Topical Immunomodulator Step Therapy Program

Policy Number: 5.01.557
Last Review: 7/2018
Origination: 7/2013
Next Review: 7/2019

Policy

Blue Cross and Blue Shield of Kansas City (Blue KC) BCBSKC will provide coverage for topical immunomodulators when the following criteria are met.

The topical immunomodulators affected are:
- Elidel® (pimecrolimus cream)
- Protopic® (tacrolimus ointment)
- Generic tacrolimus ointment

When Policy Topic is covered

This step therapy program has been developed to encourage the use of a topical corticosteroid (brand or generic) prior to pimecrolimus cream or tacrolimus ointment. If the step therapy rule is not met, coverage will be determined by prior authorization criteria.

Automation: This program uses one topical steroid (brand or generic) in the previous 130 days as a surrogate marker.

Step 1: topical corticosteroids (brand or generic)
Step 2: tacrolimus ointment, Protopic, Elidel

Criteria

1. If the patient has tried one prescription topical corticosteroid (brand or generic), then authorization for a Step 2 agent may be given.

2. Authorization for a Step 2 agent may be given if the patient has a dermatologic condition on or around the face, eyes/eyelids, axilla, or genitalia

Topical corticosteroids may cause skin atrophy. The risk for this adverse event increases when these agents are used on thinner skin, in areas such as the face or skin folds.5 Topical immunomodulators have not been found to cause skin atrophy.1,5 The 2014 American Academy of Dermatology (AAD) Guidelines of Care for the Management of AD indicate that topical immunomodulators are effective for acute and chronic AD treatment, especially in patients with AD in sensitive areas (e.g., face, genitalia, skin folds), steroid-refractory AD, steroid-induced atrophy, or a history of long-term uninterrupted topical steroid use.

3. Authorization for a Step 2 agent may be given if the patient has steroid-induced rosacea.

Preliminary reports indicate 7 to 10 days of therapy with topical tacrolimus (extemporaneously compounded) is effective for steroid-induced rosacea when combined with avoidance of all other topical therapy including topical corticosteroids.10-11 In one small (n = 18), investigator-blind, split-face study, topical pimecrolimus (formulation not specified) was effective in treating steroid-induced rosacea.12 In
another small (n = 35), open-label study, topical pimecrolimus (formulation not specified) was effective in treating steroid-induced rosacea. The American Acne & Rosacea Society (AARS) consensus guidelines on the management of rosacea (2014) state that both tacrolimus ointment and Elidel cream have been used in the treatment of patients with steroid-induced rosacea. When used in combination with steroid discontinuation, these agents have been observed to reduce erythema and other rosacea symptoms.

4. No other exceptions are recommended.

When Policy Topic is not covered
The use of topical immunomodulators is considered investigational for all other indications.

Considerations
Topical immunomodulators require prior authorization through the Clinical Pharmacy Department.

This Blue Cross and Blue Shield of Kansas City policy Statement was developed using available resources such as, but not limited to: Food and Drug Administration (FDA) approvals, Facts and Comparisons, National specialty guidelines, Local medical policies of other health plans, Medicare (CMS), Local providers

Description of Procedure or Service
Atopic Dermatitis (AD)
AD is a genetically transmitted, chronic inflammatory skin disease that affects 10% to 20% of children and 1% to 3% of adults. Pruritis, scratching, and chronic and/or relapsing eczematous lesions are major hallmarks of the disease. In infants and young children, there is a characteristic pattern of involvement of the face, neck, and extensor skin surfaces. In older children and adults, the skin lesions often involve lichenification and are usually localized to the flexural folds of the extremities. The diagnosis of AD is based on clinical presentation rather than results of diagnostic testing. The effective management of AD involves a combination of trigger avoidance, measures to restore skin barrier function (e.g., emollients), and anti-inflammatory medications (e.g., topical corticosteroids, Protopic, and Elidel).

Protopic and Elidel are topical calcineurin inhibitors (immunomodulators) indicated as second-line therapy for the short-term and non-continuous chronic treatment of AD in non-immunocompromised patients who have failed to respond adequately to other topical prescription treatments, or when those treatments are not advisable. Protopic is indicated for moderate to severe AD while Elidel is indicated for mild to moderate AD. Protopic 0.03% ointment and Elidel are indicated in adults and children aged ≥ 2 years. Although there are data documenting the Protopic 0.1% strength’s safety and efficacy in children, this product is not approved for use in pediatric patients. Neither Protopic nor Elidel are indicated for use in children < 2 years of age; however, both agents have been studied in this patient population.

Based on concerns of the potential carcinogenicity (skin cancer and lymphomas) that may be associated with using a topical immunomodulator continuously over a prolonged period of time, a Black Box Warning was added to Elidel and Protopic product labeling. There have been no empirical data to date definitively linking Elidel and Protopic to an increased cancer risk in humans and a causal relationship has not been established. A case-control study of nearly 300,000 patients with AD did not demonstrate an increased risk of lymphoma in patients who received therapy with a topical calcineurin inhibitor. There are data in three different animal species which demonstrated that the risk of cancer increased as the amount of drug given increased and that immunosuppressant use in transplant patients has led to an increase in cancer incidence. Data reviewed also included a small number of reports of cancers in children and adults. The Food and Drug Administration (FDA) Pediatric Advisory Committee expressed concern over the widespread off-label use of these agents as first-line treatment and in children ≤ 2 years of age. The FDA emphasized that these agents should be used
only as directed and as indicated and only after other eczema treatments have failed to work. The prescribing information for both products was updated to clarify that these drugs are recommended for use as second-line therapy for the short-term and non-continuous treatment in non-immunocompromised patients. Elidel and Protopic should be used for short periods of time and patients should use only the minimum amount necessary to control symptoms.

**Rationale**

According to the 2012 Joint Task Force (American Academy of Allergy, Asthma, and Immunology [AAAAI], the American College of Allergy, Asthma, and Immunology [ACAAI], and the Joint Council of Allergy, Asthma, and Immunology [JCAAI]) AD practice parameter, topical corticosteroids are appropriate for the vast majority of patients. The 2014 American Academy of Dermatology (AAD) Guidelines of Care for the Management of AD also indicate that topical steroids are the mainstay of therapy for AD in both adults and children. The intensity of management and treatment of AD is dictated by the severity of illness. Clinicians should use a multifaceted approach that includes skin hydration, topical anti-inflammatory medications, antipruritic therapy, antibacterial measures, and elimination of exacerbating factors. Moisturizers should be recommended as first-line therapy. If AD is not controlled by moisturizers alone, a topical corticosteroid should be used. Low-potency corticosteroids are recommended for maintenance therapy, while intermediate- and high-potency corticosteroids should be used for the treatment of exacerbation over short periods of time. Potent fluorinated corticosteroids should not be used on the face, eyelids, genitalia, and intertriginous areas or in young infants; a low-potency corticosteroid preparation is generally recommended for these areas. Ultrahigh-potency corticosteroids should only be used for very short periods (1 to 2 weeks) and in non-facial, non-skinfold areas.

The Joint Task Force guidelines note that Protopic should be considered for AD that is unresponsive to low-potency topical steroids. Protopic, unlike topical glucocorticoids, is not atrophogenic and has a greater therapeutic margin of safety than medium-strength corticosteroids for facial and eyelid eczema. Studies have demonstrated that Protopic 0.1% ointment has the strength of a mid-potency topical corticosteroid and should be considered first-line therapy for facial eczema where treatment with corticosteroids is limited to low-potency corticosteroids due to safety concerns. According to guidelines, Elidel decreases the number of AD flares, reduces the need for corticosteroids, does not cause skin atrophy, and controls pruritus. The AAD guidelines also confirm that the topical immunomodulators are effective for acute and chronic AD treatment, especially in patients with steroid-refractory AD, AD in sensitive areas (e.g., face, genitalia, skin folds), steroid-induced atrophy, and long-term uninterrupted topical steroid use. Furthermore, the AAD guidelines recommend intermittent use of a topical immunomodulator as maintenance therapy (two to three times per week) to help prevent relapses in areas that commonly flare. In this setting, the topical immunomodulators are more effective treatment than emollients alone and also reduce the need for topical corticosteroids.

**Off-Label Use**

There is widespread off-label use of the topical immunomodulators in several dermatologic conditions. In these conditions, topical immunomodulators are used when patients have failed standard therapy or in patients with contraindications to standard therapy agents. Data on the use of the topical immunomodulators are available in patients with lichen planus, cutaneous lupus erythematosus (CLE), psoriasis, and vitiligo, as well as numerous other rare dermatologic conditions. In these conditions, topical corticosteroids remain first line-therapy, with tacrolimus and Elidel utilized as second-line therapy when patients have failed primary treatment.

**References**


**Other References Utilized**

**Billing Coding/Physician Documentation Information**
Topical immunomodulators are considered a pharmacy benefit.

**Additional Policy Key Words**
Policy Number: 5.01.557

**Policy Implementation/Update Information**
- 08/2013 New Policy titled Topical Immunomodulator Step Therapy Program
- 08/2015 Annual Review- updated References; no changes in policy statement
- 12/2015 Added generic tacrolimus ointment
- 08/2016 Annual Review- updated References; no changes in policy statement
- 08/2017 Annual review- no changes to policy statement
- 08/2018 Annual review – no changes made

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