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Honorable Henry A. Waxman
House of Representatives
Committee on Government Reform
2157 Rayburn House Office Building
Washington DC 20515 – 6143

September 29, 2002

Dear Representative Waxman,
You asked my opinion on the content of 74 direct-to-consumer broadcast advertisements submitted to FDA by drug manufacturers during late 2001 and 2002, in terms of whether they accurately represent product characteristics or whether they are in any way false and misleading, in terms of for example a fair balance of benefit and risk information, advertising only for approved uses, etc. Given the short time frame, these are mainly general impressions with a few examples of areas of concern. This is not in any way a complete or systematic overview.

Presentation of risk information: In most ads, the voice speeds up for the risk information and/or a different, softer voice is used, and there is often distracting music as well as images that are not consistent with the content of the risk information. This is a ubiquitous problem, rather than one that is product-specific, and it leads to a consistent de-emphasis of important patient safety information. An example would be the visuals of happy smiling people during the voice-over on risks of liver problems with Zocor.

One ad for Paxil states that it is 'non-habit forming'. Some users have experienced severe withdrawal reactions when they stopped taking Paxil and 35 people have started a class action suit against the manufacturer, GSK. The federal judge in this suit has ordered GSK to stop making this claim in television commercials. *[Lota L. Los Angeles, Associated Press. Judge bans TV ads claiming anti-depressant Paxil is non-habit forming. Aug 20, 2002]*

Some ads precede lists of side effects with a minimizing statement. An example is: *"Prevacid has a low occurrence of side effects such as diarrhea, abdominal pain and nausea,"* as opposed to a statement that "Side effects of Prevacid include diarrhea, abdominal pain and nausea," followed by information on frequency. Another example is the statement for Clarinex which says that: "*Side effects are similar to sugar pill, including sore throat, dry mouth...*" instead of a less confusing and more direct statement that: 'Side effects include...", followed by a statement about frequency relative to

placebo. I did not come across any claims of product benefit preceded by similar types of minimizing statements.

Information that does not accurately reflect the product label:
The ad for Ambien states that: "Patients who abuse prescription sleeping pills may become dependent." The product label clearly states that anyone can become dependent, regardless of abuse history:

" Sleep medicines can cause dependence, especially when these medicines are used regularly for longer than a few weeks or at high doses...
All people taking sleep medicines have some risk of becoming dependent on the medicine. However, people who have been dependent on alcohol or other drugs in the past may have a higher chance of becoming addicted to sleep medicines."

Reminder ads with strong hints about product indications:
Reminder ads are allowed to state the brand name of a product, but not indications. If an ad states both the name and the indication, it is considered full product advertising and thus manufacturers must provide legally required risk information.

Two reminder ads for Viagra are stretching the limits of legality with strong hints about the product's indication. In the first, a race car driver lifts off his helmet and says "...bet you thought I was Bob Dole." Bob Dole had featured in Pfizer ads on erectile dysfunction during Viagra's launch. In the second ad, the race car driver says, "six, that's my number" with a strong Southern accent, making it easy to mistake the 'six' for 'sex'.

Implied overstatements of efficacy:
The ads omit information on how likely treatments are to work, and whether they are more or less effective than alternatives. However, the visuals and voice-over often suggest that products are highly effective. This is not just a product-specific problem; again, like the speeding up of verbal presentations of risk information, it is ubiquitous. Ads often include print statements that 'your results may vary' or that results may not be seen immediately. These are almost never included in the audio portion of the ad and were easy to miss. For example Flonase ads say "maximum relief may take several days" in white letters on a light blue background, which is easy to miss. Only one ad included limits to efficacy in the audio portion (an ad for Valtrex).

Another example is the two ads for Lipitor. The ads highlight healthy, thin and fit people who suddenly fall or flop down as if with a heart attack, to the horror of those around them. The ads imply that no matter how healthy you are, if you don't lower your cholesterol (presumably with Lipitor) you could suddenly die of a heart attack. The ads do say "Lipitor has not been shown to prevent heart disease or heart attacks" but this is only in print and is easy to miss. The audio portion makes no mention of this limitation, although it is highly relevant to the simulated heart attacks. The use of fear of death to sell a product is also ethically questionable.

The ads for Detrol and Ditropan, two drugs for overactive bladder, present an image of greater efficacy than is supported by the clinical trial evidence, with claims like "proven effective" (Detrol), and statements that a woman doesn't have to accept overactive bladder, she can do something about it (Ditropan). A Ditropan ad also links the decision to request this medicine with women taking control of their lives and not accepting the idea that women are the weaker sex or dressing in pink. These are treatments that aim to relieve troublesome symptoms; therefore a key question is whether the users felt better:

"Two double-blind RCTs are available comparing the effectiveness of tolterodine, 2 mg BID, with oxybutynin 5 mg TID, and placebo. .... There was no significant difference in the proportion of patients who perceived an improvement in bladder symptoms: placebo 47%, tolterodine (Detrol) 50%, and oxybutynin (Ditropan®), 49%." [Source: Therapeutics Letter, <http://www.ti.ubc.ca/pages/letter36.htm#Tolterodine>

The ads do not provide any hint that the drugs are likely to have only a modest effect, although this is an important aspect of product characteristics that potential users would want to know.

The ad for Singulair similarly says that taking this pill is "what I do every day to control my asthma." It does not explain that the effect of this class of asthma drugs is mild or that this product has been found to be less effective than inhaled steroids. To quote an independent assessment again: *"The average effects in the trials, though statistically significant, are small and of questionable clinical significance."* <http://www.ti.ubc.ca/pages/letter29.htm>

The FDA does not require manufacturers to state the likelihood of treatment success, and images often convey misleading impressions. The FDA did address this problem for ads for drugs for HIV/AIDS: in 2001 the agency sent a letter to manufacturers telling them to stop showing unrealistic images of patients on anti-retroviral therapy, after a San Francisco city health department survey found that young gay men with higher self-reported exposure to DTC drug advertising were less likely to practice safe sex. http://www.aegis.com/news/bar/2001/BR010501.html

Implied broader indications:

A Paxil ad for generalized anxiety disorder only states in print that anxiety from everyday stresses usually doesn't require medication. The testimonials in the audio portion include anxieties that could easily be mistaken for everyday problems. Similarly the ad for Zoloft for depression includes the qualification that symptoms must persist for at least two weeks only in print. This information is omitted from the audio portion of the ad, which lists symptoms that many people also experience as transient events, such as loss of sleep or depressed mood. If symptoms are more transient a person would not be diagnosed with clinical depression; similarly, a person with everyday anxiety would not be diagnosed with generalized anxiety disorder. In both cases the audio portion of the ad omits important limitations in terms of who the drug is indicated to treat.

In conclusion, the advertisements consistently treat benefit and risk information differently, in ways that tend to minimize even the relatively brief statements of major risks required by the FDA guidance on broadcast advertising. They also fail to provide

key information allowing viewers to obtain a realistic sense of how effective a product is or how it compares to other treatment options. I cannot comment on the legality of the ads, but I would question whether they are consistent with the aim of regulatory requirements for a fair balance of benefit and risk information in pharmaceutical advertisements and accurate representation of product characteristics. Additionally, offers of financial incentives including free trial prescriptions, rebates and other gifts were common in this series of ads.

The FDA found in its 1999 survey on DTCA that 28% of respondents believed only the safest drugs could be advertised on TV, and researchers in California found that 43% of a random sample of Sacramento residents believed that only completely safe drugs could be advertised to the US public. Any drug may be advertised to the public regardless of its safety profile. Thus, these studies suggest that a significant minority of viewers of television advertising obtain a false impression of product safety.

Sincerely,

Barbara Mintzes
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University of British Columbia