

Paxil is an antidepressant drug (selective serotonin re-uptake inhibitors or SSRI) used to treat major depression, obsessive-compulsive disorder, panic disorder, social anxiety, post-traumatic stress disorder and generalized anxiety disorder in adult patients.

It shares the common side effects and contraindications of other SSRIs, with high rates of nausea, somnolence [sleepiness], and sexual side effects. Paxil is associated with clinically significant weight gain.

Discontinuing Paxil is associated with a high risk of withdrawal syndrome.

Several studies have suggested that Paxil can be used in the treatment of premature ejaculation. The reason it causes a delay in ejaculation is because it greatly reduces sex drive, in some cases, causing an inability to gain an erection or ejaculate.

Sexual dysfunction is a common side effect with SSRIs. Specifically, side effects often include difficulty becoming aroused, lack of interest in sex, and anorgasmia (trouble achieving orgasm). Genital anesthesia, loss of or decreased response to sexual stimuli, and ejaculatory anhedonia are also possible. Although usually reversible, these sexual side effects can last for months or years after the drug has been completely withdrawn. This is known as post SSRI sexual dysfunction.

Among the common adverse effects listed in the prescribing information, those with the greatest difference from placebo are

- nausea (26% vs 9% on placebo)
- somnolence (23% vs. 9% on placebo)
- ejaculatory disturbance (13% vs. 0% on placebo)
- other male genital disorders (10% vs. 0% on placebo)
- asthenia (15% vs. 6% on placebo)
- sweating (11% vs. 2% on placebo)
- dizziness (13% vs. 6% on placebo)
- insomnia (13% vs. 6% on placebo)
- dry mouth (18% vs. 12% on placebo)
- constipation (14% vs. 9% on placebo)
- tremor (8% vs. 2% on placebo).

Other side effects include high blood pressure, headache, agitation, weight gain, impaired memory and paresthesia, decreased fertility.

Withdrawal can cause a rebound effect with symptoms re-emerging in an exaggerated form for very long periods of time. Almost all SSRIs are known to cause either one or more of these symptoms.

The European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) gave a warning to prescribers recommending close monitoring of adult patients at high risk of suicidal behaviour and/or suicidal thoughts. CHMP does not prohibit use of Paxil with high risk adults but urges extreme caution. Due to reports of adverse withdrawal reactions upon terminating treatment

Paxil and other SSRIs have been shown to cause sexual side effects in most patients, both males and females. In males, it is also linked to sperm DNA fragmentation.

Mania or hypomania may occur as a serious side effect of Paxil, affecting up to 8% of psychiatric patients treated. This side effect can occur in individuals with no history of mania but it is more likely to occur in those with bipolar or with a family history of mania.

Schmitt et al. (2001) suggested that Paxil negatively affects long-term memory, but not short-term, although the result has not been independently verified. In their study, healthy participants given Paxil for 14 days (20 mg for days 1–7 and 40 mg days 8–14) showed poorer recall of words on day 14 compared to those receiving a placebo.

Paxil may also be contraindicated in many adult men due to sexual and reproductive side effects described below. In the United States, the Food and Drug Administration requires this drug to carry a black box warning, its "most serious type of warning in prescription drug labeling", due to increased risk of suicidal ideation and behavior. The warning also applies to other SSRIs.

SSRI discontinuation syndrome

Many psychoactive medications can cause withdrawal symptoms upon discontinuation from administration. Evidence has shown that Paxil has among the highest incidence rates and severity of withdrawal syndrome of any medication of its class. Common withdrawal symptoms for Paxil include nausea, dizziness, lightheadedness and vertigo; insomnia, nightmares and vivid dreams; feelings of electricity in the body, as well as crying and anxiety.

GlaxoSmithKline cautions that drug interactions may create or increase specific risks, including Serotonin Syndrome or Neuroleptic Malignant Syndrome (NMS)-like Reactions: The development of a potentially life-threatening serotonin syndrome or Neuroleptic Malignant Syndrome (NMS)-like reactions have been reported with SNRIs and SSRIs alone, including treatment with PAXIL, but particularly with concomitant use of serotonergic drugs (including triptans) with drugs that impair metabolism of serotonin (including MAOIs), or with antipsychotics or other dopamine antagonists.

For 10 years, GlaxoSmithKline (GSK) marketing of the drug stated that it was "not habit forming", which numerous experts and at least one court found to be incorrect. In 2001, the BBC reported the World Health Organization had ranked Paxil as the most difficult antidepressant to withdraw from. In 2002, the U.S. FDA published a new product warning about the drug, and the International Federation of Pharmaceutical Manufacturers Associations said GSK had misled the public about Paxil and breached two of the Federation's codes of practice. The British Medical Journal quoted Charles Medawar, head of Social Audit: "This drug has been promoted for years as safe and easy to discontinue.... The fact that it can cause intolerable withdrawal symptoms of the kind that could lead to dependence is enormously important to patients, doctors, investors, and the company. Since the FDA approved paroxetine in 1992, approximately 5,000 U.S. citizens have sued GSK. Most of these people feel they were not sufficiently warned in advance of the drug's side effects—particularly the withdrawal syndrome discussed above, after GSK had specifically advertised the drug as non-habit forming.

In 2001, GSK increased its American TV advertising of Paxil after the September 11 attacks; in October 2001, GSK spent nearly twice as much as in October 2000. In early 2004, GSK agreed to settle charges of consumer fraud for \$2.5 million (a tiny fraction of the over \$2.7 billion in yearly Paxil sales at that time). The legal discovery process also uncovered evidence of deliberate, systematic suppression of unfavorable Paxil research results.

The court documents released as a result of one of the lawsuits in October 2008 indicated that GSK "and/or researchers may have suppressed or obscured suicide risk data during clinical trials" of paroxetine. One of the investigators, "Charles Nemeroff, former chairman of the Department of Psychiatry at Emory University, was the first big name 'outed' ...In early October 2008, Nemeroff stepped down as department chair amid revelations that he had received over \$960,000 from GSK in 2006, yet reported less than \$35,000 to the school. Subsequent investigations revealed payments totaling more than \$2.5 million from drug companies between 2000 and 2006, yet only a fraction was disclosed."

The suppression of unfavorable research findings on Paxil by GSK — and the legal discovery process that uncovered it — is the subject of Alison Bass's 2008 book *Side Effects: A Prosecutor, a Whistleblower, and a Bestselling Antidepressant on Trial*. The book chronicles the lives of two women - a prosecutor and a whistleblower - who exposed deception in the research and marketing of Paxil. The book shows the connections between pharmaceutical giant GlaxoSmithKline, a top Ivy League research institution, and the government agency designed to protect the public - conflicted relationships that arguably compromised the health and safety of vulnerable children. *Side Effects* received the NASW Science in Society Award for 2009.

In 2012 the U.S. Justice Department announced that GSK had agreed to plead guilty and pay a \$3 billion fine, in part for promoting the use of Paxil for children.

