

September 13, 2002

Dockets Management Branch  
HFA-305  
Food and Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, MD 20852

Re: Comments to Docket 02N-0209

Dear Sir or Madam:

The Blue Cross and Blue Shield Association (BCBSA) strongly supports the Food and Drug Administration's (FDA's) continued regulation of direct-to-consumer (DTC) promotion of prescription drugs as a critical function of its public health and safety mission. As such, we appreciate the opportunity to comment on FDA's policies related to commercial speech, advertising and the First Amendment.<sup>1</sup>

BCBSA has two recommendations in response to the FDA notice:

1. We believe that it is critical, in light of recent statutory violations by advertisers, that the FDA retain strong oversight of DTC promotion to assure that consumers receive clear and understandable information about the risks and benefits of prescription drugs; and
2. We believe that DTC ads should emphasize, when appropriate, that a particular drug is only one of a range of treatment choices available to patients.

BCBSA agrees with a prior FDA statement that although DTC advertising "may alert consumers to new information and facilitate treatment of their medical problems, it also may confuse consumers and adversely impact the relationship between patients and their health care providers."<sup>2</sup> BCBSA believes that use-inducing promotion raises issues with respect to consumer safety, including inappropriate demand for and use of advertised drugs. This is especially a concern since a review of recent warning letters and notice of violation letters from the agency regarding DTC advertisements

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<sup>1</sup> See 67 Fed. Reg. 34,942 (May 16, 2002).

<sup>2</sup> See 66 Fed. Reg. 15,494 (March 19, 2001).

demonstrates that drug manufacturers do not always present DTC advertisements that are truthful and not misleading.

As DTC ads for new therapies continue to saturate the media, the FDA must likewise continue to ensure that consumers receive clear and understandable information about the risks and benefits of prescription drugs. In addition, BCBSA recommends that FDA take steps to assure that consumers, in consultation with their health care providers, understand the full range of treatment alternatives, including lower-cost generic drugs, that may be available.

BCBSA comprises 42 independent, locally operated Blue Cross and Blue Shield companies that collectively provide healthcare coverage for 84.7 million -- nearly 30 percent of all Americans. Blue Cross and Blue Shield Plans have extensive experience in providing prescription drug coverage through a variety of products and delivery mechanisms designed to meet the quality and value demands of their customers.

## **I. Background On FDA Regulation of Advertising**

The Federal Food, Drug, and Cosmetic Act (FDCA) requires that advertisers of prescription drugs disclose in advertisements certain information about the advertised product's uses and risks. For prescription drugs, the FDCA requires advertisements to contain "information in brief summary relating to side effects, contraindications, and effectiveness."<sup>3</sup> The resulting information disclosure is commonly called the "brief summary."

The prescription drug advertising regulations distinguish between print and broadcast advertisements.<sup>4</sup> Print advertisements must include the brief summary, which contains each specific risk and contraindication from the product's approved package labeling. Broadcast advertisements must disclose the product's major risks in either the audio or audio and visual parts of the presentation; this is sometimes called the "major statement."

Broadcast advertisements are also required to present a brief summary or, alternatively, may make "adequate provision ... for dissemination of the approved or permitted package labeling in connection with the broadcast presentation."<sup>5</sup> This is referred to as the "adequate provision" requirement. The regulations thus specify that the *major statement*, together with *adequate provision* for dissemination of the product's approved labeling, can provide the information disclosure required for broadcast advertisements.

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<sup>3</sup> See 21 U.S.C. 352(n).

<sup>4</sup> See 21 CFR § 202.1.

<sup>5</sup> See 21 CFR § 202.1(e)(1).

The advertising regulations further list 33 ways in which prescription drug advertisements can be false or misleading. In practice, such ads are most commonly judged to be false or misleading because they: (1) selectively or inaccurately represent or report data; (2) make claims of superiority based on less than adequate, well-controlled scientific studies; (3) use in vitro or animal data to suggest clinical significance when such significance has not been demonstrated; or (4) represent that the product's indications are broader than those actually approved by the FDA.

## **II. FDA's Role Is To Insure That Consumers Receive Clear and Understandable Information About The Risks and Benefits of Prescription Drugs**

Although BCBSA believes that DTC advertisements may provide some positive benefits, these potential benefits are negated when consumers do not receive accurate, understandable and truthful information. As commercial speech is protected by the First Amendment only so long as it is truthful and not misleading, FDA must not treat the decision in *Western States Medical Center*<sup>6</sup> as a repudiation of its mandate to protect consumers from false or misleading advertising. Furthermore, despite some of the potential positive benefits that may result from the use of DTC advertising, it is clear that the primary purpose of DTC advertising, as with all advertising, is to stimulate demand for a product.

### **A. DTC Ads are Effective in Stimulating Demand For Prescription Drugs**

The volume of DTC advertising continues to increase. According to a 2000 study by the National Institute for Healthcare Management (NIHCM), spending on DTC ads increased to \$2.5 billion in 2000, from \$1.8 billion in 1999 and \$791 million in 1996. This investment translates to explosive sales of newly approved drugs and steep market penetration.

For example, increases in the sales of the 50 drugs most heavily advertised to consumers in 2000 were responsible for almost half of the \$20.8 billion (18.8%) one year increase in retail spending on prescription drugs from 1999 to 2000. Retail sales of these 50 drugs rose an aggregate 32 percent from 1999 to 2000 compared to less than 14 percent for all other prescription drugs (numbering about 9,850), the study shows. This use-inducing advertising raises issues with respect to consumer safety in the absence of complete information about product benefits and risks.

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<sup>6</sup> *Thompson v. Western States Medical Center*, 535 U.S. \_\_\_\_, (slip opinion)(2002). The Supreme Court in *Thompson* struck down, as violative of the First Amendment, restrictions in the Food and Drug Administration Modernization Act related to the advertising or promotion of the compounding of any particular drug, class of drug, or type of drug. The Court ruled that even assuming the restrictions directly advanced the government's important interest in maintaining the integrity of FDA's new drug approval process, that interest could have been attained without imposing such restrictions. However, the decision did not address or concern any restrictions or regulations dealing with the advertising of non-compounded prescription drug products.

Both consumer and physician surveys suggest that DTC ads for prescription drugs are effective in stimulating demand for branded products. Prevention magazine conducted a consumer survey in 1998, 1999, and 2000 and found that the number of U.S. adults who had seen or heard a DTC prescription drug advertisement rose sharply over this time period. By March 2000, 80 percent of respondents could recall seeing or hearing an ad for a specific product compared to 63 percent in 1997. Prevention estimated that by early 2000, between 148 and 169 million U.S. adults had seen or heard a prescription drug ad.<sup>7</sup>

This same survey also showed that such ads did impact the relationship between patients and their health care providers. In 2000, 32 percent of respondents who had seen a prescription drug ad talked with their doctors about an advertised medication. Within this group, 26 percent reported that they had asked their doctors for a prescription and 81 percent reported that their physicians complied with their request.

This increased demand for prescription products raises the issue of whether patient requests for particular drugs represent the best available therapy including alternatives and whether DTC advertising may actually impair a physician's ability to prescribe the best available therapy by creating unrealistic consumer demands and preferences.

***B. Consumers May Not Receive Fair, Balanced and Non-Misleading Information***

BCBSA has reviewed numerous warning letters and notice of violation letters recently issued by FDA relating to DTC advertisements.<sup>8</sup> A review of these letters suggests that such ads do not always convey fair and balanced information to consumers.

According to BCBSA's review, during the past two years some of the most heavily promoted drug products have been the target of warning letters or notice of violation letters charging that their DTC advertisements were "false, lacking in fair balance, or otherwise misleading in violation of the Federal Food, Drug, and Cosmetic Act" in some manner. These include:

- Avapro (irbesartan);
- Celebrex (celecoxib);

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<sup>7</sup> Prevention Magazine, "International Survey on Wellness and Consumer Reaction to DTC Advertising of Rx Drugs" (Emmaus, Pennsylvania: 2000): 46.

<sup>8</sup> FDA warning and notice of violation letters are one of the enforcement mechanisms employed by FDA. A Warning Letter is a written communication from FDA notifying a company that the agency considers one or more products, practices, processes, or other activities to be in violation of the FDCA. A Warning Letter states that the failure to take appropriate and prompt action to correct and prevent any future repeat of the violations noted in the Warning Letter may result in an administrative or regulatory action. Warning Letters are typically issued for repeated or significant violations. Notice of violation letters are issued for less serious violations, but nevertheless communicate FDA's belief that a violation of the FDCA has occurred. Such letters will normally request that a violative promotion be ceased immediately.

- Claritin (loratadine);
- Glucophage (metformin hydrochloride);
- Lipitor (atorvastatin calcium);
- Prevacid (lansoprazole);
- Prilosec (omeprazole);
- Sarafem (fluoxetine HCl);
- Taxol (paclitaxel); and
- Viagra (sildenafil citrate)

A review of FDA's Web site reveals that the agency issued nearly 50 warning and notice of violation letters regarding specific violations related to DTC advertisements since January 2000. A sampling of these violations is included below.

In a warning letter to the maker of Prilosec the agency said:

- “Your broadcast advertisement #161827 for Prilosec contains audio representations and suggestions about Prilosec yet fails to include information relating to Prilosec's major side effects and contraindications. In addition, in the absence of a brief summary, the advertisement fails to make adequate provision for disseminating the approved product labeling.”<sup>9</sup>

In a warning letter to the maker of Viagra:

- “Your ‘Valentine's Day’ broadcast advertisement for Viagra contains written and graphic representations and suggestions about Viagra, yet fails to include information relating to Viagra's major side effects and contraindications. In addition, in the absence of a brief summary, the advertisement fails to make adequate provision for disseminating the approved product labeling.”<sup>10</sup>

In a warning letter to the maker of Celebrex:

- “The 60-second ‘full product’ TV advertisement is misleading because the totality of the images, the music, and the audio statements that you present overstate the efficacy for Celebrex.”<sup>11</sup>

In a Notice of Violation letter to the manufacturer of Lipitor:

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<sup>9</sup> See FDA Warning Letter dated February 4, 2000 to Douglas N. Dobak, Quality Liason Leader, AstraZeneca L.P.

<sup>10</sup> See FDA Warning Letter dated February 2, 2000 to Rita Wittich, Director, Regulatory Affairs, Pfizer Pharmaceuticals.

<sup>11</sup> See FDA Warning Letter dated November 14, 2000 to Jerome M. Prah, Associate Director, Regulatory Affairs, G.D. Searle & Co.

- The ad misleadingly suggests that Lipitor is safer than other statins. ... The Lipitor "Brief Summary" part of the DTC print ad is misleading because it indicates that Lipitor may lack the side effects of other members of the statin class of lipid-lowering medications.<sup>12</sup>

In a Notice of Violation letter to the manufacturer of Prevacid:

- "This TV Ad is misleading because it fails to clearly communicate to the typical consumer the definition and limitations of the approved indications for Prevacid. . ." <sup>13</sup>

A review of these warning and notice of violation letters demonstrate that consumers cannot always be assured that truthful and accurate information will be communicated in DTC advertisements. In addition, FDA enforcement occurs after the potentially misleading information has been disseminated to a wide audience. For example, on average, one primetime advertising spot airing nationwide on a major network reaches more than 11 million adults age 18 and over.<sup>14</sup> Similarly, a DTC ad in *Time* magazine is seen by nearly 22 million adults age 18 and over.<sup>15</sup> Because most prescription drug companies run more than one ad in a given month, this audience begins to increase dramatically. According to one media source, 52 primetime spots for Celebrex were aired in July 2002, reaching nearly 300 million adults age 18 and over, or 60 percent of the American population in that demographic.<sup>16</sup>

Furthermore, while the volume of DTC advertising continues to increase, FDA has designated just five full-time employees to review ads, creating increased difficulties in attempting to police such advertising. Thus while commercial speech may be protected where it is truthful and not misleading, FDA's responsibility to ensure drug advertisements are truthful and accurate should be paramount and undeterred.

This sampling of warning and notice of violation letters also is consistent with physician viewpoints on the quality and objectivity of the information presented in DTC ads. In a 1998 survey of 3,000 doctors, Scott-Levin found that more than half of physicians disagreed with the statement, "DTC advertising is a reliable source of information." In addition, more than 60% disagreed with the statement, "DTC advertising is an objective source of information."

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<sup>12</sup> See FDA Notice of Violation Letter dated August 12, 2002 to Christopher A. Graham, Director Worldwide Regulatory Strategy, Pfizer Inc.

<sup>13</sup> See FDA Notice of Violation Letter dated August 2, 2002 to Una Oretell, Assistant Director, Regulatory Affairs, TAP Pharmaceutical Products Inc.

<sup>14</sup> Nielsen DMA Planners Guide, February 2002.

<sup>15</sup> MRI Doublebase, 2001.

<sup>16</sup> CMR, July 2002.

### **III. BCBSA Recommendations For Continued FDA Regulation and Oversight**

#### **A. *FDA Should Continue To Monitor DTC Advertisements For Truthfulness and Accuracy***

Because prescription drug advertising is not subject to preapproval requirements, in order to adequately protect the public from false and misleading advertising, FDA must continue to monitor DTC advertisements. Although the post-marketing reporting requirements require the submission of advertisements at the time of initial publication, it is clear that this requirement is not complied with in all instances.<sup>17</sup>

BCBSA believes that, unlike many other consumer-advertised products, prescription drugs have significant benefits, but also significant risks that must be adequately conveyed to consumers. This critical function to ensure that prescription drugs are advertised in this manner rests squarely with the agency, and the agency must balance the requirements of free speech with vigilant to protection of the public health and safety.

#### **B. *DTC Ads Should Emphasize The Range of Treatment Choices Available***

The role of a physician is to advise patients about the choice of available therapies, including both prescription and non-prescription alternatives, and to recommend a therapy based on potential side effects from treatments, relative efficacy of treatments and cost factors — including the availability of generic drugs. Advertisements that provide consumers information only on a single treatment may impair the ability of prescribers to substitute alternative or even non-prescription treatments.

Studies have suggested that physicians may sometimes accommodate patient requests for particular drugs not because they believe such treatments represent the best available therapy, but because they fear alienating the patient by refusing to prescribe specific brand products.<sup>18</sup> Thus DTC ads should emphasize that a particular drug is only one of a range of treatment choices available. BCBSA recommends that FDA require in DTC ads language such as "Consult your health care provider about the range of treatment alternatives that may be available."

### **IV. Conclusion**

BCBSA applauds the FDA for addressing this critical health care issue and appreciates this opportunity to comment on these issues. BCBSA supports FDA's continued regulation of DTC promotion of prescription drugs and is hopeful that the agency will

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<sup>17</sup> See 21 CFR § 314.81(b)(3)(i).

<sup>18</sup> Rebecca K. Schwartz, Stephen B. Soumerai and Jerry Avorn, "Physician Motivations for Non Scientific Drug Prescribing", *Social Sciences and Medicine*, Vol. 28, No. 6 (1989): 577-582.

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continue to ensure that consumers and their doctors receive complete, clear and accurate information on the full range of available treatments.

Sincerely,

A handwritten signature in black ink, appearing to read "Mary Nell Lehnhard". The signature is written in a cursive, flowing style.

Mary Nell Lehnhard  
Senior Vice President

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