trials to date have tested tacrolimus with this particular group of people, so it is difficult to say how well it will work for 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. These symptoms generally disappear within a week of use.

Other side effects include changes in skin colouration (skin becoming red or darker) on the area of application, a sensation of warmth on the area of application, and 'pins and needles'. A few people also experienced blocked skin pores (folliculitis) and viral skin infections such as cold sores and warts. In children, impetigo is more common in children using TCIs.

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

Tests have also been carried out to see whether TCIs can pass into the bloodstream. 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 longer-term side effects of using TCIs for many years might be. However, this treatment has been a prescribed topical eczema treatment in the UK for nearly 20 years, with a very good safety record.

Can TCIs be used for other types of eczema?

TCIs have only been licensed to treat adults and children (over 2 years of age) with atopic eczema. However, dermatologists can use their professional judgment and prescribe them to patients with other types of eczema, if they consider it appropriate to do so.

Further information

As well as reading the patient information leaflet that came in the box with your treatment, you may wish to find out more by visiting the electronic Medicines Compendium (eMC) and 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 research trials and product knowledge, and approved by the UK product licensing authority, the Medicines and Healthcare products Regulatory Agency (MHRA). The eMC's website is www.medicines.org.uk/emc.

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 found at www.nice.org.uk/guidance/TA82.

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