Food and Drug Administration
Center for Drug Evaluation and Research

Summary Minutes of the Nonprescription Drugs Advisory Committee Meeting
April 15, 2016

Location: Hilton Washington DC North/Gaithersburg
The Ballrooms, 620 Perry Parkway, Gaithersburg, MD 20877

Topic: The committee discussed data submitted by Galderma Laboratories, L.P. to support supplemental new drug application (sNDA) 20-380, for over-the-counter (OTC) marketing of adapalene gel 0.1%. The proposed OTC use is for the treatment of acne and to clear up acne pimples and acne blemishes. The applicant proposes to label the product for 12 years and older. The committee was asked to consider whether data support an acceptable risk/benefit profile for the nonprescription use of adapalene gel 0.1% by OTC consumers.

These summary minutes for the April 15, 2016 meeting of the Nonprescription Drugs Advisory Committee of the Food and Drug Administration were approved on June 27, 2016.

I certify that I attended the April 15, 2016 meeting of the Nonprescription Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/s/
Moon Hee V. Choi, PharmD
Designated Federal Officer, NDAC

/s/
Christianne L. Roumie, MD, MPH
Chairperson, NDAC

Summary Minutes of the Nonprescription Drugs Advisory Committee Meeting
April 15, 2016

The following is the final report of the Nonprescription Drugs Advisory Committee meeting held on April 15, 2016. A verbatim transcript will be available in approximately six weeks, sent to the Division of Nonprescription Drug Products and posted on the FDA website at: http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/NonprescriptionDrugsAdvisoryCommittee/ucm487180.htm.

All external requests for the meeting transcript should be submitted to the CDER Freedom of Information Office.

The Nonprescription Drugs Advisory Committee (NDAC) of the Food and Drug Administration, Center for Drug Evaluation and Research, met on April 15, 2016, at the Hilton Washington DC North/Gaithersburg, The Ballrooms, 620 Perry Pkwy., Gaithersburg, Maryland. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA and Galderma Laboratories, L.P. The meeting was called to order by Christianne L. Roumie, MD, MPH (Chairperson). The conflict of interest statement was read into the record by Moon Hee V. Choi, PharmD (Designated Federal Officer). There were approximately 120 people in attendance. There were 2 Open Public Hearing (OPH) presentations.

Issue: The committee discussed data submitted by Galderma Laboratories, L.P. to support supplemental new drug application (sNDA) 20-380, for over-the-counter (OTC) marketing of adapalene gel 0.1%. The proposed OTC use is for the treatment of acne and to clear up acne pimples and acne blemishes. The applicant proposes to label the product for 12 years and older. The committee was asked to consider whether data support an acceptable risk/benefit profile for the nonprescription use of adapalene gel 0.1% by OTC consumers.

Attendance:
NDAC Members Present (Voting): Michael R. Cohen, RPh, MS; Ralph B. D'Agostino, Sr., PhD; Janet P. Engle, PharmD, FAPhA; Lorraine J. Gudas, PhD; Paul Pisarik, MD, MPH, FAAFP; Maria C. Pruchnicki, PharmD, BCPS, BCACP, CLS; Christianne L. Roumie, MD, MPH (*Chairperson*)

NDAC Members Not Present (Voting): Michael K. Paasche-Orlow, MD, MA, MPH; Estela M. Pledge, MS, LCPC, MAC, ACS; Lee M. Sanders, MD, MPH

Temporary Members (Voting): Cheryl K. Bernstein, RN, BSN, CCRC (*Acting Consumer Representative*); Michael E. Bibgy, MD; Elizabeth A. Joniak-Grant, PhD (*Patient Representative*); Kenneth A. Katz, MD, MSc, MSCE; Stephen B. Harris, PhD, FATS, FRSB; Sarah Gloria Obican, MD; Sonja A. Rasmussen, MD, MS; Anthony R. Scialli, MD; Victor Wu, MD, MPH

Acting Industry Representative to the Committee (Non-Voting): Marla Sultan, MD, MBA

FDA Participants (Non-Voting): Charles Ganley, MD; Theresa Michele, MD; Tatiana Oussova, MD, MPH; Jane Filie, MD; Paul Brown, PhD

Open Public Hearing Speakers: David Spangler (Consumer Healthcare Products Association); Adam Friedman, MD, FAAD

The agenda proceeded as follows:

Call to Order and Introduction of Committee	**Christianne L. Roumie, MD, MPH** Chairperson, NDAC
Conflict of Interest Statement	**Moon Hee V. Choi, PharmD** Designated Federal Officer, NDAC
FDA Introductory Remarks	**Theresa Michele, MD** Director, Division of Nonprescription Drug Products (DNDP) Office of Drug Evaluation IV (ODE IV) Office of New Drugs (OND), CDER, FDA
APPLICANT PRESENTATIONS	**Galderma Laboratories, L.P.**
Introduction	**Howard Marsh, MD** Vice President of Medical Affairs, Galderma
Dermatologist Perspective	**Guy Webster, MD, PhD, FAAD** Webster Dermatology and Professor of Clinical Dermatology Jefferson College, Philadelphia
Efficacy and Safety	**Matthew Meckfessel, PhD** Medical Lead, Self-Medication, Galderma
Toxicology	**John DeSesso, PhD, DABFM, DABFE, FACFEI, DABCHS, Fellow ATS** Director, Center for Toxicology and Mechanistic Biology, Exponent Professor of Biochemistry, Molecular & Cellular Biology Georgetown University School of Medicine
Consumer Studies	**Julie Aker, MT (ASCP)** President and CEO, Concentrics Research
Benefit-Risk Assessment	**Jonathan Wilkin, MD** Director of Dermatology at Ohio State University (Retired) Founding Director of FDA Division of Dermatology & Dental Products (Retired)
Conclusion	**Howard Marsh, MD**
Clarifying Questions	

BREAK

FDA PRESENTATIONS

Maximal Usage Trial (MUsT) Data	**Chinmay Shukla, PhD** Clinical Pharmacologist Division of Clinical Pharmacology III Office of Clinical Pharmacology Office of Translational Sciences, CDER, FDA
Nonclinical Summary	**Cindy Li, PhD** Toxicologist DNDP, ODE IV, OND, CDER, FDA
Label Comprehension and Self-Selection Studies	**Barbara Cohen, MPA** Social Science Analyst DNDP, ODE IV, OND, CDER, FDA
Actual Use Trial & Clinical Perspective	**Ryan Raffaelli, MD** Medical Officer DNDP, ODEIV, OND, CDER, FDA
Postmarketing Prescription Safety Data	**Lopa Thambi, PharmD** Safety Evaluator Division of Pharmacovigilance II Office of Pharmacovigilance and Epidemiology Office of Surveillance and Epidemiology, CDER, FDA
Benefit: Risk Profile	**Jane Filie, MD** Lead Medical Officer DNDP, ODE IV, OND, CDER, FDA

Clarifying Questions

LUNCH

OPEN PUBLIC HEARING

Charge to the Committee	**Valerie Pratt, MD** Deputy Director for Safety DNDP, ODE IV, OND, CDER, FDA

Questions to the Committee/Committee Discussion

BREAK

Questions to the Committee/Committee Discussion

Adjournment

Questions to the Committee:

1. **DISCUSSION**: Discuss the safety profile of adapalene gel 0.1% in the over-the-counter (OTC) setting. In your discussion, please consider the following:

    a. use by females with reproductive potential (i.e., teratogenic risk),

    b. pediatric use (i.e., use by adolescents and/or younger children), and

    c. potential for misuse (e.g., excessive use or use for non-acne conditions) and the consequences of such use.

    Committee Discussion: *There was an overall consensus that use of adapalene gel 0.1% would be safe, in the over-the-counter (OTC) setting, by females with reproductive potential which could be at risk of fetal harm with exposure to potentially teratogenic drugs. One committee member noted that pregnant women will use the drug but, based on the reassuring animal data, he saw no signal for teratogenicity. Other members agreed, noting that the evidence demonstrating no teratogenicity risk is substantial. One committee member raised the point that counseling about teratogenicity risk of retinoids as a class, and explaining why topical adapalene is different from other drugs in the class, might be useful in patient-provider discussions. In regard to the safety of adapalene in pediatrics (i.e., use by adolescents and/or younger children), it was noted that this group seemed to have used higher quantities ("more is better" approach) based on the data (higher plasma concentrations observed in adolescents vs. adults, and 5 of the 13 subjects that used 80 gm or more were between the ages of 12 – 17), thus raising potential safety concerns as a consequence of this higher quantity use. In terms of the potential for misuse, it was noted that the term "blemishes" may be misconstrued and use of the product misunderstood as a treatment for hyperpigmentation or a skin lightening agent. Please see the transcript for details of the committee discussion.*

2. **VOTE**: Has the safety of adapalene gel 0.1% for OTC use for the treatment of acne been adequately demonstrated?

    a. If not, what additional data, if any, should be obtained to demonstrate safety in the OTC setting?

    Vote Result: YES: 16 NO: 0 ABSTAIN: 0

    Committee Discussion: *The committee members unanimously agreed that the safety of adapalene gel 0.1% for OTC use for the treatment of acne has been adequately demonstrated. Please see the transcript for details of the committee discussion.*

3. **DISCUSSION**: Discuss the proposed Drug Facts Label and Consumer Information Leaflet.

    a. **DISCUSSION**: If your review of the label and leaflet identifies concerns, please discuss ways in which the documents could be revised to encourage the safe and proper use of the product by consumers.

Committee Discussion: *Overall, the committee was split in its recommendations regarding the inclusion of the cautionary language "If pregnant or breast-feeding, ask a health professional before use" in the labeling. The committee members who recommended removal of this language stated that if the drug is deemed to be safe for OTC use and without risk for pregnant consumers, the language may be misunderstood by both consumers and healthcare professionals. The committee members who recommended retaining this language asserted that because consumers are used to seeing it in Drug Facts labeling, its absence might convey to them more of a safety assurance than is warranted. The committee members who recommended strengthening this language asserted that many consumers do not pay attention to it currently because it is seemingly ubiquitous. Some committee members noted that there was inconsistency between the Drug Facts labeling and the Consumer Information Leaflet regarding the directions on the areas where the drug needs to be applied (affected area vs. entire face), as well as how to cleanse the skin (thoroughly vs. gently) before applying the drug. They recommended that information in both the Drug Facts labeling and leaflet be consistent. Additionally, given the majority of the data presented were from trials conducted over a maximum of12 weeks, it was recommended that the labeling include duration of use and language directing consumers to see a health care professional if the product is used longer than a specified time. Please see the transcript for details of the committee discussion.*

4. **VOTE**: The sponsor proposes OTC use of adapalene gel 0.1% for the treatment of acne in consumers ages 12 years and older. Does the totality of the data support the use of this product OTC?

   a. If yes, do you have additional comments or recommendations for labeling?

   b. If not, what further data, if any, should be obtained to support such use?

   Vote Result: YES: 16 NO: 0 ABSTAIN: 0

   Committee Discussion: *The committee members unanimously agreed that the totality of the data support the OTC use of adapalene gel 0.1% for the treatment of acne in consumers ages 12 years and older. Regarding the labeling statement about breastfeeding, opinions varied: keep the statement, remove the statement, leave a statement about breastfeeding and remove the pregnancy warning, change the breastfeeding warning and add not to apply product to the breast, or remove the breastfeeding warning and keep the pregnancy warning. Some committee members recommended that breastfeeding be uncoupled from pregnancy in the labeling. Some committee members also agreed that more specific information is needed on the product's labeling, such as amount of drug to use, frequency of use, duration of use, etc. One committee member noted that although adapalene 0.1% gel has been demonstrated to be safe for OTC use, this should not be a precedent for other drugs in the same class to follow. Please see the transcript for details of the committee discussion.*

The meeting was adjourned at approximately 2:35 p.m.