

FDA Approves Eucrisa (crisaborole) for Eczema

(Atopic dermatitis)

Atopic dermatitis (AD) is the most common of the many types of eczema, and onset typically begins in childhood and can last through adulthood. It is characterized by red, scaly and crusted bumps, which are extremely itchy. Scratching leads to swelling, cracking, “weeping” clear fluid, and finally, coarsening and thickening of the skin. The cause of AD is a combination of genetic, immune and environmental factors. ^[1]

In December 14, 2016 FDA approves Eucrisa (Crisaborole) for eczema. Crisaborole, applied topically twice daily, is a phosphodiesterase-4 (PDE-4) inhibitor, although its specific mechanism of action in AD is not well defined. However, overactive PDE-4 has been shown to contribute to the signs and symptoms of AD. ^[1]

The approval of crisaborole is based on a clinical development program, including the results of two large, identical, multicenter, randomized, double-blind, parallel-group, vehicle-controlled (nonmedicated ointment) trials (Trials 1 and 2) that treated 1,522 patients with mild to moderate AD between 2 and 79 years of age. In both trials, participants were randomly assigned 2:1 to receive crisaborole or a nonmedicated ointment applied to the skin with signs and symptoms of AD twice daily for 28 days. At baseline, 38.5% of the patients had an Investigator’s Static Global Assessment (ISGA) score of 2 (mild), and 61.5% had an ISGA score of 3 (moderate). The ISGA score includes erythema, induration/papulation and oozing/crusting on a severity scale of 0 to 4. ^[2]

The primary efficacy end point was success in ISGA at day 29, defined as the proportion of patients achieving an ISGA score of 0 (clear) or 1 (almost clear), with at least a 2-grade improvement from baseline. These data showed crisaborole to be an effective treatment that achieved statistically significant results versus vehicle for the primary efficacy end point in adults and children 2 years of age and older (32.8% vs. 25.4% [$P=0.038$] for Trial 1; 31.4% vs. 18.0% [$P<0.001$] for Trial 2). Efficacy results were seen in some patients as early as day 8 (first post-baseline assessment), with 13.4% of crisaborole patients achieving success in ISGA versus 4.5% with vehicle in Trial 1 and 15.9% of crisaborole

patients versus 6.3% with vehicle in Trial 2. Crisaborole-treated patients achieved improvement in pruritus earlier than vehicle-treated patients (pooled data, 1.37 vs 1.70 days, $P = .001$).^[2]

Treatment with crisaborole was well tolerated; with similar rates of adverse effects as vehicle. The majority of treatment-related adverse effects were application site pain, primarily reported as burning or stinging.^[2]

The results seen in these pivotal Phase III studies show the efficacy and safety of Eucrisa as a steroid-free treatment option for people as young as two living with mild to moderate atopic dermatitis.^[2]

In conclusion, crisaborole represents a promising new option for patients with mild to moderate AD based on the favorable safety profile and improvement in AD seen in these studies. Future studies could apply alternative AD severity grading scales that may provide additional efficacy information by anatomic region to further our understanding and elaborate on the role crisaborole could play in the treatment of AD.

References:

- 1- www.fda.gov last accessed 8/1/2017
<http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm533371.htm>
- 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 Sep; 75(3):494-503.e4. doi: 10.1016/j.jaad.2016.05.046. Epub 2016 Jul 11.

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