# How Does Pharmaceutical Advertising Affect Consumer Search?

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**Abstract**

This paper explores how restricting pharmaceutical search advertising affects the types of information that consumers seek online about drugs. We examine how consumer search patterns changed after the FDA issued warnings to pharmaceutical companies, prohibiting their use of Internet search ads. Our results suggest that, after the reduction in pharmaceutical search advertising, consumers were more likely to seek information from websites based on user-generated content or websites that focused on medical treatments not regulated by the FDA, such as Canadian pharmacies and herbal remedies.

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# 1 Introduction

The desirability of direct-to-consumer pharmaceutical advertising is disputed. On the one hand, pharmaceutical advertising may inform consumers about potential treatments and even encourage check-ups with health providers or increase compliance with drug therapy (Iizuka and Jin, 2005; Wosinska, 2005). On the other hand, it may induce consumers to choose unnecessary and expensive treatments (Donohue, 2006). It may even not be particularly effective at influencing consumer behavior at all, relative to other types of expenditures (Calfee et al., 2002; Narayanan et al., 2004). Much of this ambiguity exists because previous research has focused on aggregate outcomes and has not used data specifically on how pharmaceutical advertising affects the types of information that consumers are seeking. By contrast, in this paper, we directly analyze how pharmaceutical advertising affects which websites consumers acquire information from online. We find evidence that the effect of pharmaceutical advertising is largely neutral for consumers seeking information on pharmaceutical brands. However, if pharmaceutical advertising is not present, then consumers are more likely to seek information about medical conditions from unverified or less regulated sources of information.

Search engines are now the dominant way that consumers seek information on the Internet. Each month, Americans conduct around 14.3 billion searches using search engines. We investigate how online pharmaceutical advertising affects the types of websites consumers visit after consulting a search engine. There are many reasons to expect search advertising to be correlated with consumer behavior, so we study an event that exogenously shifted the ability of pharmaceutical companies to advertise on search engines. On March 26, 2009, the US Food and Drug Administration (FDA) issued notices to the manufacturers of 48 drugs regarding their online search ads. The letters stated that the ads contradicted existing regulations on pharmaceutical advertising by not conveying any risk information. Since

search ads have a 3-line text limit, many pharmaceutical companies could not adequately document the side effects and consequently removed their ads. Industry estimates suggest that pharmaceutical ads fell by 84 percent immediately after the ruling.[1]

We use unique data on consumer search behavior for the period before and after the FDA warning letters, from February to June 2009. Our data derive from comScore, which tracks 2 million web-users and the webpages they visit after querying any of the three major search engines. We focus on the three major search engines (Google, Live and Yahoo!), which account for approximately 92 percent of search activity in the US. We investigate queries associated with the brand names of the drugs that received the FDA warnings and the medical conditions they treat (e.g., "breast cancer", "hair loss").

Our results indicate that when pharmaceutical search advertising is not present, consumers behave differently in their search patterns and acquisition of information. Consumers seeking information on a medical condition are less likely to visit the webpages of pharmaceutical companies relative to other commercial websites, and they are also more likely to visit websites that feature health sectors that are not regulated by the FDA, such as herbal remedies and pharmacies based in Canada. In the absence of pharmaceutical advertising, consumers who seek information on a specific brand of pharmaceutical product were just as likely to visit that product's website, and were also more likely to visit community-based forums, non-profit, government, and medical school websites.

In our analysis, we also compare whether the consumer reached a website through a "paid link", that is, an ad that the website purchased from the search engine, or through a "non-paid link", that is, a link that appeared in the main body of results displayed by the search engine. Our findings suggest that among consumers who were seeking information on a brand, the restriction on advertising did not affect the number of visits to pharmaceutical company websites. In the absence of a paid link, consumers simply clicked on the non-

[1] "Fearing FDA, pharma abandons search ads", Tracy Staton, Adage, October 7, 2009.

paid links. However, consumers who were seeking information on medical conditions were less likely to click on pharmaceutical websites through either paid ads or non-paid links. This suggests that the presence of a paid ad for search, even if not clicked on, can encourage people to visit the website through the main search results. In addition, after pharmaceutical company ads were removed, paid ads by government agencies, non-profits, and medical schools attracted relatively more clicks for consumers who searched for a particular brand name. We check the robustness of our results to multiple specifications. We also show that no such changes in behavior occurred during the same period in the previous year, again suggesting that it was the FDA's warning driving our findings.

Our paper makes several distinct contributions to the literature. First, we provide direct evidence on how pharmaceutical advertising affects the set of information that a consumer acquires. In economics, limited empirical research exists due to the lack of behavioral data. Calfee et al. (2002) found that direct-to-consumer advertising had no effect on prescriptions after an FDA policy change in 1997, which facilitated the use of broadcast media for the advertisement of the statin class of cholesterol-reducing drugs, although the advertising did have a positive effect on a patient's compliance with drug therapy. Iizuka and Jin (2005) found that prescription drug advertising increased the number of doctor visits. Outside of the economics literature, most studies of how direct-to-consumer advertising affects behavior have focused on the use of surveys. For example, Emmaus (2001) finds that less than 6 percent of patients received a prescription for the advertised drug after being prompted by direct-to-consumer advertising to ask their doctor about the drug. Our research complements this existing literature by demonstrating the role that pharmaceutical advertising has on the set of information that a potential patient initially gathers about a pharmaceutical product.

Second, this is one of the first studies of the effectiveness of online advertising for pharmaceutical companies. Online expenditures for advertising have become increasingly important for pharmaceutical firms. In the year prior to the shift in FDA policy that we study, phar-

maceutical spending had increased by 36 percent $101 million in 2007, to $137 million in 2008.[2] Research on pharmaceutical advertising online has been mainly speculative. For example, Rosenthal et al. (2002) suggest that the underlying reason behind the growth of direct-to-consumer (DTC) pharmaceutical advertising may have been the "desire of patients to be involved in decisions about their health care, driven in part by the plethora of health-related information available on the Internet, [which] may have motivated pharmaceutical companies to reach out to consumers". Our research shows that while pharmaceutical advertising does divert a consumer's attention away from websites that could be considered less commercial, it also plays a role in diverting consumers' attention away from medical avenues not regulated by the FDA.

Finally, our paper demonstrates how restrictions imposed by the pre-Internet 1987 Pharmaceutical Marketing Act are shaping consumer search patterns and pharmaceutical advertising on the Internet. The Act mandated that firms had a responsibility to inform consumers about one approved use for the drug, the generic name of the drug, and the most important risks of the drug. Under the Act's "fair balance" requirement, the ads must present side effect information in a manner similar to that used in the presentation of the benefits of the drug.[3] Our results suggest that the enforcement of these requirements can dramatically change the information set on pharmaceutical products that consumers are exposed to. Questions still remain over how these restrictions should apply in an era of the Internet, where the ability of pharmaceutical advertisers to present textual information in ads is limited.

[2] Advertising Age, 2009.

[3] Various ways of presenting information that can affect fair balance include font size, use of bullets, amount of white space, and headlines.

# 2 Institutional Background and Data

## 2.1 FDA Ruling

The Food and Drug Administration (FDA) has regulated prescription drug advertising since 1962. The FDA's actions in recent years reflect a relative increase in its attention towards the regulation of direct-to-consumer advertising as opposed to physician advertising. As pointed out by Donohue et al. (2007), the proportion of promotion-related regulatory letters that cited 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.

On March 26, 2009, the FDA issued letters of warning to 14 major pharmaceutical companies, regarding their Internet ads that accompanied keyword searches on Google and other search engines. The FDA stated that the ads were misleading because they did not include information on the risks or side effects associated with a drug. These warnings were one of the first major actions by the FDA to crack down on Internet promotions. The companies that received letters were Biogen, Sanofi-Aventis SA, Johnson & Johnson, GlaxoSmithKline PLC, Forest Laboratories Inc., Cephalon Inc., Bayer AG, Novartis AG, Merck & Co., Eli Lilly & Co., Pfizer, Roche Holding AG, Genentech Inc. (now acquired by Roche), and Boehringer Ingelheim Pharmaceuticals Inc. Nineteen of the 48 drugs cited in the letters carry a black box, which is the FDA's strongest warning concerning possible side effects.[4]

A typical FDA letter resembled the one sent to Hoffmann-La Roche, regarding its drugs Boniva, Pegasys, and Xeloda. We quote the full text of the letter in the Appendix to this article. The letter cited ads that had the message, "XELODA Information www.xeloda.com Learn About An Oral Chemotherapy Treatment For Colon Cancer." The FDA criticized these ads, saying "By omitting the most serious and frequently occurring risks associated

[4]FDA Warns Drug Firms Over Internet Ads, Wall Street Journal, April 4, 2009.

with the drugs promoted in the links above, the sponsored links misleadingly suggest that Boniva, Pegasys and Xeloda are safer than has been demonstrated." Even though the ad included a link to the website for the drug, which did contain the relevant risk information, the FDA said the link was "insufficient to mitigate the misleading omission of risk information from these promotional materials," and it gave the company until April 9, 2009 to prove compliance.

## 2.2 Data

We obtain data on search advertising and consumer online behavior from the comScore Marketer database, which tracks the online activity of a panel of more than 2 million users. Our data span the period from February 2009 to June 2009. We collected information on keyword searches that contained the brand name for each of the 48 pharmaceutical products targeted by the FDA. We identified 350 different combinations of search terms and the resulting websites that consumers reached. For 33 out of the 48 drugs that were targeted by the FDA, we observed consumers in our data visiting the drug's website though a keyword search of its brand name. For the remaining 15 drugs, comScore did not observe enough panelists visiting their websites through a brand name search to record click activity. In the Appendix, Table A-1 records for each of the different drugs targeted by the FDA, the medical conditions it treats, major side effects and treatment protocols, and its webpage. Table A-2 contains a list of the keywords for the corresponding medical conditions.

We collected information on keyword searches for medical conditions by identifying the top two medical condition phrases that were used by consumers to navigate to a pharmaceutical website in February 2009, where such data was available. These medical conditions were terms such as "breast cancer" and "hypertension." These keywords terms closely aligned with the medical conditions mentioned in the FDA warning letters.

Our dataset includes 4,230 different combinations of brand and medical condition search

terms and websites subsequently visited by consumers. For 11 drugs, no search data either in the form of medical conditions searches or brand searches was recorded, presumably due to the narrowness of the condition they treated.[5] Some overlap of websites across search terms occurs; for example, many people who searched for information on various medical conditions visited the same website such as webmd.com. In sum, our panel data contains information on search terms used to reach 1057 unique websites.

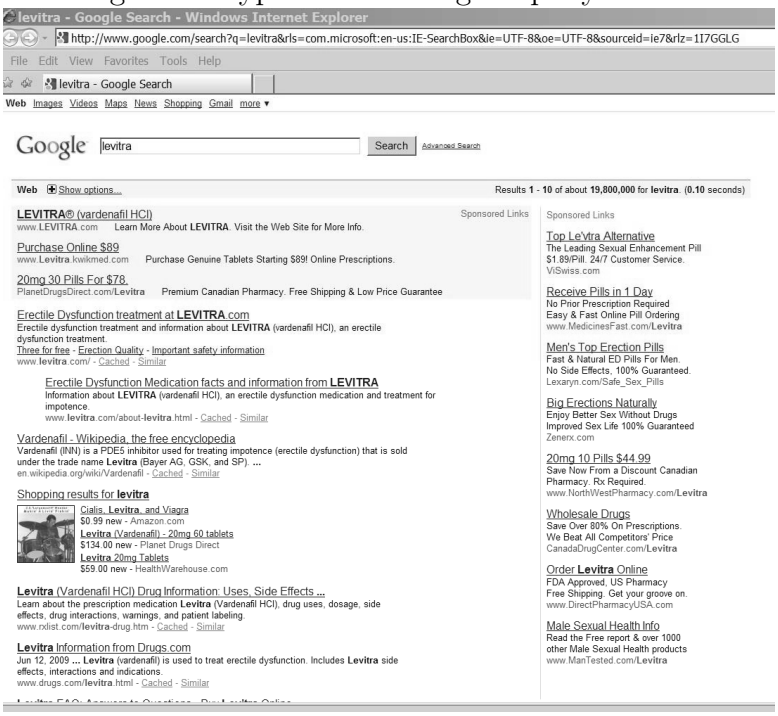
For each search term used to reach a website, we have information on how many consumers clicked on either a paid link or a non-paid link during each month. This distinction between paid and non-paid links is important, both for understanding how a search engine works and because it was the paid links that were targeted by the FDA. Figure 1 depicts the search results from a query on the keyword "Levitra" using the Google search engine. As shown in the figure, the search engine returns a list of paid and non-paid (also called "organic") results. The search ads appear in the paid results section (at the top and to the right) of the search results page, and they are listed separately from the main search results. Advertisers bid for text ads in response to consumers' keyword searches, and when a user clicks on the paid ad, the advertiser must pay the search engine.

In addition to pharmaceutical companies, many different types of advertisers place ads on keywords containing a pharmaceutical brand name or medical condition. For instance, most ads for the keyword "Levitra" are either for online pharmacies (often Canadian) such as northwestpharmacy.com or kwikmed.com, or for alternative natural remedies for erectile dysfunction like zernerx.com. These sites are able to advertise because no legal restriction exists on bidding for a pharmaceutical brand name. For example, in *Merck & Co. v. Mediplan Health Consulting, 2006 WL 800756 (SDNY Mar. 30, 2006)*, Merck lost its attempt to prevent Mediplan, a Canadian internet pharmacy, from bidding on keywords such as "Zocor".

[5]These were Avandaryl, Emend, Evista, Exjade, Fentora, Gleevec, Lucentis, Prezista, Treanda, Tykerb, and Xolair.

In the case, Merck claimed patent infringement, trademark infringement and dilution, and false advertising. The court dismissed Merck's claims on the grounds that Mediplan's actions did not represent a use of a trademark in commerce.

Figure 1: Typical search engine query results




Notes: This is the results page from a keyword search on "Levitra" in Google. The paid search ads appear in the paid results sections at the top and on the right side of the page. The non-paid (organic) results appear separately.

Our data report online behavior by the three major search engines (Google, Live and Yahoo!), which collectively account for approximately 92 percent of search activity in the US. Since Microsoft rebranded its search engine in the month after our study, we check robustness to the inclusion of observations from Live Search in Column (1) of Table A-3 in our Appendix.

A vast set of combinations of search terms and websites exist. Therefore, comScore imposes some selection criteria for inclusion into its database. ComScore only collects data on websites that receive search visits from at least 30 panel members, and it also only

collects data on specific phrases that arise from queries by at least two different members. For websites with fewer than three unique clicks, no statistics are reported. In the regressions we report in the paper, we assume that such advertisers receive two clicks, but as shown in Column (2) of Table A-3 in the Appendix, our results are also robust to assuming they receive one click.[6] We also restrict our sample to websites that have at least two non-zero clicks during the sample period, to eliminate websites that appear only in one or two months of the data. This allows us to identify website fixed effects.

ComScore recruits its panel members through affiliate programs and partnering with third party application providers, and it emphasizes and discusses the representativeness of their sample to the general population in their User Guide. For example, it states that "The accuracy and representivity [sic] of the comScore panel has been validated by several leading industry bodies and the use of independent third-party data sources". The comScore data have also been used in several academic studies (Montgomery et al., 2004; Santos et al., 2009).

### 2.2.1 Categories of Websites

We distinguish between four catgories of websites in our dataset: pharmaceutical, non-commercial, non-regulated, and other commercial. Pharmaceutical product websites are sites that are owned by pharmaceutical companies. For instance, Bayer (the manufacturer of Levitra) maintains the website levitra.com. In cases where a single product had two websites (e.g., Yaz.com and Yaz-US.com), we included data for both websites in our sample.

We also identified non-commercial websites in our sample by whether the website address contained a suffix of .ORG, .EDU, or .GOV. The motivation behind this grouping is to identify a set of websites that are more likely to provide impartial, balanced, and educational information because of their governmental or non-profit status. This category also included

[6]The results are also similar when we assume they receive zero clicks in the specifications where we do not use a log-dependent variable.

Wikipedia.org. Since Wikipedia is a unique non-profit, we tested the robustness of our results with and without Wikipedia sites in Column (3) of Table A-3. The results are qualitatively similar.

We identified community websites by whether they contained the words "community", "groups", "answers", or "forum" in their URL. We also included websites that allowed users to pose questions, which are then answered by other community members such as "Yahoo! Answers". The idea behind this categorization is to identify a set of websites where information is provided by members of the public rather than by verified or official sources. Given the FDA's emphasis in its letters on ensuring that information was complete and balanced, this is a category of websites where information is likely to be diffuse and not balanced in any one posting.

In addition, we identified websites that promoted medical solutions that are either prohibited by the FDA or that are not subject to strict control and testing by the FDA. These websites fall into three groups. The first are websites such as discountdrugsfromcanada.com that allow consumers to order prescription medications from outside of the US. Federal law prohibits consumers obtaining prescription drugs from Canada where they are cheaper due to government price caps, because of safety concerns over whether the drugs are genuine or fake. The second group are websites that offer herbal remedies such as nativeremedies.com. Though homeopathic remedies are regulated by the FDA, they do not have to undergo the same testing and review by the FDA before being sold as pharmaceutical products do; these manufacturers are not subject to the same fair-balance requirements in advertising as pharmaceutical products. The third group of websites offers advice about the consumption of marijuana, such as weedsthatplease.com. Thirteen states have approved the use of marijuana for medical purposes, but the FDA has not approved a medical use for marijuana.

Our last category consists of commercial websites, such as www.webmd.com. Commercial websites provide medical content information and may be supported by revenues from

Table 1: Summary Statistics

| | Mean | Std Dev | Min | Max | Observations |
|---|---|---|---|---|---|
| Non-Paid Clicks | 5637.9 | 11174.6 | 0 | 299024 | 25233 |
| Total Clicks | 6009.5 | 11337.6 | 50 | 305233 | 25233 |
| Paid Clicks | 371.5 | 1950.2 | 0 | 56387 | 25233 |
| Post-FDA | 0.60 | 0.49 | 0 | 1 | 30495 |
| Pharma Website | 0.022 | 0.15 | 0 | 1 | 30495 |
| Non-Regulated Website | 0.020 | 0.14 | 0 | 1 | 30495 |
| Non-Commercial Website | 0.16 | 0.36 | 0 | 1 | 30495 |
| .ORG Website | 0.099 | 0.30 | 0 | 1 | 30495 |
| .EDU Website | 0.013 | 0.11 | 0 | 1 | 30495 |
| .GOV Website | 0.044 | 0.20 | 0 | 1 | 30495 |
| Community Forum Website | 0.044 | 0.21 | 0 | 1 | 30495 |
| Brand search term | 0.074 | 0.26 | 0 | 1 | 30495 |
| Observations | 30495 | | | | |

advertising. These websites provide the baseline time-trend in our analysis.

Table 1 reports summary statistics for our panel of website and search combinations. Most of the visits to the websites originated from clicks on unpaid links. The average website in our sample received 6000 total clicks, of which 5600 were unpaid. Pharmaceutical websites comprise a small fraction of the sample (2 percent). People visited a greater diversity of sites as a result of medical condition searches than for searches that used a brand name; website visits to brand searches consist of 7 percent of the sample. Non-commercial websites are 16 percent of the sample, with the majority of these websites containing a .ORG suffix.

The FDA warning reduced the number of search ads by pharmaceutical firms. As displayed in Figure 2, from March to April 2009, the fraction of pharmaceutical websites in our sample that purchased a search ad for the brand keyword of their drug dropped from 82 to 28 percent.[7] For non-pharmaceutical websites, no corresponding change in ad behavior occurred, with 12 percent of these websites displaying paid ads in March and April 2009.

Though the majority of search ads was removed, some pharmaceutical companies con-

[7]For websites with fewer than three unique clicks and therefore below the comScore minimum reporting standards, we assume that no paid ads were present. A similar pattern is found if we graph the number of paid clicks over this period, assuming that such advertisers receive either one or two clicks.

tinued displaying their ads, but with dramatically changed text. For example, Eli Lilly tried to circumvent the fair balance requirements by removing any mention of treatment in their ads. An ad for the drug Cialis might provide a link to the official website and text that merely states, "Official Site. Free Trial Voucher."[8] Therefore, our results capture both the removal of actual ads by pharmaceutical companies and the removal of informative content within ads by pharmaceutical companies.

We also checked that the dramatic shift in pharmaceutical advertising behavior was linked to the FDA warning letters, and did not represent changing seasonality in behavior. Figure 3 shows the proportion of paid ads for same months in the year 2008. In this previous year within the same time frame, pharmaceutical companies slightly increased their paid search advertising for pharmaceutical sites from 68 percent to 70 percent.

We also investigated whether any major shifts in other types of ad spending occurred during this period. With the worsening economic cycle, advertising spending decreased across the largest media outlets. Arnold (2009) suggests that pharmaceutical ad spending on TV fell by 6% to $1.5 billion for the period that we study compared to 2008. However, this decrease occurred across February to June 2009 and does not appear to be related to the change in FDA policy in April.

[8] "Drug Makers to Press for Guidance on Web Marketing, Wall Street Journal, Emily Steel, November 12, 2009.

Figure 2: Fraction of pharmaceutical and non-pharmaceutical websites with paid search ads before and after FDA policy change

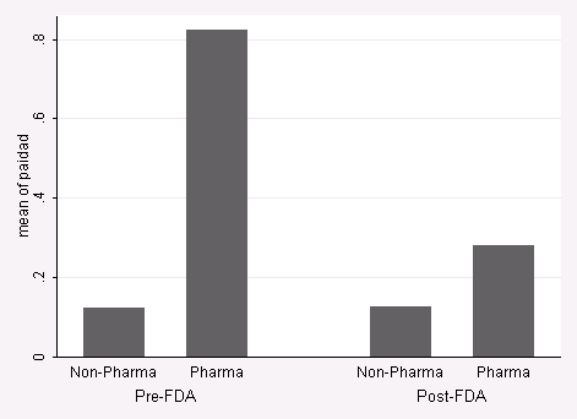
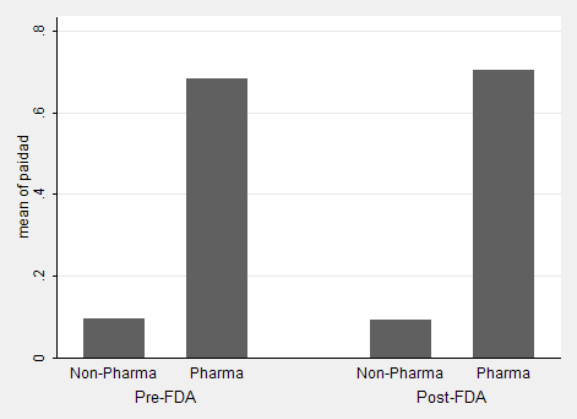



Figure 3: Fraction of pharmaceutical and non-pharmaceutical websites with paid search ads in comparable months to the FDA policy change but in 2008



# 3 Estimation and Results

We use the following specification to track how the FDA warnings affected consumer searches. For each website $i$ reached by a consumer using search term $j$ in month $t$, we model the log of total clicks as:

$$\begin{aligned} log(clicks_{ijt}) &= \beta_0 + \beta_1 Pharma_i * PostFDA_t + \beta_2 Noncommercial_i * PostFDA_t \\ &+ \beta_3 Nonregulated_i * PostFDA_t + \beta_4 CommunityForum_i * PostFDA_t \\ &+ \beta_5 PostFDA_t + \gamma_i + \alpha_j + \epsilon_{ijt} \end{aligned}$$

where $Pharma$ is an indicator variable equal to 1 if the website is owned by the pharmaceutical company, $NonCommercial$ is an indicator variable equal to 1 if the website is a non-commercial site with an address that contains a suffix of .ORG, .EDU, or .GOV, $NonRegulated$ is an indicator variable equal to 1 if the website directs consumers to products that are not regulated by the FDA, $CommunityForum$ is an indicator variable equal to 1 if the website is a community forum, and $PostFDA$ is an indicator variable equal to 1 if the month occurs after March 26, 2009, when the FDA issued the letters. The controls $\gamma$ and $\delta$ are website and search term fixed effects. The coefficient on the interaction term $Pharma * PostFDA$ captures the effect of the FDA ruling on consumer visits to pharmaceutical websites. The coefficients on the interaction terms $NonCommercial * PostFDA$, $Nonregulated * PostFDA$, and $CommunityForum * PostFDA$ capture the effects of the FDA ruling on consumer visits to medical information, non-regulated, and community forum sites. The omitted category consists of commercial websites that are not owned by pharmaceutical companies, so the interaction terms capture the effect on clicks within a particular category of websites in the months following the FDA warning letters relative to these commercial websites.

Table 2 presents our initial results. Columns (1)-(4) display the estimates from the incremental addition of the various components of equation (1), with Column (4) capturing the full specification. Columns (5)-(6) show how the results vary by whether the search term included a brand name or a medical condition.

Table 2 suggests that in the absence of pharmaceutical search ads, total clicks to pharmaceutical websites declined relative to commercial websites by approximately 80 percent. Columns (5) and (6) reveal that the decline in visits to pharmaceutical websites resulted primarily from a decrease in visits from consumers using medical conditions search terms; total clicks for consumers searching on brand terms remain relatively unchanged. This suggests that advertising encourages traffic to a website when a consumer is searching for general information on a medical condition and may not be aware of a pharmaceutical brand. However, for consumers already aware of and searching on a pharmaceutical brand, advertising does not significantly increase total clicks to the website.

Visits to non-commercial sites increased after the FDA letters by 140 percent for customers who were searching for information using a brand name keyword. Traffic to non-commercial websites from medical conditions searches declined by 18 percent. A potential explanation for this asymmetry is that consumers who are seeking information on brand terms are already informed about the brand's general characteristics and want specific information, perhaps about dosage or side effects. Therefore, without a paid ad to click on, these consumers are more likely to seek this information from other plausibly unbiased sources. By contrast, consumers who are seeking information on a medical condition may not already be aware of the brand. If product ads are present, these consumers may seek out information about that brand from what they perceive to be an unbiased website. However, when there are no pharmaceutical ads or there are uninformative pharmaceutical ads, consumers are not informed about the product, so they are not likely to try to seek information about it elsewhere.

Table 2: Restricted pharmaceutical advertising changes search behavior

| | All terms | | | | Brand Terms | Medical Conditions |
|---|---|---|---|---|---|---|
| | (1) | (2) | (3) | (4) | (5) | (6) |
| | Log Clicks | Log Clicks | Log Clicks | Log Clicks | Log Clicks | Log Clicks |
| Post-FDA*Pharma Website | -0.827*** | -0.827*** | -0.827*** | -0.827*** | 0.00234 | -1.783*** |
| | (0.279) | (0.279) | (0.279) | (0.284) | (0.302) | (0.533) |
| Post-FDA*Non-Commercial Website | -0.151 | -0.151 | -0.151 | -0.151 | 1.398* | -0.184* |
| | (0.105) | (0.105) | (0.105) | (0.107) | (0.718) | (0.108) |
| Post-FDA*Non-Regulated Website | 0.568*** | 0.568*** | 0.568*** | 0.568*** | 0.134 | 0.760*** |
| | (0.166) | (0.166) | (0.166) | (0.169) | (0.347) | (0.230) |
| Post-FDA*Community Forum Website | 0.172 | 0.172 | 0.172 | 0.172 | 0.805** | 0.115 |
| | (0.172) | (0.172) | (0.172) | (0.175) | (0.390) | (0.181) |
| Post-FDA | -0.201*** | -0.201*** | -0.201*** | -0.201*** | -0.391** | -0.188*** |
| | (0.0503) | (0.0503) | (0.0504) | (0.0513) | (0.158) | (0.0524) |
| Pharma Website | 0.826*** | 0.984*** | 1.398*** | | | |
| | (0.240) | (0.260) | (0.220) | | | |
| Non-Commercial Website | 0.304* | 0.326 | 0.305 | | | |
| | (0.184) | (0.200) | (0.212) | | | |
| Non-Regulated Website | -0.795** | -0.786* | -0.704* | | | |
| | (0.362) | (0.403) | (0.378) | | | |
| Community Forum Website | 0.115 | 0.0398 | 0.0146 | | | |
| | (0.223) | (0.232) | (0.243) | | | |
| Constant | 6.594*** | 6.755*** | 5.863*** | 6.858*** | 3.158*** | 6.769*** |
| | (0.104) | (0.117) | (0.138) | (0.101) | (0.306) | (0.102) |
| Search Engine Fixed Effects | No | Yes | Yes | Yes | Yes | Yes |
| Website Fixed Effects | No | No | No | Yes | Yes | Yes |
| Keyword Fixed Effects | No | No | Yes | Yes | Yes | Yes |
| Observations | 30495 | 30495 | 30495 | 30495 | 2270 | 28225 |
| R-Squared | 0.00371 | 0.0133 | 0.0334 | 0.236 | 0.282 | 0.248 |

Robust standard errors clustered at the keyword level. $^{*}p < 0.1$, $^{**}p < 0.05$, $^{***}p < 0.01$.

Websites that focused on medical treatments not regulated by the FDA received more clicks after the FDA warning. This appears to have been driven by consumers who were searching for information using medical conditions rather than brand names. Consumers searching for pharmaceutical brands increased their visits to community forum websites by almost 80 percent; no corresponding increase occurred for consumers searching on medical conditions. The negative coefficient on $PostFDA$ indicates that over the sample period, total clicks on commercial websites declined.

After the FDA warning, search patterns and the resulting information that search engine

users acquired changed. The policy change had different effects on consumers, depending upon their prior knowledge of the product and medical condition. An unintended consequence of the FDA warning was to shift the patterns of consumers' online behavior. If the intent of the warning was to deter consumers from misleading advertisements, the FDA policy had no such effect for consumers that were already aware of the pharmaceutical brand. The absence of the ads did not affect the number of visits to pharmaceutical websites. However, the removal of the ads did decrease traffic for consumers who were searching on general medical conditions. Given the larger volume of searches on medical conditions as opposed to brand keywords, the overall effect of the FDA warning appears to have diverted online traffic to websites that promote health sectors not regulated by the FDA.

When evaluating the desirability of direct-to-consumer advertising, it is important to recognize that, particularly on the Internet, alternative sources of information do exist. In the absence of advertisements, consumers may seek information from other sources that may not necessarily be more balanced in their presentation of the product.

# 4 Investigating the difference between paid and non-paid search

The results in Table 2 to do not distinguish between clicks that the website paid for and clicks that the website did not pay for. Since this distinction has commercial implications and also can serve as a robustness check, we explore this further in this section. Table 3 presents stratified results for the specification in Column (4) of Table 2. Column (1) reports the results for non-paid clicks, that is the number of clicks generated by users who navigated to the website through the main search results as opposed to the paid ads. Column (2) reports the results for consumers who navigated to the website through a paid search link.

As expected, with the removal of paid search ads by pharmaceutical companies, paid

Table 3: Separate results for non-paid and paid search terms

| | All terms | | Brand Terms | | Medical Terms | |
|---|---|---|---|---|---|---|
| | (1) | (2) | (3) | (4) | (5) | (6) |
| | Log Non-Paid | Log Paid | Log Non-Paid | Log Paid | Log Non-Paid | Log Paid |
| Post-FDA*Pharma Website | -0.0956 | -2.753*** | 0.380 | -2.938*** | -0.609** | -2.337*** |
| | (0.191) | (0.379) | (0.288) | (0.431) | (0.304) | (0.497) |
| Post-FDA*Non-Commercial Website | -0.116 | 0.00207 | 1.380* | 0.0809** | -0.146 | -0.00478 |
| | (0.106) | (0.0589) | (0.717) | (0.0349) | (0.107) | (0.0603) |
| Post-FDA*Non-Regulated Website | 0.467*** | 0.168 | 0.342* | -0.151 | 0.543*** | 0.300** |
| | (0.143) | (0.124) | (0.178) | (0.269) | (0.191) | (0.122) |
| Post-FDA*Community Forum Website | 0.200 | -0.0168 | 0.662** | 0.323 | 0.158 | -0.0471 |
| | (0.174) | (0.0482) | (0.314) | (0.266) | (0.179) | (0.0460) |
| Post-FDA | -0.239*** | 0.0209 | -0.373** | -0.0809** | -0.229*** | 0.0281 |
| | (0.0493) | (0.0269) | (0.155) | (0.0349) | (0.0501) | (0.0284) |
| Constant | 6.669*** | 1.667*** | 2.800*** | 2.535*** | 6.597*** | 1.572*** |
| | (0.104) | (0.0748) | (0.305) | (0.126) | (0.107) | (0.0706) |
| Search Engine Fixed Effects | Yes | Yes | Yes | Yes | Yes | Yes |
| Website Fixed Effects | Yes | Yes | Yes | Yes | Yes | Yes |
| Keyword Fixed Effects | Yes | Yes | Yes | Yes | Yes | Yes |
| Observations | 30495 | 30495 | 2270 | 2270 | 28225 | 28225 |
| R-Squared | 0.326 | 0.554 | 0.311 | 0.601 | 0.348 | 0.563 |

Robust standard errors clustered at the keyword level. *$p < 0.1$, **$p < 0.05$, ***$p < 0.01$.

clicks for pharmaceutical websites decreased substantially. Site traffic was diverted to other forms of online information, depending on the type of search conducted by the consumer.

The results support our preliminary analysis that paid search ads act as a substitute for people who are already aware of a brand, but as a complement for people who are not. As shown in Columns (3) and (4) for brand term searches, the decrease in paid clicks was offset by an increase in non-paid clicks (though this is imprecisely estimated). Consistent with this evidence, total clicks for brand searches remained unchanged as discussed earlier for Table 2. This suggests that in the absence of a pharmaceutical ad, consumers (who were already aware of and searching on a brand name) simply clicked on the non-paid link of the pharmaceutical website. On the other hand, for searches on medical terms as shown in Columns (5) and (6), the removal of pharmaceutical ads led to a decrease in clicks for both paid and non-paid links. The presence of a pharmaceutical ad or paid link encourages consumers (who may not be aware of a particular brand) to visit the brand's website either

through the paid or unpaid link.

This finding sheds light on a small but newly emerging literature on search advertising by firms. Rutz and Bucklin (2008) analyze the effect of a paid search campaign from a major lodging chain on consumer search behavior in Google. They find that search ads increase paid clicks for websites. In a controlled field experiment, Ghose and Yang (2010) find that paid ads also often complement non-paid links. Our results contribute to this prior work by emphasizing that the relationship between paid and non-paid links varies crucially with the keyword concerned.

Our findings suggest that positive spillovers between paid and non-paid links exist for a consumer who is not already informed about the product, but that for a consumer who already has some knowledge about the product (in our case, is informed about the brand name), simple substitution occurs between paid and non-paid links. This suggests that while a large majority (74 percent) of pharmaceutical companies advertise on their brand keywords, no corresponding increase in traffic occurs as a result. Instead, the advertisements on keywords for general medical conditions generate increased website traffic and also serve to increase awareness of the brand.

Our results also indicate that the increased traffic to non-commercial and non-FDA-regulated websites for brand searches is due primarily to an increase in non-paid clicks. While total clicks remain the same for pharmaceutical websites, non-paid clicks for these pharmaceutical websites increase as well as those for non-commercial (138 percent), non-FDA-regulated (34 percent), and community forum (66 percent) websites. One interpretation is that in the absence of paid links, people must scan non-paid results to locate the link to the pharmaceutical company's website; with their attention refocused on the organic results, they are now more likely to be diverted to other types of non-paid results as well. In fact, eye-tracking studies have shown that consumers tend to focus their attention on the upper left

triangle of the browser, which often includes the paid links.[9] For those consumers interested in obtaining information for a specific brand, their active search for the brand's website in the non-paid results may shift their attention. The results indicate that the other non-paid links do not crowd out visits to pharmaceutical websites. Traffic to pharmaceutical and other non-paid links both increase, suggesting that consumers now visit several paid links from one keyword search query. Therefore, the FDA warning appears to have expanded the set of information accumulated by consumers; rather than just diverting consumers from paid to non-paid links of pharmaceutical websites, consumers visit a greater variety of sources online due to the increased attention on non-paid results.

# 5 Discussion and Conclusion

On March 26, 2009, the FDA issued letters of warnings to manufacturers of 48 drugs, indicating that their online ads did not properly convey any risk information. As many pharmaceutical companies could not adequately disclose the side effects in the 3-line text limit of the ad, many companies removed their online ads. We study the effect of these FDA warnings sent to pharmaceutical companies, which severely restricted their use of search advertising. Our work sheds light on the current debate over the desirability of direct-to-consumer pharmaceutical advertising. We provide direct evidence of how pharmaceutical advertising changes the set of information that a consumer seeks and acquires online. Our results also are the first to provide evidence on the use of online search by consumers seeking medication advice. This paper also directly examines how advertising regulations imposed in the pre-Internet era affect these new emerging, online markets.

Our empirical analysis suggests that restricting pharmaceutical advertising does not necessarily lead consumers to seek more balanced sources of information. The major benefi-

[9] "Google Eye Tracking Report", Enquiro white paper, 2005.

ciaries of the restrictions appear to have been channels not regulated by the FDA, such as Canadian pharmacies and purveyors of alternative homeopathic remedies. Although some evidence exists that people who are already aware of the brand name of pharmaceutical products are more likely to consult non-commercial sources for information, evidence also persists that a smaller but still sizable number of consumers are increasingly relying on non-verified information from the public.

We also find that positive spillovers exist between search ads for pharmaceutical brands and non-paid results when consumers are not aware of the brand and searching for information on general medical conditions; the presence of an ad encourages consumers to visit pharmaceutical websites. On the other hand, when consumers are already aware of and conducting a search on a brand, the absence of a pharmaceutical ad does not affect visits to the website; instead, consumers simply visit the website through the main search results.

Our results have a direct public policy implication for the regulation of advertising in online markets. We find that pharmaceutical advertising does have a direct effect on which websites consumers acquire information from online, especially for individuals seeking general information on medical conditions. In the absence of pharmaceutical advertising, consumers are more likely acquire information from other less-regulated channels. The shift in consumers' search behavior may or may not be desirable, depending on the quality of the alternative sources of information.

This paper documents how the types of information that consumers gather about treatment options varies with advertising regulation. Future avenues of work can investigate how consumers use the information they have collected and how it affects prescriptions for pharmaceutical products. While we study the immediate aftermath to the warning letter, other changes in the structure of pharmaceutical advertising are likely to arise in the long run. For example, major search engines indicate that they are developing special formats for drug advertising that could accommodate the need to warn consumers about side effects.

The consequences of the FDA warning for pharmaceutical advertising are likely to shape the way in which the market for online advertising develops in the future.

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# Appendix

Table A-1: Full Listing of Drugs, FDA approved use, Webpage and Keywords

| Drug | FDA-approved use | Webpage | Brand Keyword |
|---|---|---|---|
| Aromasin | Aromasin is indicated for adjuvant treatment of postmenopausal women with estrogen-receptor positive early breast cancer who have received two to three years of tamoxifen and are switched to Aromasin for completion of a total of five consecutive years of adjuvant hormonal therapy. Aromasin is indicated for the treatment of advanced breast cancer in postmenopausal women whose disease has progressed following tamoxifen therapy. | AROMASIN.COM | |
| Avandamet | Avandamet is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus when treatment with dual rosiglitazone and metformin therapy is appropriate. The PI includes important limitations to use, such that Avandamet should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis, the co-administration of Avandamet and insulin is not recommended, and the use of Avandamet with nitrates is also not recommended. | AVANDAMET.COM | avandamet |
| Avandia | Avandia is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Avandia should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis, the co-administration of Avandia and insulin is not recommended, and the use of Avandia with nitrates is also not recommended. | AVANDIA.COM | avandia |
| Avastin | Avastin is indicated, among other things, in combination with intravenous 5-fluorouracil-based chemotherapy for first- or second-line treatment of patients with metastatic carcinoma of the colon or rectum. | AVASTIN.COM | avastin |
| Avodart | Avodart is indicated for the treatment of symptomatic benign prostatic hyperplasia (BPH) in men with an enlarged prostate to improve symptoms, reduce the risk of acute urinary retention (AUR), and reduce the risk of the need for BPH-related surgery. | AVODART.COM | avodart |
| Boniva | Boniva is indicated for the treatment and prevention of osteoporosis in postmenopausal women. Boniva increases bone mineral density (BMD) and reduces the incidence of vertebral fractures. | BONIVA.COM | boniva |
| Bystolic | Bystolic is indicated for the treatment of hypertension. Bystolic may be used alone or in combination with other antihypertensive agents. | BYSTOLIC.COM | bystolic |
| Caduet | Caduet (amlodipine and atorvastatin) is indicated in patients for whom treatment with both amlodipine and atorvastatin is appropriate. The Indications and Usage section provides a detailed description of the indications for each of the drug's two active ingredients. | CADUET.COM | caduet, novasc |
| Campral | Campral is indicated for the maintenance of abstinence from alcohol in patients with alcohol dependence who are abstinent at treatment initiation. Treatment with Campral should be part of a comprehensive management program that includes psychosocial support. The efficacy of Campral in promoting abstinence has not been demonstrated in patients who have not undergone detoxification and have not achieved alcohol abstinence before initiation of Campral treatment. Additionally, the efficacy of the drug in promoting abstinence from alcohol in polysubstance abusers has not been adequately assessed. | CAMPRAL.COM | campral |
| Celebrex | Carefully consider the potential benefits and risks of CELEBREX and other treatment options before deciding to use CELEBREX. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals....CELEBREX is indicated [among other things]: 1) For relief of the signs and symptoms of osteoarthritis. 2) For relief of the signs and symptoms of rheumatoid arthritis in adults. 3) For relief of the signs and symptoms of juvenile rheumatoid arthritis in patients 2 years and older.... | CELEBREX.COM | celebrex |
| Chantix | Chantix is indicated as an aid to smoking cessation treatment. | CHANTIX.COM | chantix |
| Cymbalta | Cymbalta is indicated, among other things, for the acute and maintenance treatment of major depressive disorder (MDD). | CYMBALTA.COM | cymbalta |

Continued on next page

Table A-1 – continued from previous page

| Drug | FDA-approved use | Webpage | Brand Keyword |
|---|---|---|---|
| Detrol | Detrol LA Capsules are once daily extended release capsules indicated for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency. | DETROLLA.COM | detrol |
| Diovan | Diovan is indicated, among other things, for the treatment of hypertension. It may be used alone or in combination with other antihypertensive agents. | DIOVAN.COM | diovan |
| Exforge | Exforge is indicated for the treatment of hypertension. Exforge may be used in patients whose blood pressure is not adequately controlled on either [amlodipine or valsartan as] monotherapy. Exforge may also be used as initial therapy in patients who are likely to need multiple drugs to achieve their blood pressure goals. The choice of Exforge as initial therapy for hypertension should be based on an assessment of potential benefits and risks including whether the patient is likely to tolerate the lowest dose of Exforge.... | EXFORGE.COM | exforge |
| Femara | Femara is indicated for the adjuvant treatment of postmenopausal women with hormone receptor positive early breast cancer. Femara is indicated for the extended adjuvant treatment of early breast cancer in postmenopausal women who have received 5 years of adjuvant tamoxifen therapy. Femara is indicated for first-line treatment of postmenopausal women with hormone receptor positive or hormone receptor unknown locally advanced or metastatic breast cancer. Femara is also indicated for the treatment of advanced breast cancer in postmenopausal women with disease progression following antiestrogen therapy. The Indications and Usage section of the PI includes important limitations for Femara's use in the adjuvant setting, including that the effectiveness of Femara in early breast cancer is based on an analysis of disease-free survival in patients treated for a median of 24 months and followed for a median of 26 months and follow-up analyses will determine long-term outcomes for both safety and efficacy. This section also includes important limitations for Femara's use in the extended adjuvant setting, including that the effectiveness of Femara in extended adjuvant treatment of early breast cancer is based on an analysis of disease-free survival in patients treated for a median of 24 months and further data will be required to determine long-term outcome. | FEMARA.COM | femara |
| Flomax | Flomax is indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH). Flomax is not indicated for the treatment of hypertension. | 4FLOMAX.COM | flomax |
| Gemzar | Gemzar is indicated, among other things, in combination with cisplatin for the first-line treatment of patients with inoperable, locally advanced (Stage IIIA or IIIB), or metastatic (Stage IV) non-small cell cancer. | GEMZAR.COM | gemzar |
| Herceptin | Herceptin is indicated for adjuvant treatment of HER2 overexpressing node positive or node negative (ER/PR negative or with one high risk feature) breast cancer: as part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel; with docetaxel and carboplatin; as a single agent following multi-modality anthracycline based therapy. Herceptin is also indicated in combination with paclitaxel for first-line treatment of HER2-overexpressing metastatic breast cancer, or as a single agent for treatment of HER2-overexpressing breast cancer in patients who have received one or more chemotherapy regimens for metastatic disease. | HERCEPTIN.COM | |
| Januvia | Januvia is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. The PI includes important limitations of use, such that Januvia should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings, and that Januvia has not been studied in combination with insulin. | JANUVIA.COM | januvia |
| Levitra | Levitra is indicated for the treatment of erectile dysfunction. | LEVITRA.COM | levitra |
| Lexapro | Lexapro is indicated, among other things, for the acute and maintenance treatment of major depressive disorder (MDD) in adults and in adolescents 12 to 17 years of age. | LEXAPRO.COM | lexapro |
| Lyrica | Lyrica is indicated, among other things, for: . . . Management of neuropathic pain associated with diabetic peripheral neuropathy; . . . Adjunctive therapy for adult patients with partial onset seizures [and] . . . Management of fibromyalgia. | LYRICA.COM | lyrica |

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Table A-1 – continued from previous page

| Drug | FDA-approved use | Webpage | Brand Keyword |
|---|---|---|---|
| Mirapex | Mirapex is indicated, among other things, for the treatment of moderate-to-severe primary Restless Legs Syndrome (RLS). | MIRAPEX.COM | mirapex |
| Mirena | Mirena is indicated for intrauterine contraception for up to 5 years. Thereafter, if continued contraception is desired, the system should be replaced. Mirena is recommended for women who have had at least one child. | MIRENA-US.COM | mirena |
| Namenda | Namenda is indicated for the treatment of moderate to severe dementia of the Alzheimer's type. | NAMENDA.COM | namenda |
| Pegasys | Pegasys is indicated, among other things, alone or in combination with Copegus (ribavirin) for the treatment of adults with chronic hepatitis C (CHC) virus infection who have compensated liver disease and have not been previously treated with interferon alpha. | PEGASYS.COM | |
| Plavix | For patients with a history of recent myocardial infarction (MI), recent stroke, or established peripheral arterial disease, PLAVIX has been shown to reduce the rate of a combined endpoint of new ischemic stroke (fatal or not), new MI (fatal or not), and other vascular death. | PLAVIX.COM | plavix |
| Propecia | PROPECIA is indicated for the treatment of male pattern hair loss (androgenetic alopecia) in MEN ONLY. Safety and efficacy were demonstrated in men between 18 to 41 years of age with mild to moderate hair loss of the vertex and anterior mid-scalp area. Efficacy in bitemporal recession has not been established. PROPECIA is not indicated in women . . . [or] children . . . | PROPECIA.COM | propecia |
| Pulmozyme | Daily administration of Pulmozyme (dornase alpha) Inhalation Solution in conjunction with standard therapies is indicated in the management of cystic fibrosis patients to improve pulmonary function. In patients with an FVC 40% of predicted, daily administration of Pulmozyme has also been shown to reduce the risk of respiratory tract infections requiring parenteral antibiotics. The Indications and Usage section of the PI also includes the important limitation that the safety and efficacy of daily administration have not been demonstrated in patients for longer than 12 months. | PULMOZYME.COM | |
| Rituxan | Rituxan is indicated for the treatment of non-Hodgkin's Lymphoma (NHL) patients with: Relapsed or refractory, low-grade or follicular, CD-20-positive, B-cell, NHL as a single agent; Previously untreated follicular, CD-20-positive, B-cell NHL in combination with CVP chemotherapy; Non-progressing (including stable disease), low-grade, CD-20-positive, B-cell NHL, as a single agent, after first-line CVP chemotherapy; Previously untreated diffuse large B-cell, CD20-positive, NHL in combination with CHOP or other anthracycline-based chemotherapy regimens. Rituxan in combination with methotrexate is also indicated to reduce signs and symptoms and to slow the progression of structural damage in adult patients with moderately-to-severely-active rheumatoid arthritis who have had an inadequate response to one or more TNF antagonist therapies. | RITUXAN.COM | rituxan |
| Singulair | Singulair is indicated, among other things, for the relief of symptoms of allergic rhinitis (seasonal allergic rhinitis in adults and pediatric patients 2 years of age and older, and perennial allergic rhinitis in adults and pediatric patients 6 months of age and older). | SINGULAIR.COM | singulair |
| Spiriva | Spiriva is indicated for the long-term, once-daily, maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema. | SPIRIVA.COM | spiriva |
| Tysabri | TYSABRI is indicated as monotherapy for the treatment of patients with relapsing forms of multiple sclerosis to delay the accumulation of physical disability and reduce the frequency of clinical exacerbations . . . . Because TYSABRI increases the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability, TYSABRI is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, alternate multiple sclerosis therapies. Because of the risk of PML, a consequence of TYSABRI use that is fatal or severely debilitating, TYSABRI is available only through a special restricted distribution program. | TYSABRI.COM | |

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Table A-1 – continued from previous page

| Drug | FDA-approved use | Webpage | Brand Keyword |
|---|---|---|---|
| Xeloda | Xeloda is indicated, among other things, as a single agent for adjuvant treatment in patients with Dukes' C colon cancer who have undergone complete resection of the primary tumor when treatment with fluoropyrimidine therapy alone is preferred. Xeloda was non-inferior to 5-flourouracil and leucovorin (5-FU/LV) for disease-free survival and while neither Xeloda nor combination therapy increases overall survival, combination therapy has been shown to improve disease-free survival compared to 5-FU/LV. Xeloda is also indicated as first-line treatment of patients with metastatic colorectal carcinoma when treatment with fluoropyrimidine therapy alone is preferred. Combination chemotherapy demonstrated a survival benefit compared to 5-FU/LV alone, however, a survival benefit over 5-FU/LV has not been demonstrated with Xeloda monotherapy. | XELODA.COM | xeloda |
| Yaz | YAZ is indicated for the prevention of pregnancy in women who elect to use an oral contraceptive. YAZ is also indicated for the treatment of symptoms of premenstrual dysphoric disorder (PMDD) in women who choose to use an oral contraceptive as their method of contraception. The effectiveness of YAZ for PMDD when used for more than three menstrual cycles has not been evaluated. YAZ has not been evaluated for the treatment of premenstrual syndrome (PMS). YAZ is also indicated for the treatment of moderate acne vulgaris in women at least 14 years of age, who have no known contraindications to oral contraceptive therapy, and have achieved menarche. YAZ should be used for the treatment of acne only if the patient desires an oral contraceptive for birth control. | YAZ-US.COM | yaz |

Table A-2: Medical Condition Keywords

| Medical Condition Keywords | |
|---|---|
| aids | hay fever |
| alcoholism | hct |
| allergies | headaches |
| alopecia | heart attack |
| alzheimer | hepatitis c |
| anxiety | hiv |
| arthritis | hypertension |
| asthma | incontinence |
| baldness | iud |
| birth control | leukemia |
| blood clots | lung cancer |
| blood pressure | lymphoma |
| blood sugar | macular degeneration |
| bph | mdd |
| breast cancer | multiple sclerosis |
| bronchitis | neuropathy |
| carcinoma | norvasc |
| chemotherapy | osteoporosis |
| cll | ovarian cancer |
| colon cancer | overactive bladder |
| contraception | pms |
| contraceptive | prostate cancer |
| cystic fibrosis | rheumatoid arthritis |
| dementia | runny nose |
| depression | sarcoma |
| diabetes | shingles |
| diabetic | smoking |
| diabetic neuropathy | stomach cancer |
| emphysema | stroke |
| enlarged prostate | vomiting |
| erectile dysfunction | |
| erection | |
| fibromyalgia | |
| finasteride | |
| hair loss | |

Table A-3: Robustness Checks

| | No Live Search | Assume 1 click | No Wiki | No June | March+April | No Search Sites |
|---|---|---|---|---|---|---|
| | (1) | (2) | (3) | (4) | (5) | (6) |
| | Log Clicks | Log Clicks | Log Clicks | Log Clicks | Log Clicks | Log Clicks |
| Post-FDA*Pharma Website | -0.696** | -0.827*** | -0.821*** | -1.259*** | -1.673*** | -0.858*** |
| | (0.299) | (0.284) | (0.285) | (0.363) | (0.480) | (0.285) |
| Post-FDA*Non-Commercial Website | -0.143 | -0.151 | -0.177 | -0.0119 | -0.0452 | -0.181* |
| | (0.107) | (0.107) | (0.113) | (0.103) | (0.125) | (0.108) |
| Post-FDA*Non-Regulated Website | 0.581*** | 0.568*** | 0.575*** | 0.481*** | 0.270 | 0.538*** |
| | (0.178) | (0.169) | (0.170) | (0.171) | (0.196) | (0.170) |
| Post-FDA*Community Forum Website | 0.202 | 0.172 | 0.187 | 0.0964 | -0.0710 | 0.141 |
| | (0.176) | (0.175) | (0.203) | (0.162) | (0.207) | (0.176) |
| Post-FDA | -0.232*** | -0.201*** | -0.208*** | 0.0447 | -0.0907 | -0.171*** |
| | (0.0525) | (0.0513) | (0.0540) | (0.0496) | (0.0594) | (0.0531) |
| Constant | 6.860*** | 6.858*** | 6.729*** | 7.903*** | 8.277*** | 6.747*** |
| | (0.102) | (0.101) | (0.103) | (0.107) | (0.125) | (0.102) |
| Search Engine Fixed Effects | Yes | Yes | Yes | Yes | Yes | Yes |
| Website Fixed Effects | Yes | Yes | Yes | Yes | Yes | Yes |
| Keyword Fixed Effects | Yes | Yes | Yes | Yes | Yes | Yes |
| Observations | 28920 | 30495 | 28545 | 24396 | 12198 | 28855 |
| R-Squared | 0.245 | 0.236 | 0.235 | 0.255 | 0.317 | 0.223 |

Robust standard errors clustered at the keyword level. $^{*}p < 0.1$, $^{**}p < 0.05$, $^{***}p < 0.01$. Table A-3 replicates the results for Table 2 under various robustness checks: omitting Microsoft Live search, redefining data below the minimum reporting standards as one click, omitting Wikipedia, restricting the months to March and April, and omitting search sites. In June 2009, Microsoft switched its search engine from the "Live" to the "Bing" platform. Therefore in Column (1) we exclude "Live" from our analysis. Its inclusion does not change our results substantively.

Table A-4: Restricted pharmaceutical advertising changes search behavior: Total Clicks

| | All terms | | | | Brand Terms | Medical Conditions |
|---|---|---|---|---|---|---|
| | (1) | (2) | (3) | (4) | (5) | (6) |
| | Total Clicks | Total Clicks | Total Clicks | Total Clicks | Total Clicks | Total Clicks |
| Post-FDA*Pharma Website | -2297.0*** | -2297.0*** | -2297.0*** | -2297.0*** | -2193.7** | -2840.8*** |
| | (666.3) | (666.3) | (667.4) | (679.2) | (1063.0) | (809.6) |
| Post-FDA*Non-Commercial Website | -463.3** | -463.3** | -463.3** | -463.3** | 1072.9*** | -470.6** |
| | (228.0) | (228.0) | (228.4) | (232.5) | (371.0) | (233.4) |
| Post-FDA*Non-Regulated Website | 325.4** | 325.4** | 325.4** | 325.4** | 288.1 | 265.4 |
| | (154.2) | (154.2) | (154.5) | (157.2) | (249.6) | (169.1) |
| Post-FDA*Community Forum Website | 66.15 | 66.15 | 66.15 | 66.15 | -29.04 | 68.00 |
| | (211.3) | (211.3) | (211.7) | (215.4) | (469.7) | (249.4) |
| Post-FDA | -295.4*** | -295.4*** | -295.4*** | -295.4*** | -16.13 | -315.2*** |
| | (106.1) | (106.1) | (106.2) | (108.1) | (151.2) | (111.5) |
| Pharma Website | 2783.7** | 3375.6*** | 4903.6*** | | | |
| | (1175.6) | (1236.9) | (1121.0) | | | |
| Non-Commercial Website | 897.7 | 1011.0 | 898.9 | | | |
| | (734.5) | (787.0) | (883.0) | | | |
| Non-Regulated Website | -2472.4*** | -2275.0*** | -1882.6** | | | |
| | (602.4) | (817.1) | (803.9) | | | |
| Community Forum Website | 522.1 | 249.1 | 187.9 | | | |
| | (944.3) | (1000.0) | (1081.6) | | | |
| Constant | 5042.3*** | 5819.5*** | 5258.9*** | 9271.0*** | 1154.4 | 9029.8*** |
| | (442.6) | (547.1) | (778.3) | (668.9) | (1609.2) | (639.7) |
| Search Engine Fixed Effects | No | Yes | Yes | Yes | Yes | Yes |
| Website Fixed Effects | No | No | No | Yes | Yes | Yes |
| Keyword Fixed Effects | No | No | Yes | Yes | Yes | Yes |
| Observations | 30495 | 30495 | 30495 | 30495 | 2270 | 28225 |
| R-Squared | 0.00254 | 0.0169 | 0.0424 | 0.280 | 0.443 | 0.296 |

Table A-4 replicates the results for Table 2 using total clicks (as opposed to log of clicks) as the dependent variable. Robust standard errors clustered at the keyword level. *$p < 0.1$, **$p < 0.05$, ***$p < 0.01$.

# Sample Warning Letter from FDA

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service Food and Drug Administration Silver Spring, MD 20993

TRANSMITTED BY FACSIMILE

Margaret J. Jack Director, DRA Hoffmann-La Roche Inc., Bldg 1/2 340 Kingsland Street Nutley, NJ 07110 RE: NDA #21-455, 21-858 BONIVA (ibandronate sodium) Tablets BLA #103964 PEGASYS (peginterferon alfa-2a) for Injection NDA #20-896 XELODA (capecitabine) Tablets MACMIS ID #17318

Dear Ms. Jack:

As part of its monitoring and surveillance program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) of the U.S. Food and Drug Administration (FDA) has reviewed Hoffmann-La Roche Inc.'s (Hoffmann-La Roche) sponsored links on internet search engines (e.g., Google.com) for the following products: BONIVA (ibandronate sodium) Tablets (Boniva), PEGASYS (peginterferon alfa-2a) for Injection (Pegasys), and XELODA (capecitabine) Tablets (Xeloda). The sponsored links are misleading because they make representations and/or suggestions about the efficacy of Boniva, Pegasys, and Xeloda, but fail to communicate any risk information associated with the use of these drugs. In addition, the sponsored links for Pegasys and Xeloda inadequately communicate the drugs' indications and also fail to use the required established name. Thus, the sponsored links misbrand the drugs in violation of the Federal Food, Drug, and Cosmetic Act (the Act) and FDA implementing regulations. See 21 U.S.C. 352(a) & (n), 321(n); 21 CFR 201.10(g)(1), 202.1(b)(1), (e)(3)(i), (ii) & (e)(6)(i).

**Background**

Boniva

According to its FDA-approved product labeling (PI), Boniva is indicated for the treatment and prevention of osteoporosis in postmenopausal women. Boniva increases bone mineral density (BMD) and reduces the incidence of vertebral fractures. Boniva is associated with a number of risks, as reflected in the Contraindications, Warnings, Precautions, and Adverse Reactions sections of its PI.

Pegasys

According to its FDA-approved PI, Pegasys is indicated, among other things, alone or in combination with Copegus (ribavirin) for the treatment of adults with chronic hepatitis C (CHC) virus infection who have compensated liver disease and have not been previously treated with interferon alpha. Margaret J. Jack Page 2 Hoffmann-La Roche Inc. NDA #21-455, 21-858, 20-896, BLA 103964 MACMIS #17318 Pegasys is associated with a number of risks, as reflected in the Boxed Warning, Contraindications, Warnings, Precautions, and Adverse Reactions sections of its PI.

Xeloda

According to its FDA-approved PI, Xeloda is indicated, among other things, as a single agent for adjuvant treatment in patients with Dukes' C colon cancer who have undergone complete resection of the primary tumor when treatment with fluoropyrimidine therapy alone is preferred. Xeloda was non-inferior to 5-flourouracil

and leucovorin (5-FU/LV) for disease-free survival and while neither Xeloda nor combination therapy increases overall survival, combination therapy has been shown to improve disease-free survival compared to 5-FU/LV. Xeloda is also indicated as first-line treatment of patients with metastatic colorectal carcinoma when treatment with fluoropyrimidine therapy alone is preferred. Combination chemotherapy demonstrated a survival benefit compared to 5-FU/LV alone, however, a survival benefit over 5-FU/LV has not been demonstrated with Xeloda monotherapy Xeloda is associated with a number of risks, as reflected in the Boxed Warning, Contraindications, Warnings, Precautions, and Adverse Reactions sections of its PI. Omission of Risk Information

Promotional materials, other than reminder pieces, which include the name of the drug product but do not include indications or other representations or suggestions relative to the drug product (see 21 CFR 200.200, 201.100(f), 202.1(e)(2)(i)), are required to disclose risk and other information about the drug. Such materials are misleading if they fail to reveal facts that are material in light of the representations made by the materials or with respect to consequences that may result from the use of the drug as recommended or suggested by the materials. The sponsored links present the following claims:

- Free Trial Offer www.Boniva.com BONIVA (ibandronate sodium). Learn About Postmenopausal Osteoporosis.
- PEGASYS Official Site www.PEGASYS.com Learn About PEGASYS & Hepatitis C Register For The E-Mail Newsletter.
- XELODA Information www.xeloda.com Learn About An Oral Chemotherapy Treatment For Colon Cancer.

These sponsored links make representations and/or suggestions about the efficacy of Boniva, Pegasys, and Xeloda, respectively, but fail to communicate any risk information. This omission of risk information is particularly concerning as two of the products, Pegasys and Xeloda, have Boxed Warnings. For promotional materials to be truthful and non-misleading, they must contain risk information in each part as necessary to qualify any claims made about the drug.

By omitting the most serious and frequently occurring risks associated with the drugs promoted in the links above, the sponsored links misleadingly suggest that Boniva, Pegasys and Xeloda are safer than has been demonstrated. We note that these sponsored links contain a link to the products' websites. However, this is insufficient to mitigate the misleading omission of risk information from these promotional materials.

**Inadequate Communication of Indication**

The sponsored links for Pegasys and Xeloda provide very brief statements about what the drugs are for; however, these statements are incomplete and misleading, suggesting that the drugs are useful in a broader range of conditions or patients than has been demonstrated by substantial evidence or substantial clinical experience.

Specifically, the sponsored link for Pegasys misleadingly broadens the indication for Pegasys by implying that all patients with hepatitis C are candidates for Pegasys therapy (Learn About PEGASYS & Hepatitis C...), when this is not the case. Rather, Pegasys is only indicated (alone or in combination) for the treatment of chronic hepatitis C virus infection in adults who have compensated liver disease and who have not been

treated with interferon alpha previously. Similarly, the sponsored link for Xeloda misleadingly broadens the indication for Xeloda by implying that the drug is approved to treat any type of colon cancer (Learn About An Oral Chemotherapy Treatment For Colon Cancer), when this is not the case. Rather, Xeloda's indication is limited to adjuvant treatment in patients with Duke's C colon cancer and as first-line treatment for metastatic colorectal carcinoma. Furthermore, the sponsored link fails to communicate any of the limitations to either of these indications or the drug's limited proven survival benefits.

**Failure to Use Required Established Name**

The sponsored links for Pegasys and Xeloda fail to present the full established name of the drugs being promoted, despite the requirement to do so. See 21 CFR 201.10(g)(1) & 202.1(b)(1).

**Conclusions and Requested Action**

For the reasons discussed above, the sponsored links misbrand Boniva, Pegasys and Xeloda, in violation of the Act and FDA regulations. See 21 U.S.C. 352(a) & (n), 321(n); 21 CFR 201.10(g)(1), 202.1(b)(1), (e)(3)(i), (ii) & (e)(6)(i). DDMAC requests that Hoffmann-La Roche immediately cease the dissemination of violative promotional materials for Boniva, Pegasys and Xeloda, such as those described above.

Please submit a written response to this letter on or before April 9, 2009, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) in use for these drugs as of the date of this letter, identifying which of these materials contain violations such as those described above, and explaining your plan for discontinuing use of such materials. Finally, we encourage you to review your promotional materials for the Margaret J. Jack Page 4 Hoffmann-La Roche Inc. NDA #21-455, 21-858, 20-896, BLA 103964 MACMIS #17318 other prescription drug products that Hoffmann-La Roche promotes in the United States and to discontinue or revise any materials with the same or similar violations, and request that your response address this issue as well.

Please direct your response to the undersigned at the Food and Drug Administration, Center for Drug Evaluation and Research, Division of Drug Marketing, Advertising, and Communications, 5901-B Ammendale Road, Beltsville, MD, facsimile at 301-847-8444. In all future correspondence regarding this matter, please refer to MACMIS # 17318 in addition to the NDA numbers. We remind you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for Boniva, Pegasys, and Xeloda comply with each applicable requirement of the Act and FDA implementing regulations.

Sincerely,

Michael Sauers Regulatory Review Officer Division of Drug Marketing, Advertising and Communications