



BlueCross BlueShield  
of Alabama

## Atopic Dermatitis (Elidel<sup>®</sup>, Eucrisa<sup>™</sup>, Protopic<sup>®</sup>, tacrolimus ointment) Step Therapy Program Summary

This step therapy and quantity limit criteria applies to Commercial, SourceRx and Health Insurance Marketplace.

### OBJECTIVE

The intent of the Atopic Dermatitis Step Therapy program is to encourage the use of topical corticosteroid or topical corticosteroid combination preparations prior to, or concurrent with target agents. The program allows use of target agents when the patient has had a trial, documented intolerance, FDA labeled contraindication, or hypersensitivity to a topical corticosteroid or topical corticosteroid combination preparation, or when the requested agent is for use on the face, neck or skin folds. Requests for target agents will be reviewed when patient-specific documentation has been provided.

### TARGET AGENTS

**Elidel<sup>®</sup>** (pimecrolimus cream)

**Eucrisa<sup>™</sup>** (crisaborole ointment)

**Protopic<sup>®</sup>** (tacrolimus ointment)<sup>a</sup>

<sup>a</sup> generic available, targeted in program

### PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

**Target Agents** will be approved when ONE of the following is met:

1. The patient is requesting the requested agent for use on the face (including eyelids), neck, or skin folds (e.g. groin, armpit/under arm)

**OR**

2. The patient's medication history includes use of any topical corticosteroid or topical corticosteroid combination preparation in the past 120 days

**OR**

3. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to topical corticosteroids or topical corticosteroid combination preparations

**Length of approval:** 12 months

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## FDA APPROVED INDICATIONS AND DOSAGE<sup>1,2,10</sup>

Available Products	Indication	Dosage and Administration
<b>Elidel</b> (pimecrolimus Cream 1%)	Second-line therapy for the short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis (AD) in nonimmunocompromised adults and children 2 years of age and older, who have failed to respond adequately to other topical prescription treatments, or when those treatments are not advisable.	Apply a thin layer (minimum amount to control signs and symptoms of AD) to affected skin twice daily.
<b>Eucrisa</b> (crisaborole ointment 2%)	Topical treatment of mild to moderate atopic dermatitis in patients 2 years of age and older.	Apply a thin layer twice daily to affected areas
<b>Protopic<sup>a</sup></b> (tacrolimus Ointment 0.03%, 0.1%)	Second-line therapy for short-term and non-continuous chronic moderate to severe AD in nonimmunocompromised adults and children who have failed to respond adequately to other topical prescription treatments for AD, or when those treatments are not advisable. (0.03% and 0.1% for adults; 0.03% only for children ages 2-15).	Apply a thin layer (minimum amount to control signs and symptoms of AD) to affected skin twice daily.

AD=atopic dermatitis

<sup>a</sup> generic available

## CLINICAL RATIONALE

### Atopic Dermatitis

Management of atopic dermatitis [AD] (also known as atopic eczema) consists of relieving symptoms and lengthening time between flare-ups. Regular, liberal use of emollients is recommended. The primary pharmacologic treatment is topical corticosteroids. The principal complication of prolonged application of topical corticosteroids, especially those of higher potency, is skin atrophy. Other local complications include telangiectasia, striae, hypopigmentation, and acne.<sup>4,11,12</sup>

Topical calcineurin inhibitors (TCI); e.g. topical pimecrolimus, topical tacrolimus; are recommended for use as second line agents in AD in certain situations:<sup>4,6,8,11,12</sup>

- Individuals at risk of atrophy from topical corticosteroids
- Reduce the long-term use of topical corticosteroids
- For use on areas of thinner skin such as on the face, neck, anogenital region, and skin folds
- For use in AD which is recalcitrant to topical corticosteroids

A meta-analysis (2016; 12 RCTs) compared calcineurin inhibitors (n = 3492) vs. corticosteroids (n = 3462) in treatment of atopic dermatitis. Calcineurin inhibitors and corticosteroids had similar rates of improvement of dermatitis (81% vs. 71%; p = 0.01)

and treatment success (72% vs. 68%;  $p = 0.04$ ). Calcineurin inhibitors were associated with higher costs and had more adverse events (74% vs. 64%;  $p = 0.02$ ) including a higher rate of skin burning (30% vs. 9%;  $p < 0.00001$ ) and pruritus (12% vs. 8%;  $p < 0.00001$ ). There were no differences in atrophy, skin infections, or adverse events that were serious or required discontinuation of therapy.<sup>9</sup>

Crisaborole 2% ointment appears modestly effective for short-term treatment of mild to moderate atopic dermatitis. How it compares in efficacy to topical corticosteroids or calcineurin inhibitors remains to be established.<sup>11,12</sup>

### **Psoriasis (off-label use)**

The American Academy of Dermatology Guidelines (2009-2011) state that although corticosteroids remain the mainstay of topical therapy for psoriasis, the most potent and efficacious of these agents are approved for only short term treatment (2-4 weeks). Consideration should be given to use of medications that have been developed to either replace potent topical corticosteroids in longer term treatment, or to be used in combination to provide greater efficacy with lesser exposure to steroid containing agents. Pursuit of these goals with agents including vitamin D analogues, topical retinoids, and TCIs has shown benefit.<sup>5</sup> Although tacrolimus and pimecrolimus [off-label] have not been found beneficial for plaque psoriasis, these agents have shown some benefit for intertriginous and facial psoriasis.<sup>3,5</sup>

A review (2013) on treatment of psoriasis suggests tacrolimus and pimecrolimus generally improve symptoms with less skin atrophy than topical corticosteroids, and are considered first-line treatments for facial and flexural psoriasis. Tacrolimus is superior to pimecrolimus in reducing psoriasis symptoms.<sup>7</sup>

For additional clinical information see the Prime Therapeutics Formulary Chapter 14.5Y: Topical Immunomodulators.

### **Safety**

Elidel is contraindicated in individuals with a history of hypersensitivity to pimecrolimus or any of the components of the cream. Elidel also carries the following black box warning:<sup>1</sup>

- Long-term safety of topical calcineurin inhibitors has not been established
- Although a causal relationship has not been established, rare cases of malignancy (e.g., skin and lymphoma) have been reported in patients treated with topical calcineurin inhibitors, including Elidel Cream, 1%. Therefore:
  - Continuous long-term use of topical calcineurin inhibitors, including Elidel Cream, 1%, in any age group should be avoided, and application limited to areas of involvement with atopic dermatitis
  - Elidel Cream, 1% is not indicated for use in children less than 2 years of age

Eucrisa is contraindicated in individuals with known hypersensitivity to crisaborole or any component of the formulation.<sup>10</sup>

Protopic is contraindicated in patients with a history of hypersensitivity to tacrolimus or any other component of the ointment. Protopic also carries the following black box warning:<sup>2</sup>

- Long-term safety of topical calcineurin inhibitors has not been established
- Although a causal relationship has not been established, rare cases of malignancy (e.g., skin and lymphoma) have been reported in patients treated with topical calcineurin inhibitors, including Protopic Ointment. Therefore:

- Continuous long-term use of topical calcineurin inhibitors, including Protopic Ointment, in any age group should be avoided, and application limited to areas of involvement with atopic dermatitis.
- Protopic Ointment is not indicated for use in children less than 2 years of age. Only 0.03% Protopic Ointment is indicated for use in children 2-15 years of age.

## References

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6. Krakowski A, Eichenfield L, Dohil M. Management of atopic dermatitis in the pediatric population. Pediatrics. 2008;122:812-824.
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9. Journal of the American Academy of Dermatology. 2016;75(2):410-419.e3.
10. Eucrisa prescribing information. Anacor Pharms Inc. December 2016.
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12. Up to Date: Treatment of atopic dermatitis (eczema). Current through: Jan 2017. Updated: Feb 2017. Accessed 2/15/2017

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