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COVINGTON & BURLING LLP

# E-ALERT | Food & Drug

August 12, 2013

## SUMMARY OF FDA ADVERTISING AND PROMOTION ENFORCEMENT ACTIVITIES

## JULY 2013

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 prescription drugs, medical devices, and biologics.

In July 2013, FDA's Office of Prescription Drug Promotion (OPDP) posted the following enforcement letters on FDA's website[1]:

- Warning letter to Acorda Therapeutics, Inc., re: NDA #022250 AMPYRA (dalfampridine) Extended Release Tablets MA #223 (July 25, 2013) ("Acorda Warning Letter")
- Untitled letter to Spectrum Pharmaceuticals re: BLA #125019, ZEVALIN (ibritumomab tiuxetan) Injection for Intravenous Use MA #195 (July 23, 2013) ("Spectrum Untitled Letter")

The Office of Compliance and Biologics Quality (OCBQ) in FDA's Center for Biologics Evaluation and Research (CBER) and the Office of Compliance in FDA's Center for Devices and Radiological Health (CDRH) did not post any enforcement letters relating to advertising and promotion on FDA's website.

***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.***

## LETTERS ISSUED BY OFFICE OF PRESCRIPTION DRUG PROMOTION (OPDP)

### Acorda Warning Letter

OPDP alleged that a print ad for Ampyra was false or misleading because it omitted risk information.

*Minimization of Risk Information:* The print ad for Ampyra included the following claims: (1) The company logo and name of the drug, with the question, "**Has Multiple Sclerosis affected you or someone you care for?**"[2] and (2) "AMPYRA (dalfampridine) Extended Release Tablets, 10 mg is indicated as a treatment to improve walking in patients with Multiple Sclerosis (MS). This was demonstrated by an increase in walking speed."

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[1] Only enforcement letters posted to FDA's website in July 2013 are included herein. Letters issued in July but not posted to the website by July 31, 2013 will be summarized in our alerts for the months in which those letters are posted.

[2] Emphasis in print ad.

OPDP alleged that the print ad was misleading because it entirely omitted risk information. OPDP noted that the print ad stated, "This presentation is not medical advice or an attempt to provide medical advice. Talk to your healthcare provider to determine if AMPYRA is right for you." OPDP claimed, however, that this statement did not mitigate the omission of risk information in the print ad.[3]

## Spectrum Untitled Letter

OPDP alleged that a sales aid for Zevalin was false or misleading because it minimized the risks associated with Zevalin, overstated its efficacy, and omitted material facts in violation of 21 U.S.C. §§ 352(a), 321(n). Zevalin is indicated for the treatment of (1) relapsed or refractory, low-grade or follicular B-cell non-Hodgkin's lymphoma (NHL) and (2) previously untreated follicular NHL, with patients who achieve a partial or complete response to first-line chemotherapy.

*Minimization of Risk Information:* The front cover of the sales aid included a picture of an archer taking aim at a target populated with lymphoma cells. The back cover included an arrow lodged within the lymphoma cells on the bulls-eye. Page seven of the sales aid included the claims, "ZEVALIN **delivers radiation precisely** where it's needed"[4] and "Monoclonal antibody **specifically** targets the CD20 antigen found on **95%** of B-cell lymphomas."[5] The sales aid also included headers stating that Zevalin's side effects are "predictable and manageable."

According to OPDP, the sales aid misleadingly implied that Zevalin selectively targets lymphoma cells without harming healthy cells and tissues. OPDP contended the mechanism of action section of the approved product label states that Zevalin can damage healthy cells neighboring target cells. Further, FDA alleged that the clinical trial cited by the sales aid in support of the targeted destruction claim failed to support those claims. The sales aid cited a phase I/II study. According to FDA, however, this was insufficient because the objective of the phase I/II study was only to determine the maximum single tolerated dose of Zevalin without stem cell support. Further, although the sales aid included an asterisked disclosure that "Severe cytopenias persisting more than 12 weeks following administration can occur," OPDP stated that this did not mitigate the sales aid's overall misleading impression.

*Overstatement of Efficacy:* The sales aid included the following statements: "Patients reaching complete response after first-line treatment are more likely to experience improved overall survival" and "[d]ata from this study suggest a strong correlation between response quality after first-line treatment (complete response) and survival." According to OPDP, these statements (among others) misleadingly overstated Zevalin's efficacy by implying that Zevalin improved overall survival when used after first line treatment. OPDP contended that a study supporting Zevalin's approval showed that there was no improvement in overall survival for patients treated with Zevalin after first-line induction. Further, OPDP alleged that a study cited in the sales aid to support these claims did not contain any data evaluating Zevalin on any efficacy endpoint.

The sales aid also contained the following statements: "**Earlier treatment with Zevalin treatment regimen was shown to provide benefits**"[6] and "Earlier treatment with Zevalin may improve [overall response rate] ORR." According to OPDP, these and other similar claims of enhanced efficacy with earlier treatment of Zevalin were misleading. OPDP stated that the reference cited in support of these claims did not evaluate earlier versus delayed initiation of treatment over the same disease

[3] OPDP also stated that Acorda violated 21 C.F.R. 314.81(b)(3)(i) because it failed to submit Form FDA 2253 at the time of initial publication of the alleged drug advertisement.
[4] Emphasis provided by OPDP.
[5] Emphasis provided by OPDP.
[6] Emphasis in sales aid.

progression points (e.g., at first, second, third relapse, etc.). Instead, the study presented a retrospective comparison of outcomes across different patient populations. OPDP alleged that the higher ORR achieved by patients in first relapse (as opposed to after multiple relapses) may be attributable to the nature of the disease rather than Zevalin treatment.

Finally, OPDP noted that pie charts on pages 14 and 15 of the sales aid presented claims about enhanced complete response rates resulting from consolidation therapy with Zevalin. OPDP claimed that these charts misleadingly implied that consolidation therapy with Zevalin enhanced complete response rates for patients who had a response after first-line induction therapy, when this is not the case. According to OPDP, the trials cited in support of the pie charts did not include specified endpoints for improvements in complete response rates, and the claims in the sales aid were based on a post-hoc, exploratory subgroup analysis of the trial data.

*Omission of Material Fact:* The sales aid stated that "ZEVALIN patients experienced a median time to progression of 12.1 months vs. 10.1 months for rituximab patients." According to OPDP, this claim was misleading because it failed to disclose that, per Zevalin's product label, differences in time to progression were statistically insignificant between study arms.

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If you have any questions concerning the material discussed in this client alert, please contact the following members of our Food & Drug Practice Group:


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