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E-ALERT | Food & Drug

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SUMMARY OF FDA ADVERTISING AND PROMOTION ENFORCEMENT ACTIVITIES

AUGUST 2012

This e-alert is part of a series of monthly e-alerts summarizing publicly-available FDA enforcement letters (i.e., warning letters and untitled letters) relating to the advertising and promotion of drugs, biologics, and medical devices. In August 2012, FDA's Office of Prescription Drug Promotion (OPDP) posted the following enforcement letters on its website:[1]

- Untitled letter to Valeant Pharmaceuticals North America, LLC re: Zovirax® (acyclovir) Cream 5% (July 18, 2012) ("Valeant Untitled Letter")[2]
- Untitled letter to Forest Laboratories, Inc. re: Daliresp® (roflumilast) tablets (August 1, 2012) ("Forest Untitled Letter")

The Office of Compliance in FDA's Center for Devices and Radiological Health (CDRH) posted the following letters on FDA's website:

- Warning letter to Quanta Aesthetic Lasers USA, LLC re: Quanta System Q-Plus T (June 16, 2012) ("Quanta Warning Letter")
- Warning letter to Augustine Biomedical & Design LLC re: Hot Dog Patient Warming System (July 24, 2012) ("Augustine Warning Letter")

During August 2012, the Office of Compliance and Biologics Quality (OCBQ) in FDA's Center for Biologics Evaluation and Research (CBER) did not post any enforcement letters relating to the advertising and promotion of biologics on FDA's website. The letters posted by OPDP and the Office of Complaince at CDRH raise a variety of allegations and conclude that the cited advertising/promotional issues render the subject product misbranded and/or adulterated.

This e-alert represents a change in format from previous editions. Previous versions of this alert grouped FDA's observations by observation type (e.g., grouping together all of FDA's observations in a given month related to Overstatement of Efficacy). For this and future alerts, we will summarize each letter individually, discussing FDA's observations on a letter-by-letter basis. We hope that this change makes these alerts more useful for our readers.

This alert merely summarizes the allegations contained in FDA's letters. It does not contain any analysis, opinions, characterizations, or conclusions by or of Covington & Burling LLP. As a result, the information presented herein does not necessarily reflect the views of Covington & Burling LLP or any of its clients.

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[1] Only enforcement letters posted to FDA's website in August 2012 are included herein. Letters issued in August but not posted to the website by August 31, 2012 will be summarized in our alerts for the months in which those letters are posted.

[2] The dates referenced for the letters are the issue dates.

Valeant Untitled Letter

Zovirax is indicated for the treatment of recurrent herpes labialis (cold sores) in adults and adolescents. OPDP concluded that Valeant's webpage for Zovirax was misleading because it overstated Zovirax's efficacy and made unsubstantiated superiority claims about the drug.

Overstatement of Efficacy: Valeant's webpage made the claim: "PROVEN EFFECTIVE AT ANY STAGE, Even When Therapy Is Initiated Late." The claim was presented alongside a chart showing six progressive stages of an untreated herpes lesion.[3] According to OPDP, this presentation misleadingly suggested that Zovirax is effective during the later stages of a herpes lesion, when this has not been demonstrated by substantial evidence or substantial clinical experience. Valeant's webpage cited two references in support of its claim. OPDP, however, determined that both were inadequate. The first reference relied solely on Valeant's two pivotal trials (where patients were instructed to initiate treatment within an hour of noticing symptoms). The second reference was a review article. Additionally, OPDP pointed to Zovirax's prescribing information (PI), which provides that "therapy should be initiated as early as possible following onset of signs and symptoms (i.e., during the prodrome or when lesions appear)." OPDP also found that although the webpage included a footnote that stated "[t]herapy should be initiated as soon as possible following onset of signs and symptoms," this did not mitigate the overall misleading impression caused by the claims.

Unsubstantiated Superiority Claims: The above-mentioned chart also claimed that the competitor product Valtrex is effective only when initiated at the first stage of a herpes lesion. OPDP found the presentation misleading because it implied that "Zovirax is clinically superior to Valtrex due to an extended timeframe of treatment initiation." According to OPDP, it was not aware of any evidence that supports this implication.

Forest Untitled Letter

According to its PI, Daliresp is indicated as "a treatment to reduce the risk of COPD exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations." Daliresp's PI also provides a limitation of use, stating "Daliresp in not a bronchilator and is not indicated for the relief of acute bronchospasm." OPDP found that oral statements made by two Forest sales representatives to a healthcare professional on October 12, 2011 were false or misleading because they broadened Daliresp's indication and minimized the drug's serious risks. The incident was submitted pursuant to OPDP's Bad Ad Program.[4]

Broadening of Indication: OPDP concluded that the Forest sales representatives' statements during the October 12th call misleadingly broadened the indication for Daliresp. Although the sales representatives communicated that Daliresp is effective for COPD exacerbations, they did not present the appropriate patient population. Additionally, the sales representatives failed to disclose that Daliresp is not a bronchilator and is not indicated for the relief of acute bronchospasm. OPDP found that the sales representatives' statements misleadingly suggested that Daliresp is safe and effective in a broader range of patients and conditions than has been demonstrated.

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[3] The stages presented in the chart included: prodrome or early (stage 1), papule or swelling (stage 2), vesicle or blistering (stage 3), ulcer or weeping (stage 4), crust or scabbing (stage 5), and healing (stage 6).

[4] OPDP found Forest's violative conduct particularly troubling given: (1) Forest's September 2012 Corporate Integrity Agreement with the Office of Inspector General of HHS mandating Forest's compliance with FDA promotional requirements, (2) similar violative promotional activities by Forest sales representative in April 2011, and (3) prior communications from OPDP to Forest advising Forest about launch promotional materials for Daliresp.

Minimization of Risk: Daliresp's PI contains warnings and precautions regarding weight loss, psychiatric events (including suicidality), and drug interactions. During the October 12th call, the Forest sales representatives responded to direct questions regarding these warnings and precautions in a manner consistent with Daliresp's PI. OPDP found, however, that the sales representatives then downplayed the risks "with anecdotal claims regarding other physicians who have prescribed the drug, were pleased with it, and were not reporting **any** adverse events."[5] The sales representatives further minimized the risk of weight loss "by indicating that this adverse reaction may actually be beneficial in COPD patients who are overweight." OPDP explained that this is in direct contrast to Daliresp's PI, which directs that discontinuation of Daliresp should be considered if unexplained or clinically significant weight loss occurs.

Quanta Warning Letter

Quanta obtained clearance of the Quanta System Q-Plus T ("Q-Plus") for "the treatment of vascular lesions, pigmented lesions, and for hair, tattoo removal and the incision, excision, ablation, vaporization of soft tissue for general dermatology" and "for use for cutting, vaporization and ablation of soft tissue and the removal of tattoos and benign pigment lesions." CDRH reviewed Quanta's website and found several claims outside Quanta's cleared use of the Q-Plus.

Claims Outside Cleared Use:[6] Quanta's website included claims such as the Q-Plus "effectively perform[s] . . . skin rejuvenation and tightening," and "reduces the sebaceous secretion and activating the porphyrins, leads to the formation of oxygen which causes the death of the microorganism causing acne." CDRH found that Quanta's promotion of the Q-Plus for skin rejuvenation, skin lifting, skin tightening/smoothness, acne treatments, anti-aging, firming, and treatment of scars and keloids represented a major change in the intended use of the device. According to CDRH, these claims rendered the Q-Plus adulterated and misbranded.

Augustine Warning Letter

Augustine obtained several clearances for the Hot Dog Patient Warming System, each of which is "intended to prevent or treat hypothermia and to provide warmth to patients." Each device is "intended primarily for use in hospitals and surgical centers including, without limitation, operating, recovery and emergency rooms and on medical/surgical floors." CDRH determined that several claims on Augustine's website were outside Augustine's cleared use of the Hot Dog Patient Warming System.

Claims Outside Cleared Use:[7] CDRH found that Augustine's website made several claims regarding reduced infection rates, even though none of Augustine's 510(k)s for the Hot Dog Patient Warming System included this intended use. Specifically, CDRH pointed to the claim: "unlike forced-air, air-free HotDog warming doesn't generate waste heat that can contaminate the sterile field . . . . Hospitals that have switched to HotDog report significant reduction in deep joint SSIs. For example a # 1 rated hospital in Minnesota experienced an 81% reduction after switching to air-free warming." Additionally, under its webpage titled "HOTDOG IS SAFER," Augustine's website summarized an article in the Journal of Bone and Joint Surgery as finding a 74% reduction in implant infections resulting from the change to air-free Hot Dog patient warming. Because Augustine did not have clearance for this indication of use, CDRH found that these claims rendered the Hot Dog Patient Warming System adulterated and misbranded.

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[5] Emphasis added by OPDP.
[6] The letter issued by CDRH does not explicitly use this subheading, but the allegation fits within this category.
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