

## Topical calcineurin inhibitors factsheet

Topical calcineurin inhibitors (TCIs) are a type of medicine used to treat atopic eczema in adults and children. 'Topical' means that they are applied to the skin. 'Calcineurin inhibitor' means that they block calcineurin, a protein that contributes to the inflammation in atopic eczema. There are two types of TCI, Protopic ointment (tacrolimus) for treating moderate to severe eczema, and Elidel cream (pimecrolimus) for mild to moderate eczema. Protopic comes in two strengths, 0.1% and 0.03%. TCIs can be used for both treating and preventing flares. They may be prescribed as a treatment to use with topical steroids or as an alternative to topical steroids.

### How do they work?

The immune system of people with atopic eczema overreacts to certain irritants and allergens in the environment (for example, house dust mite droppings, mould and pollen). Calcineurin inhibitors work with the immune system by blocking a specific protein called calcineurin, which plays a role in the activation of immune cells, such as T-cells. T-cells are involved in various aspects of atopic eczema, including inflammation and itch. Calcineurin inhibitors act on T-cells to dampen down the immune response. This helps reduce inflammation and itch.

## Who are they for?

Protopic 0.1% is used to treat atopic eczema in adults and children aged 16 and older. The weaker version of Protopic, 0.03%, is used to treat atopic eczema in adults and children from the age of 2 years. Elidel is used to treat atopic eczema in anyone aged 3 months of age and older.

### How do I go about getting them?

TCIs are only available on prescription. They can be prescribed by any doctor who has experience in the diagnosis and treatment of atopic eczema, including GPs. You will usually need to have tried topical steroids first.

### Where are they used?

TCIs can be used on any area of affected skin, but are particularly suitable for delicate areas, such as the face, neck, eyelids, skin folds and outer genital skin, where

prolonged treatment with topical steroids may be inappropriate. Both Protopic and Elidel can be used for short periods to treat flares and also longer-term to prevent them.

### How are they used?

TCIs are usually applied twice a day for short periods to treat flares, or twice a week on non-consecutive days as maintenance treatment. When treating flares, TCIs can be used for up to 6 weeks, or until the eczema is under control. After 6 weeks or when the eczema is under control, twice weekly maintenance treatment can begin if needed. The purpose of maintenance treatment is to prevent flares.

TCIs should be applied thinly to the areas of skin affected by eczema. Quantities are measured using the fingertip unit (FTU). For more information about the FTU, please see our Topical steroids factsheet. TCIs should not be applied to mucous membranes (that is, inside the nose or mouth, eyes or on moist genital skin).

TCIs are sometimes used with topical steroids in a 'combination' treatment approach. In this approach, when a flare is at its worst, only topical steroids are used. As the flare improves, TCIs are added. Initially, TCIs are used once a day (e.g. in the evening) alongside topical steroids (e.g. in the morning). As improvement continues, topical steroids are reduced to every other day. When the eczema is well controlled, topical steroids are stopped and TCIs are used twice a day, then reduced to once a

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day. When the skin is clear, TCIs are used every other day and eventually just twice a week on non-consecutive days. In large clinical trials, this approach has been shown to reduce the chances of a flare recurring.

Some doctors might advise alternating between a TCI and a topical steroid if flares are not controlled and/or prevented by the TCI when used by itself.

It's important to use TCIs as your doctor has advised, as they might recommend a different regime to those described above to suit your specific circumstances.

Protopic ointment comes in two strengths: 0.1%, which is stronger, and 0.03%, which is weaker. Adults and children aged 16 years and older should start with Protopic 0.1%. After an initial twice-daily treatment period of up to 6 weeks, Protopic 0.1% can continue to be used as maintenance treatment twice weekly (for example, on Monday and Thursday nights) to prevent or reduce the number of eczema flares. Studies have shown this to be effective over a 1-year period. If eczema flares recur, Protopic 0.1% can be restarted, but it's 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 skin is clear. When the skin is clear, maintenance treatment can begin (as above).

Generally, you should see an improvement with Protopic within a week of starting treatment. If there is no sign of improvement after 2 weeks, other treatment options should be explored.

Elidel cream can be prescribed from 3 months of age. Elidel should be applied twice daily at the first appearance of inflammation or itching, or to treat established eczema. It should be used this way for as short a time as possible, until the eczema is under control. If there's no improvement after 6 weeks, Elidel should be stopped. When prescribed for maintenance, it should be applied twice a week on non-consecutive days (for example, on Monday and Thursday nights).

If in any doubt as to how to use 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. TCIs should always be used in conjunction with emollients (leave-on moisturisers and wash products). Emollients are a very important part of eczema management and need to be used every day. Apply them liberally and as often as needed to keep the skin well-moisturised.

There are some important rules to follow when using TCIs with emollients. The manufacturer of Protopic recommends that emollients should not be used within 2 hours of applying Protopic. This means you should use leave-on emollients and bath/wash products and then leave a 2-hour gap before applying Protopic.

In the case of Elidel, 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, your doctor may advise you to use a TCI at the same time as a topical steroid on different parts of the body. For example, a TCI may be prescribed for unresponsive facial eczema, and a topical steroid for your arms. Or you might be advised to use TCIs and topical steroids in a 'combination' treatment approach, or to alternate between them, as described above.

As TCIs work by damping down the immune system, they can 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 to treat infected eczema.

# Can I use them while pregnant or breastfeeding?

It's recommended not to use TCIs if you're pregnant or breastfeeding, unless you've been advised to do so by a dermatologist.

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### What are the risks of TCIs?

A common side effect of TCIs is a burning or stinging sensation experienced when they're first applied, which lasts for about 15-20 minutes. This is a side effect, not an allergic reaction, and usually settles down within the first week of use.

The main precaution for TCIs is to protect the skin from the sun, as they can make the skin more sensitive to sunlight. Avoid prolonged sun exposure, sunbeds or phototherapy. Use SPF 30-50 sunscreen, avoid direct sunlight from 11:00am to 3:00pm and wear sunprotective clothing such as long sleeves and a sunhat.

TCIs should not be used in people 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.

Although drinking alcohol at safe levels (14 units per week) is fine to do when using TCls, some people experience increased skin irritation and facial flushing if they drink alcohol while using Protopic.

Tests have 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 doesn't happen. TCIs have been a prescribed eczema treatment in the UK for over 20 years and have a good safety record.

When TCIs started being prescribed more than 20 years ago, they had a 'black triangle' warning (meaning they were more closely monitored), as there were reviews suggesting a theoretical cancer risk. However, more recently, a huge systematic review looked at 3.4 million people with eczema worldwide who are treated with TCIs. This research study provided clear evidence that there is no increased risk of cancer, for infants, children or adults.

# Can TCIs be used to treat other types of eczema?

TCIs have only been licensed to treat adults and children 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.

## Can I have vaccinations while using TCIs?

Yes. Clinical trials have shown that neither Protopic nor Elidel affect responses to vaccinations.

#### DISCLAIMER

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