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March 16, 2007

By Facsimile [301-796-9877]
and First-Class Mail

Thomas Abrams, RPh, MBA
Director
Division of Drug Marketing, Advertising, and Communications
10903 New Hampshire Ave.
Bldg 22 Rm 1400
Silver Spring, MD 20993-0002

Re: NDA # 20-717
Provigil® (modafinil) Tablets [C-IV]
MACMIS # 14707

Dear Mr. Abrams:

On February 27, 2007, the Division of Drug Marketing, Advertising, and Communications (DDMAC) sent a warning letter to Cephalon, Inc. alleging that a handout for Provigil® (modafinil) Tablets "misbrands the drug in violation of" 21 U.S.C. §§ 352(a) & (f)(1) and 321(n) in that it recommends or suggests uses for Provigil that are not in the FDA-approved labeling, and thus creates new "intended uses" for Provigil for which the product lacks adequate directions for use, broadens the indication for Provigil, and fails to communicate any of the risks associated with its use. For the reasons set forth below, we request that DDMAC withdraw this warning letter. Further, we request once again that DDMAC respond to our numerous letters and citizen petition raising legal and policy concerns with DDMAC's regulation of materials disseminated about prescription drug products.

Inappropriate Regulation of Pharmacy and Therapeutics Committee Materials

DDMAC alleges that the handout was distributed to the Maryland Department of Health and Mental Hygiene's Pharmacy and Therapeutics Committee (P&T Committee) when Dr. Henry Kerasidis spoke at a public meeting regarding the inclusion of Provigil on the Committee's Preferred Drug List.

P&T committees receive information about drug products in a variety of ways, and different regulatory requirements apply depending on the type of information provided (*e.g.*, pharmacoecomic data provided to P&T committees in promotional labeling is governed by 21 U.S.C. § 352(a), scientific exchange is addressed in 21 C.F.R. § 312.7, and formulary dossiers submitted in response to unsolicited requests are outside of FDA's promotional authority entirely by operation of FDA policy). DDMAC has apparently determined that the handout, even though a preferred drug list communication, is subject to the same content regulation as conventional promotional labeling and advertising. This position is problematic.

Traditionally, DDMAC has implemented the promotional labeling and advertising provisions of the Federal Food, Drug, and Cosmetic Act by focusing on detail aids, print advertisements, and other promotional materials aimed at prescribers or (more recently) patients. These communications qualify as promotion because they recommend or suggest use of a product in a promotional context and propose that the prescriber order (or that the patient request an order of) the drug. It is inappropriate, we submit, for DDMAC to turn its attention to materials, like the handout, that are aimed at P&T committees.

As the FDCA recognizes, 21 U.S.C. § 352(a), such committees are capable of evaluating complex drug information for the purpose of making formulary decisions. Members of P&T committees and similar entities have extensive experience and expertise relevant to assessing scientific data relating to drugs. Members are charged with rendering decisions about the relative utility of drugs for a wide range of patients, and therefore such committees regularly seek and receive data that could be relevant to their decisions. Congress recognized the unique expertise of this audience when it passed the pharmacoeconomic language appearing in 21 U.S.C. § 352(a). *See* S. Rep. No. 105-43, at 42-43 (1997); H.R. Rep. No. 105-310, at 65-67 (1997). DDMAC's determination to treat the handout as essentially identical to conventional promotional labeling is, at best, in tension with that recognition.

This is at least the second occasion on which WLF has raised concerns about DDMAC's intrusion into reimbursement-related communications by regulated firms. WLF is concerned that DDMAC has adopted a policy—not expressly announced to the public but operational nonetheless—of scrutinizing reimbursement-related communications in the same manner as promotional labeling without first engaging in rulemaking or (at least) articulating its position in publicly available guidance. Such action would be cause for extreme concern from a policy perspective, given the increasing importance of information relating to the costs associated with various health-care interventions. We therefore urge DDMAC to ventilate these issues publicly, and to refrain from issuing further warning or untitled letters until a coherent policy has been adopted based on input from interested parties and based on considered evaluation of the relevant legal and policy considerations.

<u>Unsubstantiated Allegations of Misleadingness</u>

DDMAC alleges that the handout is false or misleading because it states or suggests that Provigil is safe and effective for use in the treatment of various disorders that do not appear in the FDA-approved labeling. This allegation is also problematic.

DDMAC presents no data to corroborate its interpretation of the handout. The only apparent basis for DDMAC's analysis of the meaning of the piece is the judgment of the DDMAC personnel involved in preparing and reviewing the warning letter. As we explained in the other letter we sent you today, regarding Rozerem, DDMAC's approach in this regard presents substantial issues under the First Amendment and under the Administrative Procedure Act. 5 U.S.C. § 706.

DDMAC does not even allege that anyone was actually misled by the handout. To the contrary: in the warning letter to Cephalon, DDMAC "acknowledge[s] that the claims [about Provigil] may be true." Rather, DDMAC appears to be merely fearful that someone might be misled by the handout—despite DDMAC's concession and despite the sophistication of the intended audience. This approach is incompatible with the First Amendment. *See Virginia State Bd. v. Virginia Citizens Consumer Council*, 425 U.S. 748, 769, 773 (1976).

Procedural Irregularities

We are troubled by how long DDMAC waited before issuing the warning letter. The allegedly violative communication occurred on August 17, 2006, which means that DDMAC waited almost six months to issue the warning letter. Perhaps the delay in issuing a letter reflects internal disagreement over the appropriateness of DDMAC action, or concerns about the public health effects of DDMAC regulation of reimbursement-related communications. In any event, as a matter of sound administrative procedure, DDMAC should not issue letters objecting to conduct that is so dated. Otherwise, regulated firms have no way of knowing whether a communication they made many months ago might someday be the subject of a DDMAC complaint. The more time that elapses, the more difficult it becomes for companies to respond comprehensively to DDMAC's expressed concerns, and the less likely it is that the matter will be resolved satisfactorily. Whatever the reason, DDMAC should take greater care to ensure that its warning and untitled letters are issued in a timely fashion.

Conclusion and Requested Action

We request that DDMAC immediately withdraw the warning letter to Cephalon concerning Provigil. We urge DDMAC to cease the issuance of warning and untitled letters and advisory correspondence that contain allegations the same as or similar to those described above.

The deficiencies described in this letter do not necessarily constitute an exhaustive list. DDMAC must ensure that its actions with respect to prescription drug promotion, and to other forms of commercial speech, comply with the First Amendment, and do not exceed FDA's statutory authority under the Federal Food, Drug, and Cosmetic Act.

Sincerely,

Richard A. Samp

Chief Counsel

cc: Sheldon Bradshaw (GCF-1)