Off-Label Marketing is the promotion of a pharmaceutical product by manufacturers for a purpose other than what the United States Food and Drug Administration (FDA) has approved it for. Off-label marketing or promotion is one of the more high-profile and dangerous forms of pharmaceutical fraud. The practice has harmed thousands of people and defrauded Medicare and Medicaid of billions of dollars. It is punishable under the False Claims Act (FCA), which imposes liability on companies that defraud the United States government.

Overview

In the interest of protecting the public, the FDA maintains a strict set of clinical trials, evaluations, and performance standards that new drugs and treatments must satisfy before being approved for public sales. Part of this approval process includes creating the "drug label." This specifies the exact uses the pharmaceutical compound may be prescribed for, including the patient populations and dosages. Although many pharmaceutical products have potential alternate applications, approval is only given for those treatments that meet the most stringent testing. Using a drug to treat an illness in a way other than what the FDA has approved is known as "Off-label usage."

"Off-label usage" can be a valuable tool for doctors. Many medicines have secondary effects that they find useful for certain patients. More than half of all cancer-treating drugs, for example, are prescribed in this way. This is especially true in the case of cancers are too rare to have merited a full FDA clinical trial.

"Off-label marketing" by contrast, is an act of criminal and civil fraud. It occurs when a drug manufacturer advertises the potential off-label uses of a drug to healthcare providers and the public. A prescription drug might be approved by the FDA to treat blood pressure, but the drug manufacturer seeks to grow their profits by informing doctors that this drug is also effective at treating migraines. As the drug has not undergone the rigorous testing for safety and effectiveness required by the FDA, there may be hidden dangers.

While healthcare providers employ off-label usage for the benefit of their patients, off-label marketing is conducted as part of a corporate financial strategy. Patient welfare becomes secondary to the expansion of profits. This has led to numerous cases of inadequate testing, falsified research, and increased levels of consumer risk in the rush to market. In many cases, this has resulted in serious harm to patients.

Off-Label Marketing Strategies

There are three main off-label marketing strategies that pharmaceutical companies employ to increase the number of prescriptions to new patients:

- Promoting the treatment for unapproved diseases
    - The most common off-label marketing strategy, it encourages doctors to prescribe a medication for diseases outside of those the FDA has approved the drug to treat.

- Promoting for unapproved indications of a disease
    - Often, the FDA will approve a drug to treat only certain severities or types of a disease. For example, a drug approved to treat depression in adults may be promoted to children. This can be dangerous because different populations may experience different side effects while taking the same drug.

- Promoting different dosages
    - In some cases, pharmaceutical companies have promoted higher dosages of a drug in order to increase revenue. This is also quite risky, as increased dosages may cause new or more severe side effects than those observed during clinical trials.

Types of Off-Label Marketing

In a 2011 Harvard School of Public Health study, researchers identified the most common methods that pharmaceutical companies have use to encourage Off-Label prescriptions.

- Promoting Off-Label Use to Doctors
    - Pharmaceutical sales representatives are legally prohibited from discussing off-label usage unless a physician asks. However, many companies have trained their sales representatives to ignore this rule and tout all alleged benefits.

- Providing Free Samples
    - Sales representatives will often be instructed to provide free samples of a drug to encourage doctors to give it to patients. In some of the more egregious cases, companies have sent free samples to pediatricians for drugs that have never been tested in children.

- Financial incentives and kickbacks
    - Pharmaceutical companies have been known to give doctors expensive gifts, provide lavish vacations, or provide exorbitant speaking fees for them to advocate the product at conferences. Cooperative doctors have

also been known to receive lucrative consultant contracts.

- Teaching and research activities
    - After identifying doctors and healthcare thought leaders who support off-label use, pharmaceutical companies will often arrange for them to give lectures and Continuing Medical Education (CME) seminars to promote off-label use. In some instances, shell-corporations have been used to create the illusion of independent advocacy.

- Helping Doctors receive reimbursements for off-label sales
    - Doctors are often unable to receive Medicare/Medicaid and insurance reimbursements for prescribing drugs outside the range of FDA approval. However, multiple pharmaceutical companies have instructed healthcare providers how to manipulate their billing systems in such a way to receive reimbursements regardless.

- Patients gifts and incentives
    - Companies have targeted potential populations who could request an off-label prescription by sending gift certificates and other items of value.

- Reviewing Patient Charts
    - Pharmaceutical companies have reviewed doctors' patient charts in order to identify potential candidates for off-label prescription. This practice violates patient confidentiality laws.

The Cost and Dangers of Off-Label Marketing

As off-label marketing often occurs on a massive scale and produces significant public risk, the penalties associated with it have been some of the largest in the history of the False Claims Act. Between the years 2009 and 2014, the Department of Justice (DOJ) collected over $13 billion in settlement fees from major pharmaceutical manufacturers in FCA cases related to this practice.

Identifying Off-Label Marketing Fraud and Taking Action

Most Off-Label promotion strategies are company-wide and are usually spread through marketing departments during meetings and seminars. This often makes the practice an open secret, or at the very least provides strong clues to employees regarding the

impropriety. Roughly 95% of all FCA lawsuits are *qui tam* cases brought forward by company insider whistleblowers.

Off-Label marketing cases often originate from the pharmaceutical representatives who are charged with executing the fraud. If you suspect that you are being asked to perpetrate such a fraud, there are several signs you can look for:

- Company's legal department explicitly warns employees against off-label marketing, while simultaneously continuing an off-label marketing strategy.

- Company gives verbal orders or directions that differ from written company policy about how to market a drug.

- Company instructs sales representatives to focus their pitch on the symptoms that a product might cure, rather than the larger illness context of the illness itself.

- Company provides explicit instructions to delete documents, emails, or brochures that mention specific off-label uses. This is particularly noteworthy if the instructions violate the company's own record retention policy.

- Company gives some sort of incentive tied to off-label promotion. In some instances, sales representatives have been tasked with meeting prescription quotas that can only be met through off-label use.

Past Off-Label Marketing Cases

- January 2009: The company Eli Lilly pled guilty to criminal charges of off-label marketing for its drug Zyprexa, paying a combined criminal and civil fine of $1.415 billion. In March 2000, the FDA had approved the drug for the short term treatment for both Type 1 Bipolar mania and psychosis from schizophrenia. Eli Lilly proceeded to market the drugs for these purposes as well as for the unapproved treatment of anxiety, Alzheimer's Disease, depression, insomnia, and dementia. The company's sales force was instructed to market directly to doctors, and were to focus on symptoms instead of larger medical issues. This campaign was bolstered by massive spending in medical education grants to disseminate false information in the medical community. Qui Tam Whistleblowers split a total of $79 million from the money collected by the government.

- September 2009: Pfizer paid $2.3 billion for criminal and civil charges pertaining to the off-label marketing of four of its top selling drugs. Included in this suit was Bextra, which had been approved by the FDA in 2005 for the treatment of minor pain. Pfizer instructed its sales teams to promote it for use against acute pain, while concealing the health risks that higher dosages brought to the kidneys, heart, and skin. Pfizer's actions

also placed undue financial strain on its patients, as Medicaid policy prevented it from reimbursing charges for off-label drug usage. Six whistleblowers split $102 million of the settlement.

- May 2012: Abbott Labs pays $1.5 billion to the Department of Justice for the off-label promotion of the drug Depakote. The FDA had previously approved this drug for use as an antipsychotic, but the manufacturer began to promote its effectiveness in combating schizophrenia and elderly dementia, as well. This off-label promotion came several years after the FDA ordered Abbott to stop clinical trials for these treatments, after the company's internal research found that the drug could cause aggression, confusion, and agitation in the elderly. Despite these risks, the manufacturer invested considerable resources into promoting Depakote off-label, instructing their sales staff to target nursing homes while providing millions of dollars in rebate incentives to pharmacies. The group of whistleblowers who brought the initial qui tam suit against Abbott split an $84 million reward.

- November 2013: A landmark case where Johnson & Johnson paid a fine of $2.2 billion to the Department of Justice to resolve criminal and civil charges of off-label marketing and kickbacks. The violations involved several of the company's medications, most notably the best-selling drug, Risperdal. The FDA had approved this drug explicitly for managing schizophrenia in adults. To expand profits, Johnson & Johnson incentivized their sales representatives to promote Risperdal for the treatment of dementia in the elderly and for ADHD in children. Studies later found that Risperdal caused premature and abnormal breast growth in prepubescent boys and girls. The wrongdoing was brought to light through the efforts of multiple whistleblowers, who split a $167 million reward.

- October 2015: The Swiss drug manufacturer Serono paid $704 million to settle civil and criminal liability charges for the off-label marketing of its drug Serostim, which is designed to combat the rapid loss of weight experienced by AIDS patients, known as "AIDS Wasting". However, shortly after Serono was granted FDA approval in 1996, a series of more effective drugs from a rival company were also approved, threatening Serono's profit potential. The company broadened their internal definition of "AIDS Wasting" to include a much larger patient group, including those who did not actually have the disease. This was a Qui Tam case brought forth by five whistleblowers. They split $51 million worth of settlement money.