DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

Marianne Frost, MA
Senior Vice President, Regulatory Affairs
Biohaven Pharmaceuticals
215 Church Street
New Haven, CT 06510

RE: NDA 212728
NURTEC ODT (rimegepant) orally disintegrating tablets, for sublingual or oral use
MA 71

Dear Ms. Frost:

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 Khloé Kardashian, which identifies her as a paid Biohaven Pharmaceuticals spokesperson (Spokesperson).[1] This promotional communication, a video, states it is "SPONSORED BY: Nurtec™ ODT" (rimegepant) orally disintegrating tablets, for sublingual or oral use (Nurtec ODT). In addition, the video includes the web-address, "takebacktoday.com," which redirects the viewer to www.nurtec.com. The video originally appeared on ABC's *The View* on July 15, 2020 and can also be accessed through *The View*'s YouTube page.[2] The FDA Bad Ad Program also received a complaint regarding this video.

This video makes false or misleading claims and representations about the risks associated with and the efficacy of Nurtec ODT. Thus, the video misbrands Nurtec ODT 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)(i); (e)(5); (e)(7)(viii). In addition, these materials were not submitted at the time of initial dissemination or publication as required by 21 CFR 314.81(b)(3)(i). These violations are concerning from a public health perspective because the promotional communication creates a misleading impression regarding the overall benefit a patient may expect as a result of Nurtec ODT treatment and minimizes the risks associated with taking the drug.

Background

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

[1] In the video, a host of *The View* describes Biohaven Pharmaceuticals as "one of our sponsors."
[2] This video is available on the internet at https://www.youtube.com/watch?v=Fc_nSDnwOrE (last accessed date March 8, 2021).
[3] 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.

NURTEC ODT is indicated for the acute treatment of migraine with or without aura in adults.

Limitations of Use
NURTEC ODT is not indicated for the preventive treatment of migraine.

Nurtec ODT is contraindicated in patients with a history of hypersensitivity reaction to rimegepant, Nurtec ODT, or any of its components. The PI contains a warning and precaution regarding hypersensitivity reactions. The most common adverse reaction is nausea.

False or Misleading Claims about Efficacy

Prescription drug advertisements and labeling (promotional communications) misbrand a drug if they are false or misleading with respect to efficacy. 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 video features an interview with a Spokesperson, as acknowledged both verbally and in text during the video. In the video, the Spokesperson makes claims such as (in pertinent part):

- ". . . something that works in about 15-30 minutes . . ."

- "It literally works within, for me, 15 minutes. And anyone with a migraine, for 15 minutes, of pure agony, they're like knives in my head. So to have this relief, and to not be in a fog afterwards . . . I'm able to just go with the rest of my day."

These claims misleadingly suggest that patients treated with Nurtec ODT will experience "relief" within 15 to 30 minutes of taking the drug. While these claims may be an accurate reflection of the Spokesperson's own experience with Nurtec ODT, their personal experience does not adequately support the suggestion that the drug will provide "relief" within 15 to 30 minutes. According to the CLINICAL STUDIES section of the PI, the co-primary endpoints (freedom from pain and most bothersome symptoms) were measured beginning at 2 hours after dosing with Nurtec ODT and placebo. In addition, the PI states that, "In Study 1, statistically significant effects of NURTEC ODT compared to placebo were demonstrated for the additional efficacy endpoints of pain relief at 2 hours . . . ." Claims that Nurtec ODT provides relief in 15-30 minutes are not supported by the clinical trial data. There were no pre-specified endpoints that evaluated the efficacy of the drug at 15 or 30 minutes after dosing. OPDP notes that the video includes the SUPER, "AS EVERYONE EXPERIENCES MIGRAINE DIFFERENTLY. TREATMENT RESULTS MAY VARY" (emphasis original, in pertinent part). However, this does not mitigate the misleading impression. FDA is not aware of any data to support the claims that patients treated with Nurtec ODT will experience "relief" within 15 to 30 minutes of taking the drug. If you have data to support these claims, please submit to FDA for review.

The video also includes the following claims (emphasis added, in pertinent part):

- "I have been on handfuls of different prescriptions and over-the-counter medications, and none of them have really worked for me. Or if they worked, and maybe it was a one or two time thing and then they didn't work consistently after that. And I was given Nurtec ODT, I tried it, it was a **gamechanger**[.]"

- "So to have this relief, and to not be in a fog afterwards, **to not like, other medications would give me rebound headaches, and this one doesn't** . . ."

These comparative claims are misleading because they suggest that Nurtec ODT is clinically superior to or more effective than other prescription and over-the-counter (OTC) products, when this has not been demonstrated. In addition, the use of the word "gamechanger" in the context of the comparative claim misleadingly suggests that Nurtec ODT represents a significant advance over other currently available products, when this has not been demonstrated. While these claims may be an accurate reflection of the Spokesperson's own experience with Nurtec ODT, their personal experience does not support the suggestion that Nurtec ODT is more advanced than or superior to other migraine drug products on the market. FDA is not aware of evidence to support these claims. If you have data to support these claims, please submit to FDA for review.

Additionally, the video is misleading because the interview portion of the video communicates that Nurtec ODT is for the treatment of migraine but it fails to adequately communicate Nurtec ODT's full FDA-approved indication and limitations of use. Specifically, the interview portion of the video fails to convey that Nurtec ODT is approved for the acute treatment of migraine, and that it is not indicated for the preventive treatment of migraine. OPDP notes that the full indication with limitations of use is presented briefly, at the end of the video, after the interview portion, in a script/text format on the screen. However, this does not mitigate the misleading impression.

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 video is misleading because it fails to present information relating to the contraindications, warnings, precautions, and adverse reactions for Nurtec ODT with a prominence and readability reasonably comparable with the presentation of information relating to the benefits of Nurtec ODT. Specifically, the video contains claims and/or representations about the benefits of Nurtec ODT in the audio portion, while the risk information is presented in text only format and in small font. Moreover, the risk information only appears briefly for four seconds at the end of the video, after the close of the Spokesperson's presentation, where it is unlikely to draw the viewer's attention.

Additionally, the video does not present any signal to alert the viewer that important risk information follows after the close of the Spokesperson's presentation. In fact, the host of the interview states, "we'll be right back," which typically signals the close or end of a presentation. The overall effect of disclosing risk information in this manner undermines the communication of risk information and thereby misleadingly minimizes the risks associated with the use of Nurtec ODT.

Failure to Submit Under Form FDA-2253

FDA regulations require any labeling or advertising devised for promotion of the drug product to be submitted at the time of initial dissemination of the labeling and at the time of initial publication of the advertisement for a prescription drug product. Each submission is required to be accompanied by a completed transmittal Form FDA-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) and is required to include a copy of the product's current professional labeling. A copy of the video was not submitted to OPDP under cover of Form FDA-2253 at the time of initial dissemination as required by 21 CFR 314.81(b)(3)(i).

Conclusion and Requested Action

For the reasons discussed above, the video misbrands Nurtec ODT 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)(i); (e)(5); (e)(7)(viii). Furthermore, Biohaven Pharmaceuticals did not comply with 21 CFR 314.81(b)(3)(i).

This letter notifies you of our concerns and provides you with an opportunity to address them. OPDP requests that Biohaven Pharmaceuticals 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 other promotional communications (with the 2253 submission date) for Nurtec ODT that contain representations like those described above, and explaining any plan for discontinuing use of such communications, or for ceasing distribution of Nurtec ODT.

If you believe that your products are 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 71 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}

Dhara Shah, PharmD, RAC
Regulatory Review Officer
Division of Advertising & Promotion Review 1
Office of Prescription Drug Promotion

{See appended electronic signature page}

Aline Moukhtara, RN, MPH
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/s/

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for Aline Moukhtara