

Warnings of Psychiatric Drug Causing Aggression, Hostility, Violence, Mania, Psychosis, Homicidal Thoughts/Actions, etc.

Across 5 countries (US, UK, Canada, Australia, and Japan) and Europe, there have been 24 drug regulatory and pharmaceutical company warnings about psychiatric drugs causing violence and aggression.

These warnings are as follows:

1995:

1. **October 1995:** The U.S. Drug Enforcement Administration (DEA) said Ritalin use could lead to addiction and that “**psychotic episodes, violent behavior** and bizarre mannerisms had been reported” with its use.¹

2003:

2. **July 2003:** Health Canada’s Health Products and Food Branch warned health care professionals, “Until further information is available, Paxil should not be used in...pediatric patients...**due to a possible increased risk of suicide-related adverse events in this patient population.**” Further, incidents of suicidal thoughts and self-harm were nearly twice as high on Paxil as on placebo (5.3% vs. 2.8%).²
3. **August 22 2003:** Wyeth Pharmaceuticals, the makers of SSRI antidepressant Effexor, issued a warning to U.S. doctors that use of the drug could cause **hostility, suicidal ideation and self-harm** in patients under the age of 18. In September, a similar alert was sent to Canadian doctors telling them Effexor had been linked with a possible increase in suicidal thinking in children.³

2004:

4. **March 22 2004:** The FDA Public Health Advisory was issued, stating: “**Anxiety, agitation, panic attacks, insomnia, irritability, hostility, impulsivity, akathisia [severe restlessness], hypomania [abnormal excitement, mild mania] and mania [psychosis]** have been reported in adult and pediatric patients being treated with [Paxil-like] antidepressants...both psychiatric and non-psychiatric.”⁴
5. **April 22, 2004:** The European Agency for the Evaluation of Medicinal Products issued a press release to the press and public. In this press release, they report that, according to clinical trials, Paroxetine (**Paxil**) **containing medicines can cause** suicidal behavior **and hostility in children.** It recommends that Paroxetine

not be used in children and recommends that young adults be observed carefully for signs and symptoms of suicidal behavior or hostility. Paroxetine is shown to have little effectiveness in children according to clinical trials. The committee also recommends strengthened warnings on the withdrawal symptoms of paroxetine, which are common.⁵

6. **June 3, 2004:** Health Canada issued an Advisory to the public. Stronger warnings have been placed on SSRIs and other newer anti-depressants. These warnings indicate that people taking these drugs at any age are at greater risk of behavioral or emotional changes including self-harm or harm to others. The advisory said, "A small number of patients taking drugs of this type may feel worse instead of better.... For example, they may experience **unusual feelings of agitation, hostility or anxiety, or have impulsive or disturbing thoughts that could involve self-harm or harm to others.**" The drugs mentioned in this Advisory are Welbutrin, Zyban, Celexa, Prozac, Luvox, Remeron, Paxil, Zoloft and Effexor.⁶
7. **September 21 2004:** The British Healthcare Products Regulatory Authority advised that it had issued guidelines that children should not be given most SSRI antidepressants because of clinical trial data showing an increased rate of harmful outcomes, **including hostility.**⁷
8. **December 2004:** The Australian Therapeutic Goods Administration published an Adverse Drug Reactions Bulletin recommending that any use of SSRIs in children and adolescents should be carefully monitored for the emergence of suicidal ideation. In a recent study involving Prozac, it said, there was an increase in adverse psychiatric events of **suicide, self-harm, aggression and violence.**⁸

2005:

9. **April 25 2005:** The European Medicines Agency's scientific committee, the Committee for Medicinal Products for Human Use (CHMP) concluded that Prozac-type SSRIs and SNRIs antidepressants were associated with increased **suicide-related behavior and hostility** in young people. The London-based watchdog said it was recommending the inclusion of strong warnings across the whole of the European Union to doctors and parents about these risks and that the drugs should not be used in children and adolescents in off label situations.⁹
10. **June 28 2005:** The FDA announced its intention to make labeling changes for Concerta and other methylphenidate (Ritalin) products (stimulants) to include, "psychiatric events such as **visual hallucinations, suicidal ideation, psychotic behavior, as well as aggression or violent behavior.**"¹⁰ The FDA announced its intention to also investigate possible cardiac concerns with these drugs.¹¹

11. **August 19 2005:** The Commission of the European Communities, representing 25 European countries, endorsed and issued the strongest warning yet against child antidepressant use as recommended by Europe's Committee for Medicinal Products for Human Use (CHMP). Clinical trials had shown that the drugs caused suicidal behavior including suicide attempts and suicidal ideation, **aggression, hostility (predominantly aggression, oppositional behavior and anger) and/or related behavior.**¹²
12. **November 2005:** The FDA's Safety Information and Adverse Event Reporting Program reported "**homicidal ideation**" as an adverse event of Effexor ER (extended release).¹³

2006:

13. **February 2006:** Health Canada approved a new warning label for Paxil that read, in part: "A small number of patients taking drugs of this type may feel worse instead of better. For example, they may experience unusual feelings of **agitation, hostility or anxiety, or have impulsive or disturbing thoughts, such as thoughts of self-harm or harm to others.**" Health Canada required Paxil's product information to detail a list of "rare" side effects, affecting fewer than one in 1,000 patients. These include **delusions, hostility, psychosis, and psychotic depression.** That's 1,000 cases in a million who could all potentially kill one or more people.¹⁴
14. **August 21, 2006:** FDA said "ADHD" stimulant manufacturers have to strengthen their warning labels to warn that the drugs can cause suppression of growth, **psychosis**, bipolar illness, **aggression**, and 'serious' cardiovascular side effects. GlaxoSmithKline and Shire company posted a letter to doctors about the revised prescribing information.¹⁵
15. **October 18, 2006:** The Australian Therapeutic Goods Administration ordered manufacturers of "ADHD" drugs, Ritalin, Strattera and dexamphetamine to add stronger warnings to their information packaging after receiving 200 complaints about the drugs. The TGA had received 123 reports of adverse reactions involving Ritalin, including complaints that it caused headache, nausea, anorexia, somnolence and depression; 23 **reports about atomoxetine (Strattera), including aggression**, and 60 reports about dexamphetamine, including seven of agitation, five of tachycardia (rapid heartbeat) and four reports each of hypertonia (abnormally tight muscles), hyperkinesia (muscle spasm) and insomnia.¹⁶

2007:

16. **February 21, 2007:** The FDA directed ADHD drug manufacturers to distribute "patient friendly" guides to consumers warning about serious psychiatric and

cardiovascular problems, including stroke, heart attack, sudden death and **psychotic reactions** caused by ADHD drugs.¹⁷

2008:

17. **November 20, 2008:** ELI LILLY STRATTERA WARNING: Eli Lilly including in their Strattera label in Europe to include warnings that Strattera causes "hallucinations, delusional thinking, **mania or agitation in children and adolescents without a prior history of psychotic illness or mania...**"¹⁸ Strattera is an antidepressant prescribed as a "non stimulant" drug to treat ADHD.

2009:

18. **February 2009:** AUSTRALIAN METHYLPHENIDATE WARNING: **A Boxed Warning (the strongest warning) was placed onto the ADHD drug Methylphenidate (Concerta and Ritalin)** by the Australian Therapeutic Goods Administration **for drug dependence.** It warns that chronic abuse of Methylphenidates can lead to a marked tolerance and psychological dependence with varying degrees of abnormal behaviour and **frank psychotic episodes can also occur.**¹⁹

19. **March 2009:** UK STRATTERA WARNING: Medicines and Healthcare products Regulatory Agency (UK) published in their *Drug Safety Update* newsletter new information about Atomoxetine (Strattera, a non-stimulant ADHD drug). They warned that Atomoxetine is associated with **treatment-emergent psychotic or manic symptoms in children without a history of such disorders.**²⁰

20. **May 2009:** JAPANESE SSRI WARNING. The Japanese Ministry of Health, Labor and Welfare investigated news reports of antidepressant users "who developed increased feelings of hostility or anxiety, and have even committed sudden acts of violence against others." After its investigation, the Ministry decided to revise the label warnings on SSRI antidepressant stating, "**There are cases where we cannot rule out a causal relationship [of hostility, anxiety, and sudden acts of violence] with the medication.**"²¹

21. **July 2009:** US WELLBUTRIN WARNING UPDATE: The FDA updated the warning label for the antidepressant Wellbutrin (bupropion) to include Boxed Warnings that patients being treated with it for smoking cessation should be observed for neuropsychiatric symptoms and **changes in behavior such as hostility agitation,** suicidal ideation as well as attempted suicide. They also updated the patient medication guide.²²

22. **July 2009:** US ZYBAN WARNING: The FDA updated the warning label for Zyban (an antidepressant used for smoking cessation) to include that all patients being treated with Zyban should be **observed for neuropsychiatric symptoms including**

changes in behavior, hostility, agitation, depressed mood, and suicide-related events, including ideation, behavior, and attempted suicide. Completed suicides have been reported in some patients attempting to quit smoking while on Zyban. The label was also updated to include precautions and a medication guide.²³

23. July 1, 2009: US BENZO/ANTIDEPRESSANT WARNING: The FDA has required the manufacturers of the smoking cessation aids varenicline (Chantix) and bupropion (Zyban, aka Wellbutrin) to add new Boxed Warnings and develop patient Medication Guides highlighting the **risk of serious neuropsychiatric symptoms** in patients using these products. **These symptoms include changes in behavior, hostility, agitation**, depressed mood, suicidal thoughts and behavior, and attempted suicide.²⁴

2010:

24. October 2010: US WAKEFULNESS PROMOTING AGENT WARNING: The FDA added data to Provigil's package insert, which now includes the Psychiatric Symptom **"aggression"** in the Warnings section.²⁵

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List provided by CCHR (www.cchr.org) / NCRM (www.ncrm.nl)

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⁴ "Worsening Depression and Suicidality in Patients Being Treated with Antidepressant Medications," US Food and Drug Administration Public Health Advisory, 22 Mar. 2004.

⁵ Martin Harvey Allchurch – EMEA press officer, "PRESS RELEASE European Agency for the Evaluation of Medicinal Products: Committee for proprietary Medicinal Products 20-22 April 2004," EMEA, ref: EMEA/D/11206/04/Final, Apr 22, 2004.

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⁸ "Use of antidepressants in children and adolescents," *The Australian Therapeutic Goods Administration (TGA) published an Adverse Drug Reactions Bulletin*, Vol 23, No. 6, Dec. 2004, p. 22.

⁹ "EU calls for tougher warnings on antidepressants for kids," *News-Medical.Net*, 25 Apr. 2005.

¹⁰ FDA "Statement on Concerta and Methylphenidate for the June 30 Pediatric Advisory Committee," 28 June 2005.

¹¹ "FDA Raises Concerns About ADHD Drugs," *The Wall Street Journal*, 29 June 2005.

¹² Commission of the European Communities Commission Decision concerning the placement on the market, under Article 21 of the Directive 2001/83/EC of the European Parliament and of the Council, of the medicinal products for human use which contain (lists of SSRI/SNRI antidepressants)," *Brussels 19-VIII-2005, C (2205) 3256*.

¹³ FDA's Safety Information and Adverse Event Reporting Program, Effexor XR, Nov. 2005.

¹⁴ Kate Jaimet, "I've learned a lesson in the worst way possible: What drove a loving father to kill his son?," *Ottawa Citizen*, 27 Aug. 2006.

¹⁵ “Glaxo, Shire strengthen drug warnings, Firms say ADHD treatments may cause heart attacks,” *The Boston Globe*, 22 Aug. 2006.

¹⁶ Matthew Franklin, “ADHD drug risk for kids,” *The Australian*, 18 Oct. 2006.

¹⁷ “FDA Directs ADHD Drug Manufacturers to Notify Patients about Cardiovascular Adverse Events and Psychiatric Adverse Events,” FDA News, Feb. 21, 2007.

¹⁸ Janne Larsson, “Official Warning issued: The ADHD drug Strattera Causes psychosis, hallucinations, mania and agitation,” *Trans World News*, Dec 01, 2008

¹⁹ CONCERTA® Extended-Release Tablets PRODUCT INFORMATION, late updated 17 Feb. 2009; “Dear Healthcare Professional” Navartis Letter to doctors;

²⁰ “Atomoxetine: risk of psychotic or manic symptoms,” *Drug Safety Update*, MHRA, Vol. 2, Iss. 8, March 2009.

²¹ “Japan Revises SSRI Warnings--Hostility, Violence,” *Medical News Today*, 28 May 2009, web URL, <http://www.medicalnewstoday.com/printerfriendlynews.php?newsid=151688>

²² “Wellbutrin (bupropion hydrochloride) tablets and Sustained-Release tablets,” FDA.gov, July 2009. URL <http://www.fda.gov/safety/medwatch/safetyinformation/ucml176817.htm>

²³ “Zyban (bupropion hydrochloride) Sustained-Released tablets” FDA.gov, July 2009, www.fda.gov/safety/medwatch/safetyinformation/ucml176815.htm

²⁴ “Information for Healthcare Professionals: Varenicline (marketed as Chantix) and Bupropion (marketed as Zyban, Wellbutrin, and generics),” FDA.gov, July 1, 2009.

²⁵ “Provigil (modafinil) tablets,” FDA Center for Drug Evaluation and Research, October 2010.