



TRANSMITTED BY FACSIMILE

Kathryn A. Roberts
Director, Regulatory Affairs
Johnson & Johnson
Pharmaceutical Research and Development, L.L.C.
420 Delaware Drive
Suite 300, Mailstop 964
Fort Washington, PA 19034

**RE: NDA # 21-121
CONCERTA[®] (methylphenidate HCl) Extended-release Tablets [CII]
MACMIS ID # 15567**

Dear Ms. Roberts:

The Division of Drug Marketing, Advertising, and Communications (DDMAC) of the U.S. Food and Drug Administration (FDA) has reviewed professional convention panels (CON06-107 A,B,D,E,F,G) for Concerta (methylphenidate HCl) Extended-release Tablets [CII] (Concerta) submitted by Johnson & Johnson Pharmaceutical Research and Development, L.L.C. (Johnson & Johnson) under cover of Form FDA 2253, as well as a consumer webpage¹ for Concerta. These pieces are false or misleading because they overstate the efficacy of Concerta and omit material facts regarding use of Concerta. Thus, the promotional materials misbrand the drug in violation of the Federal Food, Drug, and Cosmetic Act (Act), 21 U.S.C. 352(a), 352(n), & 321(n), and FDA's implementing regulations. Cf. 21 CFR 202.1(e)(3)(i) & (e)(6)(i).

Background

According to its FDA-approved product labeling (PI)², Concerta is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD). The Indications and Usage section of the PI also includes information regarding special diagnostic considerations, the need for comprehensive treatment, and information about long-term use.

¹ Available at <http://www.concerta.net/concerta/pages/teens-after.jsp>. Last accessed September 25, 2008.

² The PI submitted with the convention panels and referred to within this letter is dated February 2006. The most recent PI is dated March 2007. Although not relevant to this letter given the date the piece at issue was disseminated, we note that the current PI includes changes to the Warnings section.

The Concerta PI contains a Boxed Warning regarding drug dependence. The PI also contains numerous contraindications, including use in patients with marked anxiety, tension, and agitation, use in patients with glaucoma, use in patients with motor tics or with a family history or diagnosis of Tourette's syndrome, and use during treatment with monoamine oxidase inhibitors or within a minimum of 14 days following discontinuation of a monoamine oxidase inhibitor. Additionally, the PI contains warnings regarding use for depression, use for fatigue, potential for long-term suppression of growth, use in patients with psychosis, use in patients with seizures, potential for gastrointestinal obstruction, sudden death in patients with structural cardiac abnormalities, use in patients with hypertension and other cardiovascular conditions, visual disturbances, and use in children under six years of age. Periodic CBC, differential, and platelet counts are advised during prolonged therapy. The most common treatment-emergent adverse events reported in children relative to placebo include headache (14%, 10%), upper respiratory tract infection (8%, 5%), and abdominal pain (7%, 1%). The most common treatment-emergent adverse events reported in adolescents relative to placebo include headache (9%, 8%), accidental injury (6%, 3%), and insomnia (5%, 0%).

Overstatement of Efficacy

The convention panels claim, "CONCERTA[®] helps children improve academic performance throughout the day." This presentation is misleading because it implies that use of Concerta will lead to an improvement in academic performance throughout the day when this has not been shown by substantial evidence or substantial clinical experience. We acknowledge that the cited reference³ does support improvement in math scores for patients treated with Concerta compared with placebo, and that improvement in math scores is commonly used to assess level of attention. However, the claim implies a much broader academic improvement; specifically, by stating that Concerta will "Improve academic performance throughout the day." A student studies many subjects throughout the school day, including math, and your claim suggests that the student will achieve better academic performance throughout the day in all of their subjects. Improvement in attention, as evidenced by increased numbers of math problems answered correctly, has not been correlated with an improvement in academic performance throughout the day, an endpoint which has not been studied. While the available data supports the presentation in the graph regarding percentage of math problems answered correctly, they do not support the broader claim made in the convention panels about academic performance throughout the day.

Similarly, the webpage, entitled "After School," presents claims about the impact of treatment with Concerta on after school activities. Specifically, the page states:

Adolescence is a time of greater independence and responsibility. For most teens, the after-school hours are filled with plenty of activities, including:

- sports

³ Pelham WE, Gangy EM, Burrows-Maclean L, et al. Once-a-day Concerta methylphenidate versus three-times-daily methylphenidate in laboratory and natural settings. *Pediatrics*. 2001;107(6)

- o clubs
- o part-time jobs
- o socializing with friends
- o household chores
- o and, of course, homework

ADHD can have an impact on all of these activities, so you want to be sure your teen's medication is doing its job.

CONCERTA® provides consistent symptom management throughout the day, for up to 12 hours, helping your teen focus and manage behavior. This may benefit your teen's ability to socialize with family and friends, and pursue interests and hobbies outside of school. You also won't have to worry about whether your teen needs another dose of medication, because a single dose in the morning is all it takes.

As a parent, you naturally want your teen to do well in all areas of his or her daily life. With once-daily CONCERTA®, you can be confident that symptoms are being managed no matter what he or she is doing.

This presentation is misleading because it asserts improvement with Concerta in a broad array of adolescent after school activities, such as athletics, clubs, and performance in part-time jobs, when this has not been demonstrated by substantial evidence. While Concerta has been shown to improve total scores on the Attention Deficit Hyperactivity Disorder Rating Scale (ADHD-RS), which measures ADHD symptoms such as fidgeting, not listening, and talking excessively, what has not been shown is that this improvement in ADHD-RS total scores is correlated with a positive effect on adolescents' ability to pursue interests and hobbies outside of school and to do "well in all areas of [their] daily life."

Omission of Material Fact

Promotional materials are misleading if they fail to reveal material facts with respect to consequences that may result from the use of the drug as recommended or suggested by the materials. The convention panels omit material facts regarding the risk of long-term growth suppression in five of the six convention panels. According to the Warnings section of the PI (in pertinent part):

...[G]rowth should be monitored during treatment with stimulants, and patients who are not growing or gaining height or weight as expected may need to have their treatment interrupted.

The presentation of this risk information on one panel is not sufficient to ensure that the claims in each convention panel are truthful and non-misleading.

Conclusion and Requested Action

For the reasons discussed above, the professional convention panels and webpage misbrand Concerta in violation of the Federal Food, Drug, and Cosmetic Act (Act), 21 U.S.C. 352(a), 352(n), & 321(n), and FDA's implementing regulations. *Cf.* 21 CFR 202.1(e)(3)(i) & (e)(6)(i).

DDMAC requests that Johnson & Johnson immediately cease the dissemination of violative promotional materials for Concerta such as those described above. Please submit a written response to this letter on or before October 7, 2008, stating whether you intend to comply with this request, listing all violative promotional materials for Concerta the same as or similar to those described above, and explaining your plan for discontinuing use of such materials. Please direct your response to me at the Food and Drug Administration, Center for Drug Evaluation and Research, Division of Drug Marketing, Advertising, and Communications, 5901-B Ammendale Road, Beltsville, MD 20705-1266, or facsimile at 301-847-8444. In all future correspondence regarding this matter, please refer to MACMIS # 15567 in addition to the NDA number. We remind you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for Concerta comply with each applicable requirement of the Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Robert Dean, M.B.A.
Group Leader
Direct to Consumer (DTC) Group 1
Division of Drug Marketing,
Advertising, and Communications

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this page is the manifestation of the electronic signature.**

/s/

Robert Dean
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