http://ijhpm.com
Int J Health Policy Manag 2015, 4(12), 813–821

doi 10.15171/ijhpm.2015.157

IJHPM International Journal of Health Policy and Management

Original Article

Trouble Spots in Online Direct-to-Consumer Prescription Drug Promotion: A Content Analysis of FDA Warning Letters

Hyosun Kim*

Abstract

Background: For the purpose of understanding the Food and Drug Administration's (FDA's) concerns regarding online promotion of prescription drugs advertised directly to consumers, this study examines notices of violations (NOVs) and warning letters issued by the FDA to pharmaceutical manufacturers.

Methods: The FDA's warning letters and NOVs, which were issued to pharmaceutical companies over a 10-year period (2005 to 2014) regarding online promotional activities, were content-analyzed.

Results: Six violation categories were identified: risk information, efficacy information, indication information, product labeling, material information issues, and approval issues. The results reveal that approximately 95% of the alleged violations were found on branded drug websites, in online paid advertisements, and in online videos. Of the total 179 violations, the majority of the alleged violations were concerned with the lack of risk information and/or misrepresentation of efficacy information, suggesting that achieving a fair balance of benefit versus risk information is a major problem with regard to the direct-to-consumer advertising (DTCA) of prescription drugs. In addition, the character space limitations of online platforms, eg, sponsored links on search engines, pose challenges for pharmaceutical marketers with regard to adequately communicating important drug information, such as indication information, risk information, and product labeling.

Conclusion: Presenting drug information in a fair and balanced manner remains a major problem. Industry guidance should consider addressing visibility and accessibility of information in the web environment to help pharmaceutical marketers meet the requirements for direct-to-consumer promotion and to protect consumers from misleading drug information. Promotion via social media warrants further attention, as pharmaceutical manufacturers have already begun actively establishing a social media presence, and the FDA has thus begun to keep tabs on social media promotions of prescription drugs.

Keywords: Pharmaceutical, Direct-to-Consumer Advertising (DTCA), Food and Drug Administration (FDA), Fair Balance of Information, Online Promotion of Prescription Drugs

Citation: Kim H. Trouble spots in online direct-to-consumer prescription drug promotion: a content analysis of FDA warning letters. *Int J Health Policy Manag.* 2015;4(12):813–821. doi:10.15171/ijhpm.2015.157

Article History:
Received: 27 May 2015
Accepted: 21 August 2015
ePublished: 25 August 2015

View Video Summary

***Correspondence to:**
Hyosun Kim
Email: hskim.kor@gmail.com

Key Messages

Implications for policy makers

- Risk information is not easily accessible on the drugs' websites, where unlimited pages and bandwidth space are available for information.
- Limited space, ie, sponsored links on search engines, on online venues often creates challenges for pharmaceutical marketers to adequately present product labeling and indication information.
- In the regulatory guidance for online direct-to-consumer advertising (DTCA), fair balance of information, as well as visibility and accessibility of information, should be considered to protect consumers from misleading information.

Implications for public

The online promotion of prescription drugs directly to consumers has become an increasingly popular method of drug advertising in the United States. Though the Food and Drug Administration (FDA) oversees direct-to-consumer advertising (DTCA) in order to protect consumers from misleading advertisements, some advertising may be violative because the promotional materials are not regulated by law before being aired in the market. Further, DTCA is more common for treatments for chronic conditions, which require regular prescriptions for a long battle, placing many vulnerable patients at risk. This study discusses the FDA's concerns regarding online promotional activities of prescription drugs in an attempt to give context to pharmaceutical marketers on what to avoid in their online promotional materials, so that truthful and useful drug information is provided to consumers online.

School of Media and Journalism, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

Background

The online promotion of prescription drugs directly to consumers has become an increasingly popular method of drug advertising in the United States. Traditionally, pharmaceutical companies' promotional efforts were directed almost exclusively to physicians and healthcare providers.[1] In the 1990s, however, pharmaceutical manufacturers took their promotional efforts one step further and began marketing prescription drugs directly to consumers. At that time, the Food and Drug Administration (FDA) guidelines, which were tailored to print media, made it impractical to advertise prescription drugs in television commercials due to extensive disclosure requirements.[1] In 1997, in response to advertisers' needs in the pharmaceutical market and the changing media environment, the FDA updated its regulatory guidelines for broadcast direct-to-consumer advertising (DTCA) and clarified ways that information about prescription drugs could be presented in broadcast media, subsequently leading to an exponential increase in television commercials for prescription drugs.[1] These new FDA guidelines thus opened a new marketing era, bringing with it broader opportunities for consumers to make informed decisions about health-related concerns, in addition to flooding the pharmaceutical market with DTCA.[2]

Consequently, pharmaceutical marketing expenditures for DTCA have increased rapidly since the end of the last millennium. For example, although the pharmaceutical industry spent $12 million on DTCA in 1989, its marketing expenditures skyrocketed to $2.38 billion in 2001, an almost 200-fold increase in 12 years.[2,3] Furthermore, in 2008, $4.7 billion was spent on DTCA, accounting for almost one-fourth of the pharmaceutical companies' marketing expenditures for all promotional activities.[4] Due to new drugs being launched in the pharmaceutical market, DTCA spending reached its peak between 2004 and 2006, evidenced by the fact that the most heavily advertised drugs were also the top-selling drugs in the US market.[1] A recent study reported that pharmaceutical manufacturers continue to spend significant amounts on DTCA ($3.1 billion in 2012),[5] although health professional-directed promotions are still dominant.

Currently, the DTCA of prescription drugs in broadcast and print media encourages consumers to visit drug websites for further information about the product.[6] This allows advertisers to take advantage of online platforms and use more diverse approaches to reach consumers than was possible even a decade or two ago. They are actively engaging with consumers online and experimenting with new online media platforms, eg, social media, establishing an online presence and promoting their prescription drugs.[7,8] However, as online advertising becomes an increasingly integral part of prescription drug promotion, the lack of clear guidance regarding online promotion has created challenges for pharmaceutical marketers.[7]

Therefore, based on an analysis of the alleged violations found in warning letters and untitled letters that have been issued to pharmaceutical manufacturers by the FDA in a recent 10-year span with regard to online DTC promotion of prescription drugs, the present study aims to diagnose issues that pharmaceutical marketers should avoid in their online promotional materials to protect consumers from misleading information. This study of FDA warning letters and notices of violations (NOVs) regarding alleged violations found in the online DTCA of prescription drugs appears to be unique in the literature at present.

Literature Review

FDA Regulation of Prescription Drug Advertising

For the purpose of protecting public health, the FDA oversees prescription drug advertising to ensure that consumers receive accurate and science-based information about prescription drugs.[9] The authority of the FDA includes determining whether the advertising contains any information that could possibly mislead consumers.[9] However, according to federal law, the FDA may not compel pharmaceutical companies to submit prescription drug-related DTCA for approval; rather, many drug companies are encouraged to seek advice from the FDA voluntarily before releasing their ads. This current scenario indicates that the public could see ads that may include false or misleading information before the FDA can take action on any unlawful claims the pharmaceutical companies may have made in their advertisements.[10]

In order to regulate drug companies' marketing activities, the usual policy is for the Office of Prescription Drug Promotion (OPDP) within the FDA to send letters to pharmaceutical companies and request that they remove ads or stop unlawful promotional activities if the OPDP alleges that their ads violate the law.[10] Generally, the FDA finds that the DTCA of prescription drugs is allegedly unlawful if such ads state or imply that unproven drugs can treat a condition, claim benefits without providing adequate evidence, falsely represent data from studies, overstate efficacy, or omit or downplay risk information.[10] The OPDP issues 2 types of letters to pharmaceutical companies to notify them of alleged violations.[2] One is a NOV, also called an untitled letter, and the other is a warning letter. Untitled letters are sent to drug companies for minor violations, whereas warning letters are issued for serious violations and imply that the FDA will proceed with further regulations if the cited company does not take corrective action or respond to the FDA.[2]

Specifically, the FDA's authority over prescription advertising is based on the Food, Drug, and Cosmetic (FDC) Act, which requires that prescription drug advertising must present information in a way that is accurate and in a non-misleading manner.[9] Also, the FDA's Center for Drug Evaluation and Research (CDER) is responsible for ensuring that pharmaceutical manufacturers present drug information in a valid and balanced manner in their claims.[9] Pharmaceutical marketers must present both the benefits and risks of a drug in a fair and balanced manner[11] and similarly in terms of content and presentation.[12] In other words, the most important risk information should not be minimized in comparison to the efficacy claims, because prescription drugs may cause substantial side effects to some patients, even though they may also provide effective medical benefits.[13]

According to the FDA's regulations regarding the DTCA of prescription drugs, advertisements must comply with the "brief summary" or the "major statement," which requires that promotional materials provide information that relates to side effects, contraindications, and effectiveness.[13] The FDA has been monitoring whether DTCA presents adequate contextual

and risk information with understandable language in a fair and balanced manner in an attempt to ensure that consumers receive non-misleading promotional claims. Although the FDA has recognized the importance of the Internet as a growing marketing channel for pharmaceutical companies, the agency has expressed concerns as to how to best achieve fair balance in the DTCA of prescription drugs in an online environment.[14,15] The growing number of available online DTCA platforms, including social media posts, banner ads, embedded videos, and sponsored links on search engines, makes it increasingly difficult for the FDA to monitor and regulate all such promotional activities. In an effort to address these concerns, in 2013, the FDA introduced draft guidelines for consumer-directed online promotional activities,[15] and 3 other draft guidelines were added in 2014.[14,16,17] However, it appears that these draft guidelines do not comprehensively address concerns related to online prescription drug promotions advertised directly to consumers.[7]

Consumer Advantages and Disadvantages of Direct-to-Consumer Advertising of Prescription Drugs

DTCA helps consumers have better discussions with their physicians and to make better health-related decisions as active consumers.[13,18] Prescription drug advertising can be useful in that it enables consumers to pay closer attention to their health conditions and learn about new medications and treatment options.[19] DTCA arguably lessens the stigma associated with many health concerns and diseases, thereby making it easier for consumers to discuss such private matters with their doctors and seek treatment,[2] while reducing unnecessary surgeries and hospitalization, which lowers overall healthcare costs.[20]

Despite the various benefits of DTCA, some have expressed considerable concern regarding the DTCA of prescription drugs due to the inadequate presentation of information in the ads, which could result in adverse effects for consumers. For instance, DTCA may cause unnecessary anxiety, in that frequent exposure to such information makes people overly concerned about their health.[21] Notably, the major problem associated with DTCA is that advertisers often overemphasize the efficacy of a prescription drug while minimizing the risks associated with the drug's use, which leads patients to conclude that certain brands of drugs are more effective and safer than others, or that certain brands have only minor risks.[18] As an example, models in ads for HIV medications are portrayed as healthy-looking people who actively engage in social activities, downplaying the cause of HIV while highlighting aspirational images.[22] Visual cues in ads serve an important persuasive role,[22] and the portrayal of drugs and medical conditions in DTCA can be problematic and misleading in this regard. Thus, given these considerations, the following sections discuss the key concerns that have been raised with regard to DTCA in both traditional media and online media.

Achieving a Fair Balance of Information in Direct-to-Consumer Advertising of Prescription Drugs

The primary key area of concern regarding prescription drugs advertised directly to consumers is that of fair balance, ie, a balanced presentation of the benefits and the risks of the drugs being advertised. This issue has been ongoing since DTCA became available in broadcast and print media. For example, a study focusing on the warning letters and untitled letters that the FDA issued to drug advertisers with regard to DTCA in broadcast and print media reveals that about 38% of the complaints centered on the fair balance issue.[20] The thrust of the complaints is that failing to achieve fair balance is primarily due to the lack or minimization of risk information in the allegedly violative ads.[20] The commercials on broadcast media, where product claims are made in a limited length of time (30 to 60 seconds), often do not adequately communicate side effects, contradictions, and precautions, which presumably could mislead consumers.[21] The inadequate presentation of risk information in DTCA can negatively affect consumers by making it difficult for them to understand the side effects of the drugs that are being promoted in televised DTCA.[20,23]

One reason that pharmaceutical marketers may fail to present information about their drugs in a fair and balanced manner might be the lack of explicit guidelines as to ways they can achieve a balanced presentation of benefit and risk information.[20] The more recent addition of online DTCA to existing broadcast and print media DTCA has created even more challenges for the FDA to ensure the balanced presentation of pharmaceutical information to the public.[7]

Direct-to-Consumer Advertising of Prescription Drugs on the Internet

The pharmaceutical industry is moving forward rapidly into online marketing, as online media platforms allow marketers to reach a larger number of consumers than traditional forms of media, help target specific patients, and are more cost efficient than TV or print.[7,24] In order to promote prescription drugs directly to consumers online, pharmaceutical manufacturers have spent their advertising budgets on online banners, streaming videos, sponsored ads on search engines, and product websites.[1] Among these online promotion types, prescription drug websites now serve as a primary source for consumers to obtain a variety of information about prescription drugs in detail, such as testimonials from the drug's users, assessment tools, and the drug's risks and benefits.[25] Because the FDA permits broadcast DTCA to refer consumers to a brand's website, print advertisements, or a toll-free telephone number, the brand websites for prescription drugs thus have become venues that consumers can visit to seek further information about particular drugs.[23]

Interestingly, however, studies have revealed that nearly half of these websites did not actually include risk information about the drugs being advertised.[25] Furthermore, any risk information included often was not designed or presented in a way that was similar to the benefit information. More significant, the risk information was not explicitly visible; for example, visitors to the site were forced to scroll down to see it, which could minimize the chance of consumers seeing the information at all.[25] In a similar vein, another study showed that the benefit information was presented in a way to attract more attention from the viewer, whereas the risk information was less eye-catching.[26] Thus, pharmaceutical marketers often fail to address risk information as adequately on their websites as they did when they advertised in broadcast and print media.

In a recent study examining pharmaceutical manufacturers' social media presence for their prescription drugs, all top 10 pharmaceutical corporations were found to have Facebook pages and Twitter feeds.[7] In addition, 8 companies had dedicated YouTube channels and healthcare-related mobile applications, suggesting that pharmaceutical marketers are actively adopting digital channels as marketing tools.[7] With the growing use of digital channels as prescription ad platforms, the FDA has begun to express concerns and send preemptive warning letters to major pharmaceutical companies advising them to stop placing sponsored link ads on search engines in a misleading way—ie, omitting risk information.[27] What's more, social media can be an incredibly complex form of media, in that marketers are unable to completely control their marketing messaging;[7] thus, scholars posit that alternative regulatory policy, eg, independent third-party oversight, is necessary to ensure public safety.[24]

Research Questions

Online media platforms provide many opportunities for pharmaceutical manufacturers to promote prescription drugs directly to consumers. Simultaneously, however, this information can be misleadingly delivered to consumers, threatening public health. Therefore, the goal of this study is to understand the FDA's concerns with regard to the online DTCA of prescription drugs by examining the FDA's warning letters and untitled letters that have been issued to pharmaceutical companies. This study identifies the most common alleged violations that pharmaceutical manufacturers often make in their online promotional activities, and thus addresses the following research questions.

RQ1. What types of online promotional platforms received the most letters from the FDA?

RQ2. What are the drug categories that have been the subject of FDA warning and untitled letters?

RQ3. What types of legal violations does the FDA allege most frequently occur in the online DTCA of prescription drugs?

RQ4. How do the types of alleged violations differ by online promotion type?

Methods

This analysis is based on the warning letters and NOVs issued by the FDA from 2005 through 2014 concerning the online DTCA of prescription drugs. The present study examined FDA letters over a recent span of 10 years when scholars began to pay particular attention to drug manufacturers' online promotional activities with regard to prescription drugs. Since the last time the FDA's warning letters with regard to traditional media—broadcast and print—were studies in 2003,[20] 2 new studies focusing on online media have come out: Huh and Cude[26] investigated the fair balance issue in direct-to-consumers prescription drug websites in 2004, and another similar study was published by Sheehan in 2007.[25] Therefore, for the purpose of expanding the current discussion of drug manufacturers' online promotional activities, the present study examined alleged violations of prescription drug promotions from 2005 to 2014.

These letters are publically accessible and available from the FDA's website. A total of 262 letters were downloaded. First, letters were categorized as being related to consumer-directed online promotion (73 letters), consumer-directed traditional media promotion (48 letters), and healthcare professional-directed promotion (141 letters). As this study is only concerned with online DTCA, the consumer-directed traditional media and healthcare professional-directed promotion category letters were discarded.

The letters that were issued for online promotional activities only were then content-analyzed into subcategories based on online promotion type, drug category, and type of alleged violation. The majority of located letters contained multiple alleged violations; thus, 179 allegations of violations were counted in total. Only 11 letters identified a single alleged violation. The rest of letters reported 2 or more violations: 24 letters with 2 violations, 32 letters with 3 violations, and 6 letters with 4 violations.

Two coders coded the letters to ensure inter-coder reliability. Coders were trained to increase inter-coder reliability and coded the data according to a structured coding scheme; further, they were instructed to examine both actual promotional materials and letters to correctly code the data into relevant categories. These actual promotional materials were also downloaded from the FDA website, along with the letters. Krippendorff's α was used for the inter-coder reliability check.[28] Krippendorff's α for the variables ranged from 0.82 to 1.0.

The coding protocol was developed based on Sheehan's study, which examined FDA warning letters regarding DTCA violations in traditional media.[20] The coding protocol included (1) issue date, (2) name of drugs, (3) drug categories, (4) online promotion type, and (5) categories of alleged violation. Coders were instructed to initially look at subheadings of violations to determine relevant categories when coding violations. Coding for online promotion type was easily identifiable because the FDA addressed the type of media they were investigating in the introductory paragraph of the letters.

Types of online promotion were categorized into website, online paid ads, online video, email, and social media. Promotional materials on manufacturers' websites were promotional messages or drug information including text and graphics. Online paid ads included text ads (ie, sponsored links) on search engine sites such as Google and online banner ads. One type of online video promotion was a video clip embedded in a manufacturer's website, either in the form of patients' testimonials or as an online video ad. Another type of online video promotion was a YouTube video clip uploaded by a drug manufacturer in the form of a video ad to be included as video streaming content on nondrug manufacturers' sites. Email was the electronic mail sent to consumers by pharmaceutical marketers. Social media promotions for the purpose of this study were mainly related to Facebook, ie, Facebook pages and the Facebook "share" button on a manufacturer's website.

Online promotion types were then grouped into 2 categories: market-controlled and market-influenced. Market-controlled promotions are websites, online paid ads, online videos, and emails in which marketers have full control of their marketing messaging. By contrast, drug manufacturers are unable to fully control their promotional activities on social media because social media platforms specifically enable consumers

add their own messages and share information with fellow consumers.[7] In fact, the FDA has indeed expressed concerns about the uncontrollability of social media promotional materials in its letters.[29,30]

These violations were then grouped into 6 categories: risk information, indication information, efficacy information, product labeling, approval issues, and material information issues. In categorizing the alleged violations, Sheehan's categories of complaints from her 2003 study were employed,[20] with the addition of categories for indication information and product labeling. According to Sheehan's types of complaints,[20] alleged violation of risk information is concerned with the omission of important risk information and minimization of risk information. If the letters cited a violation because the material in question did not disclose or clearly state risk information, it was coded as omission of risk information, whereas it was coded as minimization of risks when the promotional material downplayed the seriousness of risks. Complaints about efficacy information are often associated with misleading communication about the benefits of drugs, such as an overstatement of benefits or unsubstantiated claims of efficacy. Approval issues were coded when the pharmaceutical companies promoted drugs that were under investigation. Material information was used to indicate the type of complaints related to misleading communication of ingredients information for the drugs. Violation of product labeling, a newly added complaint category, was often related to sponsored links on a search engine. The FDA invoked this complaint when the drug manufacturers failed to adequately present both the generic name and brand name of the drug. Another newly added complaint category was indication information, aimed at material which misleadingly communicated drugs' dosage instructions by broadening the patients types who should be taking the drugs or failing to adequately present when and how to take the drugs to ensure safety.

Results

Ten Years (2005 to 2014) of FDA Allegations of Violative Direct-to-Consumer Advertising in Online Media

Seventy-three warning letters and NOVs were collected for analysis. Alleged violations were found in a variety of online promotion types. Approximately half of the letters were issued by the FDA for advertisements on drug websites. About 25% of the violations were found in the online paid ad category, such as banner ads and text ads. The letters that were issued for online video promotion accounted for 22% of the total number of letters (see Table 1). Thus, the majority (94.5%) of violations were related to promotional materials in these 3 media platform categories. Notably, over the 10 years in the time range for this study, 5 warning letters were issued concerning advertisers' promotional activities on brand websites and 3 warning letters were sent concerning online videos. Thus, it appears that the FDA has expressed considerable concern over promotional materials on drug companies' websites and online videos when determining alleged violations. Therefore, RQ1 was addressed.

Interestingly, the results revealed that pharmaceutical companies use email (2 letters were found) in an attempt to reach specific individuals. Social media widgets, the Facebook "share" button on a webpage, are also used by pharmaceutical marketers to encourage consumers to engage in the content and propagate messages.

In general, DTCA is more common for drugs intended to treat chronic condition, serving as a reminder for prescription refill.[1,7] As such, pharmaceutical manufacturers target this market, where larger number of patients regularly ask for prescriptions for extended periods of time.[1,7] The finding in the present study indicated that about 22% of the letters examined were issued for cancer treatment drugs (see Table 2). Thus, RQ2 was addressed.

Next, among the 6 violation categories, alleged violation of risk information was the most frequently reported, followed by efficacy information and indication information (see Table 3). It also appeared that alleged violation of risk information went hand in hand with efficacy information, meaning that pharmaceutical marketers seemed to downplay risk information for the sake of emphasizing the benefits of their drugs. For some letters, the FDA claimed both omission and minimization of risk information when addressing alleged violation of risk information. The most serious problem of alleged violation of efficacy information was overstating the efficacy of drugs and claiming benefits without providing substantiated evidence. The alleged violation of indication information was newly added in the present study, as it was not found in DTCA in traditional media in Sheehan's 2003 study. Specific problems found in this violation category were inadequate communication of drug indication regarding dosage instructions and broadening patient types eligible to take the drugs. These results addressed RQ3.

Finally, RQ4 asks whether the types of alleged violations differ by online promotion type. As shown in Table 4, specific alleged violations were more frequently reported in certain types of online promotional activities. For example, the majority of

Table 1. Types of Online Promotion Warned by the FDA

Online Promotion Category		Types of Promotion	No.	Percent
Marketer controlled	Website	Website/webpage	35	47.9
	Online paid ad	Sponsored links in Internet search engines/banner ads	18	24.7
	Online video	Embedded testimonial videos or promotional videos on manufacturers' websites	14	21.9
		Promotional online video on independent websites[a]	2	
	Email	Email promotion	2	2.7
Marketer influenced	Social media	Social media widgets (Facebook "Share" button) on drug manufacturers' websites/ Facebook pages	2	2.7
Total			73	99.9

Abbreviation: FDA, Food and Drug Administration.

[a] One promotional video was a YouTube video clip uploaded by a drug manufacturer and the other video was and online video ad placed as video streaming news content on CNN.

Table 2. Types of Drugs Receiving FDA Warning or Untitled Letters

Drug Category	No.	Percent
Cancer	16	21.9
Dermatological conditions	9	12.3
Urological conditions	5	6.8
Cardiovascular disease	5	6.8
Psychiatric/neurological disorders	4	5.5
Musculoskeletal ailment	4	5.5
OB/GYN conditions	3	4.1
HIV-AIDS	3	4.1
Gastrointestinal conditions	3	4.1
Infections/non-HIV disease	3	4.1
High cholesterol	3	4.1
Allergy	2	2.7
Arthritis	2	2.7
Depression	2	2.7
Diabetes	2	2.7
Osteoporosis	2	2.7
Respiratory condition	1	1.4
Weight loss	1	1.4
Hypotrichosis of eyelash	1	1.4
Serious pain relief	1	1.4
Tobacco addictions	1	1.4
Total	73	99.8

Abbreviations: OB/GYN, obstetrics and gynecology; FDA, Food and Drug Administration.

online paid ads allegedly failed to present product labeling and indication information adequately, whereas online video promotions often omitted or misrepresented risk information (see Table 4). Thus, RQ4 was addressed.

In order to provide context for each alleged violation with regard to the online promotion of prescription drugs, the following sections provide detailed analysis regarding the top 4 alleged violations, ie, risk information, efficacy information, indication information, and product labeling, which accounted for approximately 88% of the total alleged violations.

Risk Information

The FDA alleges a policy violation when the advertisement fails to communicate a drug's risk information correctly by omitting or minimizing the side effects associated with the drug.[31] For instance, in a 2006 warning letter issued to BioMarin Pharmaceutical regarding its FDA-approved drug Orapred, a prescription treatment for allergic conditions in asthma patients, the FDA alleged that the company's website for the drug was in violation because it contained efficacy claims but the risk information was not easily accessible. Also, a NOV was issued to KV Pharmaceutical for its email promotion because the benefit claims were conspicuously presented using large, bold headers with bullets, whereas all the risk information was at the end of the email, using smaller font without any bolding or bullet points.

Findings in this study revealed that the risk information for drugs was not always communicated adequately in terms of format, quantity, location, or even its level of seriousness. According to the FDA, the risk information, when compared to the benefit information, was displayed less prominently in online promotional materials. Most important, the FDA expressed concern in its letters that the lack of risk information or inadequate presentation of such information could mislead consumers by possibly causing them to believe that the advertised drug has more benefits than risks, which could ultimately threaten public health.

Efficacy Information

In general, the FDA considers promotional materials to be misleading if advertisers tout a drug as superior to other

Table 3. Types of Alleged Violations

Category of Alleged Violation	Details of Alleged Violation	No.	Percent
Risk information	Subtotal	58	32.4
	Omission of risk information	39	21.8
	Minimization of risk information	19	10.6
Efficacy information	Subtotal	51	28.5
	Overstatement of efficacy	25	14.0
	Unsubstantiated claims	12	6.7
	Unsubstantiated superiority claims	10	5.6
	Misleading claims	4	2.2
Indication information	Subtotal	34	19.0
	Inadequate communication of indication	15	8.4
	Broadening of indication	12	6.7
	Misleading communication of the indication	3	1.7
	Failure to state full indication	1	0.6
	Misleading claims regarding dosing	1	0.6
	Unsubstantiated dosing claims	1	0.6
	Omission of indication information	1	0.6
Product labeling	Subtotal	14	7.8
	Failure to use required established name	14	7.8
Material information issues	Subtotal	13	7.3
	Omission of material facts	10	5.6
	Misleading presentation	3	1.7
Approval issues	Subtotal	9	5.0
	Promotion of an investigational new drug/promotion of unproved use	9	5.0
Total		179	100

Table 4. Types of Alleged Violations by Online Promotion Type

Category of Alleged Violation	Website	Online Paid Ad (Text/Banner)	Online Video/Webcast	Social Media	Email
Risk information	27	16	15	2	2
Efficacy information	26	1	11	2	1
Indication information	13	12	6	1	2
Product labeling	1	15	0	0	1
Approval issues	6	0	2	0	0
Material information issues	8	1	2	2	0
Total	81	45	36	7	6

alternatives without basing this claim on adequate, well-controlled clinical trials and substantiated comparisons with competitors in addressing the safety and effectiveness of the product.[32] For instance, in a warning letter issued for inadequate claims of superiority, the FDA alleged that Adderall XR's video testimonial posted on YouTube misleadingly implied that Adderall XR was more likely than its competitors to treat attention deficit hyperactivity disorder (ADHD) symptoms without providing substantial evidence to support such claims in the video. This violation type was found most frequently on companies' websites, followed by online videos (see Table 4). The FDA specifically expressed public health and safety concerns about benefit claims that overstate or inflate efficacy without providing clinical evidence that would ensure the safety of the drugs.

Indication Information

Alleged violations of the inadequate communication of indication were frequently found in sponsored links on search engines, where advertisers needed to communicate key messages within the limited space allowed on the search engine websites.

According to the NOV the FDA issued to Pfizer in 2009, one of Pfizer's sponsored links provided incomplete content about dosage information for their product Aromasin. The FDA alleged in this letter that Aromasin's sponsored link broadened the indication, implying that the promoted drug was available for treatment of the broader female population, although the drug treatment was limited to only a specific type of patient, ie, postmenopausal women. Similarly, a letter regarding Orapred, a medication approved to treat only severe allergic conditions for adult and pediatric populations with asthma or respiratory disorders, found that the drug's website described only the general condition of asthma, implying that Orapred was useful for a broad range of conditions and patients, thereby failing to describe important limitations regarding Orapred's indication.

Product Labeling

The FDA warning letters and NOVs indicated that many sponsored links, ie, text ads on search engines, allegedly failed to use the required established name of the drug being promoted. According to FDA regulations, the established name, or generic name, that includes the active ingredients of the drug, must accompany the proprietary name, which is the drug's brand name. In order to provide details about the drugs to consumers, the established name should be placed to the right of or below the proprietary name.[15] Based on the requirements for the presentation of prescription drugs' product names, including the size, placement, and frequency of labeling and advertising, the FDA alleged that the sponsored links inadequately presented the product name, thereby misrepresenting the particular drug's established name (see Table 4). In addition, these sponsored links were the most frequently associated with alleged violations of the risk and indication information presentation requirements. The lack of risk information or inadequate presentation of indication information may be attributed to the limited advertising space in sponsored links.

Discussion

This study examined the FDA's concerns with regard to online promotional activities of prescription drugs advertised directly to consumers. The FDA's warning letters and NOVs, which were issued to pharmaceutical manufacturers over a recent span of 10 years, were thus content-analyzed.

The results indicate that nearly 95% of the alleged violations were found in promotional content from branded drug websites, online paid ads, and online videos. The FDA expressed considerable concern over online promotion of cancer treatments, which require regular prescriptions for long-term treatment. The most significant finding, that concerning the fair balance issue, suggests that the online promotional content of prescription drugs fails to present risks and benefits in a balanced manner. This issue has also been a primary concern for traditional forms of media, such as broadcast media and print media,[20] suggesting that presenting drug information in a fair and balanced manner remains a major problem.

New forms of advertising platforms have been accompanied by new violations as well. For instance, due to limited character space, sponsored ads on search engines frequently fail to state a drug's correct indication information fully or to present the product names as adequately as the law requires by not correctly communicating both the brand name (proprietary name) and the generic name (established name). These failures could result in safety concerns, because the lack of indication information and active ingredient information could lead to misuse of the drug. The FDA expresses particular concern about sponsored links on search engines, as evidenced by preemptive untitled letters sent to major pharmaceutical manufacturers in 2009 to advise drug advertisers about the need for the adequate presentation of product labels.[27] As a result, the FDA published draft guidelines for this type of advertising, providing guidance about ways to present drug information, specifically risk information associated with drug usage, on sponsored links where advertising space is relatively limited.[15] In the draft guidelines,

the FDA acknowledges that character space limitations on online platforms might pose challenges for pharmaceutical manufacturers in delivering both benefits and risks in a fair and balanced manner. This guidance therefore specifically addressed the importance of the adequate presentation of risk information that could prevent consumers from viewing misleading drug information.[15]

In addition, the FDA is increasingly concerned over the growing popularity of social media as a pharmaceutical marketing channel, as evidenced by the recent industry guidance for social media published in 2014. However, researchers have suggested that the guidelines do not adequately troubleshoot issues pertaining to social media marketing.[24] Though only 2 letters were found regarding social media promotions in this study, top pharmaceutical manufacturers have already been developing their social media presence, actively adopting social media in their marketing communication strategy.[7,24] Moreover, their Facebook pages appear to be accessible to non-US consumers, although the pages do indicate that they are designated only for US consumers, creating further regulatory concerns.[7,33] According to the letters studied, the FDA specifically expressed concerns about the uncontrollability of social media, in that regulators can hardly oversee content created by consumers on social media and message-sharing through the media, which makes it difficult for marketers to predict a message's viral impact.

Pharmaceutical marketers are also trying to reach specific patients through personal email, and the FDA finds that important risk information and indication information are not adequately communicated in email promotions. In general, consumers perceive individually tailored promotional materials as easier to understand and more attention-catching than non-tailored ones;[34] thus, promotional emails that are sent individually to specific patients can be quite problematic with regard to fair balance issues. It is clear that pharmaceutical marketing through social media and tailored emails warrants close attention and further research to respond to growing industry inquiries.

Online platforms allow pharmaceutical manufacturers to create content in a variety of formats. Benefit and risk information about drugs can be presented in different ways, too. It is possible to overstate benefit information by presenting efficacy information on the first page of a website, for example, or by using larger font in an email. By the same token, the risks of a drug can be perceived as less significant if the information is presented in a smaller font or requires many clicks to reach the relevant page. Although prescription drugs provide many benefits to patients, they also may be accompanied by serious risks.[24] Due to the side effects that might affect some patients significantly, prescription drugs traditionally have been prescribed by and their use advised under the guidance of physicians. As the present study indicates, it is still challenging to present risk information adequately on online platforms.

Consumers acquire information either poorly or well depending on the way the information is presented.[35] In fact, different types of information presentation on online platforms significantly affect consumers' perceptions and attitudes differently. For example, animated banner ads, as opposed to static banner ads, lead to higher recall, click intent, and a positive attitude toward the ads due to their attention-grabbing capabilities.[36] Moreover, the visual appeal of website designs for the DTCA of prescription drugs may impede people's ability to process information correctly.[37] Therefore, the inadequate presentation of drug information could result in informed but unsafe healthcare decisions and put public health and safety at risk.[25] In this vein, the FDA has insistently warned about visibility and accessibility of information in the online environment. It is increasingly clear that merely requesting that drug marketers present balanced information may not provide an ideal system of guidance in the online environment; rather, comprehensive guidelines that address the accessibility and visibility of information would help pharmaceutical marketers avoid putting so many misleading promotional activities online.

This study, however, has some limitations worth noting. One potential limitation of this study is that the letters issued by the FDA are only allegations of violations and not findings by a court. Second, the results are descriptive and do not represent all the online marketing issues with regard to DTCA in the pharmaceutical market. Despite these limitations, the present study does make meaningful contributions to the current discussion of online promotion of prescription drugs being advertised directly to consumers by identifying the FDA's concerns as revealed by their recent warning letters and NOVs. Furthermore, the findings from the current study provide pharmaceutical marketers with a note of caution about common mistakes to avoid in online promotions in order to meet the regulatory requirements while protecting consumers from misleading information.

Acknowledgements

I would like to thank Dr. Michael Hoefges, who guided me to explore research in DTCA of prescription drugs, and Dr. Francesca Dillman Carpentier, for her excellent support as a mentor. I would also like to express my sincere gratitude to the anonymous reviewers whose constructive and thoughtful comments were so conducive to improving this manuscript.

Ethical issues

This research does not involve human subjects; thus, ethical issue regarding treatment of human samples is not applicable.

Competing interests

Author declares that she has no competing interests.

Author's contribution

HK is the single author of the manuscript.

References

1. Campbell S. Promotional Spending for Prescription Drugs. https://www.cbo.gov/sites/default/files/111th-congress-2009-2010/reports/12-02-drugpromo_brief.pdf. Accessed April 16, 2015. Published December 2, 2009.
2. Palumbo FB, Mullins CD. The development of direct-to-consumer prescription drug advertising regulation. *Food Drug Law J*. 2002;57(3):423-443.
3. Calfee J. Public policy issues in direct-to-consumer advertising of prescription drugs. *J Public Policy Mark*. 2002;21(2):174-193.
4. Campbell S. Potential Effects of a Ban on Direct-to-Consumer Advertising of New Prescription Drugs. https://www.cbo.gov/sites/default/files/112th-congress-2011-2012/reports/5-25-prescriptiondrugadvertising.pdf. Published May 2011.

5. Dobrow L. DTC Report: DTC Gets Smart - Medical Marketing and Media. *Med Mark Media*. http://www.mmm-online.com/features/dtc-report-dtc-gets-smart/article/339357/. Accessed August 22, 2015. Published 2014.
6. Lorence D, Churchill R. A study of the web as DTC drug marketing agent. *J Med Syst.* 2007;31(6):551-556. doi:10.1007/s10916-007-9098-4
7. Liang BA, Mackey TK. Prevalence and global health implications of social media in direct-to-consumer drug advertising. *J Med Internet Res*. 2011;13(3):e64.
8. Thomaselli R. Web thrives as DTC platform. http://adage.com/article/digital/web-thrives-dtc-platform/96790/. Accessed April 16, 2015. Published November 10, 2003.
9. Food and Drug Administration (FDA). Prescription Drug Advertising - Background on Drug Advertising. http://www.fda.gov/Drugs/ResourcesForYou/Consumers/PrescriptionDrugAdvertising/ucm071964.htm. Accessed April 16, 2015.
10. Food and Drug Administration (FDA). Prescription Drug Advertising - Prescription Drug Advertising: Questions and Answers. http://www.fda.gov/Drugs/ResourcesForYou/Consumers/PrescriptionDrugAdvertising/UCM076768.htm. Accessed April 16, 2015.
11. Food and Drug Administration (FDA). Guidance for Industry: Consumer Directed Broadcast Advertisements. http://www.fda.gov/RegulatoryInformation/Guidances/ucm125039.htm. Accessed April 16, 2015. Published 1999.
12. Food and Drug Administration (FDA). Prescription Drug Advertising - Drug Advertising: A Glossary of Terms. http://www.fda.gov/Drugs/ResourcesForYou/Consumers/PrescriptionDrugAdvertising/ucm072025.htm. Accessed April 16, 2015.
13. Aikin KJ, Swasy JL, Braman A. Patient and Physician Attitudes and Behaviors Associated With DTC Promotion of Prescription Drugs — Summary of FDA Survey Research Results. http://www.fda.gov/Drugs/ScienceResearch/ResearchAreas/DrugMarketingAdvertisingandCommunicationsResearch/ucm151498.htm. Published May 19, 2004.
14. Food and Drug Administration (FDA). Guidance For Industry: Internet/Social Media Platforms: Correcting Independent Third-Party Misinformation About Prescription Drugs and Medical Devices. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM401079.pdf. Accessed April 16, 2015.
15. Food and Drug Administration (FDA). Product Name Placement, Size, and Prominence in Advertising and Promotional Labeling. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070076.pdf. Accessed April 27, 2015. Published 2013.
16. Food and Drug Administration (FDA). Draft Guidance for Industry: Internet/Social Media Platforms with Character Space Limitations - Presenting Risk and Benefit Information for Prescription Drugs and Medical Devices. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM401087.pdf. Accessed April 27, 2015. Published 2014.
17. Food and Drug Administration (FDA). Guidance for Industry: Fulfilling Regulatory Requirements for Postmarketing Submissions of Interactive Promotional Media for Prescription Human and Animal Drugs and Biologics. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM381352.pdf. Accessed April 16, 2015. Published 2014.
18. Schwartz V, Silverman C, Hulka M, Appel C. Marketing pharmaceutical products in the twenty-first century: an analysis of the continued viability of traditional principles of law in the age of direct-to-consumer advertising. *Harv J Law Public Policy*. 2009;32:333-354.
19. Bell R, Kravitz R, Wilkes M. Direct-to-consumer prescription drug advertising and the public. *J Gen Intern Med*. 1999;14(11):651-657.
20. Sheehan K. Balancing acts: an analysis of Food and Drug Administration letters about direct-to-consumer advertising violations. *J Public Policy Mark*. 2003;22(2):159-169.
21. Vogt DU. CRS Report for Congress: Direct-to-Consumer Advertising of Prescription Drugs. Congressional Research Service; 2005.
22. Welch Cline RJ, Young HN. Marketing drugs, marketing health care relationships: a content analysis of visual cues in direct-to-consumer prescription drug advertising. *Health Commun*. 2004;16(2):131-157.
23. Lurie P. DTC advertising harms patients and should be tightly regulated. *J Law Med Ethics*. 2009;37(3):444-450. doi:10.1111/j.1748-720X.2009.00405.x
24. Gibson S. Regulating direct-to-consumer advertising of prescription drugs in the digital age. *Laws*. 2014;3(3):410-438.
25. Sheehan K. Direct-to-consumer (DTC) branded drug web sites risk presentation and implications for public policy. *J Advert*. 2007;36(3):123-135. doi:10.2753/JOA0091-3367360310
26. Huh J, Cude B. Is the information “fair and balanced” in direct-to-consumer prescription drug websites? *J Health Commun*. 2004;9(6):529-540.
27. Miley M. Big Pharma Taking Steps to Reach Patients With Digital Media. http://adage.com/article/news/big-pharma-taking-steps-reach-patients-digital-media/136538/. Accessed April 16, 2015.
28. Hayes A, Krippendorff K. Answering the call for a standard reliability measure for coding data. *Commun Methods Meas*. 2007;1(1):77-89.
29. Food and Drug Administration (FDA). Letter to Novartis Pharmaceuticals. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceutical Companies/UCM221325.pdf. Accessed July 15, 2015. Published 2010.
30. Food and Drug Administration (FDA). Letter to Institut Biochimique SA. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM388800.pdf. Accessed July 15, 2015. Published 2014.
31. Food and Drug Administration (FDA). Letter to BioMarin Pharmaceutical. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/ucm053647.pdf. Accessed April 28, 2015. Published 2006.
32. Food and Drug Administration (FDA). Letter to Astellas Pharma. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/UCM208795.pdf. Accessed April 28, 2015. Published 2010.
33. Liang BA, Mackey T. Direct-to-consumer advertising with interactive internet media: global regulation and public health issues. *J Am Med Assoc*. 2011;305(8):824-825. doi:10.1001/jama.2011.203
34. Kreuter M, Bull F, Clark E, Oswald D. Understanding how people process health information: a comparison of tailored and nontailored weight-loss materials. *Heal Psychol*. 1999;18(5):487-494.
35. Bettman J, Kakkar P. Effects of information presentation format on consumer information acquisition strategies. *J Consum Res*. 1977;3(4):233-240.
36. Yoo CY, Kim K, Stout PA. Assessing the effects of animation in online banner advertising: hierarchy of effects model. *J Interact Advert*. 2004;4(2):49-60.
37. Sewak S, Wilkin N, Bentley J, Smith M. Direct-to-consumer advertising via the Internet: The role of Web site design. *Res Social Adm Pharm*. 2005;1(2):289-309. doi:10.1016/j.sapharm.2005.03.012