Atopic Dermatitis
(Elidel, Eucrisa, Protopic, tacrolimus ointment)
Step Therapy Program Summary

This program applies to FlexRx Open, FlexRx Closed, GenRx Open, GenRx Closed, Health Insurance Marketplace, and KeyRx.

This is a FlexRx standard and GenRx standard step therapy program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

Program specific denial language for prerequisite step therapy component does not apply. Instead, supplemental program denial language will apply.

FDA APPROVED INDICATIONS AND DOSAGE1,2,8

<table>
<thead>
<tr>
<th>Available Products</th>
<th>Indication</th>
<th>Dosage and Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Elidel®</strong> (pimecrolimus Cream 1%)a</td>
<td>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.</td>
<td>Apply a thin layer (minimum amount to control signs and symptoms of AD) to affected skin twice daily.</td>
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<tr>
<td><strong>Eucrisa™</strong> (crisaborole ointment 2%)</td>
<td>Topical treatment of mild to moderate atopic dermatitis in patients 2 years of age and older.</td>
<td>Apply a thin layer twice daily to affected areas</td>
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<tr>
<td><strong>Protopic®</strong> (tacrolimus Ointment 0.03%, 0.1%)a</td>
<td>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).</td>
<td>Apply a thin layer (minimum amount to control signs and symptoms of AD) to affected skin twice daily.</td>
</tr>
</tbody>
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AD=atopic dermatitis
a 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.4

Topical calcineurin inhibitors (TCI); e.g. topical pimecrolimus, topical tacrolimus; are recommended for use as second line agents in AD in certain situations:

- 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 corticosteroids6

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<0.0001). There were no differences in atrophy, skin infections, or adverse events that were serious or required discontinuation of therapy.7

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.9

**Psoriasis**

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.5 Although tacrolimus and pimecrolimus have not been found beneficial for plaque psoriasis, these agents have shown some benefit for intertriginous and facial psoriasis.3

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.5

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:1

- 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.⁸

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:²

- 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
Atopic Dermatitis (Elidel, Euceris, Protopic, tacrolimus ointment)
Step Therapy

TARGET AGENTS
- **Elidel®** (pimecrolimus cream)\(^a\)
- **Euceris™** (crisaborole ointment)
- **Protopic®** (tacrolimus ointment)\(^a\)
  - \(^a\) generic available, targeted in program

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
**Target Agents** will be approved when ONE of the following is met:
1. The requested agent is 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
**Step Therapy Supplement**

This program applies to FlexRx Closed, FlexRx Open, GenRx Closed, GenRx Open, Health Insurance Marketplace, FocusRx and KeyRx formularies.

Please note, this does not include or apply to quantity limit questions.

**STEP THERAPY SUPPLEMENT**

**OBJECTIVE**
The intent of the Step Therapy Supplement is to provide additional questions, to ensure compliance to MN Statute 62Q.184. These questions will apply if the step therapy component within a Prior Authorization or Step Therapy program is not able to be approved.

**CONDITIONS FOR APPROVAL**
The requested agent will be approved when ONE of the following are met:

1. The patient is currently being treated with the requested agent as indicated by ALL of the following:
   a. A statement by the prescriber that the patient is currently taking the requested agent  
      AND
   b. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent  
      AND
   c. The prescriber states that a change in therapy is expected to be ineffective or cause harm

   **OR**

2. The patient's medication history include the required prerequisite/preferred agent(s) as indicated by:
   a. Evidence of a paid claim(s) within the past 999 days  
      **OR**
   b. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days AND the required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event

   **OR**

3. The prescriber has provided documentation that the required prerequisite/preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

**Length of Approval:** As per program specific criteria