STEP THERAPY CRITERIA

BRAND NAME*
(generic)

PRUDOXIN
(doxepin)

ZONALON
(doxepin)

Status: CVS Caremark Criteria
Type: Initial Step Therapy with Quantity Limit;
Post Step Therapy Prior Authorization with Quantity Limit ***Ref # 1496-E***

**Drugs that are listed in the target drug box include both brand and generic and all dosages forms and strengths unless otherwise stated*

FDA-APPROVED INDICATIONS
Prudoxin and Zonalon are indicated for the short-term (up to 8 days) management of moderate pruritus in adult patients with atopic dermatitis or lichen simplex chronicus.

INITIAL STEP THERAPY with QUANTITY LIMIT*
If the patient has filled a prescription for at least a 7 day supply of a generic topical corticosteroid **AND** at least a 7 day supply of topical tacrolimus (Protopic) or Elidel (pimecrolimus) or Eucrisa (crisaborole) within the past 120 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit.* If the patient does not meet the initial step therapy criteria, then the claim will reject with a message indicating that a prior authorization (PA) is required. The prior authorization criteria would then be applied to requests submitted for evaluation to the PA unit.

*If the patient meets the initial step therapy criteria, then the initial limit criteria will apply. If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating that a PA is required.

***INITIAL LIMIT CRITERIA**

Drug	**1 Month Limit* and 3 Month Limit***
Prudoxin (doxepin)	90 grams/25 days
Zonalon (doxepin)	90 grams/25 days

** This drug is indicated for short-term acute use; therefore, the 1 month, 3 month, retail, and mail limits will be the same.*
**The limit criteria apply to both brand and generic, if available.*

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for short-term (up to 8 days) management of moderate pruritus in an adult patient with atopic dermatitis or lichen simplex chronicus
- The patient has experienced an inadequate response to a topical corticosteroid or topical tacrolimus (Protopic) or pimecrolimus (Elidel) or crisaborole (Eucrisa)

Quantity limits apply.

RATIONALE

If the patient has filled a prescription for at least a 7 day supply of a generic topical corticosteroid AND at least a 7 day supply of topical tacrolimus (Protopic) or Elidel (pimecrolimus) or crisaborole (Eucrisa) within the past 120 days under a prescription benefit administered by CVS Caremark, then the requested drug will be paid under that prescription benefit. An initial quantity limit is set at 90 grams per month.

If the patient does not meet the initial step therapy criteria, then prior authorization (PA) is required. If the patient is requesting more than the initial quantity limit the claim will reject with a message indicating that a PA is required.

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Prudoxin and Zonalon cream are indicated for the short-term (up to 8 days) management of moderate pruritus in adult patients with atopic dermatitis or lichen simplex chronicus.

A thin film of Prudoxin and Zonalon cream should be applied four times each day with at least a 3 to 4 hour interval between applications. There are no data to establish the safety and effectiveness of Prudoxin and Zonalon cream when used for greater than 8 days. Chronic use beyond eight days may result in higher systemic levels and should be avoided. Use of Prudoxin and Zonalon cream for longer than 8 days may result in an increased likelihood of contact sensitization.

The Compendia state that topical corticosteroids provide relief of inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.[3,4] The American Academy of Dermatology (AAD) Guidelines of Care for the Management of Atopic Dermatitis states that studies investigating topical doxepin have demonstrated a short-term decrease in pruritus in some cases, but with no significant reduction in disease severity or control.[5] The AAD guideline recommends topical corticosteroids for atopic dermatitis affected individuals who have failed to respond to good skin care and regular use of emollients alone.[5] Topical calcineurin inhibitors are also recommended by the AAD guideline as effective for acute and chronic treatment in both adults and children with atopic dermatitis.[5] Eucrisa (crisaborole) is a topical phosphodiesterase-4 (PDE-4) inhibitor that is indicated for topical treatment of mild to moderate atopic dermatitis in patients 2 years of age and older.[8] Therefore, the initial step requirement will be trial of two treatment options, a topical corticosteroid AND a topical calcineurin inhibitor (tacrolimus, or pimecrolimus) OR a PDE-4 inhibitor (crisaborole). Topical tacrolimus and pimecrolimus are FDA-approved as second-line therapy for the short-term and non-continuous chronic treatment of atopic dermatitis in non-immunocompromised adults and children who have failed to respond adequately to other topical prescription treatments, or when those treatments are not advisable.[6,7] Crisaborole significantly reduced the signs and symptoms of atopic dermatitis in two phase III studies and demonstrates a reduce in risk of systemic side effects. The data show efficacy for crisaborole but did not compare directly to topical corticosteroids or topical calcineurin inhibitors. Therefore, the criteria for approval will be an inadequate response with a trial of ONE of the following medications: topical corticosteroid OR topical tacrolimus (Protopic) OR Elidel (pimecrolimus) OR Eucrisa (crisaborole).[9]

The risk for sedation may increase with greater body surface area application of doxepin 5% cream (Zonalon, Prudoxin). Patients with greater than 10% of body surface area affected should be particularly cautioned concerning possible drowsiness and other systemic adverse effects of doxepin. If excessive drowsiness occurs, it may be necessary to reduce the body surface area treated, reduce the number of applications per day, reduce the amount of cream applied, or discontinue the drug.

According to the AAD guidelines, no universal standard exists for quantity of application, although suggested methods include use of the adult fingertip unit (the amount from the distal interphalangeal joint to the fingertip, or approximately 0.5grams, being applied over an area equal to 2 adult palms), following the rule of 9's that measures the percent affected area, and use of charts that propose amounts based on patient age and body site.[5] Utilizing these methods 90 grams should be sufficient for application up to 10% of body surface area 4 times daily for 8 days, allowing for at least 2.5 grams per application. Post limit quantities for these drugs are set to the same quantity as the initial quantity limit. Doxepin 5% cream, Prudoxin, and Zonalon are available in 30gm and 45gm tubes.

REFERENCES

1. Prudoxin [package insert]. Newtown, PA: Prestium Pharma, Inc.; February 2015.

2. Zonalon [package insert]. Newtown, PA: Prestium Pharma, Inc.; October 2014.
3. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed June 2018.
4. Micromedex Solutions [database online]. Greenwood Village, CO: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed June 2018.
5. Eichenfield L, Tom W, Berger T, 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;71:116-32. Available at: https://www.aad.org/practice-tools/quality-care/clinical-guidelines/atopic-dermatitis/. Accessed June 2018.
6. Elidel [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; August 2014.
7. Protopic [package insert]. Parsippany, NJ: LEO Pharma. Inc.; June 2016.
8. Eucrisa [package insert]. New York, NY: Pfizer Inc.; October 2017.
9. Paller AS, Tom WL, et. al. Efficacy and safety of crisaborole ointment, a novel, nonsteroidal phosphodiesterase 4 (PDE4) inhibitor for the topical treatment of atopic dermatitis (AD) in children and adults. *J Am Acad Dermatol.* 2016 Jul 11; 75 (3) 494-503.e4

Written by:	UM Development (RP)
Date Written:	06/2016
Revised:	08/2016, (TM) 02/20017 (add generic & limit, change prereqs), (TM) 06/2017 (removed q3, revised q4), (SF) 06/2018 (added Eucrisa to pre-requisites)
Reviewed:	Medical Affairs (MC) 06/2016, 08/2016, (JG) 02/2017, (AN) 06/2017, 06/2018 External Review: 08/2016, 04/2017, 10/2017, 10/2018

CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for short-term (up to 8 days) management of moderate pruritus in an adult patient with atopic dermatitis or lichen simplex chronicus?	Yes	No
2	Has the patient experienced an inadequate response to any of the following: A) topical corticosteroid, B) topical tacrolimus (Protopic), C) Elidel (pimecrolimus), D) Eucrisa (crisaborole)?	Yes	No
3	Does the patient require more than the plan allowance of 90 grams? [RPh Note: If yes, then deny and enter a partial approval for 90 grams/25 days of doxepin 5% cream (Zonalon or Prudoxin).]	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Go to 2	Deny	You do not meet the requirements of your plan. Your plan covers this drug when it is prescribed for the following: - Short-term (up to 8 days) management of moderate pruritus in an adult patient with atopic dermatitis or lichen simplex chronicus Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you have tried any of the following and they did not work for you: - a topical corticosteroid - topical tacrolimus (Protopic) - Elidel (pimecrolimus) -Eucrisa (crisaborole) Your request has been denied based on the information we have.

			[Short Description: No inadequate response to prerequisite drug]
3.	Deny	Approve, 3 months, 90 grams/25 days*	You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 90 grams/month of the doxepin 5% cream (Zonalon or Prudoxin). You have been approved for the maximum quantity that your plan covers. Your request for additional quantities of the requested drug and strength has been denied. [Short description: Over max quantity]
** This drug is indicated for short-term acute use; therefore, the 1 month, 3 month, retail, and mail limits will be the same.* **The limit criteria apply to both brand and generic, if available.*			