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Joan Claybrook, President

Public Citizen's Health Research Group's Comments On:
Draft Guidance for Industry; Consumer-Directed Broadcast Advertisements; Availability

[Docket No. 97D-0302]

Submitted - October 14, 1997

Since 1972, Public Citizen's Health Research Group has been promoting research-based, system-wide changes in health care policy as well as advocating for the appropriate prescribing and use of prescription drugs. The Health Research Group testifies before Congress and petitions the Food and Drug Administration (FDA) on issues such as banning or relabeling of drugs and the misleading advertising of prescription and non-prescription drugs by their manufacturers. Our publications help consumers make informed decisions about the health care they receive and the drugs they are prescribed.

The combination of the FDA's failure to issue regulations on direct-to-consumer (DTC) prescription drug advertising and the agency's draft guidance for industry on DTC ads, allowing radio and television ads for prescriptions drugs, is an ill-advised policy that promotes the distribution of misleading information to the public. The FDA deludes itself by believing that this guidance, loosely applying statutory and regulatory requirements intended to regulate direct-to-doctor advertising, can provide a fair balance of benefit and risk information to consumers. The notion that broadcast drug commercials can include a thorough major statement conveying all of the product's most important risk information in 60 seconds is irresponsible. The agency's assumption is fallacious that increased dissemination of a drug's approved labeling (package insert) or a brief summary of the product's labeling to consumers through mechanisms given in broadcast ads — such as toll free telephone numbers for drug companies, referring consumers to print ads for the brief summary of the advertised drug's approved labeling, and company Internet addresses — furnishes consumers with adequate access to information about a drug's risks. Equally fallacious is the presumption that doctors always protect consumers asking for prescription drugs by brand names from being prescribed an inappropriate product. Doctors are influenced by advertising[1,2,3] and consumers who request drugs by brand name may get them because of DTC advertising.[4]

Current FDA policy on DTC broadcast and print advertising, and the absence of regulations, leaves consumers naked in the viciously competitive marketplace for

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prescription drugs without the protection of accessible objective, independent information about risks and benefits. Market competition breeds winners and losers: for drug companies the risk is only in a percentage of market share; for the consumers who may lose when the wrong drug is chosen, it can mean at the very least economic harm, possibly drug induced injury, or even worse, death. FDA policy has apparently withered to the stage that the agency now sees prescription drugs like any other type of consumer good. If this is the case, then the agency has the responsibility to ensure that consumers have access to accurate comparative information about prescription drugs and their risks just as they do before buying a step-ladder, power tool, or an automobile.

At this time, to the best of our knowledge, three drugs are currently being advertised on television under the FDA's new guidance policy: valacyclovir (Valtrex); fexofenadine (Allegra); and loratadine (Claritin). Less than a week after it first aired the ad for loratidine was banned because it was found to be misleading.[5] We have just become aware that a television ad is now airing for the migraine drug sumatriptan (Imitrex) that may also be misleading. The migraine drug market is becoming increasingly crowded and competitive for Glaxo Wellcome, the maker of sumatriptan, with the approval of zolmitriptan (Zomig), rizatriptan (Maxalt), and the dihydroergotamine nasal (Migranal) expected before the end of the year.[6] The FDA sees no problems with the drugs that are currently being advertised on television ads seems content in its belief that additional dangerous drugs will not be promoted because of the time necessary, and thus the prohibitive expense, to communicate major risks on radio and television. The FDA should make no mistake that as competitive pressures increase in the drug industry, as they surely will and now have with sumatriptan, drug companies will do whatever is necessary to ensure a drug's market share. This is the nature of business.

PRESCRIPTION DRUG ADVERTISING IS MISLEADING AND NOT EDUCATIONAL

Advertising by its very nature is all-to-often misleading. Its sole purpose is to sell by generating brand-name awareness, and differentiating the advertised product from other similar products in the market by accentuating benefits and downplaying potential risks, the evidence be damned. Consumers face enormous barriers to obtaining objective, comparative information about prescription drugs. This single fact, that objective, comparative information is not available creates an information imbalance that makes DTC prescription drug advertising to consumers misleading.

A myth promoted by the drug industry and its Madison Avenue allies is that the purpose of DTC advertising is altruistic, to educate the public about prescription drugs. For-profit corporations do not spend $610 million for DTC ads, as they did in 1996[7], simply to inform consumers of ways to improve their health. If the prescription drug industry was truly interested in educating the public about the safe and effective use of their products, this industry would not have been instrumental in blocking FDA initiatives to provide consumers with useful written prescription drug information in the form of patient package

inserts in 1982.[8] Prescription drug manufacturers who are committed to educating consumers about drugs will provide complete comparative disclosure of adverse effects, contraindications and the effectiveness of their products with respect to those of their competitors to consumers.

APPROVED PRODUCT LABELING AND BRIEF SUMMARIES ARE MISLEADING TO CONSUMERS

The FDA guidance states that either a highly inclusive brief summary must be presented with printed advertising or, in the case of broadcast advertisements, substitution may be made by ensuring dissemination of a drug's approved product labeling, or referring consumers to a brief summary of the approved labeling in a print ad. A drug's approved labeling is written for professionals in technical language, and by virtue of years of education, health professionals have the contextual knowledge required to critically evaluate this information. Many consumers do not have this extensive knowledge background to evaluate such materials and, in addition, the small print precludes many older Americans from even being able to read the approved labeling. Consumers are perfectly capable of evaluating and using the information in a drug's labeling if it is written in non-technical language and the risk information is presented in a properly framed context. Nevertheless, this would still leave consumers without a source of objective, comparative information about other drugs or non-drug treatment options for their illnesses.

Statute and regulation require that the brief summary for a drug includes information on a product's effectiveness and discloses all risk related information in a product's approved labeling.[9] A clear example of a DTC advertisement containing a misleading brief summary is from a print ad appearing in recent issues of *Arthritis Today* magazine for the drug nabumetone (Relafen). Nabumetone is a nonsteroidal anti-inflammatory drug (NSAID), produced by SmithKline Beecham Pharmaceutical of Philadelphia, approved for rheumatoid and osteoarthritis and heavily promoted direct to arthritis sufferers. Appendix I below contains information taken directly from the approved product labeling for nabumetone that does not appear in the brief summary in the *Arthritis Today* magazine promotion. Kept from consumers is information in the Clinical Trials section of the approved labeling comparing nabumetone to aspirin and naproxen (Naprosyn and generics). More importantly, vital risk information has been deleted from the brief summary in this ad that would inform consumers of potentially life threatening adverse effects, gastrointestinal (GI) ulceration, bleeding, and perforation.

In January 1997, SmithKline Beecham Pharmaceuticals was found distributing false and misleading advertising about the safety and cost-effectiveness of nabumetone compared to other NSAID's to doctors in violation of regulations and the Federal Food, Drug, and Cosmetic Act.[10] While the FDA's Division of Drug Marketing, Advertising and Communications (DDMAC) required SmithKline Beecham to immediately stop distributing the misleading materials to doctors, DDMAC has done nothing about correcting the

misleading safety information in the nabumetone ad directed at consumers. The following statement is made in the nabumetone ad appearing in *Arthritis Today* when the GI adverse effects of the drug are mentioned: "Relafen, however, has been found to have a low potential for such ulcers." This lack of regulatory action by DDMAC places in serious question if the FDA has the resources to protect consumers from misleading DTC ads.

EFFECT OF DTC ADS ON THE PUBLIC'S HEALTH

While the FDA plans to evaluate the effect of DTC advertising on the public's health by August 1999, there are already examples of the harm that has been caused. The recent withdrawal of the diet drug fenfluramine (Pondimin), one-half of the once popular "fen/phen" combination, because of heart valve damage in potentially tens of thousand of consumers, is one example of the adverse effects of DTC drug advertising on the public's health. Though we have no reason to believe that the manufacturers of fenfluramine or phentermine (Fastin and generics) promoted their products directly to consumers, it was not necessary. The DTC advertising was done for them by an unscrupulous diet clinic industry. It makes no difference who promoted the use of these drugs directly to consumers because both drug manufacturers and diet clinics use the same marketing strategy, overstate benefits and de-emphasize the risks.

Nabumetone is also an example of DTC drug advertising that may cause both economic and potentially physical harm as well. The misleading nature of SmithKline Beecham's promotion of this drug to doctors and consumers was discussed above. Nabumetone sales jumped during the second quarter of 1994 by 52 percent boosted by a DTC advertising campaign.[11] In 1995, SmithKline Beecham invested $11 million in their DTC promotion of nabumetone[12] and the drug moved from the 48th most frequently dispensed drug in the U.S. in 1994 to number 44 in 1995.[13] Nabumetone moved up two spots more in 1996 to number 42 on the list with more than 7.4 million prescriptions having been sold.[14]

By 1994, evidence was emerging of differences in the risk of the NSAID's most common serious adverse effect, GI toxicity. Ibuprofen (Motrin and many generics) has shown the least risk, and naproxen, another NSAID compared with nabumetone in the Clinical Trials section of the nabumetone package insert, shows an intermediate risk of GI toxicity.[15] These differences in the GI risks of various NSAIDs have recently been confirmed in a comprehensive summary of the medical literature.[16] The risk of GI toxicity with nabumetone in relation to other NSAIDs remains unknown.

Nabumetone is substantially more expensive than other NSAIDs. Using the 1995 Drug Topics Red Book, a standard drug pricing guide, the wholesale cost to the pharmacist for enough nabumetone to last 30 days at the minimum recommended dose of 1,000 milligrams per day was $58.68. By comparison the cost to the pharmacist for sufficient generic naproxen to last one month at its minimum recommended dose of 500 milligrams

per day was only $8.08. For ibuprofen, the safest of the NSAIDs, the wholesale cost of a month's supply at its usual starting dose of 1,200 milligrams per day was $8.64. The difference in average wholesale cost for nabumetone and naproxen in 1995, in doses shown to be equally effective, was over seven-fold.

It is difficult to imagine a scenario in which a well informed consumer given objective, comparative information about nabumetone would accept the unknown risk of GI toxicity and the economic harm from the higher cost of nabumetone over treatment with ibuprofen or naproxen.

In light of the DTC promotion of fen/phen and resulting disaster and the success of nabumetone in the marketplace despite its high cost and unknown toxicity, the argument that doctors always protect consumers from inappropriate drugs and potential drug induced injury is unsound. We are aware of no valid scientific evidence that suggests DTC prescription drug advertising leads to better health outcomes for the public. On the contrary, based on the prevailing evidence presented above, DTC advertising may cause needless economic hardship and perhaps serious physical harm to consumers.

WILL THE FDA HAVE THE RESOURCES TO MONITOR DTC ADS?

Public Citizen has little confidence that DDMAC, the division of the FDA responsible for monitoring advertising, has been given or will be given in the future the resources necessary to fulfil that mission. Recent studies have shown that print advertisements for prescription drugs appearing in medical journals and DTC print ads are misleading over 40 percent of the time.[17,18] The table below shows that from 1993 to 1996 there was almost a tripling in the number of labor-intensive drug advertising launch campaigns DDMAC had to monitor with only a slight increase in the Division's personnel (FTEs).[19]

Year	Number of Launch Campaigns	Number of Warning Letters	Number of Notice of Violation Letters	FTE Staff (by calendar years
FY 1993	118	4	247	NA
FY 1994	185	2	210	26
FY 1995	306	0	163	30
FY 1996	>300	2	137	29

The most common kind of regulatory action, a notice of violation letter from the FDA to a drug company, always cites a violation of FDA advertising laws and/or regulations and asks the company to cease such activity. In the same interval of 1993 to 1996, there was almost a 50 percent decrease in the number of such letters. We are very discouraged that DDMAC has posted only 62 notices of violation or warning letters on the FDA's website in the first 9 months of 1997.

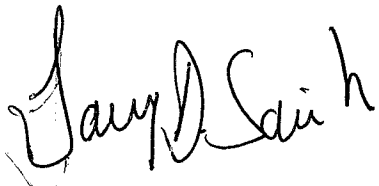
Legislation that recently passed both houses of Congress fundamentally changes the Food, Drug and Cosmetic Act and its implementing regulations and weakens the FDA's ability to protect the public. In addition, this legislation may have a profound impact on DDMAC's responsibilities and work load. This legislation allows drug companies to distribute copies of medical journal articles promoting uses for their drugs that have not been shown to be safe and effective by FDA review directly to doctors. The FDA will have 60 days to review the medical journal articles for accuracy and balance before they are sent to doctors, but prior review does not permit the agency to prohibit dissemination of the articles.

It is our understanding that at least part of the task of reviewing what could be thousands of medical journal articles in 60 days or less would fall to the staff of the DDMAC. Public Citizen sees no feasible way, without additional resources, for the DDMAC to monitor hundreds of direct-to-doctor print ads, and direct-to-consumer print and broadcast promotions, in addition to evaluating what may be thousands of journal articles used to promote unapproved uses of prescription drugs.

CONCLUSION

Current FDA policy on DTC prescription drug advertising as exemplified by the "Draft Guidance for Industry; Consumer-Directed Broadcast Advertisements" promotes the distribution of misleading information to consumers with potentially serious consequences to the public's health. Public Citizen finds it illogical and dangerous that the FDA is allowing the commercial promotion of prescription drugs directly to consumers without first issuing regulations to ensure the public's protection from misleading advertisements for a class of products that when prescribed inappropriately create a serious personal risk to consumers and add a significant burden to the cost of health care. We strongly urge the FDA to immediately declare a moratorium on all DTC prescription drug advertising until appropriate regulations have been issued.

Sincerely,



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APPENDIX I

Important Consumer Information Missing from the Relafen Brief Summary in an Ad Appearing in *Arthritis Today* Magazine.

CLINICAL TRIALS

Osteoarthritis: The Use of Relafen in relieving the signs and symptoms of osteoarthritis was assessed in double-blind controlled trials in which 1,047 patients were treated for 6 weeks to 6 months. In these trials, Relafen in a dose of 1,000 mg/day administered at night was comparable to naproxen 500 mg/ day and to aspirin 3,600 mg/day.

Rheumatoid Arthritis: The use of Relafen in relieving the signs and symptoms of rheumatoid arthritis was assessed in double-blind, randomized, controlled trials in which 770 patients were treated for 3 weeks to 6 months. Relafen, in a dose of 1000 mg/day administered at night was comparable to naproxen 500 mg/day and to aspirin 3600 mg/day.

WARNINGS

Risk of G.I. Ulceration, Bleeding and Perforation with NSAID Therapy: Serious gastrointestinal toxicity such as bleeding, ulceration and perforation can occur at any time, with or without warning symptoms, in patients treated chronically with NSAID therapy.

INFORMATION FOR PATIENTS

Relafen, like other drugs of its class, is not free of side effects. The side effects of these drugs can cause discomfort and, rarely, there are more serious side effects, such as gastrointestinal bleeding, which may result in hospitalization and even fatal outcome.

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