DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

Bharathi Devarakonda, SVP,
Regulatory Affairs & Technical Services
Eton Pharmaceuticals, Inc.
21925 West Field Parkway, Suite 235
Deer Park, IL 60010

RE: NDA 213876
ALKINDI® SPRINKLE (hydrocortisone) oral granules
MA 13

Dear Ms. Devarakonda:

The Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has reviewed the promotional communication, sponsored links[1], for ALKINDI® SPRINKLE (hydrocortisone) oral granules (Alkindi Sprinkle), submitted by Eton Pharmaceuticals (Eton) under cover of Form FDA 2253. These sponsored links are false or misleading in that they present information about the benefits of Alkindi Sprinkle, but fail to include **any** risk information about the drug. Thus, the sponsored links misbrand Alkindi Sprinkle within the meaning of the Federal Food, Drug, and Cosmetic Act (the Act) and make its distribution violative. 21 U.S.C. 352(a),(n); 321(n); 331(a). *See* 21 CFR 202.1(e)(5). These violations are especially concerning from a public health perspective because the promotional communications create a misleading impression about the safety of Alkindi Sprinkle, a drug that is used in a vulnerable pediatric patient population, and may cause serious adverse reactions such as adrenal crisis, infections, and growth retardation, among others.

Background

Below are the indication and summary of the most serious and most common risks associated with the use of Alkindi Sprinkle.[2]

According to the FDA-approved product labeling (PI)[3]:

> ALKINDI SPRINKLE is indicated as replacement therapy in pediatric patients with adrenocortical insufficiency.

Alkindi Sprinkle is contraindicated in patients with hypersensitivity to hydrocortisone or any of the ingredients in Alkindi Sprinkle. The PI contains warnings and precautions regarding adrenal crisis, infection, growth retardation, Cushing's Syndrome due to use of excessive doses of corticosteroids,

[1] Available at https://www.google.com (Last accessed July 27, 2021).
[2] This information is for background purposes only and does not necessarily represent the risk information that should be included in the promotional piece(s) cited in this letter.
[3] The version of the Alkindi Sprinkle PI that was submitted to FDA when the piece was disseminated, and the version referred to in this letter is dated September 2020. Subsequently, a new version of the PI was approved in June 2021. We note that the current version of the PI, approved in June 2021, includes additional risk information in the WARNINGS AND PRECAUTIONS section.

decrease in bone mineral density, psychiatric adverse reactions, ophthalmic adverse reactions, and gastrointestinal adverse reactions. The most common adverse reactions are fluid retention, alteration in glucose tolerance, elevation in blood pressure, behavioral and mood changes, increased appetite and weight gain.

False or Misleading Risk Presentation

Prescription drug advertisements and labeling (promotional communications) misbrand a drug if they are false or misleading with respect to risk. The determination of whether a promotional communication is misleading includes, among other things, not only representations made or suggested in the promotional communication, but also the extent to which the promotional communication fails 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 promotional communication.

The sponsored links are misleading because they present claims and/or representations about the use and/or benefits for Alkindi Sprinkle but fail to communicate **any** risk information. For example, the sponsored links present the following claims (emphasis original):

- "**Hydrocortisone Oral Granules I Alkindi Sprinkle Now Available**
  Accurate and individualized dosing for infants and children with adrenal insufficiency. Strengths as low as 0.5 mg without splitting or manipulation."

- "**Hydrocortisone Oral Granules I Cortisol Replacement Therapy**
  ALKINDI SPRINKLE: low-strength hydrocortisone for children with adrenal insufficiency. Individualized hydrocortisone dosing with no bitter taste, pill cutting or dissolving."

- "**Alkindi Sprinkle for Kids I Micro-Granular Hydrocortisone**
  Alkindi Sprinkle for pediatric adrenal insufficiency; strengths as low as 0.5 mg. No cutting, no splitting, just sprinkles for neonates and children <17 years of age."

By omitting the risks associated with Alkindi Sprinkle, the sponsored links fail to provide material information about the consequences that may result from the use of Alkindi Sprinkle and create a misleading impression about the drug's safety.

Conclusion and Requested Action

For the reasons discussed above, the sponsored links misbrand Alkindi Sprinkle within the meaning of the FD&C Act and make its distribution violative. 21 U.S.C. 352(a), (n); 321(n); 331(a). *See* 21 CFR 202.1(e)(5).

This letter notifies you of our concerns and provides you with an opportunity to address them. OPDP requests that Eton cease any violations of the FD&C Act. Please submit a written response to this letter within 15 working days from the date of receipt, addressing the concerns described in this letter, listing all promotional communications (with the 2253 submission date) for Alkindi Sprinkle that contain representations like those described above, and explaining any plan for discontinuing use of such communications, or for ceasing distribution of Alkindi Sprinkle.

If you believe that your product is not in violation of the FD&C Act, please include in your submission to us your reasoning and any supporting information for our consideration within 15 working days from the date of receipt of this letter.

The concerns discussed in this letter do not necessarily constitute an exhaustive list of potential violations. It is your responsibility to ensure compliance with each applicable requirement of the FD&C Act and FDA implementing regulations.

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 13 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.

Sincerely,

{See appended electronic signature page}

Charuni Shah, PharmD
Regulatory Review Officer
Division of Advertising & Promotion Review 2
Office of Prescription Drug Promotion

{See appended electronic signature page}

Melinda Wilson, PharmD, MPH, BCPS, RAC
Team Leader
Division of Advertising & Promotion Review 2
Office of Prescription Drug Promotion

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/

CHARUNI P SHAH
08/09/2021 01:54:59 PM

MELINDA M WILSON
08/09/2021 02:16:56 PM