

**Comments of
The Prescription Project, Community Catalyst and
Prescription Access Litigation, Community Catalyst**

**Concerning
Limitations and Risks of Direct-to-Consumer Advertising
Docket No. FDA-2008-N-0226**

September 26, 2008

The Prescription Project of Community Catalyst, Inc., a non-profit health care advocacy organization based in Boston (www.prescriptionproject.org) and Prescription Access Litigation LLC, a coalition of over 130 organizations representing consumers, health care advocates, seniors, labor union members, legal services organizations, and others (www.prescriptionaccess.org) submit to the FDA that direct-to-consumer advertising (DTCA) produces no proven public health benefits and likely plays a role in driving unnecessary use of pharmaceuticals. Manufacturer-sponsored television advertisements, in particular, are ill-suited to effective communication of risk-benefit information about prescription drugs. Elderly consumers, the less-educated and those with English as a second language may be at particular risk for misunderstanding the potential risks and benefits associated with advertised drugs.

There are few reliable studies establishing the effect of DTCA on prescribing trends and health outcomes. However, available research largely shows that: DTCA influences patients to discuss advertised treatments and conditions with their doctors; ¹⁻³ patient requests for specific treatments are frequently successful; ^{3,4} and DTCA campaigns are correlated in time with increased prescriptions for the advertised drug. ^{3, 5-7}

DTC advertising is overwhelmingly concentrated in a few drug classes, ⁸ which may not represent important therapeutic advances. Moreover, advertising does not correlate with the burden of disease. Advertised products are almost always new to market and therefore, by definition, have unknown safety profiles. Encouraging unnecessary use of new products that provide no clear clinical benefit puts consumers at risk. When the advertised drug has risks which have not been fully or appropriately conveyed, such increased prescribing jeopardizes the public health.

DTCA YIELDS LOW COMPREHENSION OF RISK INFORMATION, PARTICULARLY IN ADULTS WITH LOW LITERACY

Evidence suggests that many consumers fundamentally misunderstand the basis under which FDA allows DTCA. One survey of consumers (reviewed by Wilkes *et al.*)⁹ found that 21 percent believed that only “extremely effective” drugs could be marketed directly to consumers. In addition, consumers held other mistaken beliefs:

43 percent believed that only “completely safe” drugs could be advertised directly to consumers, 22 percent thought that advertising of drugs with serious side effects had been banned.

Of course, no drug is “completely safe.” DTC advertising does not provide consumers with the information to assess the severity or likelihood of potential risks, or the likelihood of obtaining clinical benefit. Certain demographic groups – particularly the elderly, those with less education or English as a second language – may be less able to adequately assess such risks and benefits, and less able to evaluate the rapid-fire information presented in a television commercial. In a study assessing comprehension of direct-to-consumer ads, adults with limited literacy were much less likely to understand risk information compared with the company’s positive messaging (OR 0.28; CI 0.20-0.40).¹⁰

THE MESSAGE FROM TELEVISION

DTC television advertising is ubiquitous. However, the true message of such ads is conveyed through images (healthy, beautiful people), which provide no basis for a rational assessment of potential drug risks or benefits. Cline, in her analysis of drug advertisement imagery, reports that more than 90% of examined print ads depicted “identity rewards” – personal models that consumers identify with and want to emulate.¹¹ Ruth S. Day, researcher and Director of the Medical Cognition Laboratory at Duke University, has presented testimony to the House

Committee on Energy and Commerce describing her research on consumer comprehension of drug information. Her major finding has been that overall, subjects are able to report the benefits discussed in drug ads with much greater accuracy than the risks – a striking 80% versus 20% on average. Her analysis focuses on cognitive accessibility, which she asserts is much higher for the presentation of benefit information. Cognitive accessibility is heightened for drug benefits by devoting more time to them, by frequently repeating the drug name and benefits, and by using easy to understand language. By contrast, drug risks are often presented with more difficult language in a shorter time span, are placed in unfavorable locations, or are reported simultaneously with audio or visual distractions.¹²

DTCA DRIVES PRESCRIBING, BUT NOT ALWAYS IN THE PATIENT'S BEST INTEREST

Proponents of DTCA often proclaim the benefits of increased communication between patients and doctors. It is certainly true that patient prescription requests stimulated by DTCA are not in and of themselves inappropriate. However they become a serious problem when they result in medically unnecessary treatment.. At best such treatment needlessly inflates health costs. At worst this spike in prescribing exposes a large population to the health risks of a newer (thus less-tested) drug. This was clearly illustrated when prescriptions for cyclooxygenase-2 (COX-2) inhibitors soared between 1999 and 2002. Vioxx (a COX-2) was the most heavily promoted drug in 2000 and was subsequently determined to be responsible for an estimated 88,000 to 140,000 cases of serious coronary heart disease and an estimated 38,000 to 61,000 deaths in the USA.¹³

For a small subgroup of patients (those at risk of gi bleeds), Vioxx may have been an appropriate first-choice medication. But 63% of the growth in COX-2 prescriptions between 1999 and 2002 was for patients at low risk for adverse events from traditional NSAIDs, who thus should not have been prescribed Vioxx as a first-line therapy.¹⁴ Advertising drove indiscriminate and costly use of this new drug.

The elderly population may bear an increased risk of the effects of inappropriate prescribing due to greater susceptibility to certain adverse effects. For example, elderly patients prescribed sleeping pills are at high risk of falling.¹⁵ Yet, DTCA campaigns for widely advertised sleeping

pills fail to make this risk clear. This is particularly important given that sleep-enhancing effects of these drugs may be statistically significant, but clinically of little importance (for example, sleep latency of 30 minutes for one widely advertised pill versus 45 minutes for placebo, with a difference in total sleep duration of only 15 minutes).¹⁶ And some evidence indicates that elderly patients may be especially likely to receive treatment in response to DTCA-inspired requests.¹⁷

Other heavily advertised products that provide little or no meaningful clinical benefit for many patients include cholesterol-lowering agents (for patients without heart disease), allergy treatments, and Alzheimer's drugs. DTC advertising for these products increases the likelihood that patients will be unnecessarily exposed to adverse events.

DTCA's ability to promote unnecessary prescribing is further demonstrated by a 2005 study published in *JAMA*, which showed the influence of patients' DTCA-prompted requests for antidepressants -- one of the drug classes most heavily advertised to consumers. Trained actors posing as patients were sent into clinics presenting signs of either major depression or adjustment disorder. "Patients" with symptoms of depression requesting Paxil (the antidepressant chosen for the study) were more likely to receive Paxil than those making a general request for medication or no request (27%, 2% and 4.2%, respectively; $p < 0.001$). For symptoms of adjustment disorder, antidepressant prescribing rates were 36.7%, 10.2%, and 0%, respectively ($p < 0.001$). Importantly, the authors report that no evidence supports the use of Paxil for adjustment disorder and minimal evidence for the use of the drug for minor depression.⁴ Thus, DTCA has the demonstrated potential to drive medically inappropriate use. This may be particularly true of "reminder ads," which mention a product, but not an indication.

SYSTEMATIC REVIEW OF THE DTCA LITERATURE: NO EVIDENCE OF BENEFITS

Most published academic studies of the effects of DTCA are patient and prescriber perception surveys. There are few reliable data examining the effects of DTCA on prescribing and health. The only systematic review and evaluation of studies on the effects of DTCA found that just four of 2853 citations met strict inclusion criteria. Of these four publications, none found evidence

that DTCA imparts health benefits, and some reported concerns.¹⁸ The authors of the systematic review conclude that the onus is on the proponents of DTCA to demonstrate its benefit.

One striking survey compared responses of patients and doctors before and after appointments at two primary care practices to establish the effect of DTCA on prescribing. In both locations, patients reporting higher exposure to advertising also requested more advertised drugs. In both locations, around 75% of those requesting advertised drugs received a prescription. Yet 50% of prescribing physicians reported that choice of drug as “possible” or “unlikely” choice for similar patients,³ suggesting the role of DTCA in influencing prescribing choices. FDA’s own 2002 physician survey reports that nearly 50% of doctors reported feeling some pressure to prescribe the drug requested by the patient.¹

INDUSTRY ASSERTIONS

Industry representatives assert that “a wealth of data from independent studies... show that direct-to-consumer advertising of prescription medications has a positive impact on public health.”¹⁹ It may be useful to review the sources cited by industry to support this assertion. It is important to note that of the eight publications cited, only one (Weissman *et al.*, 2003) examines the actual effects of DTCA on prescribing. Four are patient and physician opinion surveys; one is a report by the US General Accounting Office; and two are communications made by Pfizer Inc. or PhRMA, an industry trade group, to the FDA. In addition, we note that some of these sources express concerns about DTCA that are not reflected in the industry comments.

DTCA’s effects on prescribing have been examined by Weissman *et al.*, who found, based on telephone surveys of patients, that one in four patients who asked about an advertised drug received a new diagnosis, and that 43% of these new diagnoses were for high priority conditions (as defined by AHRQ/IOM criteria); 57% were not high priority conditions. However, study respondents with multiple DTCA-inspired visits were asked to focus only on the visit that was most important to their health, likely skewing responses toward high priority conditions. Moreover, the study provides no information on whether high-priority diagnoses were more or less common in DTCA-inspired physician visits than in those not inspired by advertising.

Patients schedule visits with a physician for a variety of reasons, based on a variety of sources of information. In this study, patients were about equally likely to receive a new diagnosis whether DTCA played a small or large role in the decision to see a doctor. This undermines the suggestion that DTCA plays an important role in the identification of serious health conditions. In addition, it is important to note that the methodology of this study did not allow for any assessment of the validity of diagnoses or appropriateness of treatment. No differences in health effects were identified between patients who received the advertised drug and those who took other drugs. As the authors note, retrospective patient self-reports of outcomes may be of limited utility.

It may be important to note that a subsequent physician survey by the same researchers found that erectile dysfunction (E.D) was by far the most common new diagnosis stimulated by patients asking about an advertised drug.²⁰ That E.D. was not among the 6 most common diagnoses on the earlier patient survey suggests possible limitations of the self-report methodology. The estimate of new high-priority diagnoses is lower in physician survey study: just 7.5% of all DTCA visits resulted in a high-priority diagnosis. In both studies, it is impossible to estimate what proportion of high-priority diagnoses would have been made irrespective of exposure to DTCA.

Industry submissions cite the FDA's own 2004 report on their 1999 and 2002 patient and physician surveys on DTCA to state that DTC raises consumer awareness of health conditions and issues. However the discussion section of this same report states: "Both patients and doctors indicate that DTC advertisements overstate drug efficacy and do not present a fair balance of benefit and risk information."¹ Further, as noted above, the FDA reports that nearly half of the physicians surveyed reported feeling some pressure to prescribe the drug requested.¹

An industry submission cites a Kaiser Family Foundation survey of physicians²¹ asserting that doctors are twice more likely to say DTC-prompted inquiries have a positive effect than negative. However, a fuller reading of the study results shows that while 42% of physicians reported positive effects of DTC-inspired patient queries, 56% of physicians reported that DTCA produced either negative effects or no effect (21% and 35% of physicians, respectively).

Industry representatives also make frequent reference to Prevention Magazine's annual consumer perception survey on DTCA. One of the most used data points from these surveys is consumer awareness of risk information in DTC TV Ads (79% in 2004).²² It is important to note that this data measures consumer awareness of the *existence* of risk information, not comprehension of that information.

OTHER CONCERNS

DTCA has also been used for "disease mongering" – growing the market for particular pharmaceutical products through disease awareness campaigns that use advertising to "widen the boundaries of illness."²³ The medical literature contains examples of pharmaceutical industry disease mongering for bipolar disorder, female sexual dysfunction, erectile dysfunction, acid reflux, insomnia and allergies.²⁴⁻²⁷ Further, the indirect costs of DTCA to public and private programs covering prescription drugs are clear. Rosenthal estimated that "\$2.6 billion or 12% of the growth in total prescription drug spending between 1999 and 2000 was attributable to DTCA" resulting in \$4.20 in increased sales "for every dollar spent on 19 DTC advertising."²⁸ Since 2000, spending on DTC advertising has increased. Both public programs, such as Medicare and Medicaid, and private insurance are increasingly burdened by rising prescription drugs spending.

CONCLUSION

In conclusion, The Prescription Project and Prescription Access Litigation urge the FDA to closely review the cognitive effects of television advertisements when establishing regulations that guide compliance with the "fair balance" requirement. More broadly, if DTCA has the ability to stimulate powerful conversations between patients and doctors, a larger focus on public service announcements (PSAs) seems warranted. PSAs are devoid of the inherent bias of commercial DTCA and can be geared towards the highest-priority conditions.

DTC television advertisement compliance with the adequate provision and fair balance requirement must be reexamined. More importantly, the claim that stimulation of discussions and increased awareness of treatments is a public health benefit must be disregarded when stated out of context. Overall it must be remembered that DTCA drives attention to conditions chosen for their return on investment, not their importance in improving the public health.

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REFERENCES

1. Akin KJ, Swasy JL, Braman AC. Patient and physician attitudes and behaviors associated with DTC promotion of prescription drugs - summary of FDA survey research results. CDER, FDA; 2004.
2. Weissman J,S., Blumenthal D, Silk A,J., Zapert K, Newman M, Leitman R. Consumers' reports on the health effects of direct-to-consumer drug advertising. *Health Aff (Millwood)*. 2003;Feb 26.
3. Mintzes B, Barer ML, Kravitz RL, et al. How does direct-to-consumer advertising (DTCA) affect prescribing? A survey in primary care environments with and without legal DTCA. *CMAJ*. 2003;169:405-412.
4. Kravitz RL, Epstein RM, Feldman MD, et al. Influence of patients' requests for direct-to-consumer advertised antidepressants: A randomized controlled trial. *JAMA*. 2005;293:1995-2002.
5. Basara LR. Impact of a direct-to-consumer prescription medication advertising campaign on new prescription volume. *Drug Inf J*. 1996;30:715.
6. Zachry III, Woodie M., Shepherd MD, Hinich MJ, Wilson JP, Brown CM, Lawson KA. Relationship between direct-to-consumer advertising and physician diagnosing and prescribing. *Am J Health Syst Pharm*. 2002;59:42..
7. Jong GW, Stricker, Bruno H. Ch., Sturkenboom, Miriam C. J. M. Marketing in the lay media and prescriptions of terbinafine in primary care: Dutch cohort study. *BMJ*. 2004 April 17; 328(7445): 931.;328:931.

8. Donohue JM, Cevasco M, Rosenthal MB. A decade of direct-to-consumer advertising of prescription drugs. *N Engl J Med.* 2007;357:673-681.
9. Wilkes MS, Bell RA, Kravitz RL. Direct-to-consumer prescription drug advertising: Trends, impact, and implications. *Health Aff.* 2000;19:110-128.
10. Kaphingst KA, Rudd RE, DeJong W, Daltroy LH. Comprehension of information in three direct-to-consumer television prescription drug advertisements among adults with limited literacy. *J Health Comm.* 2005;10:609-619.
11. Cline RJW, Young HN. Marketing drugs, marketing health care relationships: A content analysis of visual cues in direct-to-consumer prescription drug advertising. *Health Communication.* 2004;16:131.
12. Day RS. Direct-to-consumer drug ads: What do people understand and remember? testimony to the U.S. congress, may 8, 2008. house committee on energy and commerce, subcommittee on oversight and investigations. 2008.
13. Graham DJ, Campen D, Hui RH, et al. Risk of acute myocardial infarction and sudden cardiac death in patients treated with cyclo-oxygenase 2 selective and non-selective non-steroidal anti-inflammatory drugs: Nested case-control study. *The Lancet.* 2005;365:475-481.
14. Dai C, Stafford RS, Alexander GC. National trends in cyclooxygenase-2 inhibitor use since market release: Nonselective diffusion of a selectively cost-effective innovation. *Arch Intern Med.* 2005;165:171-177.
15. Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. *N Engl J Med.* 1988;319:1701-1707.
16. Krystal AD, Walsh JK, Laska E, et al. Sustained efficacy of eszopiclone over 6 months of nightly treatment: Results of a randomized, double-blind, placebo-controlled study in adults with chronic insomnia. *Sleep.* 2003;1:793-799.
17. Datti B, Carter MW. The effect of direct-to-consumer advertising on prescription drug use by older adults. *Drugs & Aging.* 2006;23:71-81.
18. Gilbody S, Wilson P, Watt I. Benefits and harms of direct to consumer advertising: A systematic review. *Qual Saf Health Care.* 2005;14:246-250.
19. Jon Richter, Pfizer, Inc. Comments to FDA-2008-N-0226 of pfizer, inc regarding the proven health benefits of direct-to-consumer advertising data from publicly available studies. 2008.
20. Weissman J,S., Blumenthal D, Silk A,J., et al. Physicians report on patient encounters involving direct-to-consumer advertising. *Health Aff (Millwood).* 2004;Apr 28.
21. Kaiser Family Foundation. Understanding the effects of direct-to-consumer prescription drug advertising. Menlo Park, CA:2006.

22. 8th annual survey on consumer reaction to DTC advertising of prescription drugs. *Women's Health, Prevention, Men's Health*; 2008.
23. Moynihan R, Henry D. The fight against disease mongering: Generating knowledge for action. *PLoS Med.* 2006;3:e191.
24. Healy D. The latest mania: Selling bipolar disorder. *PLoS Med.* 2006;3:e185.
25. Tiefer L. Female sexual dysfunction: A case study of disease mongering and activist resistance. *PLoS Med.* 2006;3:e178.
26. Lexchin J. Bigger and better: How pfizer redefined erectile dysfunction. *PLoS Med.* 2006;3:e132.
27. Applbaum K. Pharmaceutical marketing and the invention of the medical consumer. *PLoS Med.* 2006;3:e189.
28. Rosenthal MB, Berndt ER, Donohue JM, Epstein AM, Frank RG. Demand effects of recent changes in prescription drug promotion. Menlo Park, CA: Kaiser Family Foundation; 2003; Report No. 6085.