CENTENE PHARMACY AND THERAPEUTICS
DRUG REVIEW
2Q17 April – May

BRAND NAME
Eucrisa™

GENERIC NAME
Crisaborole

MANUFACTURER
Anacor Pharmaceuticals, Inc.

DATE OF APPROVAL
12/14/2016

PRODUCT LAUNCH DATE
12/20/2016

REVIEW TYPE

☒ Review type 1 (RT1): New Drug Review
Full review of new chemical or biologic agents

☐ Review type 2 (RT2): New Indication Review
Abbreviated review of new dosage forms of existing agents that are approved for a new indication or use

☐ Review type 3 (RT3): Expedited CMS Protected Class Drug Review
Expedited abbreviated review of Centers for Medicare & Medicaid Services protected class drugs (anticonvulsants, antidepressants, antineoplastic, antipsychotics, antiretrovirals, and immunosuppressants)

FDA APPROVED INDICATION[1]
Eucrisa (crisaborole) is a phosphodiesterase 4 inhibitor indicated for topical treatment of mild to moderate atopic dermatitis in patients 2 years of age and older.

OFF-LABEL USES
None reported

CLINICAL EFFICACY

[2] Two identical multicenter, randomized, double-blind, vehicle-controlled phase III trials (AD-301 and AD-302) assessed the safety and efficacy crisaborole ointment in the treatment of mild

to moderate atopic dermatitis (AD). Patients were randomized in a 2:1 ratio to twice daily treatment with topical crisaborole 2% ointment or vehicle for 28 days. The trials included 1522 patients aged 2-79 years with mild to moderate AD as determined by the Investigator's Static Global Assessment (ISGA) score of 2 (mild – faint pink erythema with mild induration/papulation and no oozing/crusting) or 3 (moderate – pink-red erythema with moderate induration/papulation with or without oozing/crusting), and at least 5% body surface area (BSA) involvement.

Key exclusion criteria were use of topical corticosteroids or a topical calcineurin inhibitor within 14 days of study entry, significant active infection and any previous use of biologic therapy.

The primary efficacy endpoint for both studies was an ISGA score of 0 (clear) or 1 (almost clear) at day 29 with a 2 or more point improvement from baseline.

Secondary efficacy endpoints included the proportion of patients with an ISGA score of 0 or 1 (clear or almost clear) at day 29 with at least a 1 point improvement from baseline and time needed to achieve an ISGA score of 0 or 1. Additional pre-specified endpoints were self-(parent/caregiver) reported severity of pruritus and investigator-assessed severity of signs and symptoms of AD (erythema, exudation, excoriation, induration/papulation, lichenification). Severity of pruritus and AD symptoms were reported on a 0-3 scale (0=none, 1=mild, 2=moderate, 3=severe).

Significantly more patients in the crisaborole group met the primary endpoint of and ISGA score of 0 (clear) or 1 (almost clear) at day 29 with at least a 2 point improvement from baseline. See table below.

Study	AD-301		AD-302	
Treatment	Crisaborole 2% N = 503	Vehicle N = 256	Crisaborole 2% N = 513	Vehicle N = 250
Primary endpoint	32.8%	25.4%	31.4%	18.0%
	Difference 7.4% P = 0.038		Difference 13.4% P < 0.001	

No patients withdrew from the studies due to lack of efficacy.

CONTRAINDICATIONS
Eucrisa (crisaborole) is contraindicated in patients with known hypersensitivity to crisaborole or any component of the formulation.

BLACK BOX WARNINGS
Not applicable

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DRUG INTERACTIONS
There are no known drug interactions.

ADVERSE REACTIONS
The most common adverse reaction occurring in ≥ 1% of subjects in clinical trials was application site pain, including burning or stinging. Less common adverse reactions (<1%) included contact urticaria. If severe pruritus, swelling and erythema occur, hypersensitivity reaction should be suspected, crisaborole should be immediately discontinued and appropriate therapy initiated.

DOSAGE AND ADMINISTRATION
Apply a thin layer of Eucrisa twice daily to affected areas.
Eucrisa is for topical use only. It is not for ophthalmic, oral or intravaginal use.

PRODUCT AVAILABILITY
Ointment 2% (20 mg crisaborole per gram)

THERAPEUTIC ALTERNATIVES

DRUG NAME	USAGE REGIMEN (route of admin/ frequency of use)	COMMENTS
Low Potency Topical Corticosteroids		
Aclometasone dipropionate 0.05% (Aclovate®) cream, ointment **Desonide 0.05% (Desowen®) cream, ointment, lotion** **Fluocinolone acetonide 0.01% (Synalar®) solution** **Hydrocortisone 2.5% (Hytone®) cream, ointment**	Apply topically to the affected area(s) twice daily	Should not be used for longer than 2 consecutive weeks
Medium Potency Topical Corticosteroids		
Desoximetasone 0.05% (Topicort®) cream, ointment, gel **Fluocinolone acetonide 0.025% (Synalar) cream, ointment** **Mometasone furoate 0.1% (Elocon®) cream, ointment, lotion** **Triamcinolone acetonide 0.025% (Aristocort®) cream, ointment**	Apply topically to the affected area(s) twice daily	Should not be used for longer than 2 consecutive weeks
Topical Calcineurin Inhibitors		

Pimecrolimus (Elidel®) 1% cream	Apply a thin layer to affected area twice daily.	Limit use to affected areas. Discontinue when symptoms have cleared.
Tacrolimus (Protopic®) **0.03% or 0.1% ointment**	Apply a thin layer to affected area twice daily. Age 2-15 years, use 0.03% ointment only.	Limit use to affected areas. Discontinue when symptoms have cleared.

Boldface indicates generic availability

Utilization Management Recommendation
• There is not significant potential for inappropriate use.
Product Comparison
• CPAC score: 52 vs. pimecrolimus (Elidel) – Equal therapeutic outcomes anticipated. • Equal therapeutic outcomes are anticipated for crisaborole and pimecrolimus, therefore it would be appropriate to provide equal access to both or to require a trial of one before the other. • It would be clinically appropriate to require a trial of a low to medium potency topical corticosteroid prior to initiation of Eucrisa.

REFERENCES

[1] Eucrisa prescribing information. Anacor Pharmaceuticals, Inc. December 2016.

[2] Paller AS, Tom WL, Lebwohl MG, 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;75:3:494-503.