Wyoming Drug Utilization Review

Atopic Dermatitis Topical Treatments

Written by Cameron Campbell PharmD, 2024

Atopic dermatitis (AD), a type of eczema, is one of the most common inflammatory skin disorders, with rates increasing in developed and developing countries (1). Patients with AD typically present with exacerbations or "flare-ups" which are followed by remission periods. These flare-up periods can be very difficult to treat and create significant morbidity for patients and their families. AD mostly affects children, with about 85-90% of patients developing symptoms before the age of 5 and about 10-30% of these patients have symptoms continuing into adulthood. Patients can have mild, moderate, or severe AD, and classification is based on scoring tests which use a combination of subjective and objective measures (1).

Atopic dermatitis occurs from a dysfunction in the skin barrier with a corresponding inflammatory response (1). This leads to the hallmark symptoms of pruritus, erythema, xeroderma, and skin lesions, and can lead to secondary infections in these sites. Topical treatments are first line and either dampen the hyperinflammatory response or target xeroderma to prevent skin barrier breakdown (1). The first and most effective intervention is the use of moisturizers (2). Atopic skin is often very dry, and exacerbations can often be prevented with good skin care. One of the newer developments in this field is the recent approval of prescription emollient devices (PED). These topical agent are designed to mimic the composition of endogenous skin secretions (2). There is some evidence that PEDs may improve symptoms of AD compared to other moisturizers, but there have been very few studies showing this benefit. PEDs are currently considered another option to be used in this patient population but not necessarily recommended over any other moisturizer (2).

If moisturizers alone are not effective in preventing exacerbations, the most used next step is topical corticosteroids (TCS) (2). TCS are considered the standard of therapy for prophylaxis and treatment with over 60 years of evidence and are the most effective agent to combat pruritus. Although they have extensive evidence behind their use, there is a lack of evidence showing efficacy of one agent in this class over any others. Since there is not a preferred agent, disease severity, cost, area of body affected, and patient age all weight heavily into the selection of which agent to use (2). There are many different classes of TCS which range from very low potency to very high potency and are used in different methods to prevent flares or gain quick control of active flares (1). Disease state control may be possible with reactive therapies using TCS only during active flares for those with mild atopic dermatitis, however patients may require prophylactic therapies if they have more severe disease (2).

Potency Rating	Corticosteroid—Topical Preparations
Class 1: Super potent	Betamethasone dipropionate ointment
	Clobetasol propionate cream/gel/ointment
Class 2: Potent	Betamethasone dipropionate cream/gel
Class 3: Upper mid-strength	Fluticasone propionate ointment
Class 4: Mid-strength	Triamcinolone acetonide ointment
	Mometasone furoate cream, lotion, solution
Class 5: Lower mid-strength	Fluticasone propionate cream and lotion
Class 6: Mild (low potency)	Betamethasone valerate cream and ointment
	Desonide cream, ointment, gel
Class 7: Least Potent	Hydrocortisone cream, lotion, and ointment

WY-DUR
University of Wyoming
School of Pharmacy
Dept. 3375
1000 E. University Ave
Laramie, WY 82071
307-766-6750
www.uwyo.edu/DUR

Edited by
Aimee Lewis, PharmD, MBA
Karly Bentz

Another option for moisturizer resistant or TCS resistant AD are the topical calcineurin inhibitors (TCI). There are only 2 of these agents currently approved: Protopic (tacrolimus ointment) and Elidel (pimecrolimus cream). These agents inhibit calcineurin-dependent T-cell activation which play a large role in inflammatory mediated skin barrier dysfunction (1). TCIs are very efficacious and have been shown to decrease the extent and severity of symptoms and help prevent flare ups in adults and children (2). These agents may cause transient initial worsening of symptoms upon starting. To combat this, patients sometimes require an initial treatment with a TCS before starting a TCI. Tacrolimus is considered the more potent TCI and it is approved for moderate to severe disease whereas pimecrolimus is only approved for mild to moderate AD (2). There is some evidence that shows tacrolimus is more effective for all severities of AD, but due to its increased risk of adverse reactions, it is reserved for more severe disease states (2,3). One benefit of TCI therapy is that these agents do not have the risk of cutaneous atrophy that TCS have, as TCIs have no effect on collagen synthesis and skin thickness (2). Given the skin barrier dysfunction that is already occurring with AD, this is theoretically a major benefit for TCIs over TCS if being used long term.

Some of the newer agents that have been added to the guidelines are the PDE-4 inhibitors and JAK inhibitors (2). These agents are both "highly recommended" but the guidelines did not give either of these agents a specific place in therapy. Crisaborole (Eucrisa) is currently the only topical PDE-4 inhibitor approved for AD. AD is characterized by overactive PDE activity, crisaborole inhibits this activity to work as anti-inflammatory agent and prevents the stimulation of inflammatory cells (1). It is highly recommended for mild to moderate AD with it showing a small but significant improvement in disease state (2,4,5). Topical ruxolitinib (Opzelura) is the only topical JAK inhibitor currently approved for use in AD. Ruxolitinib is strongly recommended for the treatment of flares and prophylactic therapy for those 12 year of age or older with mild to moderate AD (2). Treatment with ruxolitinib should not exceed 20% of total body surface area and a maximum of 60 g can be applied per week (2,6). These restrictions are in place to prevent systemic absorption and the corresponding black box warning of malignancies, infections, mortality, major cardiovascular events, and thrombosis (2).

There are several other topical agents that have been studied for use in AD but have not shown a benefit for use. There is some data to recommend the use of dilute bleach baths and/or intranasal mupirocin, but there is no data supporting the use of any pharmacological topical antimicrobials or antiseptics (2). Another medication that has been studied is topical antihistamines. Topical doxepin has shown a slight short-term decrease in pruritus but had no effect on disease state severity. Doxepin also showed significant signs of systemic absorption and subsequent sedation/systemic toxicities, particularly in children (2). Some patients who are looking for a more holistic approach previously have used coal tar. There are very few trials that have investigated the efficacy of coal tar, so its benefit is largely unknown. Munkvad (7) investigated coal tar's efficacy and found that it had a similar efficacy to 1% hydrocortisone cream. However, this study was only 4 weeks long and only 5 out of the 30 patients reported itching or soreness at baseline (7). Due to the lack of adequate data, there is no current recommendations for or against the use of coal tar (2).

Medication Class	Indications	Adverse Reactions	Dosing/Application frequency
Topical corticosteroids: multiple	Prophylaxis or treatment of AD for any age	Skin atrophy, acne, rosacea, telangiectasias, purpura, hypertrichosis, spontaneous scars, Potential for systemic side effects	Treatment: Twice a day (some data for once daily application with high potency steroids) Prophylaxis: One to two times weekly
Topical calcineurin inhibitors: tacrolimus, pimecrolimus	Prophylaxis or treatment of AD (tacrolimus 0.1% only in those 15 and older)	Burning/stinging sensation at application site, worsening of skin conditions, photosensitivity, infection risk (not to be used in those with active infections), BBW for potential cancer risk	Treatment: Twice daily Prophylaxis: Twice weekly
PDE-4 Inhibitor: crisaborole	Treatment of mild to moderate AD in patients >3 months old	Application site pain including burning and stinging, urticaria, allergic contact dermatitis (rare)	Twice daily until signs/symptoms resolve
JAK inhibitor: ruxolitinib	Treatment of AD in those 12 years or older	Serious infections, mortality, malignancies (lymphoma), major adverse cardiovascular events, thrombosis	Twice daily until signs/symptoms resolve (max 60 g per week not to exceed 20% BSA)

The Wyoming Medicaid PDL, updated October 10, 2023, includes all topical medication classes that are currently recommended for the treatment of AD (8). The PDL includes a wide range of low, moderate, and high potency corticosteroids which are first line agents. TCI can be used after trial and failure of a medium or high potency TCS for at least 21 days within the last 90 days. The preferred agents are tacrolimus and brand name Elidel. The step 3 agent is Eucrisa (crisaborole). To receive a step 3 agent, the patient must have inadequate response to a preferred step 2 agent for at least 21 days in the last 30 days. The last option are the JAK inhibitors. The preferred agent here is a systemic therapy, but topical Opzelura (ruxolitinib) is an option for a non preferred agent. For a patient to receive Opzelura they must meet the same criteria for the PDE-3 inhibitors and have a 56-day treatment failure of the preferred biologic Dupixent (8).

Topical therapies are first-line and standard of therapy for patients with atopic dermatitis. These agents have great evidence behind their use for treatment, prevention, and slowing of disease progression. There are several different medications and classes that can be used for the treatment of atopic dermatitis and if used correctly patients can experience less symptoms, longer remission periods, and improved quality of life.

References

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The P&T Committee met for its quarterly business meeting on August 8, 2024.

Highlights of this meeting include:

Change Healthcare experienced a cyber threat-related outage on February 21, 2024. The prior authorization system was stood up on July 16th. Any prior authorization that would have expired during the outage was extended for six months.

The State plans to permanently suspend patient cost sharing (copays) for all Medicaid outpatient drug prescriptions processed through the pharmacy system, effective July 1, 2024.

Rivfloza, Libservant, Filsuvez, Ohtuvayre and Zoryve were reviewed with no evidence of a difference in safety or efficacy versus the current products in their respective class. All were limited to indication and referred to the Department of Health for cost analysis and PDL placement.

Adzynma, Lenmeldy, and Beqvez were all limited to indication with prior authorization.

Kisunla was limited to indication with prior authorization. In addition, treatment duration will be limited to 18 months and the medication cannot be used with Leqembi.

All prior authorization criteria are open for public comment. Comments should be sent by email to alewis13@uwyo.eduby September 15, 2024.

The next P&T Committee meeting will be held November 14, 2024 in Cheyenne. An agenda will be posted approximately two weeks prior to the meeting.

Wyoming Drug Utilization Review
University of Wyoming
School of Pharmacy
Dept. 3375
1000 E. University Avenue
Laramie, WY 82071

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