DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

Colleen Matkowski
Senior Director, Regulatory Affairs
Aclaris Therapeutics, Inc.
640 Lee Road, Suite 200
Wayne, PA 19087

RE: NDA 209305
ESKATA® (hydrogen peroxide) topical solution
MA 56

Dear Ms. Matkowski:

The Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has reviewed a direct-to-consumer video of an interview featuring a paid Aclaris spokesperson regarding ESKATA® (hydrogen peroxide) topical solution (Eskata), as well as the corresponding script (PP-ESK-US-0482) submitted by Aclaris under cover of Form FDA 2253. The video was originally broadcast on ABC's *The View* on September 19, 2018,[1] and can also be accessed through the Eskata Facebook page and the Aclaris LinkedIn page (both last accessed June 14, 2019), both submitted by Aclaris under cover of Form FDA 2253. The video makes false or misleading claims and/or representations about the risks associated with and the efficacy of Eskata. Thus, the video misbrands Eskata within the meaning of the Federal Food, Drug and Cosmetic Act (FD&C Act) and makes its distribution violative. 21 U.S.C. 352(a), (n); 321(n); 331(a). *See* 21 CFR 202.1(e)(3)(iii); (e)(5). This video is especially concerning from a public health perspective because it fails to include information regarding the serious risks associated with Eskata, which bears warnings and precautions related to the risks of serious eye disorders (such as permanent eye injury including blindness) in the case of exposure to the eye and severe skin reactions including scarring.

Background

Below are the indication and summary of the most serious and most common risks associated with the use of Eskata.[2] According to the FDA-approved product labeling (PI)[3]:

> Eskata is indicated for the treatment of seborrheic keratoses (SK) that are raised.

The WARNINGS AND PRECAUTIONS section of the PI includes risk information regarding eye disorders and local skin reactions. In addition, the most common adverse reactions associated with Eskata are erythema, stinging, edema, scaling, crusting, and pruritis.

[1] This video is available on the internet at https://youtu.be/QncHius7UAU (last accessed June 14, 2019).
[2] This information is for background purposes only and does not necessarily represent the risk information that should be included in the promotional piece cited in this letter.
[3] The version of the Eskata PI referred to in this letter is dated December 2017.

Prior Communications

OPDP notes that our advisory comments dated March 29, 2018, addressed draft Aclaris presentations for Eskata with certain similarities to the video in this letter. In these advisory comments, OPDP recommended that Aclaris revise proposed presentations so that they did not omit material information regarding the risks associated with Eskata or otherwise misrepresent important risk information. We also recommended that Aclaris revise proposed presentations so that they did not overstate the efficacy of Eskata. We are concerned that Aclaris is promoting Eskata in a manner that fails to adequately present the serious risks of the drug or describe the efficacy of the drug in a truthful and non-misleading manner despite this direction from OPDP.

False or Misleading Risk Presentation

Promotional materials misbrand a drug if they are false or misleading with respect to risk. The determination of whether promotional materials are misleading includes, among other things, not only representations made or suggested in promotional materials, but also failure to reveal facts material in light of the representations made or with respect to consequences that may result from the use of the drug as recommended or suggested in the materials.

The video features a discussion with a physician who is a paid spokesperson for Aclaris (Physician Spokesperson), as acknowledged both verbally and in text during the video. The video contains claims and/or representations about the benefits of Eskata. However, as described below, the video fails to include prominent, balancing risk information about Eskata.

First, the video fails to reveal the serious risks that are reflected in the warnings and precautions for the drug and are intended to be communicated to patients as described in the PI and Patient Information (PPI). We acknowledge that in addition to the Physician Spokesperson referring consumers to Eskata.com for more information, the video includes superimposed text (SUPERs) listing the drug's most common side effects and directing consumers to Eskata.com for full safety and prescribing information. However, this does not mitigate the video's omission of the serious risk information regarding the warnings and precautions about serious eye disorders that can result from unintended exposure and about severe local skin reactions. By omitting the warnings and precautions associated with Eskata, the video fails to provide material information about the consequences that may result from the use of the drug and creates a misleading impression about the drug's safety. This misleading presentation is especially problematic from a public health perspective given the serious and potentially permanent risks associated with the drug including the risk for corneal injury such as erosion, ulceration, perforation, and scarring; chemical conjunctivitis; eyelid edema; severe eye pain; or permanent eye injury, including blindness, if there is inadvertent eye exposure, as well as the risk for severe local skin reactions including erosion, ulceration, vesiculation and scarring.

Second, the claims and presentations in the video with respect to the drug's common adverse reactions create misleading impressions regarding Eskata treatment and the safety profile of the product. In particular, the Physician Spokesperson makes the following claim (emphasis added):

- "And, typically in one or two treatments the lesions go away, they resolve, and that's the end of it."

This claim is followed by side-by-side images of two patients with SKs "BEFORE," at "3 WEEKS," and on "DAY 106 (Final Result)" of Eskata treatment.

As the "before" and "after" images are presented, the following exchange takes place:

- Interviewer: "Does it burn as you're doing it?"

- Physician Spokesperson: "It can sting as you apply it."

We note that one of the most common adverse reactions (i.e. stinging) is presented. However, according to the PI, the most common local adverse reactions (with percentages of Eskata patients who reported such effects in clinical trials supporting approval) include not only stinging (97%), but also erythema (99%), edema (91%), scaling (90%), crusting (81%), and pruritus (58%). Furthermore, we note that many of these common adverse reactions occurred immediately after treatment.[4] Therefore, it is misleading for the Physician Spokesperson to state that patients can experience stinging upon application, without disclosing the other most common local adverse reactions, many of which occur within minutes of treatment with Eskata.

Moreover, many patients experience local adverse reactions not only as Eskata is being applied or immediately after, but also at a longer interval after the application of Eskata. Specifically, the PI states that common local skin reactions observed 1 week after treatment included scaling (72%), erythema (66%), crusting (67%), pruritus (18%), erosion (9%), and ulceration (4%). Furthermore, common local skin reactions observed 15 weeks after the initial treatment include erythema (21%), hyperpigmentation (18%), scaling (16%), crusting (12%), and hypopigmentation (7%). Therefore, given that local adverse reactions have been observed up to 15 weeks after treatment with Eskata, it is misleading for the Physician Spokesperson to suggest that typically after one or two treatments, "that's the end of it."

We acknowledge that the common side effects are listed as SUPERs simultaneously with the images depicting two patients before and after treatment with Eskata and in a separate SUPER following these visuals. However, the first of these SUPERs also contains efficacy information that is unrelated to the product's risks. Furthermore, the SUPERs are presented in conjunction with compelling and attention-grabbing photographs of patients before and after treatment and the Physician Spokesperson statements. This large amount of unrelated information is presented at a fast pace over approximately 10 seconds and all competes for the consumer's attention. As a result, it is difficult for consumers to adequately process and

[4] According to the PI, common local skin reactions observed 10 minutes after treatment include: erythema, stinging, edema, pruritus, and vesiculation.

comprehend the common side effects disclosed in the SUPERs. Therefore, the information in the SUPERs is not sufficient to mitigate the misleading impression created by the claims and presentations that suggest that patients can experience stinging as Eskata is applied with no other local adverse reactions during or after application of Eskata.

These claims and presentations, the omission of the warnings and precautions, and the lack of prominent, balancing risk information create a misleading impression regarding Eskata treatment and minimize the risks of the product.

False or Misleading Claims about Efficacy

In the video, the Physician Spokesperson makes the following claims (underlined emphasis added):

- "And, typically in one or two treatments the lesions go away, they resolve, and that's the end of it."

- "So, you can see from the before and after, what it looks like."

These claims are followed by presentations of side-by-side, before and after, visual images that contain photographs of 2 patients, 1 with "before" photographs depicting approximately 10 lesions, and the other with "before" photographs depicting 2 lesions. Both patients depicted have no visible lesions in the "after" photographs that illustrate the final results at Day 106 for these Eskata-treated individuals.

These claims and presentations misleadingly represent that the typical patient treated with Eskata will experience similar results, i.e., complete clearance of all treated SK lesions. While the images for these two patients may be an accurate reflection of their own experiences as Eskata-treated individuals, the personal experience of these two patients does not adequately support the suggestion that patients treated with Eskata will typically achieve complete clearance of their SK lesions. According to the CLINICAL STUDIES section of the PI, only 4% and 8% of subjects treated with Eskata achieved clearance of 4 out of 4 SK lesions at Day 106 in clinical studies 1 and 2, respectively. If you have data to support claims and presentations that patients treated with Eskata will typically experience complete resolution of their SK lesions that are raised, please submit such data to FDA for review.

We acknowledge that the SUPER presented in conjunction with these claims and presentations includes the proportion of patients treated with Eskata versus vehicle who achieved clearance of 3 out of 4 lesions at Day 106, and also discloses that individual results may vary. However, this SUPER is the same one described previously, and also presents the most common side effects of Eskata in addition to the efficacy information. Furthermore, the SUPERs are presented in conjunction with compelling and attention-grabbing before-and-after photographs and the Physician Spokesperson statements. This large amount of unrelated information is presented at a fast pace over approximately 10 seconds and

competes for the consumer's attention. As a result, it is difficult for consumers to adequately process and comprehend this contextual information. Therefore, these presentations are not sufficient to mitigate the misleading impression that typically patients treated with Eskata will achieve complete clearance of all raised SK lesions.

Furthermore, these claims and presentations are misleading because they suggest that more patients will achieve complete clearance of their SK lesions than has been demonstrated. Specifically, this presentation includes before and after images of patients depicting complete clearance of their SK lesions in conjunction with a SUPER that states, in pertinent part:

- "18% of patients experienced clearance of 3 out of 4 raised SKs treated with ESKATA vs 0% with vehicle (Day 106 end of study)."

Presenting images of patients depicting complete clearance, in conjunction with data for clearance of at least 3 out of 4 lesions, while omitting data for clearance of 4 out of 4 lesions, misleadingly suggests that these data apply to the results seen in the "before" and "after" images when this is not the case. According to the PI, only 4% and 8% of subjects treated with Eskata achieved clearance of 4 out of 4 SK lesions at Day 106 in clinical studies 1 and 2, respectively.

Conclusion and Requested Action

For the reasons discussed above, the video misbrands Eskata within the meaning of the FD&C Act and makes its distribution violative. 21 U.S.C. 352(a), (n); 321(n); 331(a). *See* 21 CFR 202.1(e)(3)(iii); (e)(5).

OPDP requests that Aclaris immediately cease violating the FD&C Act, as discussed above. Please submit a written response to this letter on or before June 28, 2019, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) for Eskata that contain violations such as those described above, and explaining your plan for discontinuing use of such violative materials. If you believe that your products are not in violation of the FD&C Act, include your reasoning and any supporting information for our consideration.

Please direct your response to the undersigned at the **Food and Drug Administration, Center for Drug Evaluation and Research, Office of Prescription Drug Promotion, 5901-B Ammendale Road, Beltsville, Maryland 20705-1266**. A courtesy copy can be sent by facsimile to (301) 847-8444. To ensure timely delivery of your submissions, please use the full address above and include a prominent directional notation (e.g. a sticker) to indicate that the submission is intended for OPDP. Please refer to MA 56 in addition to the NDA number in all future correspondence relating to this particular matter. All correspondence should include a subject line that clearly identifies the submission as a Response to Untitled Letter. OPDP reminds you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for Eskata comply with each applicable requirement of the FD&C Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Laurie Buonaccorsi, Pharm.D.
Regulatory Review Officer
Division of Advertising & Promotion Review 2
Office of Prescription Drug Promotion

Matthew J. Falter, Pharm.D.
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This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

JINA KWAK on behalf of LAURIE J BUONACCORSI
06/14/2019 01:18:39 PM

MATTHEW J FALTER
06/14/2019 01:20:55 PM