

2008 Trials Expected To Expose SSRI Dirty Secrets

Thursday, 24 January 2008, 9:15 am
Opinion: Evelyn Pringle

Jury Trials In 2008 Expected To Expose SSRI Maker's Dirty Secrets

By [Evelyn Pringle](#)

The blockbuster sales figures for the new generation of selective serotonin reuptake inhibitor antidepressants (SSRI's), which have resulted from their promotion for so many unapproved uses, represents the most profitable off-label marketing coup in the history of modern medicine. Sales total about \$21 billion a year, according to IMS Health.

However, in the end these drugs will probably also hold the title for the most lawsuits filed against drug companies for overstating their benefits while concealing their serious side effects from as far back as 20 years ago.

The SSRI's include Prozac by Eli Lilly; Paxil marketed by GlaxoSmithKline, Zoloft by Pfizer, and Celexa and Lexapro from Forest Laboratories. Cymbalta by Eli Lilly and Effexor by Wyeth are often called SSRI's, but they are actually serotonin norepinephrine reuptake inhibitors (SNRI's). Wellbutrin sold by Glaxo is an inhibitor of the neuronal uptake of norepinephrine and dopamine. Several of these antidepressants now have generic counterparts.

In 2008, at least a dozen jury trials are scheduled all over the country for Paxil suicide-related cases, all of which allege that Glaxo failed to warn consumers and doctors about the known risk of suicide associated with the drug. Many of these cases will be tried by Baum, Hedlund, Aristei & Goldman, the national law firm with the longest track record of handling SSRI cases.

Going into the trials, Baum Hedlund will be armed with the largest collection of internal GSK documents, depositions of GSK employees and experts, as well as the fruits of the firm's investigation of antidepressants and their makers for the past decade and a half.

During litigation, virtually every Paxil-related document obtained by Baum Hedlund was stamped "confidential" by Glaxo and sealed under a court order.

However, through a series of legal challenges, the firm was able to unseal many of the documents, in part, by forcing Glaxo to admit that they did not contain trade secrets and should never have been sealed to begin with.

Off-label Promotion and Prescribing Drive Profits

The FDA approves drugs for uses that have been tested for safety and efficacy and includes those uses on the drug's label. The term off-label means prescribing a drug for a use that has not been tested and proven safe and effective or for a different patient group, or at a different dose, or for a longer duration, or in combination with other drugs.

While doctors may legally prescribe a drug for an unapproved use, it is illegal for drug makers to promote off-label prescribing. Over the past 20 years, SSRI's have been prescribed off-label to children as young as infants, the elderly and pregnant women, and for off-label uses that include insomnia, anxiety, shyness, grief, menstrual discomfort, pain, bed wetting, ADHD, dementia, impotence and restless leg syndrome, to name just a few.

To gain FDA approval to legally sell SSRI's to kids, all the drug companies would have to do is provide two clinical studies showing that the drugs work better than a placebo in depressed children, and they can conduct 100 trials to achieve the necessary results. But after 20 years on the market, they still have not been able to give the FDA two positive studies to prove these drugs work with children, with the exception of Prozac.

Critics are quick to point out that this is certainly not for lack of trying because there have been dozens of pediatric trials conducted that show the drugs work no better than a placebo. How Prozac gained approval remains a mystery in light of the thousands of adverse events that were already recorded among children.

A study conducted at the University of Georgia and published in the June 2006 Journal of Clinical Psychiatry reviewed prescribing records for 107,000 Medicaid recipients on drugs that act on the central nervous system and found that 75% of SSRI patients received the drugs off-label and most of the time without their knowledge.

In April 2004, the CDC reported in the Journal of Women's Health that antidepressants were the top drugs prescribed to women in doctors' offices and outpatient departments, ahead of estrogens and progestins, antiarthritics and drugs for acid/peptic disorders.

According to another report by the CDC, during 2005, antidepressants were the most prescribed drugs overall in visits to doctors and hospitals and were even prescribed more often than drugs used to treat high blood pressure, cholesterol, diabetes and headaches.

Chemical Imbalance - Selling Sickness in the Absence of Efficacy

The standard line used to sell SSRI's is that mental illnesses are caused by a chemical imbalance in the brain and that SSRI's correct the imbalance. The Lexapro website even states: "Antidepressant medicines relieve the symptoms of depression by restoring chemical imbalances in the brain."

However, "Serotonin and Depression: A Disconnect between the Advertisements and the Scientific Literature," in the November 8, 2005, PLoS Journal, by Jeffrey Lacasse, a visiting lecturer at the Florida State University, and Jonathan Leo, an Associate Professor of Neuroanatomy at Lincoln Memorial University, reports that, "there is not a single peer-reviewed article that can be accurately cited to directly support claims of serotonin deficiency in any mental disorder, while there are many articles that present counterevidence."

In their most recent paper titled, "The Media and the Chemical Imbalance Theory of Depression," appearing in the February 2008 issue of Society, Mr Lacasse and Mr Leo report that, "In spite of the enormous amount of money and time that has been spent in the quest to confirm the chemical imbalance theory, direct proof has never materialized."

In fact, they advise that the Diagnostic and Statistical Manual of Mental Disorders, which almost all psychiatrists use to diagnose and treat their patients, clearly states that the cause of depression and anxiety is unknown.

Even when prescribed for their intended purpose in treating depression, many experts say SSRI's are ineffective. One of the world's most famous psychopharmacologists, Dr David Healy, author of "The Antidepressant Era," and "Let Them Eat Prozac," says that an overall review of the published clinical trial data on the new antidepressants reveals a 10% difference in the way people respond to the drugs versus a placebo.

He reports that 50% of patients taking the antidepressants showed some improvement and 40% of people taking a placebo showed improvement. And when the data from the unpublished clinical trials are added in, 45% of patients taking a placebo showed improvement.

The author of "Surviving America's Depression Epidemic," Dr Bruce Levine also says "legitimate science shows that these antidepressants are no more helpful for depression than a placebo or no treatment at all."

However, most prescribing doctors have never heard about this 5% or 10% efficacy statistic, which researchers have referred to as the "dirty little secret," because many of the studies that revealed the "secret" remained hidden for years.

In fact, much of the information is still not in the public domain. A new study in the January 18, 2008 New England Journal of Medicine reports that the makers of the new antidepressants failed to publish many of the clinical trials that were submitted to the FDA for market approval that did not show positive outcomes in patients taking the drugs.

The researchers found that a total of 37 studies were viewed by the FDA as having positive results and all but one were published. But 22 studies that were viewed as having negative or questionable results were not published and 11 were published in a way that conveyed a positive outcome.

The study compared drug efficacy inferred from the published literature with efficacy determined in the FDA reviews and found that in the published medical literature, it appeared that 94% of the trials were positive when the FDA analysis showed that only 51% were positive.

The clinical trials analyzed included the drugs, Wellbutrin, Celexa, Cymbalta, Lexapro, Prozac, Remeron, Serzone, Paxil, Paxil CR, Zoloft, Effexor, and Effexor XR.

"For each of the 12 drugs," the researchers wrote, "the results of at least one study either were unpublished or were reported in the literature as positive despite a conflicting judgment by the FDA."

A total of 12,564 patients participated in these trials and data from 3,449 patients were not published. Data from an additional 1,843 patients were reported in journal articles that highlighted findings that conflicted with the FDA-defined primary outcome.

For each of the 12 drugs, the researchers also found that the effect size derived from the journal articles exceeded the effect size in the FDA reviews, with the increases in effect size in the published reports ranging from 11% to 69%, with an average increase of 32%.

The literature-search strategy used for the study consisted of a search of articles in PubMed, references listed in review articles, and a search of the Cochrane Central Register of Controlled Trials.

The researchers also contacted the drug maker's medical-information department by phone or email; and contact was also made by way of a certified letter to the company's medical-information department, including a deadline for responding in writing as to whether the results of a study had been published. If these steps failed to reveal any publications, the researchers concluded that the results had not been published.

The researchers who conducted the study include Erick Turner, MD, Annette Matthews, MD, Eftihia Linardatos, BS, Robert Tell, LCSW, and Robert Rosenthal, PhD, from Oregon Health and Science University, Portland Veterans Affairs Medical Center; Kent State University; the University of California–Riverside, and Harvard University.

In their paper, "The Media and the Chemical Imbalance," Mr Lacasse and Mr Leo point out the problem in the media where reporters still quote the people responsible for publishing bogus studies that have long been debunked.

"For instance," they write, "several of the researchers involved with the studies of SSRIs in children are still cited in the press even though the following information has come out about their published studies: they downplayed the suicide risk; they exaggerated the benefits; and the papers published under their names were actually written by ghostwriters paid by the pharmaceutical industry."

According to Dr Levine, depression is not a biochemical disorder and he refers to it as a strategy used to shut down overwhelming pain and says if the strategy is used to excess, it can lead to immobilization and greater pain.

He explains that depressed people experience feelings of hopelessness and helplessness and that labeling them with a disease leads to more of the same feelings.

Instead of calling it an illness or weakness, Dr Levine says, depression can be lessened by helping patients understand that it is a normal human reaction and they can identify the source of the pain and heal.

More Disorders Equals More Profits

To expand the market, the SSRI makers have managed to create a whole new generation of psychiatric illnesses by simply padding the bank accounts of a few psychiatrists who determine the criteria for the inclusion of mental disorders in the DSM. With their inclusion in the billing bible comes the guaranteed payment for the cost of the SSRI's and the visits to the prescribing doctor by public and private health insurance programs.

There are also a whole new slew of SSRI treatable disorders lining up for inclusion in the next DSM edition. For instance, an August 3, 2006 article by Reuters reported that, "People with 'body dysmorphic disorder' are 45 times more likely to commit suicide than people in the general population, a new study shows."

"The findings underscore the importance of recognizing and treating this 'often secretive' psychiatric disorder," Dr Katherine Phillips, the study's co-author, told Reuters.

Individuals with body dysmorphic disorder, she said, have a distorted body image and think obsessively about their appearance, often for hours a day, but can be helped with drugs like Prozac or Zoloft and cognitive behavioral therapy.

On October 3, 2006, the New York Times ran the headline: "Can't Keep From Shopping? Help Could Be on the Way," for an article that said, compulsive buying, "in its extreme forms may be a psychiatric illness -- an impulse control disorder associated with abnormal levels of depression and anxiety."

The article discussed a study in the American Journal of Psychiatry, and the lead author, Dr Lorrin Koran, told the Times: "Many of those who come in for

treatment suffer from depression, anxiety disorders and other impulse control disorders like pathological gambling and binge eating."

She also threw in a sales pitch saying, "studies suggest that psychotherapy or medications help many compulsive buyers to stop."

This news could potentially raise SSRI profits by 10%, because the Times says a statistical analysis of the study results found 5.5% of men and 6% of women could be afflicted.

The article also points out that compulsive buying is not yet a recognized psychiatric diagnosis, but that it is being considered for inclusion in the next edition of the DSM.

Good news for Pfizer came in the October 2006, Journal of Clinical Psychiatry, from a study led by Dr Susan Kornstein, at Virginia Commonwealth University, that claims low doses of Zoloft for 2 weeks before the onset of the menstrual period may be effective and well-tolerated for treating women with moderate-to-severe PMS.

The researchers also claim that other dosing strategies are effective, including taking Zoloft daily or waiting until symptoms begin to start taking it.

Zoloft is already approved for premenstrual dysphoric disorder (PMDD), but profits could skyrocket with widespread dissemination of this study because the researchers report that up to 60% of women suffer from PMS, while only about 5% suffer from PMDD.

On October 26, 2006, an Indianapolis Star headline warned that: "Midnight munchies can signal big problems." The article explained that routine and heavy nighttime snacking can be a sign of eating for reasons other than hunger and more serious symptoms can point to "a little-known eating disorder called night-eating syndrome."

But not to worry, because the researchers who did the study told the Star that Zoloft can help these poor souls as well, along with therapy to change eating and exercise patterns.

Great news for Glaxo came on October 27, 2006, when United Press International ran the headline: "Paxil helps compulsive hoarding syndrome".

According to UPI, persons with this syndrome exhibit 3 features: failure to discard objects due to severe anxiety related to discarding what most might regard as inconsequential objects; excessive acquisition, sometimes resulting in buying sprees, and excessive clutter to the point where home and work spaces can no longer be used.

Here again, however, researchers led by Dr Sanjaya Saxena at the University of California, report that Paxil is effective in treating this dastardly new disorder.

Risks Outweigh the Benefits

Experts say that if patients were adequately informed about the long list of side effects associated with SSRI's and their dubious efficacy before they took the first pill, they would be more than a little skeptical about whether their benefits outweigh the risks.

The SSRI labels now warn patients not to take them with common over-the-counter medications such as aspirin and many other pain relievers, or with cold remedies or herbal supplements like St John's Wort, or with alcohol.

SSRI side effects include suicidality, violence and homicide, birth defects, abnormal gastrointestinal and uterine bleeding, a decrease in bone density, fertility problems, sexual dysfunction, severe withdrawal and the life-threatening condition, serotonin syndrome.

According to the SSRI labels, symptoms of serotonin syndrome include mental status changes such as agitation, hallucinations, or coma; autonomic instability like tachycardia, labile blood pressure and hyperthermia; neuromuscular aberrations such as hyperreflexia and incoordination, and gastrointestinal symptoms of nausea, vomiting and diarrhea.

All the current labels say that anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania and mania have been reported in adult and pediatric patients treated for major depressive disorder, as well as for other indications, both psychiatric and non-psychiatric.

The labels also report that infants exposed in the womb have developed complications requiring prolonged hospitalization, respiratory support and tube feeding upon delivery. Reported clinical findings have included respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability and constant crying.

The labels note that these features are consistent with either a direct toxic effect or possibly a drug discontinuation syndrome and say it should be noted that, in some cases, the clinical picture is consistent with serotonin syndrome.

On December 8, 2005, the FDA issued a public health advisory to report that women who take Paxil in early pregnancy are at an approximately 2-fold increased risk of having an infant born with a cardiac defect compared to the general population.

Also cited on the labels is a study finding that infants exposed to SSRI's in late pregnancy showed a 6-times greater risk of developing the lung disorder known as persistent pulmonary hypertension of the newborn (PPHN), a

condition that, despite treatment, results in the death of approximately 10 to 20 percent of affected infants.

In December 2006, a Journal of Clinical Psychiatry study reported that about seven of every ten people who take antidepressants have impaired driving ability and that 16% have severe motor impairments after taking the drugs.

A short list of the adverse effects listed on the various SSRI labels as "frequent," and occurring on one or more occasions in at least 1 out of every 100 patients, includes light-headed feeling, appetite increased, increased weight, heartburn, abdominal cramp, gastroenteritis, allergy, pain in limb, fever, hot flushes, chest pain, lethargy, irritability, concentration impaired, abnormal dreams, sleep disorder, menstrual cramps, menstrual disorder, impotence, anorgasmia/orgasm abnormal, bronchitis, sinus congestion, coughing, migraine, sinus headache, vision blurred, urinary frequency and urinary tract infection.

Upcoming Jury Trials

Veteran trial lawyer, Ronald Goldman, who won one of the largest verdicts for the death of an unmarried person in Ohio state's history last year, is leading the Baum Hedlund team in the trials.

Glaxo has good reason to fear jury trials. The first Paxil-related suicide trial resulted in a verdict for the plaintiff. The case took place in Wyoming in May 2001 and involved a man, Donald Schell, who shot and killed his wife, daughter, and infant granddaughter before turning the gun on himself, after being on Paxil for only 2 days.

The instructions given to the jury required a finding that, "Paxil was a proximate cause of Donald Schell committing the homicides and suicide involved in this litigation" and that Glaxo's failure to test or to warn "was a proximate cause of the homicides and suicide in this litigation."

On June 6, 2001, the jury returned a verdict in favor of the plaintiffs and the Court entered a judgment against Glaxo for more \$6 million. Glaxo filed an appeal and the parties settled out of court while the appeal was pending.

Baum Hedlund has litigated over 3,000 pharmaceutical cases in the past 18 years and the firm currently has approximately 30 SSRI suicide-related cases in litigation. The firm served on the Plaintiffs' Steering Committee in the first suicide-related case involving Prozac and served as lead counsel for the Plaintiffs' Steering Committee in Paxil Products Liability Litigation. The firm is also handling SSRI-related birth defect lawsuits.

Persons seeking legal advice regarding SSRI-antidepressants can contact the Baum, Hedlund, Aristei & Goldman Law Firm at: (800) 827-0087; <http://www.baumhedlundlaw.com/>

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Sponsored by Baum Hedlund's Pharmaceutical Antidepressant Litigation
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