



Lou Kennedy
CEO and Owner
Nephron Pharmaceuticals Corporation
4500 12th Street Extension
West Columbia, SC 29172

RE: ANDA 78202
Budesonide Inhalation Suspension, for inhalation suspension
MA 1, 3

WARNING LETTER

Dear Mr. Kennedy:

The Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has become aware of emails that you and your sales representative sent on July 14, 2020 and July 7, 2020, respectively, in your capacity as employees of Nephron Pharmaceuticals Corporation (Nephron) regarding Budesonide Inhalation Suspension, for inhalation suspension (Budesonide). These emails were submitted as complaints to the FDA Bad Ad Program. The emails provide evidence that Budesonide is intended for a new use for which it lacks approval, specifically treatment of symptoms associated with “Coronavirus Disease 2019” (COVID-19), and for which its labeling does not provide adequate directions for use. This renders Budesonide misbranded within the meaning of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and makes its distribution violative. 21 U.S.C. 352(f)(1); 331(a). See 21 CFR 201.5; 201.100; 201.115; 201.128.

The emails are also false or misleading in that they represent that Budesonide has certain benefits, but fail to include **any** risk information about the drug. Thus, the emails misbrand Budesonide 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). These violations are concerning from a public health perspective because they create a misleading impression about the safety and effectiveness of Budesonide for the treatment of COVID-19 and suggest a use for which the labeling does not provide adequate directions for safe and effective use of the product.

There is currently a global outbreak of respiratory disease caused by a novel coronavirus that has been named “severe acute respiratory syndrome coronavirus 2” (SARS-CoV-2). The disease caused by the virus has been named COVID-19. On January 31, 2020, the Department of Health and Human Services (HHS) issued a declaration of a public health

emergency related to COVID-19 and mobilized the Operating Divisions of HHS.¹ The declaration has been renewed for an additional 90 days twice, with the most recent renewal going into effect on July 25, 2020.² In addition, on March 13, 2020, the President declared a national emergency in response to COVID-19.³

Background

Below are the indication and summary of the most serious and most common risks associated with the use of Budesonide.⁴ According to the FDA-approved product labeling (PI):

Budesonide inhalation suspension is indicated for the maintenance treatment of asthma and as prophylactic therapy in children 12 months to 8 years of age.

Limitations of Use

Budesonide inhalation suspension is NOT indicated for the relief of acute bronchospasm.

Budesonide is contraindicated for primary treatment of status asthmaticus or other acute episodes of asthma where intensive measures are required and in patients with hypersensitivity to budesonide or any of the ingredients of budesonide inhalation suspension. The PI for Budesonide includes warnings and precautions regarding local effects, deterioration of disease and acute asthma episodes, hypersensitivity reactions including anaphylaxis, immunosuppression, transferring patients from systemic corticosteroids therapy, hypercorticism and adrenal suppression, reduction in bone mineral density, effects on growth, glaucoma and cataracts, paradoxical bronchospasm and upper airway symptoms, eosinophilic conditions and Churg-Strauss Syndrome, and drug interactions with strong cytochrome P450 3A4 inhibitors. The most common adverse reactions reported with use of Budesonide include respiratory infection, rhinitis, coughing, otitis media, viral infection, moniliasis, gastroenteritis, vomiting, diarrhea, abdominal pain, ear infection, epistaxis, conjunctivitis, and rash.

Lack of Adequate Directions for Use

The emails that you and your sales representative sent include claims and representations about the use and/or benefits of Budesonide as a treatment for symptoms associated with

¹ Secretary of Health and Human Services Alex M. Azar II, Determination that a Public Health Emergency Exists. Jan. 31, 2020. (Accessible at <https://www.phe.gov/emergency/news/healthactions/phe/Pages/2019-nCoV.aspx>).

² Secretary of Health and Human Services Alex M. Azar II, Renewal of Determination that a Public Health Emergency Exists. July 23, 2020. (Accessible at <https://www.phe.gov/emergency/news/healthactions/phe/Pages/covid19-23June2020.aspx>).

³ President Donald J. Trump, Proclamation on Declaring a National Emergency Concerning the Novel Coronavirus Disease (COVID-19). Mar. 13, 2020. (Accessible at <https://www.whitehouse.gov/presidential-actions/proclamation-declaring-national-emergency-concerning-novel-coronavirus-disease-covid-19-outbreak/>).

⁴ 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.

COVID-19. For example, the email that you sent on July 14, 2020 includes the prominent headline claim, “**BUDESONIDE RELIEVES RESPIRATORY SYMPTOMS ASSOCIATED WITH COVID-19**” (emphasis original), in conjunction with an image of your product and what appears to be SARS-CoV-2. This email also states, “Over the last few weeks, doctors and researchers have touted the benefits of using Budesonide as a treatment for symptoms associated with COVID-19. One physician, who went viral this month, called Budesonide a ‘silver bullet.’” Additionally, the email that your sales representative sent on July 7, 2020, with the subject line, “COVID-19 – Budesonide – Video,” links to a YouTube video that the sales representative says is of a physician discussing “treating COVID patients successfully with Budesonide and an antibiotic. . . . You may want to share this with your respiratory team and pulmonary docs. Cost effective way to treat Coronavirus!”

These claims and representations provide evidence that Nephron is promoting Budesonide for a new use for which it lacks approval and for which its labeling does not provide adequate directions for use. Budesonide is not approved as a treatment for symptoms associated with COVID-19, and its labeling does not contain adequate directions for such use, thereby rendering the drug misbranded. These claims and representations, which misleadingly suggest that Budesonide is safe and effective for a use for which it is not approved and for which you have provided no evidence to support, are particularly alarming from a public health perspective because COVID-19 has caused significant morbidity and mortality, and because there is currently no FDA-approved treatment for symptoms associated with COVID-19.⁵

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 representations made or with respect to consequences that may result from the use of the drug as recommended or suggested in the materials.

The emails cited above include claims and representations about the use and/or benefits of Budesonide, but they fail to communicate **any** risk information about the product. By omitting the risks associated with Budesonide, the emails fail to provide material information about the consequences that may result from the use of the drug and create a misleading impression about the safety of Budesonide.

Conclusion and Requested Action

For the reasons discussed above, the emails provide evidence that Budesonide is intended for a new use for which it lacks approval, and for which its labeling does not provide adequate directions for use. This renders Budesonide misbranded within the meaning of the FD&C Act and makes its distribution violative. 21 U.S.C. 352(f)(1); 331(a); see 21 CFR 201.5; 201.100; 201.115; 201.128. The emails are also false or misleading and therefore misbrand

⁵ <https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctap>.

Budesonide 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).

OPDP requests that Nephron immediately cease misbranding Budesonide and/or cease introducing the misbranded drug into interstate commerce. Please submit a written response to this letter on or before October 6, 2020, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) for Budesonide that contain statements such as those described above, and explaining your plan for discontinuing use of such materials, or, in the alternative, for ceasing distribution of Budesonide. Because the violation/violations described above are serious, we request, further, that your submission include a comprehensive plan of action to disseminate truthful, non-misleading, and complete corrective messages about the issues discussed in this letter to the audience(s) that received the violative promotional materials. In order to clearly identify the violative promotional piece(s) and/or activity and focus on the corrective message(s), OPDP recommends that corrective piece(s) include a description of the violative promotional piece(s) and/or activity, include a summary of the violative message(s), provide information to correct each of the violative message(s), and be free of promotional claims and presentations. To the extent possible, corrective messaging should be distributed using the same media, and generally for the same duration of time and with the same frequency that the violative promotional material was disseminated. If you believe that your product is 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 Amundson Avenue, 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 1, 3 in addition to the ANDA 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 Warning Letter.

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

Failure to correct the violations discussed above may result in FDA regulatory action, including seizure or injunction, without further notice.

Sincerely,

{See appended electronic signature page}

Robert Dean
Director
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/

ROBERT T DEAN
09/22/2020 03:22:53 PM