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Drug Manufacturer Challenges the Constitutionality of FDA Regulations Related to Off-Label Marketing of Drugs and Medical Devices

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p>In a federal lawsuit recently filed against the Food and Drug Administration ("FDA"), Amarin Pharma, Inc. has preemptively asserted constitutional challenges to the FDA's restrictions on the ability of drug and medical device manufacturers to promote off-label uses of their products.[1] The case may prove to be a watershed moment within the pharmaceutical and medical device industry, which has for years complained about the FDA's practice of punishing manufacturers for promoting off-label uses of their products, even if the promotion is truthful and not misleading and there is evidence supporting the safety and efficacy of the off-label use.

Amarin, joined in the case by four co-plaintiff doctors, has asserted that it has a First Amendment right to make truthful and non-misleading statements about its drug Vascepa (a prescription omega-3 fatty acid), including statements about potentially beneficial uses that have not been approved by the FDA. The plaintiffs also assert that doctors have a constitutional right to receive such truthful and non-misleading statements.

The FDA's Regulation of Off-Label Uses

As explained in a previous Advisory,[2] the FDA generally prohibits drug and medical device manufacturers from providing information about off-label uses of their products to physicians and other health care professionals, except in narrow and specifically-tailored ways. First, manufacturers may, under certain circumstances, distribute reprints of medical or scientific journal articles and reference publications discussing off-label uses of their products. Second, manufacturers may respond to unsolicited inquiries about off-label uses of their drugs or medical devices. Manufacturers must be careful, however, to distinguish either option from marketing or promotional activity. For a more complete discussion of the two permitted options, please review our previous Advisory (https://www.clm.com/publication.cfm?ID=411&Att=170).

Although the FDA's practice of prohibiting off-label marketing suffered a setback in *United States v. Caronia*, 703 F.3d 149 (2d Cir. 2012), in which the Second Circuit reversed the conspiracy conviction of a pharmaceutical sales rep on the grounds that mere promotion of a scientifically supported off-label use was protected speech under the First Amendment, the FDA has not stopped enforcing its off-label marketing regulations and still considers off-label marketing as evidence of misbranding. Indeed, the impact of *Caronia* beyond individual criminal cases remains murky at best.

Amarin's Constitutional Challenge

Against that backdrop, Amarin has now asked a federal court to provide clarity by seeking a broad declaration that the FDA regulations related to off-label marketing violate its "First Amendment right to engage in truthful and non-misleading speech" and violate the doctors' "First Amendment right to receive such truthful and non-misleading information."[3] Amarin contends that such a declaration falls squarely within the Second Circuit's precedent in *Caronia*.

In its Complaint, Amarin alleges that its drug Vascepa has been approved by the FDA "for use as an adjunct to diet to reduce triglyceride levels in adult patients with *very* high triglycerides—defined as triglyceride levels of 500 mg/dL of blood or above." Although the FDA-approved use is limited to patients with "very high" triglycerides, Amarin asserts that "many doctors, including Doctor Plaintiffs, prescribe Vascepa to treat patients with persistently high triglycerides (i.e., 200-499 mg/dL of blood, despite the use of statins) to lower those patients' triglycerides and/or non-HDL cholesterol." *See* Complaint ¶5.

Moreover, Amarin states that it "has conducted a double-blind, placebo-controlled clinical trial demonstrating that Vascepa reduces triglyceride levels and has other favorable effects in adult patients with persistently high triglycerides." Amarin asserts that "FDA does not dispute the success of this trial, but has nonetheless recently advised Amarin that it refuses to approve the promotion of Vascepa for use in treating this population." Complaint ¶7. In light of FDA's refusal, Amarin may not provide information about the use of Vascepa for patients with persistently high triglycerides without risking significant liability. Amarin complains that it is prevented from providing such information despite the fact that the use of Vascepa for treating persistently high triglycerides has become common among physicians and the fact that Amarin's own well-designed clinical trial supports the safety and efficacy of such use.

Amarin asks the Court to allow it to disclose to doctors: (1) that "supportive but not conclusive research shows that consumption of EPA and DHA omega-3 fatty acids may reduce the risk of coronary heart disease;"[4] (2) that Amarin's study "demonstrates that Vascepa lowers triglyceride levels in patients with high [ ] triglyceride levels not controlled by diet and statin therapy; and (3) that a representative sample of "peer-reviewed scientific publications" supports the "potential effect of EPA on the reduction of the risk of coronary heart disease." Amarin also notes that it would include disclaimers that the FDA has not approved Vascepa to reduce the risk of coronary heart disease or to treat patients with persistently high triglycerides.

Amarin asserts that its proposed speech and disclaimers are truthful and not misleading, and thus "FDA's actions targeting lawful off-label promotion such as Amarin's are 'presumptively invalid' and subject to 'heightened' First Amendment scrutiny. Complaint ¶156. As Amarin points out, "Government restrictions on truthful and non-misleading promotional speech are invalid *unless* such restrictions directly serve a substantial government interest and are no more extensive than necessary." Complaint ¶155.

Conclusion

A final decision in this case would likely clarify whether and to what extent the FDA may restrict truthful and non-misleading statements about off-label uses. If so, the decision would have a significant impact on the pharmaceutical and medical device industry. Pending a resolution, manufacturers should continue to exercise caution against off-label marketing and promotion of its products. Indeed, Amarin's current challenge has not yet altered the FDA's existing regulatory regime and thus manufacturers could still find themselves subject to liability if they are caught promoting off-label uses.

For more information concerning the matters discussed in this publication, please contact the author **Michael H. Bauscher** (212-238-8785, bauscher@clm.com) or your regular CL&M attorney. **Alex D. Silagi** assisted in research for this advisory.

Endnotes

[1]*See Amarin Pharma, Inc., et al. v. U.S. Food & Drug Admin., et al.*, No. 15 CV 3588 (PAE)(JLC) (S.D.N.Y.) (filed May 7, 2015).

[2]*See* William F. Sondericker & Michael H. Bauscher, *Promoting Off-Label Uses of Drugs and Medical Devices: Manufacturers Should Exercise Caution Despite Reversal of Conspiracy Conviction in U.S. v. Caronia*, Client Advisory, Carter Ledyard & Milburn LLP (December 14, 2012), available at https://www.clm.com/publication.cfm?ID=411&Att=170.

[3]*Amarin Pharma, Inc. et al. v. U.S. Food & Drug Admin., et al.*, Complaint ¶17. Alternatively, the Plaintiffs argue that the FDA's regulations are unconstitutional vague in violation of the Due Process Clause of the Fifth Amendment. Complaint ¶18.

[4]Amarin points out that manufacturers of Omega-3 dietary supplements, which are not governed by the same regulatory regime as pharmaceutical drugs, are permitted to make this same assertion.

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