STEP THERAPY POLICY

POLICY: Topical Doxepin

DATE REVIEWED: 05/13/2020

DRUGS AFFECTED:

- Generic doxepin cream 5% – Mylan/DPT Laboratories, LTD, generics
- Prudoxin™ (doxepin hydrochloride cream 5% – Mylan/DPT Laboratories, LTD, generics)
- Zonalon® (doxepin hydrochloride cream 5% – Mylan/DPT Laboratories, LTD, generics)

OVERVIEW

Topical doxepin cream 5% (Prudoxin™, Zonalon®, generics) is indicated for the short-term (up to 8 days) management of moderate pruritus in adult patients with atopic dermatitis or lichen simplex chronicus.[1-3] Doxepin has H_1 and H_2 histamine receptor blocking actions, but the exact mechanism by which it exerts its antipruritic effect is unknown. Doxepin can produce drowsiness which may reduce awareness, including awareness of pruritic symptoms. Drowsiness occurs in more than 20% of patients treated with doxepin cream, especially in patients applying the cream to > 10% of their body surface area (BSA). If excessive drowsiness occurs, it may be necessary to reduce the frequency of applications, the amount of cream applied, and/or percentage of BSA treated, or discontinue the drug. Patients are instructed to apply a thin layer of doxepin cream 4 times a day, with at least a 3 or 4 hour interval between applications. There are no data to establish the safety and effectiveness of doxepin cream when used for > 8 days. Furthermore, chronic use (beyond 8 days) may result in higher systemic levels and increased likelihood of contact sensitization. Occlusive dressings should not be used with doxepin cream.

Atopic dermatitis is a chronic, pruritic, inflammatory dermatosis that is more common in children than adults; up to 25% of children and up to 3% of adults are afflicted.[4] The pathogenesis of atopic dermatitis is complex, involving genetic, immunologic, and environmental factors that lead to a dysfunctional skin barrier and dysregulation of the immune system. The hallmark of atopic dermatitis is pruritus; other symptoms include erythema, edema, xerosis, erosions/excoriations, oozing and crusting, and lichenification. Atopic dermatitis follows a relapsing course.

Lichen simplex chronicus (LSC) is not a primary process; it is a thickening of the skin with variable scaling that arises secondary to repetitive scratching or rubbing (e.g., scratching an itchy area of the skin and causing mechanical trauma to the point of lichenification).[5] The prevalence of LSC is unknown; it occurs mostly in mid-to-late adulthood, with the highest prevalence in persons 30 to 50 years of age. Treatment is aimed at reducing pruritus and minimizing existing lesions because continuous rubbing and scratching causes LSC. The location, lesion morphology and extent of the lesions influence treatment. For example, a high potency topical corticosteroid or intralesional corticosteroids may be needed for a thick psoriasiform plaque of LSC on a limb, whereas vulvar lesions are more commonly treated with a mild topical corticosteroid or a topical calcineurin inhibitor. Systemic therapy or total body phototherapy may be necessary for widespread lesions. Topical corticosteroids are the current treatment of choice because they decrease inflammation and itch while concurrently softening the hyperkeratosis. Alternatives to topical corticosteroids include topical doxepin.

Guidelines

The American Academy of Dermatology published guidelines for the management and treatment of atopic dermatitis with topical therapies in 2014.[6] Topical agents are the mainstay of atopic dermatitis therapy; they are used alone or in conjunction with systemic or phototherapy in severe cases. Topical agents from different drug classes are frequently used in combination, in part because they address different aspects of atopic dermatitis pathogenesis. Moisturizers, often used for treatment of mild disease, are an important component of maintenance treatment. Topical corticosteroids are the mainstay of anti-inflammatory therapy for atopic dermatitis (see Table 1 for examples). Topical corticosteroids have been shown to decrease acute and chronic signs of atopic dermatitis and are used for active disease and for prevention of relapses. Comparative trials are limited in duration and scope and as a result, there are no data to show improved efficacy of one corticosteroid product over another. Selection of a topical corticosteroid is usually based on patient vehicle preference (i.e., cream, gel, ointment, foam), cost, and availability. Other topical therapies used for atopic dermatitis include topical calcineurin inhibitors (topical tacrolimus ointment [0.03% and 0.1% strengths] and topical pimecrolimus cream (1% strength), topical antimicrobials, topical antiseptics, and topical coal tar derivatives. Use of topical doxepin has demonstrated a short-term reduction in pruritus in some cases, but with no significant reduction in disease severity or control. In addition, there are multiple reports of allergic contact dermatitis secondary to the use of topical doxepin and topical doxepin is associated with local stinging/burning and sedation.

Table 1. Topical Corticosteroids, Classified According to Potency* (Adapted from Facts/Comparisons).[7]

Potency/Group	Examples
Super-high potency (Group 1)	augmented betamethasone dipropionate 0.05% gel, lotion, ointment; clobetasol propionate 0.05% cream, cream (emoliient base), foam aerosol, gel, lotion, ointment, shampoo, solution (scalp), spray aerosol; fluocinonide 0.1% cream; flurandrenolide 4 mcg/cm^2 tape; halobetasol propionate 0.05% cream, lotion, ointment.
High potency (Group 2)	amcinonide 0.1% ointment; betamethasone dipropionate 0.05% cream (augmented), ointment; clobetasol propionate 0.025% cream; desoximetasone 0.25% cream, ointment, spray; desoximetasone 0.05% gel; diflorasone diacetate 0.05% cream (emollient), ointment; fluocinonide 0.05% cream, gel, ointment, solution; halcinonide 0.1% cream, ointment; halobetasol propionate 0.01% lotion.
High potency (Group 3)	amcinonide 0.1% cream, lotion; betamethasone dipropionate 0.05% cream (hydrophilic emollient); betamethasone valerate 0.1% ointment; betamethasone valerate 0.12% foam; desoximetasone 0.05% cream; diflorasone diacetate 0.05% cream; fluocinonide 0.05% cream (aqueous emollient); fluticasone propionate 0.005% ointment; mometasone furoate 0.1% ointment; triamcinolone acetonide 0.5% cream, ointment.
Medium potency (Group 4)	betamethasone propionate 0.05% spray; clocortolone pivalate 0.1% cream; fluocinolone acetonide 0.025% ointment; flurandrenolide 0.05% ointment; hydrocortisone valerate 0.2% ointment; mometasone furaoate 0.1% cream, lotion, ointment, solution; triamcinolone acetonide 0.1% cream, ointment; triamcinolone acetonide 0.05% ointment; triamcinolone acetonide 0.2 mg aerosol spray.
Lower-mid potency (Group 5)	betamethasone dipropionate 0.05% lotion; betamethasone valerate 0.1% cream; desonide 0.05% gel, ointment; fluocinolone acetonide 0.025% cream; fludrandrenolide 0.05% cream, lotion; fluticasone propionate 0.05% cream, lotion; hydrocortisone butyrate 0.1% cream, lotion, ointment, solution; hydrocortisone probutate 0.1% cream; hydrocortisone valerate 0.2% cream; prednicarbate 0.1% cream (emollient), ointment; triamcinolone acetonide 0.1% lotion; triamcinolone acetonide 0.025% ointment.
Low potency (Group 6)	aclometasone dipropionate 0.05% cream, ointment; betamethasone valerate 0.1% lotion; desonide 0.05% cream, foam, lotion; fluocinolone acetonide 0.01% cream, oil, shampoo, solution; triamcinolone acetonide 0.025% cream, lotion.
Least potent (Group 7)	hydrocortisone 2.5% cream, ointment, solution; hydrocortisone 2% lotion; hydrocortisone 1% cream, gel, lotion, ointment, solution, spray; hydrocortisone 0.5% cream, ointment; hydrocortisone acetate 2.5% cream; hydrocortisone acetate 2% lotion.

* This table may not include all available topical corticosteroids (strength or formulation).

POLICY STATEMENT

A step therapy program has been developed to encourage the use of a generic Step 1 product prior to the use of a Step 2 product. If the step therapy rule is not met for a Step 2 agent at the point of service, coverage will be determined by the step therapy criteria below. All approvals are provided for 2 weeks in duration.

Automation: Patients with a history of one Step 1 drug within the 130-day look-back period are excluded from step therapy.

Step 1: Generic prescription topical corticosteroids (see Table 1)

Step 2: Doxepin cream, Prudoxin cream, Zonalon cream

CRITERIA

1. If a patient has tried two Step 1 products, then authorization for a Step 2 product may be given.

2. No other exceptions are recommended.

REFERENCES

1. Doxepin hydrochloride cream, 5% [prescribing information]. San Antonio, TX: DPT Laboratories; May 2017
2. .Prudoxin™ (doxepin hydrochloride) cream, 5% [prescribing information]. San Antonio, TX: DPT Laboratories; June 2017; June 2017.
3. Zonalon® (doxepin hydrochloride cream, 5% [prescribing information]. San Antonio, TX: DPT Laboratories; June 2017
4. Eichenfield LF, Tom WL, Chamlin SL, et al. Guidelines of care for the management of atopic dermatitis: section 1. Diagnosis and assessment of atopic dermatitis. *J Am Acad Dermatol*. 2014;70(2):338-51.
5. Lichen simplex chronicus: https://emedicine.medscape.com/article/1123423-treatment?src=refgatesrc1. Updated February 15, 2019 . Accessed on May 2, 2019
6. Eichenfield LF, Tom WL, Berger TG, et al. Guidelines of care for the management of atopic dermatitis: section 2. Management and treatment of atopic dermatitis with topical therapies. *J Am Acad Dermatol*. 2014;71(1):116-132.
7. Facts and Comparisons® Online. Wolters Kluwer Health, Inc.; 2019. Available at: http://online.factsandcomparisons.com/login.aspx?url=/index.aspx&qs=. Accessed on May 8, 2020. Search terms: doxepin, corticosteroid.