The Role of OPDP in Regulating Prescription Drug Promotion

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OBJECTIVES

- To better understand the role of OPDP in regulating prescription drug promotion
- To learn common violations found in prescription drug promotion
- To learn about BadAd and how you can help stop misleading drug promotion
FDA Structure

Food and Drug Administration

- CDER: Center for Drug Evaluation and Research
- CBER: Center for Biologics Evaluation and Research
- CDRH: Center for Devices and Radiological Health
- CFSAN: Center for Food Safety and Applied Nutrition
- CVM: Center for Veterinary Medicine
- CTP: Center for Tobacco Products
- ORA: Office of Regulatory Affairs
CDER Review (Approving) Divisions

Office of New Drugs

- Division of Cardiovascular and Renal Products
- Division of Neurology Products
- Division of Psychiatry Products
- Division of Antimicrobial Products
- Division of Botanical Products
- Division of Anesthesia and Analgesia Products
- Division of Metabolism and Endocrinology Products

- Division of Pulmonary, Allergy, and Rheumatology Products
- Division of Dermatology and Dental Products
- Division of Gastroenterology Products
- Division of Reproductive and Urologic Products
- Division of Medical Imaging Products
- Division of Nonprescription Drug Products
- Office of Hematology and Oncology Products
Office of Prescription Drug Promotion (OPDP)

Mission:

• To protect the public health by assuring prescription drug information is truthful, balanced and accurately communicated.

• To guard against false and misleading advertising and promotion through comprehensive surveillance, enforcement, and educational programs
What Does OPDP Do?

- **Advice to industry**
  - DRAFT promotional materials (VOLUNTARY in most cases)
  - Launch materials for new drugs or new indications
  - Direct-to-consumer (DTC) broadcast ads
  - Non-launch materials

- **Advice within FDA**
  - Draft labeling, including PPIs and Medication Guides
  - Cartons and product labels
  - Dear Healthcare Provider letters
  - Pharmacoeconomics, health-related patient-reported outcome claims
What Does OPDP Do?

- Guidances and Policy Development
- Research
What Does OPDP Do?

- Surveillance
  - Review materials submitted to OPDP at the time of initial dissemination (Form 2253)
- Conferences
- Complaints
  - Healthcare professionals
  - Consumers
  - Competitors
What Does OPDP Do?

- Enforcement
  - Untitled Letters/Notices of Violation
  - Warning Letters
  - Injunction/Consent decrees
  - Seizures/Criminal actions
  - Civil and monetary penalties
What Does OPDP Regulate?

- Written and printed prescription drug promotional materials made by the company which include:
  - TV commercials
  - Sales aids, journal ads, and patient brochures
  - Drug websites, e-details, webinars, Epocrates, and email alerts

- Oral Presentations made by representatives of the company which include:
  - Sales Reps
  - Hired Spokespeople
  - Medical Science Liaisons
# of Final Promotional Pieces Submitted (2253s) 2006 – 2011
Direct-to-Consumer Drug Advertising Trends
DTC Myths and Misperceptions

- FDA “legalized” DTC advertising in the late 1990’s
- Industry spends most of its advertising budget on DTC advertising
- FDA has the authority to ban DTC advertising
- FDA can restrict DTC advertising to certain types of products
- FDA approves DTC ads
- FDA regulates “good taste”
Federal Food, Drug and Cosmetic Act (FFD&C Act)

- Code of Federal Regulations (CFR)
  - 202.1 - Prescription Drug Advertising
  - 312.7 - Preapproval Promotion
  - 314.550 - Subpart H, Accelerated Approval
  - 601.40 - Subpart E, Accelerated Approval for Biologics
Regulatory Authority

Post-Approval Regulations located in 21 CFR 314.81(b)(3):

- Require the submission of all promotional materials at the time of *initial dissemination* or publication
- Must include Form FDA-2253 and current PI
- Received >82K submissions last year
- OPDP does not generally “pre-clear” promotional materials
Compliance with FFD&C Act

- Must be consistent with approved product labeling
- Must be supported by substantial evidence
- Must not be false or misleading
- Must have balance between efficacy and risk information
- Must reveal all material information
What is False or Misleading?

- Better or more effective than has been demonstrated by substantial evidence
- Safer (fewer side effects, lower severity) than has been demonstrated by substantial evidence
- Comparative claims (better or safer than other products) without substantial evidence
- Misleading presentation of data
- Promotion outside labeled uses
Common Violations Cited in Advisory Letters

- Omission of Risk Information
- Minimization of Risk Information
- Broadening or Inadequate Communication of Indication
- Overstatement of Efficacy/Unsubstantiated Claims
- Other Common Issues
Omission of Risk Information

- Full product pieces include the name of the drug plus any representations or suggestions about the drug
- Promotional materials that make product claims must also provide risk information
- Contraindications, Warnings, Precautions, pertinent Adverse Events
Minimization of Risk Information

- Omission of part of the risk described in the approved labeling/lack of context
- Inclusion of non-risk information in a risk section, or vice versa
- “Safety claims”
- “Framing”
- Layout/prominence
- Sequence
Broadening/Inadequate Communication of Indication

- Implying drug is useful in a broader population of patients or disease states than demonstrated
- Failing to disclose full indication, including limitations
- Misleadingly characterizing the indication or disease state
Overstatement of Efficacy/Unsubstantiated Claims

- Suggesting or representing drug is more efficacious than demonstrated
- Guarantee of efficacy
- Survival/Long-term outcome claims
- Superiority/comparative claims
Other Common Issues

- Misleading mechanism of action claims
- Minimization of role of healthcare professional
- Omission/minimization of prescription status
Communication Issues

- Consumer-Friendly Language
- Presentation of Data
- Distraction
- Competing Modalities
Consumer-Friendly Language

- Audience for DTC promotion is consumers
- Typical consumer does not have expert-level knowledge of medical terminology
- Efficacy and risk concepts should be in easily understood, “friendly” language
Presentation of Data

- Efficacy and risk data concepts may be misleading if not presented with adequate context for the consumer to understand the concepts
- Present as clearly as possible
Distraction

- Elements that distract the viewer may interfere with comprehension of both efficacy and risk concepts.
- Examples: flashing lights, quick scene changes, vivid or incompatible visuals or audio.
Competing Modalities

- TV ads present several modalities to the viewer
- Examples:
  - Voiceovers
  - Superimposed statements
  - Graphics
Promotional Categories

- Help-Seeking
- Institutional
- Reminder
- Coming Soon

Does not make representations about a specific product – Does not require fair balance

- Full Product
Help Seeking Ad

- May discuss a medical condition or disease state
- May include a company name
- Should not include drug name
"When I was first diagnosed with prostate cancer, my first concern was ridding myself of the cancer. But I was also concerned about postoperative side effects."

"The good news is that many effective treatments are available for E.D."

"Now it's up to you to get the treatment you need for E.D."
Institutional Ad

- Company name
- Area of research
- Should not mention any drug names
“Our ability to harness new technologies and our research and development resources enable us to open new doors to science-based medicine.”
Reminder Ad

- Must include proprietary and established name
- May call attention to drug name but may **NOT** contain any representation or suggestion relating to the advertised drug product
- May include dosage form, package contents, price, name of manufacturer, packer, distributor
- Not permitted for a drug with a boxed warning
Proprietary and established names

“For more information ask your doctor. Also, call toll-free ...”
Full Product Ad

- Most common type of Ad
- Includes representations or suggestions relating to the advertised drug product
- Must include indication and balanced risk presentation ("fair balance")
- Must include the Brief Summary or PI
“...I’ve found a way to fight osteoporosis with Actonel”

“Side effects are generally mild to moderate and may include joint or back pain...”

“Please see important information on the following page”
 Brief Summary
Broadcast Advertisements

- “Major Statement”
  - Information relating to the major risks of the drug and contraindications

- “Adequate Provision”
  - Included in broadcast advertisements to direct consumers on where they can obtain more information about the drug (i.e., brief summary)
Adequate Provision

Some popular ways to fulfill these provisions are:

- Toll-free number
- Simultaneously running print component
- Reference to a healthcare provider
- Website
Enforcement Action – Aricept TV Ad

CLIENT: Eisai Inc.  
Pfizer Inc.  

PRODUCT: Aricept  

TITLE: "Beach :60 SD"  

LENGTH: :60  

ISC: PFAR9031000  

DATE: 14 October 2009  
©2009 Eisai Inc. ©2009 Pfizer Inc.
Overstatement of Efficacy

- The totality of these claims and presentations imply that, as a result of Aricept treatment, patients’ cognitive and daily functioning will be restored to normal.
- Clinical trial results do not support such drastic improvement
  - Mean difference on ADAS-cog change scores were 2.8 and 3.1 units (scale of 0 – 70) for Aricept 5 mg and 10 mg after 24 weeks of treatment
  - Less than 5% of patients treated with Aricept at either dose were either “markedly” or “moderately improved.” Majority of patients experienced no change or became worse
  - Patients on Aricept continued to show clinical decline over time
Enforcement Example: Provigil (modafinil)

- Promotional piece distributed on behalf of company at the Maryland Health and Mental Hygiene’s P&T committee meeting in 2006.

Broadening of indication/Omission of risk

- Approved Indication:
  - To improve wakefulness in patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea/hypopnea syndrome, and shift work sleep disorder (SWSD)
Enforcement Example: Provigil (modafinil)

Risk Information for Provigil

- **Warning**: Patients with abnormal sleepiness who take Provigil should be advised that their level of wakefulness may not return to normal. Patients with excessive sleepiness, including those taking Provigil, should be frequently reassessed for their degree of sleepiness and if appropriate, advised to avoid driving or any other potentially dangerous activity.

- **Precaution**: Patients should be cautioned about operating an automobile or other hazardous machinery until they are reasonably certain that Provigil therapy will not adversely affect their ability to engage in such activities.
The Utility of Provigil (modafinil) in the Medical and Psychiatric Population

Harry Kerasidis M.D.

Provigil (modafinil) is categorized as a stimulant medication. It is unique in its pharmacologic effect and mechanism of action.

Sleep Disorder Related Fatigue

- Sleep Disorder Related Fatigue is the sleepiness, inattentiveness, and psychological changes resulting from disordered sleep.
- Forty million Americans suffer from a chronic sleep disorder. This translates into 17% of the workforce, working in a chronically fatigued state.
- 20% of all adults report impairing sleepiness a few days a week or more. More commonly in shift-workers (30%)
- Corporate America is losing $18 billion each year to lost productivity due to Sleep Disorder Fatigue.
- Nearly 1/3 of all fatal-to-the-driver heavy trucking accidents are due to driver fatigue. For every driver lost, an average of 4 innocent bystanders are also lost.

Provigil (modafinil) has FDA indications for the following disorders that result in Sleep Disorder Fatigue:

- Narcolepsy, a genetic disorder of primary daytime sleepiness affecting 1 of every 2500 individuals.
- **Persistent hypersomnia in treated obstructive sleep apnea.** Obstructive sleep apnea affects 5% of the population. About 15% of these individuals have persistent daytime sleepiness even when the apnea is treated.
- **Shift Work Sleep Disorder, excessive sleepiness that persists in individuals engaging in shift work despite attempts to alleviate this symptom:**
  - Up to 24 million Americans work irregular shift schedules.
  - Approximately 25% of night/rotating shift workers meet criteria for SWSD resulting in increased risks of motor vehicle accidents, work related accidents and errors, and clinically significant impairment in social and occupational function.
Provigil (modafinil) has utility in the treatment of other sleep disorders that cause excessive daytime sleepiness including idiopathic hypersomnolence syndrome, delayed sleep phase syndrome, and, paradoxically, some cases of insomnia.

Provigil (modafinil) also has utility in the treatment of other neurologic and psychiatric disorders associated with fatigue, sleepiness, or inattentiveness:

**Multiple Sclerosis Related Fatigue**
- MS affects about 300,000 Americans. 10-20% of these individuals suffer from chronic fatigue. Provigil (modafinil) is very effective in relieving the fatigue related to MS.

**Parkinson's Disease Related Fatigue**
- Parkinson's and the medications used to treat Parkinson's Disease often result in daytime sleepiness, which often can be offset with the use of Provigil (modafinil).

**Chronic Fatigue Syndrome Fibromyalgia, & chronic pain conditions**
- The fatigue related to CFS and Fibromyalgia often responds to Provigil (modafinil). Many of the medications used to treat these conditions also lead to impairing daytime sleepiness which often can be offset by Provigil (modafinil).

**Attention Deficit Disorder**
- Affects approximately 5% of the pediatric population, and 2-3% of the adult population.
- Double blind placebo controlled studies have shown significant improvements in multiple cognitive measures in this population without the risks attendant to the traditional stimulants used to treat this condition.

**Depression**
- In a retrospective case series, modafinil was found to augment actions of antidepressants, especially in patients with residual tiredness or fatigue. Clinical experience supports this published finding.

Provigil (modafinil) is a unique medication with proven efficacy, safety, utility and versatility; and low potential for abuse, dependence and diversion.
Limitations to Surveillance

- OPDP's normal surveillance activities include:
  - Monitor drug promotions sent to us
  - Monitor Medical Convention Exhibit Halls
  - Review complaints submitted by Industry Competitors

- However, these surveillance activities do not allow us to monitor certain types of drug promotion that occur in places such as physician offices and industry-sponsored dinner and lunch programs. These types of promotion include:
  - Verbal presentations from drug reps or company-paid speakers
  - Home-made promotional materials not submitted to FDA

That’s why we developed the Bad Ad Program
The Bad Ad Program

- The Bad Ad Program is an FDA-sponsored outreach program designed to educate HCPs about the role they can play in helping FDA ensure that prescription drug advertising and promotion is truthful and not misleading.

- When HCPs recognize misleading drug promotion, they can help put a stop to it by reporting it to FDA:
  - Call
    - 877-RX-BADAD (877-792-2323)
  - Email
    - BadAd@fda.gov
OPDP Contact Information

- Fax Numbers
  301-847-8444/8445

- Telephone Number
  301-796-1200

- Website
  http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm090142.htm