



**The Last Two Years:  
A Summary of 2014-2015**

**Office of Prescription Drug Promotion (OPDP)  
Enforcement and Relevant FDA Guidance**

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## The Last Two Years: A Summary of 2014-2015 Office of Prescription Drug Promotion (OPDP) Enforcement and Relevant FDA Guidance

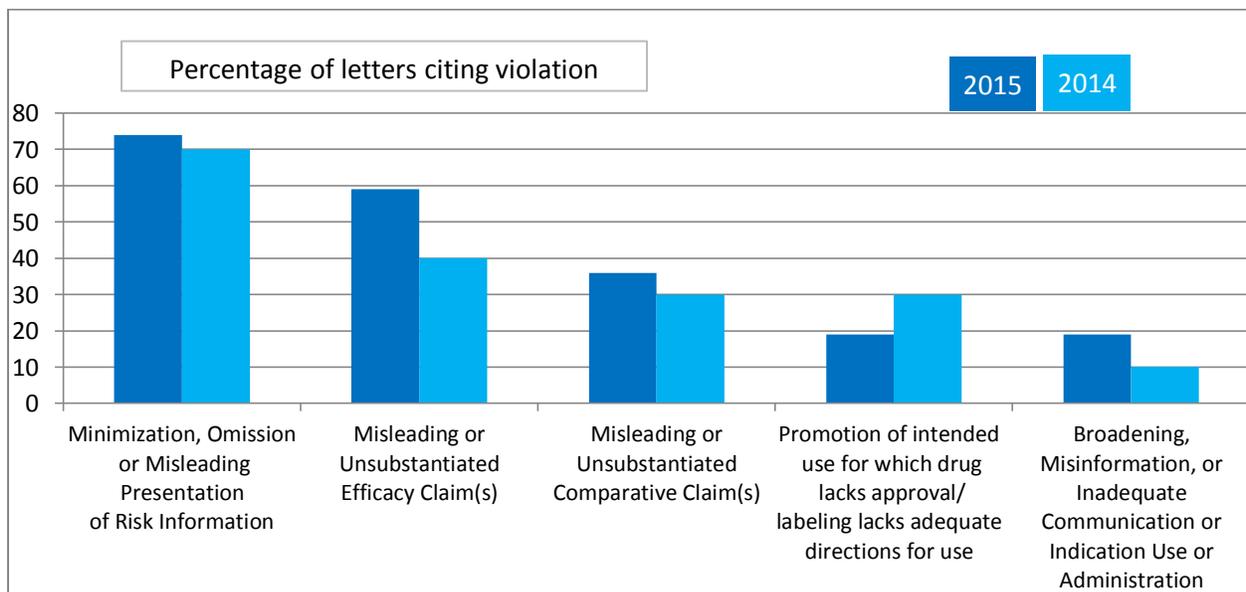
The past two years have created a bit of uncertainty for life sciences promotional review professionals. With fewer enforcement letters, high-profile lawsuits, and a shift in marketing focus as a result of the Affordable Care Act, companies are struggling for a greater understanding of the Food and Drug Administration's ("FDA") enforcement objectives and some predictability to help with sales and marketing initiatives.

In 1998, FDA's Division of Drug Marketing, Advertising, and Communications ("DDMAC"), now the Office of Prescription Drug Promotion ("OPDP"), issued 158 enforcement letters. Over the years, the number of letters issued has decreased drastically. In stark contrast to the late 1990s, OPDP issued ten letters in 2014 and nine letters in 2015. Despite fewer letters, there is still much to be learned from the content of the communications and related FDA actions.

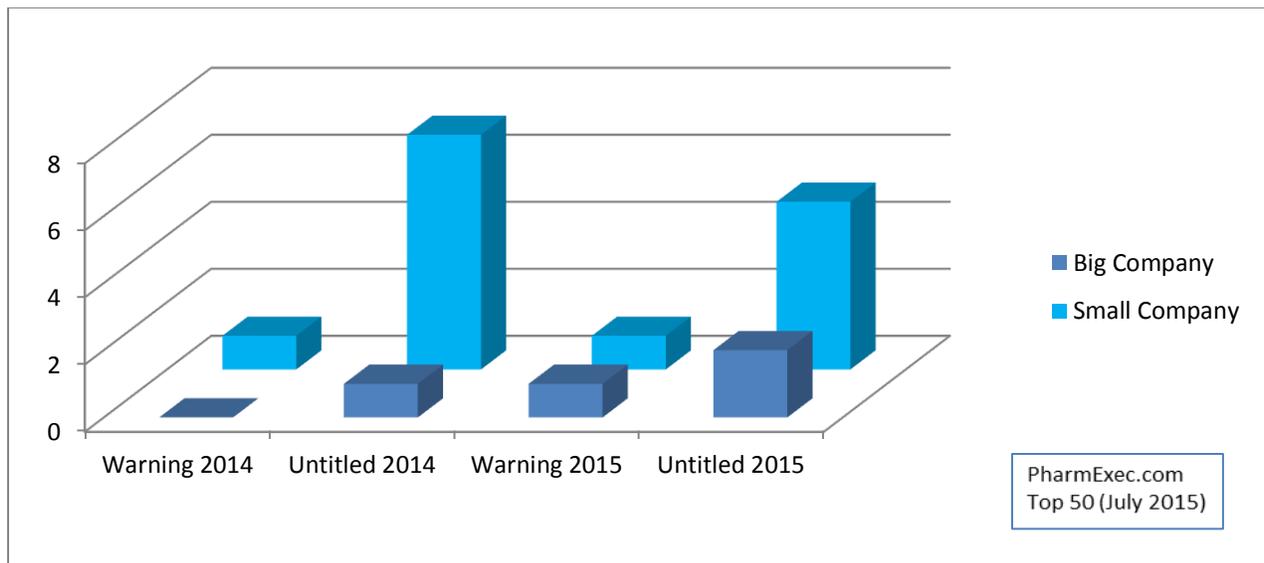
Of the ten OPDP letters issued in 2014, three identified violations concerning web promotion and the remaining letters identified violations concerning promotion directed to health care providers, including sales aids, an email, a flashcard, journal advertisements, and a telephone script. The nine 2015 enforcement letters identified violations concerning web promotion, a social media post, a sales aid, a detail aid, an exhibit booth banner, and a promotional card. The violations cited were similar to past years with minimization of risk information being the most cited, followed by misleading efficacy claims, and misleading comparative claims.

While OPDP continues to focus on violations related to promotion of unapproved drug use, FDA's description of such violations has changed post-*Caronia*. OPDP no longer includes a header listing "Unapproved New Use," but instead states that the violative piece "provides evidence that [the drug] is intended for a new use for which it lacks approval, and for which its labeling does not provide adequate directions for use."

The most frequently cited violations cited for both 2014 and 2015 are highlighted in the charts below:



Also noteworthy, the past two years have demonstrated that OPDP enforcement is not reserved for larger pharmaceutical companies. In both years, a greater number of "small pharma" companies have received warning and untitled letters than "big pharma."



## BAD AD PROGRAM

The Bad Ad Program, created in 2010, helps healthcare professionals recognize misleading prescription drug promotion and provides a way for them to report misleading promotion to the agency. To date, the Bad Ad Program has yielded eleven letters, including one in 2014 and one in 2015.

### Warning Letter to Pacira Pharmaceuticals (September 22, 2014)

OPDP issued a Warning letter to Pacira Pharmaceuticals for violative "educational technique flashcards" and a journal advertisement for Exparel (bupivacaine liposome injectable suspension). The journal advertisement was submitted as a complaint to the OPDP Bad Ad Program. According to the agency, the materials created the impression that Exparel has been approved for "new uses for which it lacks approval" and overstated the efficacy of the drug for the purposes for which it obtained approval.

According to the Dosage and Administration section of the PI, Exparel was studied and approved for use as an injectable local anesthetic agent after two specific surgeries: bunionectomy and hemorrhoidectomy. Per OPDP, however, the promotional materials suggested that the drug is safe and effective for use in laparoscopic cholecystectomy and open colectomy, neither of which are supported by data provided by Pacira. FDA acknowledged disclosures provided by the company, but noted that they do "not mitigate the overwhelming impression that Exparel is safe and effective for use in cholecystectomy and colectomy." OPDP added that other Pacira professional promotional materials, not discussed in the Warning Letter, "suggest an extensive promotional campaign ... to promote the use of Exparel in surgical procedures other than those for which the drug has shown to be safe and effective."

At the agency's direction, the company issued a statement correcting the earlier claims and agreed to stop distributing those promotional materials.

In an interesting turn of events, however, Pacira Pharmaceuticals sued the FDA on September 10, 2015, claiming a First Amendment right to promote Exparel for a wide range of surgeries, citing the *Amarin* federal court ruling that truthful off-label claims are protected free speech. In *Pacira Pharmaceuticals Inc., et. al v. Food and Drug Administration et. al*, the company maintained that its promotional information was truthful and should be allowed under the recent *Amarin* ruling.

On October 20, in an atypical move, FDA removed Pacira's Warning Letter from the FDA website. According to Janet Woodcock, M.D., FDA Director of the Center for Drug Evaluation and Research, in a letter to Pacira on December 15, 2015, ". . . in light of the agency's approval of a labeling supplement submitted by Pacira, which made certain changes to the EXPAREL label in order to clarify that its indication was not limited to bunionectomy and hemorrhoidectomy procedures, FDA removed the letter from its website."

On the same day that Dr. Woodcock issued her letter, Pacira announced that it achieved an amicable resolution with the FDA in its lawsuit. Under the settlement agreement, the FDA acknowledged that Pacira may rightfully promote Exparel for a broader range of uses than those previously recognized by the FDA, and Pacira agreed to drop its lawsuit.

#### **Warning Letter to Duchesnay, Inc. (August 7, 2015)**

OPDP issued a Warning Letter to Duchesnay, Inc. in 2015 regarding its promotion of Diclegis (doxylamine succinate and pyridoxine hydrochloride), citing a violative social media post by Kim Kardashian. The social media post was also submitted as a complaint to the OPDP Bad Ad Program.

According to FDA, Kardashian praised the drug for treating her pregnancy-related morning sickness in various social media posts on Instagram and Facebook:

"OMG. Have you heard about this? As you guys know my #morningsickness has been pretty bad . . . so I talked to my doctor," Kardashian wrote in the photo's caption. "He prescribed me #Diclegis, and I felt a lot better and most importantly, it's been studied and there was no increased risk to the baby. I'm so excited and happy with my results that I'm partnering with Duchesnay USA to raise awareness about treating morning sickness."

According to the Warning Letter, the social media post entirely omitted all risk information, and indicating at the end of the post that more information is available at [www.DiclegisImportantSafetyInfo.com](http://www.DiclegisImportantSafetyInfo.com), did not make up for the omission. OPDP also found the social media post to be misleading because it failed to provide material information regarding the approved indication, including important limitations of use, specifically, that Diclegis has not been studied in women with hyperemesis gravidarum.

On August 31, 2015, in response to the August 7<sup>th</sup> Warning Letter, Kim Kardashian posted updated endorsements of Diclegis on Instagram, Twitter, and Facebook that included acknowledgement of the drug's side effects:

"#CorrectiveAd I guess you saw the attention my last #morningsickness post received. The FDA has told Duchesnay, Inc., that my last post about Diclegis (doxylamine succinate and pyridoxine HCl) was incomplete because it did not include any risk information or important limitations of use for Diclegis. A link to this information accompanied the post, but this didn't meet FDA requirements. So, I'm re-posting and sharing this important information about Diclegis."

## **WEB PROMOTION**

#### **Untitled Letter to Institut Biochimique SA (February 24, 2014)**

FDA issued an Untitled Letter to Institut Biochimique SA ("IBSA") and Akrimax Pharmaceuticals for a violative Facebook page promoting its hypothyroid drug Tirosint (levothyroxine sodium). According to its FDA-approved product labeling, Tirosint is indicated as a replacement or supplemental therapy in congenital or acquired hypothyroidism of any etiology, except transient hypothyroidism during the recovery phase of subacute thyroiditis.

OPDP explained that the Facebook webpage was misleading because it made representations about the efficacy of Tirosint, but failed to communicate any of the risks associated with its use. OPDP noted that the omission of

risk information was particularly concerning considering that the Tirosint package insert ("PI") includes a Boxed Warning. In addition, the agency found that the Facebook webpage made suggestions regarding the use of Tirosint in patients with hypothyroidism, but failed to convey that Tirosint is not indicated for transient hypothyroidism during the recovery phase of subacute thyroiditis.

#### **Untitled Letter to Citius Pharmaceuticals (June 9, 2014)**

OPDP issued an Untitled Letter to Citius Pharmaceuticals for a webpage promoting its product Suprenza (phentermine hydrochloride). OPDP stated that the webpage omitted risk information and made exaggerated claims about the weight loss drug. According to the Untitled Letter, the Suprenza website homepage failed to state the drug's contraindications and adverse reactions. In addition, the webpage failed to disclose material facts, including the minimum initial body mass index for which Suprenza is indicated.

FDA also cited Citius for using the term "lean" in connection with the use of Suprenza, implying that patients will become more lean as a result of its use. The letter stated, "The term 'lean' is an amorphous cosmetic descriptor, commonly understood to mean thin, slim or slender, that was not associated with any clinical endpoints in the studies for phentermine."

#### **Untitled Letter to Gilead Sciences, Inc. (June 27, 2014)**

OPDP issued an Untitled Letter to Gilead Sciences, Inc. for a sponsored link on Google.com for its drug, Viread (tenofovir disoproxil fumarate). OPDP explained that the sponsored link misleadingly indicated that the drug can be used for the prevention of hepatitis B, when it is only approved for treatment of the disease.

According to the Untitled Letter, a Google search for "Hepatitis B Prevention," turned up a sponsored link to the website for Viread that listed the name of the drug and the statement, "Hepatitis B Prevention." The Untitled Letter stated that the sponsored link misbranded the drug because "[t]he approved labeling for Viread does not provide instructions for, or otherwise indicate that Viread will be safe and effective if used for the prevention of hepatitis B." OPDP also explained that the sponsored link failed to communicate serious risks associated with the drug's use, including a Boxed Warning regarding fatal cases of lactic acidosis and severe hepatomegaly with steatosis and post-treatment exacerbation of hepatitis.

OPDP noted in the letter that the sponsored link contained a link to the product's website, [www.viread.com](http://www.viread.com), but explained that "this does not mitigate the misleading omission of risk information from this promotional material."

#### **Untitled Letter to Luitpold Pharmaceuticals, Inc. (January 29, 2015)**

The first OPDP letter of 2015 addressed a violative website video. The Untitled Letter, issued to Luitpold Pharmaceuticals, Inc. for its product Injectafer (ferric carboxymaltose injection), cited the video for minimizing risk associated with the drug, as it failed to discuss risks and instead presented them in a super displayed on the screen for approximately 30 seconds of the seven minute video. OPDP stated that the website video also omitted material facts because it suggested that Injectafer can be administered as a single dose, when the PI and Patient Information explained that the drug should be given in two doses. Additionally, under the heading "Lack of Adequate Directions for Use," OPDP explained that by implying that Injectafer is used to treat all patients with iron deficiency anemia ("IDA"), the video provided "evidence that Injectafer is intended for new uses for which it lacks approval, and for which its labeling does not provide adequate directions for use." Injectafer is indicated as second line treatment in adult IDA patients who have an intolerance or unsatisfactory response to oral iron, or in patients who have non-dialysis dependent chronic kidney disease.

### **Untitled Letter to University of California, Los Angeles and Taumark, LLC (February 20, 2015)**

The second OPDP letter of 2015 was issued to the University of California, Los Angeles, as the sponsor of FDDNP, an investigational new drug, and partner of Taumark, LLC regarding its website entitled "Taumark Better Brain Diagnostics," found at <http://taumark.com>. According to the Untitled Letter, the website described FDDNP for use in brain PET scans to diagnose traumatic brain injuries, Alzheimer's disease, and other neurological conditions. Per OPDP, the website made "conclusory statements about the safety and effectiveness" of the investigational drug, including that it has a "high safety profile" with "no reported adverse events." The website therefore suggested in a promotional context that FDDNP is safe and effective for the purpose for which it was being investigated, according to FDA.

### **Untitled Letter to Discovery Laboratories, Inc. (March 3, 2015)**

OPDP issued its third letter in 2015 to Discovery Laboratories, Inc. for claims made on the homepage of its website for Surfaxin (lucinactant) Intratracheal Suspension. According to the Untitled Letter, Discovery suggested on its website that its synthetic lung drug Surfaxin is superior to competing products that are derived from animals. The webpage used images of a pig, then a cow and then a robot beside the phrase, "Join the Therapeutic Evolution." OPDP explained that the phrase "therapeutic evolution" was misleading because the ADVERSE REACTIONS section of the PI indicates that Surfaxin is not safer than animal-derived surfactants. In addition to the misleading superiority claims, OPDP cited Discovery for promoting Surfaxin with a lack of adequate directions for use. The PI for Surfaxin does not provide instructions for, or otherwise indicate that, Surfaxin will be safe and effective for the *treatment* of respiratory distress syndrome (it is indicated for the *prevention* of respiratory distress syndrome in certain premature infants), and information sufficient to demonstrate that Surfaxin is safe and effective for this new intended use was not submitted to FDA in an application, per OPDP.

### **Untitled Letter to Actavis (May 19, 2015)**

In the May 19, 2015, Untitled Letter to Actavis regarding the website for Rapaflo (silodosin), OPDP explained that the claim "works nights so he can work days," along with the picture of a man walking to the bathroom from the bed in the middle of the night, is misleading. Rapaflo is indicated for the treatment of signs and symptoms of benign prostatic hyperplasia (BPH). According to OPDP, the website presentation implied that Rapaflo improves both sleep disturbance (i.e., quality of sleep) and work productivity, but the studies cited did not use adequate endpoints or well-developed instruments to measure the impact of treatment on such individual symptoms. Therefore, per OPDP, the website did not provide the necessary substantial evidence to support the claim.

## **HCP DIRECTED PROMOTION**

### **Untitled Letter to Mission Pharmacal Company (January 23, 2014)**

OPDP issued an Untitled Letter to Mission Pharmacal Company in January 2014 for a professional sell sheet for Tindamax (tinidazole). The sales sheet included the claim, "The July 2010 issue of Treatment Guidelines from The Medical Letter recommends tinidazole as a 'drug of choice' for bacterial vaginosis ("BV") and trichomoniasis." OPDP found the sales sheet to be misleading because it failed to communicate material information from Tindamax's full FDA-approved indication for the treatment of trichomoniasis, including important information regarding diagnostic procedures and the need to treat sexual partners simultaneously.

The sales sheet also discussed the use of Tindamax for the treatment of BV, but failed to present the drug's full approved indication. For example, the following claims were presented:

- "For short, affordable treatment of bacterial vaginosis (BV)..."
- "TINDAMAX® (tinidazole tablets) is the one and only treatment for BV that gives your patients..."

According to the Untitled Letter, "Tinidazole is indicated for the treatment of bacterial vaginosis in non-pregnant women." Therefore, the sales sheet, per OPDP, misleadingly broadened the patient population or condition of Tindamax by suggesting that it is approved for the treatment of BV in all women, including those that may be

pregnant, when this was not supported by substantial evidence or substantial clinical experience. OPDP noted that the presentation also suggested that Tindamax is intended for a new use for which it lacks approval, and for which its labeling does not provide adequate directions for use. OPDP also found the sales sheet's claim of "Patient-friendly convenience" to be misleading because it is not supported by substantial evidence.

#### **Untitled Letter to Alvogen (May 6, 2014)**

OPDP issued an Untitled Letter to Alvogen, Inc. for a violative "New Product Release" sales aid for Disulfiram Tablets, USP.

The sales aid included the following statement regarding Disulfiram's indications and usage: "Disulfiram is an aid in the management of selected chronic alcohol patients who want to remain in a state of enforced sobriety so that supportive and psychotherapeutic treatment may be applied to best advantage." OPDP objected to this claim because it failed to communicate material information from the full FDA-approved indication. The Indications and Usage section of the product's PI states, "Disulfiram is not a cure for alcoholism. When used alone, without proper motivation and supportive therapy, it is unlikely that it will have any substantive effect on the drinking pattern of the chronic alcoholic."

OPDP also found the sales aid to be misleading because it made representations about the efficacy of Disulfiram but failed to communicate any risk information associated with its use, including a Boxed Warning regarding its administration.

#### **Untitled Letter to Concordia Pharmaceuticals (July 7, 2014)**

Concordia Pharmaceuticals received an Untitled Letter from OPDP for a professional telephone script about its drug, Kapvay (clonidine hydrochloride). According to OPDP, the telephone script omitted critical risk information, including warnings, precautions, and adverse events associated with the drug. While the script did direct professionals to the company's website for the full prescribing information, and offered to email the information, OPDP stated in the letter that this did not mitigate the omission of important risk information.

OPDP also found the script misleading because it omitted important material information regarding initial dosage and dosage adjustments, as well as material information regarding the drug's indication, particularly that Kapvay is part of a comprehensive treatment program that may include other measures. Also, per OPDP, the script failed to disclose the established name in direct conjunction with the proprietary name.

#### **Untitled Letter to Cipher Pharmaceuticals, Inc. (September 11, 2014)**

OPDP issued an Untitled Letter to Cipher Pharmaceuticals Inc. regarding its "e-Pharm/alert" email for Lipofen (fenofibrate capsules, USP) for oral use. According to the letter, the totality of claims and presentations in the email alert misleadingly implied that Lipofen offers a clinical advantage over other available fenofibrate products, as a result of its formulation and delivery system, when this was not demonstrated by substantial evidence. The email contained claims such as "All fenofibrates are not created equal," and "LIPOFEN Takes Particle Size Out of the Equation."

There were several references cited in support of the claims and presentations, but according to OPDP, none of the cited references described any clinical trial data comparing Lipofen to other fenofibrate products to support claims of superiority. In addition, OPDP stated that FDA is not aware of any head-to-head clinical trials comparing Lipofen to other fenofibrate products, or any evidence to support the claims that Lipofen's "Lidose" technology provides a clinical advantage over other fenofibrate products.

Although OPDP acknowledged that some of the claims in the email may be true, it explained that the totality of the claims and presentations implied that Lipofen had a clinical advantage compared to other products.

#### **Untitled Letter to Scieure Pharma (October 29, 2014)**

OPDP issued an Untitled Letter to Scieure Pharma for a sales aid promoting its product Doral (quazepam). According to the Untitled Letter, the sales aid included numerous claims and presentations regarding the benefits of using Doral for the treatment of insomnia, yet omitted all of the contraindications for the use of Doral. The sales aid also omitted the warnings and precautions regarding benzodiazepine withdrawal syndrome, the need to evaluate for co-morbid diagnoses, severe anaphylactic or anaphylactoid reactions, abnormal thinking and behavior changes, and worsening of depression. Adverse reactions such as fatigue, dizziness, dry mouth, and dyspepsia were also omitted.

OPDP acknowledged that the sales aid included the statement, "Please see accompanying full prescribing information" on the bottom of page four; however, OPDP stated that this does not mitigate the omission of the aforementioned risk information.

The sales aid also included multiple superiority claims such as, "Uniquely Selective," "The only benzodiazepine that provides BZ<sub>1</sub> receptor selectivity," and "For the effective treatment of insomnia." The Untitled Letter stated that the totality of these claims and presentations misleadingly suggested that Doral is both safer and more effective than other products for the treatment of insomnia because of a unique mechanism of action. According to OPDP, this suggestion of superior safety and efficacy, based on the mechanism of action, was not demonstrated by substantial evidence.

#### **Untitled Letter to Sunovion Pharmaceuticals (December 15, 2014)**

OPDP issued an Untitled Letter to Sunovion Pharmaceuticals for a violative print advertisement promoting its anti-seizure medication, Aptiom (eslicarbazepine acetate). According to the FDA-approved product labeling, Aptiom is indicated as adjunctive treatment of partial-onset seizures. OPDP found the advertisement to be misleading because it overstated the efficacy of Aptiom by suggesting that the drug has been shown to have treatment benefits on patients' feelings of confinement associated with seizures. The advertisement contained the statements "Seizures Can Keep Patients Feeling Confined," along with a graphic of a dark house, surrounded by a fence that was made of electroencephalogram ("EEG") brain waves. According to OPDP, claims and presentations of such treatment benefits must be supported by substantial evidence as demonstrated by adequate and well-controlled studies using well-developed instruments that can validly and reliably measure the specific concepts claimed.

#### **Untitled Letter to Otsuka Pharmaceutical (April 17, 2015)**

On April 17, 2015, OPDP issued an Untitled Letter to Otsuka Pharmaceutical Development & Commercialization, Inc. for a visual aid citing misleading claims and presentations about its drug, Abilify (aripiprazole). The FDA-approved product labeling states that Abilify is indicated for the acute treatment of manic and mixed episodes associated with bipolar I disorder, both as monotherapy and as an adjunct to lithium or valproate. It is also indicated for use as an adjunctive therapy to antidepressants for the treatment of major depressive disorder ("MDD").

According to the Untitled Letter, the visual aid showed three dimmer switches at low, high and middle heights, with the low switch representing a "full antagonist" and the high switch representing a "full agonist." The mid-height slider switch was meant to represent Abilify's pharmacology, and was accompanied by claims such as, "Modulating dopaminergic and serotonergic activity sets ABILIFY® (aripiprazole) apart" and "Unique pharmacology sets ABILIFY® (aripiprazole) apart."

OPDP found that the totality of the claims and presentations in the visual aid misleadingly implied a greater degree of certainty about the mechanism of action of Abilify in humans than is currently known and supported by

the drug label. The letter also stated that the presentation implied that Abilify has a clinical advantage over competitor drugs, which was not supported by clinical data.

#### **Untitled Letter to Oak Pharmaceuticals Inc. (May 14, 2015)**

According to the Untitled Letter issued to Oak Pharmaceuticals on May 14, 2015, the exhibit banner for Nembutal (pentobarbital sodium injection) included claims such as, "Control the Uncontrollable" and "the control you need when seizures are their worst," but it omitted all of the contraindications, warnings, precautions, and common adverse reactions associated with the use of Nembutal. This, according to OPDP, suggested that Nembutal is safer than has been demonstrated. The Untitled Letter explained that the exhibit banner included the statement "SEE BOOTH REPRESENTATIVE FOR FULL PRESCRIBING INFORMATION AND IMPORTANT SAFETY INFORMATION" at the bottom, but this statement, per OPDP, did not mitigate the omission of risk information.

In addition, OPDP stated that the exhibit banner failed to communicate material information regarding the FDA-approved indication for Nembutal, as the banner referred to control in "seizures." Nembutal is indicated, however, for use as an anticonvulsant, *in anesthetic doses, in the emergency control of certain acute convulsive episodes*, e.g., those associated with status epilepticus, cholera, eclampsia, meningitis, tetanus, and toxic reactions to strychnine or local anesthetics.

#### **Untitled Letter to Ascend Therapeutics US, LLC (June 23, 2015)**

OPDP issued an Untitled Letter to Ascend Therapeutics US, LLC in June 2015 regarding its promotional card for EstroGel® 0.06% (estradiol gel) for topical use. According to the Untitled Letter, the card included efficacy claims for EstroGel, but failed to include important risk information associated with the drug. The Untitled Letter also explained that the card failed to include information from the Boxed Warning that "EstroGel, alone or with progestin, should not be used for the prevention of cardiovascular disease or dementia." OPDP pointed out that the card failed to disclose material information about the specific risks related to cancers and cardiovascular disorders discussed in the BOXED WARNING section of the PI, which includes endometrial cancer, invasive breast cancer, deep vein thrombosis, pulmonary embolism, stroke, and myocardial infarction. The card also failed to include the drug's contraindications.

OPDP noted that while the card included the statements, "Please visit [www.estrogel.com](http://www.estrogel.com) for additional information" and "See enclosed full Prescribing Information and boxed warning," the statements did not mitigate the omission of these important risks.

#### **Warning Letter to ECR Pharmaceuticals (July 27, 2015)**

On July 27, 2015, OPDP issued a Warning Letter to ECR Pharmaceuticals, a wholly owned subsidiary of Valeant Pharmaceuticals International, regarding its professional sales aid for TussiCaps (hydrocodone polistirex and chlorpheniramine polistirex) extended-release capsules.

According to the letter, the sales aid did not disclose any risk information, including that use of TussiCaps carries a number of serious and potentially fatal risks. Per OPDP, the statement on the last page of the sales aid that the aid should remain in the representative's possession and appropriate labeling should accompany the aid did not make up for the omission.

In addition, OPDP explained that the sales aid did not provide TussiCaps' full approved indication, omitting that extended-release capsules are indicated for adults and children six years of age and older. According to the FDA-approved product labeling, TussiCaps are contraindicated in patients allergic or sensitive to hydrocodone and chlorpheniramine and in children under the age of six due to the risk of fatal respiratory depression. OPDP noted that this information is not included in the sales aid and explained that the statement on the bottom of the last page of the sales aid regarding dosing and age limitations did not correct the misleading impression.

The Warning Letter also cited unsubstantiated preference claims, including "Patient Preferred Capsule," and the statement that "73% of adult prescription cough syrup users said they prefer capsules over liquid medication." OPDP explained that these claims, combined with the presentation in the sales aid, suggest that patients prefer TussiCaps over liquid formulations, which was not supported by the referenced study.

## FDA GUIDANCE

Although the number of warning and untitled letters issued by OPDP continues to decline, the number of FDA guidances issued remains quite strong, relatively, with 2014/2015 producing one-third of CDER's advertising guidances currently in effect.

The year 2014 brought about long-awaited social media guidance, including the following:

- **Draft Guidance, "Internet/Social Media Platforms: Correcting Independent Third-Party Misinformation About Prescription Drugs and Medical Devices" (June 18, 2014)**

This draft guidance describes how drug and device manufacturers, packers and distributors should respond to misinformation about their products created and disseminated by independent third parties on the Internet or through social media platforms. The draft guidance explains that the recommendations do not apply to communications "that are owned, controlled, created, or influenced, or affirmatively adopted or endorsed, by, or on behalf of, the firm." Nor would they apply "if a firm writes, collaborates on, or exerts control or influence on product-specific content provided by a third party, to the extent that responsibility for the development of the content is imputable to the firm[.]"

The draft guidance explains that companies have no obligation to correct misleading statements or claims made about their products by third parties. For companies that choose to make corrections, however, the draft guidance sets forth recommendations for such corrections and explains that FDA will not object if the corrective information adheres to the recommendations, but does not otherwise satisfy regulatory requirements regarding labeling and advertising. The draft guidance sets forth eight recommendations for proper corrective information, including that it must be accurate, non-promotional, and relevant and responsive to the misinformation. The draft guidance also provides fifteen elaborative examples.

- **Draft Guidance, "Internet/Social Media Platforms with Character Space Limitations— Presenting Risk and Benefit Information for Prescription Drugs and Medical Devices" (June 18, 2014)**

This draft guidance explains how manufacturers, packers and distributors of prescription drugs and devices should present both benefit and risk information when using social media platforms with limited character space such as Twitter, and Google and Yahoo sponsored links. Consistent with standard requirements pertaining to promotional labeling, the draft guidance explains that product information must be truthful and non-misleading, and include the product's name, indications and limits to indications or patient populations, along with a presentation of risk information. When dealing with platforms with character limitations, the draft guidance explains that benefit information must be accurate and non-misleading, reveal material facts, and be accompanied by risk information. The risk information should include the most serious risks associated with the product, along with a link to a page that specifically presents that risk information in greater detail. The draft guidance states that if adequate benefit and risk information cannot be conveyed, then the company should reconsider using the space-limited platform.

The draft guidance also recommends that linked pages included in tweets or sponsored links not be promotional in content or tone and present the product's brand name alongside its generic name and at least one dosage form. The draft guidance uses fictional examples to demonstrate how companies should present information in tweets and sponsored links.

Additional Guidance Documents issued in 2014 included:

- **Draft Guidance**, "*Fulfilling Regulatory Requirements for Postmarketing Submissions of Interactive Promotional Media for Prescription Human and Animal Drugs and Biologics*" (**January 14, 2014**)
- **Revised Draft Guidance**, "*Distributing Scientific and Medical Publications on Unapproved New Uses — Recommended Practices*" (**March 3, 2014**)
- **Draft Guidance**, "*Distributing Scientific and Medical Publications on Risk Information for Approved Prescription Drugs and Biological Products — Recommended Practices*" (**June 11, 2014**)
- **Guidance For Industry**, "*Patient Counseling Information Section of Labeling for Human Prescription Drug and Biological Products — Content and Format*" (**December 10, 2014**)

In contrast to six FDA guidances relative to drug promotion in 2014, 2015 produced only one new guidance: "*Revised Draft Guidance for Industry: Brief Summary and Adequate Directions for Use: Disclosing Risk Information in Consumer-Directed Print Advertisements and Promotional Labeling for Prescription Drugs.*" This guidance was listed in FDA's anticipated guidance documents for 2015. The new guidance revises the draft guidance entitled "*Brief Summary: Disclosing Risk Information in Consumer-Directed Print Advertisements*" (issued January 2004). According to the agency, the draft guidance incorporates results from recent social science research that suggest consumers may get overwhelmed by large amounts of information, or may not understand the technical content. FDA regulations require print advertisements to include a "brief summary" of risk information, and promotional labeling to be disseminated with the full FDA-approved prescribing information.

The revised guidance recommends an alternative to the brief summary in consumer-directed print advertisements and the full PI in consumer-directed promotional labeling, which FDA refers to as the "consumer brief summary." In terms of language and readability, FDA recommends that drugmakers translate warnings in the PI into a casual tone, using lay language. In terms of content, the guidance suggests that the consumer brief summary include contraindications, Boxed Warnings, and the most common or serious adverse events, or those that lead to discontinuation of the drug.

In addition to introducing new guidance, FDA withdrew 47 draft guidance documents on May 6, 2015. Among them was the 2004 draft guidance on "help-seeking" and other disease awareness communications by drug and medical device manufacturers ("*Help-Seeking' and Other Disease Awareness Communications by or on Behalf of Drug and Device Firms*"). According to FDA, the documents were withdrawn "to help improve the efficiency and transparency of the guidance development process."

## LOOKING AHEAD

OPDP's enforcement has notably declined in recent years, but the ramifications of receipt of a warning or untitled letter remain consequential, as FDA activity often prompts other lawsuits or enforcement actions. The *Amarin* and *Pacira* decisions have had and will undoubtedly continue to have some impact on OPDP activity. That impact may be a more refined approach to regulatory analysis and enforcement.

The fact that OPDP issued eight letters in the last two years addressing websites, sponsored links, or social media platforms (which is 42% of letters issued), on the heels of its long awaited social media guidances, is evidence of its evolution into the social media world. Indeed, OPDP's first letter of 2016, an untitled letter to Hospira, is further evidence of its focus in this area. The subject of that letter was a video regarding Precedex (dexmedetomidine hydrochloride) Injection posted on YouTube.com, which, per OPDP, failed to include risk information and material information regarding the FDA-approved indication for the drug.

Also, a review of CDER's guidance document agenda, issued on January 22, 2016, should provide some insight as to FDA's "hot buttons," even if the guidances are not ultimately issued in 2016. The proposed advertising-related guidances include the following:

- Health Care Economic Information in Promotional Labeling and Advertising for Prescription Drugs Under Section 114 of the Food and Drug Administration Modernization Act;
- Internet/Social Media Advertising and Promotional Labeling of Prescription Drugs and Medical Devices – Use of Links to Third-Party Sites;
- Manufacturer Communications Regarding Unapproved, Unlicensed, or Uncleared Uses of Approved, Licensed, or Cleared Human Drugs, Biologics, Animal Drugs and Medical Devices; and
- Presenting Risk Information in Prescription Drugs and Medical Devices Promotion; Revised Draft.

Several of these guidances were also listed in FDA's 2015 agenda. Industry continues to anxiously await their publication, particularly guidance on health economic information. We expect 2016 to provide greater clarity on several fronts. Stay tuned.