A Decade of Direct-to-Consumer Advertising of Prescription Drugs

Julie M. Donohue, Ph.D., Marisa Cevasco, B.A., and Meredith B. Rosenthal, Ph.D.

ABSTRACT

BACKGROUND

Evidence suggests that direct-to-consumer advertising of prescription drugs increases pharmaceutical sales and both helps to avert underuse of medicines and leads to potential overuse. Concern about such advertising has increased recently owing to the withdrawal from the market of heavily advertised drugs found to carry serious risks. Moreover, the Food and Drug Administration (FDA) has been criticized for its weak enforcement of laws regulating such advertising.

METHODS

We examined industry-wide trends in spending by pharmaceutical companies on direct-to-consumer advertising and promotion to physicians during the past decade. We characterized the drugs for which such advertising is used and assessed the timing of advertising after a drug is introduced. Finally, we examined trends in the FDA's regulation of drug advertising.

RESULTS

Total spending on pharmaceutical promotion grew from $11.4 billion in 1996 to $29.9 billion in 2005. Although during that time spending on direct-to-consumer advertising increased by 330%, it made up only 14% of total promotional expenditures in 2005. Direct-to-consumer campaigns generally begin within a year after the approval of a product by the FDA. In the context of regulatory changes requiring legal review before issuing letters, the number of letters sent by the FDA to pharmaceutical manufacturers regarding violations of drug-advertising regulations fell from 142 in 1997 to only 21 in 2006.

CONCLUSIONS

Spending on direct-to-consumer advertising has continued to increase in recent years in spite of the criticisms leveled against it. Our findings suggest that calls for a moratorium on such advertising for new drugs would represent a dramatic departure from current practices.

From the Department of Health Policy and Management, University of Pittsburgh Graduate School of Public Health, Pittsburgh (J.M.D.); the Department of Health Policy and Management, Harvard School of Public Health, Boston (M.C., M.B.R.); and Vanderbilt School of Medicine, Nashville (M.C.). Address reprint requests to Dr. Donohue at the Department of Health Policy and Management, University of Pittsburgh Graduate School of Public Health, Crabtree Hall A613, 130 DeSoto St., Pittsburgh, PA 15261, or at jdonohue@pitt.edu.

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(FDA) allowed direct-to-consumer advertising of prescription drugs on television. Such advertising has been criticized for encouraging inappropriate use of medications and driving up drug spending.[1,2] Concern that such advertising may lead to increased use of expensive medications was amplified by the introduction of a prescription-drug benefit in Medicare in 2006 (Part D). Studies of the effect of advertising on prescribing practices have shown that such advertising increases classwide sales, helps to avert underuse of medicines to treat chronic conditions, and leads to some overuse of prescription drugs.[3-5]

Direct-to-consumer advertising has also been controversial in light of postmarketing revelations regarding problems with drug safety. Specifically, clinical trials that are required for drug approval are typically not designed to detect rare but significant adverse effects, and contemporary methods of postmarketing surveillance often fail to connect adverse events that have a high rate of background prevalence with the use of particular drugs. After the market withdrawal of Vioxx (rofecoxib), a drug heavily promoted to consumers,[6] critics called for the FDA to place limits on direct-to-consumer advertising, particularly for new drugs,[7] a view that was reiterated in a recent report by the Institute of Medicine on the safety of medicines.[8]

Finally, the Government Accountability Office (GAO)[9] and others[10] have criticized the FDA's enforcement of regulations governing direct-to-consumer advertising. Criticism has focused specifically on the adequacy of the FDA's review of pharmaceutical advertisements, as well as the level and speed of enforcement actions taken subsequent to review.

Since direct-to-consumer advertising has a significant effect on demand for prescription drugs, it is important to understand the evolution of such advertising and its regulation. Although one study reported that spending for such advertising increased by a factor of 3 from 1996 to 2000,[11] little is known about trends in spending and other forms of pharmaceutical promotion in recent years. In our study, we examined recent trends in the industry's use of direct-to-consumer advertising (as opposed to other forms of promotion), assessed the timing of advertising campaigns relative to the introduction of drugs in order to shed

past decade.

METHODS

DATA COLLECTION

We obtained data on industry-wide and product-specific promotional expenditures from three market-research firms that track advertising spending and specialize in forms of promotion for the pharmaceutical industry; we also obtained information from researchers and staff members at the FDA and other government agencies. These data have been widely used in studies of trends in and the effects of direct-to-consumer advertising.[3,5,11-14]

Data on expenditures for such advertising were collected by TNS Media, which tracks local and national advertising campaigns at 44 television networks (including cable), 658 magazines, 202 newspapers, the Internet, and several network and local radio stations. Data are representative of major media markets.

We obtained publicly available data on promotion to health professionals from 1996 to 2005 from IMS Health, an independent medical-information company. For the industry as a whole, we report on three major components of spending on promotion to professionals: visits of pharmaceutical sales representatives to physicians in office-based and hospital practices ("detailing"), free samples dispensed to physicians, and advertising in professional journals. IMS Health derives spending estimates on detailing from a nationally representative panel of office-based physicians and hospital pharmacy directors who track their contacts with sales representatives. IMS Health obtains data on spending on free samples from a panel of approximately 1200 office staff members in medical practices, sampled from the practices of the office-based physicians who are on the detailing panel. To estimate spending on advertising in professional journals, IMS Health tracks advertisements placed in approximately 400 medical journals and adds estimates of printing costs to the publisher's charge for the advertisements.

We obtained data on industry-wide sales from published reports on the basis of an annual survey conducted by the Pharmaceutical Research and Manufacturers of America (PhRMA). We purchased data on promotional expenditures in 2005 for products in specific classes from Verispan,

tic drug classes that had the highest U.S. sales in 2004, we obtained data on the five forms of pharmaceutical promotion that are tracked by Verispan: direct-to-consumer advertising, detailing, advertising in professional journals, meetings and educational events for physicians, and online pharmaceutical promotion to physicians. Data regarding spending on advertising are collected by TNS Media, as described previously. To track detailing, Verispan surveys approximately 13,000 office-based and hospital-based physicians and residents, nurse practitioners, and physician assistants who track their encounters with pharmaceutical sales representatives. The panel is geographically representative and includes members of 31 clinical specialties.

Verispan produces estimates of industry expenditures on professional meetings and events through a survey of more than 3500 office-based physicians representing 19 specialties who report on the events sponsored by pharmaceutical companies that they attend. This panel of physicians is also asked to report on online pharmaceutical-promotion activity, which includes digital (Internet and video) promotion and continuing medical education modules. Verispan audits approximately 600 medical journals and tabloids and calculates spending on the basis of each journal's rate-card information and premium-factor costs.

Finally, we obtained data on the number of FDA enforcement actions related to pharmaceutical promotion from 1997 to 2006 from the FDA, which posts the regulatory letters sent to pharmaceutical companies on its Web site (www.fda.gov/cder/ddmac/lawsregs.htm). FDA approval dates for specific products were obtained from the *Orange Book* of approved drug products with therapeutic equivalence evaluations.[15] We obtained data on start dates for advertising campaigns through a series of Internet searches (with specific sources available from the authors).

DATA ANALYSES

We conducted descriptive analyses. Data on promotional spending were adjusted to 2005 dollars with the use of the Consumer Price Index. We examined spending on all forms of promotion relative to sales to determine whether the intensity of pharmaceutical promotional spending has changed during the past decade. We examined the distribution of drugs in terms of dollar sales in the United States. In addition, we examined the level and timing (relative to a drug's FDA approval) of spending on advertising for the 20 drugs with the highest spending for direct-to-consumer advertising in 2005.

To characterize the nature of FDA enforcement related to advertising spending over time, we examined the numbers of enforcement letters related to promotion in each year and further calculated the percentage of promotion-related enforcement actions that were for advertising campaigns (as opposed to promotional materials aimed at health professionals). Finally, we examined the content of the notices of violation to determine the type of violation (e.g., false or misleading claims about the effectiveness or risks of drugs) and calculated the proportion related to each type.

RESULTS

INDUSTRY-WIDE TRENDS IN PROMOTION

Total real spending on promotion grew from $11.4 billion to $29.9 billion from 1996 to 2005, at an average annual rate of 10.6% (Table 1). The percentage of sales spent on promotion for the industry as a whole increased from 14.2% in 1996 to 18.2% in 2005. In the past 9 years, spending on direct-to-consumer advertising and free samples has risen as a share of total promotion, whereas investments in detailing and advertising in professional journals have fallen as a share of the total.

Real spending on direct-to-consumer advertising increased by 330% from 1996 to 2005 (Table 1). After a brief slowdown in spending on advertising in 2000 and 2001, spending grew at an average annual rate of 14.3% from 2002 to 2005. Yet, promotion to professionals still outweighs spending on direct-to-consumer advertising. In 2005, only 14% of total industry expenditures on pharmaceutical promotion were devoted to such advertising.

ROLE OF ADVERTISING FOR TOP-SELLING DRUGS

In 2005, 8 of the 10 top drug classes in terms of dollar sales had at least one product with advertising spending (Table 2). The importance of direct-to-consumer advertising varied substantially across the top classes. Manufacturers of proton-pump inhibitors, 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins), and

Variable	Annual Spending									
	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Direct-to-consumer advertising										
Total spending (millions of $)	985	1,301	1,578	2,166	2,798	2,954	2,864	3,478	4,160	4,237
Percentage of sales	1.2	1.5	1.6	1.8	2.1	2.0	1.9	2.2	2.5	2.6
Professional promotion										
Total spending (millions of $)										
Detailing	3,747	4,093	4,861	5,064	5,447	6,055	6,731	7,364	7,585	6,777
Journal advertising	571	621	597	551	549	469	474	476	516	429
Percentage of sales	5.4	5.4	5.6	4.7	4.6	4.5	4.8	5.0	4.9	4.4
Free samples										
Total retail value (millions of $)	6,104	7,358	7,910	8,476	9,021	11,539	12,928	14,362	16,404	18,438
Percentage of sales	7.6	8.4	8.1	7.1	6.9	8.0	8.6	9.1	9.9	11.2
Total promotion										
Total spending (millions of $)	11,407	13,373	14,946	16,257	17,815	21,018	22,997	25,680	28,664	29,881
Percentage of sales	14.2	15.3	15.3	13.7	13.6	14.6	15.2	16.3	17.2	18.2

* Data on promotional spending are from IMS Health (www.imshealth.com); data on sales are from PhRMA's annual report. All data were adjusted to 2005 dollars, according to the Consumer Price Index. Spending on free samples for 2005 was estimated on the basis of growth and spending rates from the previous 3 years.

erythropoietin medications spent 34%, 34%, and 31% of their total marketing budget, respectively, on direct-to-consumer advertising in 2005. The manufacturers of several drugs in these classes invested in advertising campaigns (Table 2). Spending for the advertising of antidepressant agents, seizure-disorder medications, and antipsychotic agents was lower than that for proton-pump inhibitors, statins, and erythropoietin medications as a proportion of the total marketing budget. The remaining 4 of the top 10 drug classes placed little emphasis on consumers in their promotional strategies. None of the angiotensin II antagonists used direct-to-consumer advertising in 2005. Among manufacturers of calcium-channel blockers, only non–product-specific or "disease awareness" ads were purchased. In 2005, manufacturers used direct-to-consumer advertising for only one of the cyclooxygenase-2 inhibitors (of which celecoxib was the only remaining product) and one of the angiotensin-converting–enzyme inhibitors. Since data on the retail value of free samples that are dispensed for these drug classes were not available, the overall promotion-to-sales ratios probably provide a conservative estimate.

LEVEL AND TIMING OF EXPENDITURES

Spending on direct-to-consumer advertising continued to be concentrated among a relatively small number of brands. The 20 drugs with the highest spending made up 54.4% of total industry spending on advertising in 2005 (Table 3). Drugs that are advertised to consumers are predominantly new drugs used to treat chronic conditions. Ten of the top 20 drugs, as ranked by advertising spending, were introduced in 2000 or later. Notably, nearly all (17 of 20) advertising campaigns for the most heavily advertised drugs began within a year after FDA approval of the drug.

FDA ENFORCEMENT OF REGULATIONS

The number of letters sent by the FDA to pharmaceutical manufacturers notifying them that they had violated regulations for prescription-drug advertising fell from 142 in 1997 to only 21 in 2006 (Fig. 1). During the same period, the proportion of promotion-related regulatory letters citing problems with direct-to-consumer advertisements (as opposed to promotional material aimed at health professionals) increased from 15.5% of all letters in 1997 to 33.3% in 2006. And during the years

Variable	U.S. Sales Revenues	Total Promotional Spending	Percentage of Sales	Type of Promotion					No. of Drugs in Class with Direct-to-Consumer Advertising
				Direct-to-Consumer Advertising	Detailing	Professional Meetings and Events	Journal Advertising	Online Promotion to Physicians	
	millions of dollars			*percent*					
HMG-CoA reductase inhibitors	16,000	859	5	34	52	11	2	1	4
Proton-pump inhibitors	12,900	884	7	34	57	7	1	1	4
SSRIs or SNRIs	12,500	1018	8	12	68	15	4	1	6
Antipsychotic agents	10,500	513	5	10	64	21	3	2	4
Erythropoietin	8,700	100	1	31	45	12	7	5	2
Seizure-disorder agents	8,000	348	4	12	65	16	5	2	3
Angiotensin II antagonists	5,000	598	12	0	78	19	2	1	0
Calcium-channel blockers	4,600	94	2	1	79	18	1	1	0
ACE inhibitors	3,800	251	7	2	71	24	2	1	1
COX-2 inhibitors	1,800	299	17	4	78	16	1	1	1

* Data on direct-to-consumer advertising are from TNS Media; data on detailing, professional meetings and events, journal advertising, and online promotions to physicians are from Verispan; and data on sales revenues are from IMS Health. Leading therapeutic classes of drugs were identified on the basis of publicly available IMS Health rankings of therapeutic classes according to spending for 2004. Values for selective serotonin-reuptake inhibitors (SSRIs) and selective norepinephrine-reuptake inhibitors (SNRIs) match the classification scheme used by Verispan, which was the source of our data on promotions. Values in the far right-hand column refer to product-specific advertising only. HMG-CoA denotes 3-hydroxy-3-methylglutaryl coenzyme A, ACE angiotensin-converting enzyme, and COX-2 cyclooxygenase-2.

2003–2004, nearly half of the FDA's promotion-related regulatory letters were focused on direct-to-consumer advertisements. From 1997 to 2006, nearly 84% of regulatory letters regarding direct-to-consumer advertising cited advertisements for either minimizing risks (e.g., minimizing or omitting information on side effects), exaggerating effectiveness (e.g., portraying the indication too broadly or making unsubstantiated claims of superiority over other drugs), or both.

For example, the FDA found that Eli Lilly's television broadcast advertisement for Strattera (atomoxetine) was false or misleading because it inadequately communicated the indication for the drug (attention-deficit–hyperactivity disorder) by means of competing visuals, graphics, and music presented concurrently. Similarly, serious risk disclosures were minimized for Strattera, the FDA said, by the distracting visuals and graphics (e.g., erratic camera movement, quick scene changes, and visual changes in point of view). In another case, the FDA said Pfizer's print advertisement for Zoloft (sertraline) was false or misleading because it omitted important information relating to the risk of suicidality in patients, a risk stated on the product's label at the time the advertisement ran.

DISCUSSION

Spending on direct-to-consumer advertising has continued to increase recently in absolute terms and as a percentage of pharmaceutical sales in spite of pressure on manufacturers to curtail such advertising.[8] Promotion to physicians continues to be the dominant marketing strategy, but there are some drugs in a majority of the top-selling classes that are promoted by such advertising. Driven by increases in direct-to-consumer advertising, total

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