Parker & Waichman, LLP Attorneys at Law
Wellbutrin Information Guide

Manufacturer:
GlaxoSmithKline

Generic Name:
Bupropion

Date Approved:
December 1985

Status:
On the market

Approved Uses:
Depression
Smoking Cessation

Off Label Uses:
Panic / Anxiety
Bipolar depression
Sleep disorders
Chronic fatigue
Fibromyalgia
Arthritis
Lupus
Irritable Bowel Syndrome

Serious Side Effects:
Suicide
Violence
Agitation
Panic attacks

Related Topics:
Celexa
Cymblata
Effexor
Lexapro
Luvox
Paxil
Prozac
Remeron
Serzone
Zoloft

The Case Against Wellbutrin:

Top Food and Drug Administration (FDA) officials have said publicly for the first time that scientific trials of frequently prescribed antidepressants have powerfully demonstrated that children who took the medications faced an increased risk of suicide.

Testifying before two FDA advisory committees, the officials said a recent study contracted by the FDA and conducted by Columbia University confirmed the findings of an internal analysis early this year. In clinical trials, the drugs almost doubled the incidence of suicidal behaviour in children.

In March, after hearings where parents told of the effects these drugs had on their children, the FDA ordered manufacturers of 10 frequently prescribed antidepressants: Prozac, Zoloft, Paxil, Luvox, Celexa, Lexapro, Effexor, Wellbutrin, Serzone and Remeron to include warnings about an increased risk of deepening depression or even suicide on product labels and urged patients and their families to report any changes in behaviour to their doctors.

Concerns about a possible link between the drugs and suicide were raised in the media and by some psychiatrists in 1990. The FDA convened an advisory panel on the topic but issued no warnings.

If you or a loved one has been injured by Wellbutrin, Parker & Waichman, LLP will evaluate your case for free. Click here for a free, no obligation, case evaluation.

Wellbutrin (Bupropion)

From Wikipedia, the free encyclopedia.

Bupropion (amfebutamone) is an antidepressant of the amino ketone class, chemically unrelated to tricyclics or selective serotonin reuptake inhibitors (SSRIs). It is similar in structure to the stimulant cathinone, and to phenethylamines in general. It is a chemical derivative of diethylpropion, an amphetamine-like substance used as an anorectic. Bupropion is both a dopamine reuptake inhibitor and a norepinephrine reuptake inhibitor.

History

Bupropion was first synthesized by Burroughs Research in 1966, and patented by Burroughs-Wellcome (later Glaxo-Wellcome, and, as of 2000, GlaxoSmithKline) in 1974. It was approved by the FDA in 1985 and marketed under the name Wellbutrin as an antidepressant, but clinical trials indicated that incidence of seizure was two to four times greater than other antidepressants and the drug was quickly pulled from the market. It was subsequently discovered that reducing the dose by about half greatly reduced the risk of seizures. Glaxo then developed a sustained-release (SR) version of Wellbutrin which releases bupropion hydrochloride at a slower rate. The SR formulation is taken twice a day, in order to further decrease the possibility of adverse side effects and seizures. It is also available in generic form (Bupropion SR). Extended Release bupropion, Wellbutrin XL, is the most recent formulation of bupropion and is taken orally once a day. Because of this altered mechanism of delivery and reduced dosing, incidence of seizures with bupropion is comparable to, and in some cases, lower than that of other antidepressants.

In 1997, bupropion HCl was approved by the FDA for use as a smoking cessation aid. Glaxo subsequently marketed the drug under the name Zyban to help people stop smoking tobacco by reducing the severity of craving and addiction/withdrawal symptoms. It can be used in combination with nicotine replacement therapies. Bupropion treatment course lasts for seven to twelve weeks, with the patient halting the use of tobacco around ten days into the course.

Bupropion is also being investigated as a weight loss drug.

Mode of action

Bupropion is a selective catecholamine (norepinephrine and dopamine) reuptake inhibitor. It has only a small effect on serotonin reuptake. It does not inhibit MAO. The actual mechanism behind bupropion's action is not known, but it is thought to be due to the effects on dopaminergic and noradrenergic mechanisms.

Pharmacokinetics

Bupropion is metabolised in the liver. It has at least three active metabolites: hydroxybupropion, threohydrobupropion and erythrohydrobupropion. These active metabolites are further metabolised to inactive metabolites and eliminated through excretion into the urine. The half-life of bupropion is 20 hours as is hydroxybupropion's. Threohydrobupropion's half-life is 37 hours and erythrohydrobupropion's 33 hours.

Chronic hepatotoxicity in animals

In rats receiving large doses of bupropion chronically, there was an increase in incidence of hepatic hyperplastic nodules and hepatocellular hypertrophy. In dogs receiving large doses of bupropion chronically, various histologic changes were seen in the liver, and laboratory tests suggesting mild hepatocellular injury were noted.

Indications

- management of depression
- adjunctive in tobacco withdrawal
- attention deficit disorder

Contraindications

- epilepsy and other conditions that lower the seizure-threshold
- concomitant treatment with MAO-Inhibitors
- caution with the concomitant use of sympathomimetic drugs (e.g. Ephedrine)
- active liver damage (e.g. cirrhosis)
- anorexia, bulimia
- severe kidney disease
- severe hypertension
- anxiety disorders (caution), agitated patients
- pediatric patients (see below)
- use considerable caution in treating patients where suicide may be a risk

Side effects

Common side effects include dry mouth, tremors, anxiety, loss of appetite, agitation, dizziness, headache, excessive sweating, increased risk of seizure, and insomnia. Bupropion causes less insomnia if it is taken just before going to bed, or in the morning after arising. Activation of mania and psychosis have both been encountered.

Scattered abnormalities of liver function studies are noted, without evidence of hepatotoxicity. Cases of significant liver damage with or without jaundice (icterus) have been seen rarely. In a German database covering side effects, five cases of pancreatitis with elevations of serum-amylase and lipase as well as clinical symptoms (e.g. abdominal pain, anorexia), reversible after termination of bupropion, have been reported. Currently, it is unclear, whether preexisting alcohol abuse or dependence might

predispose patients to develop pancreatitis.

Infrequently, dose dependent hypertension is noted. Single cases of myocardial infarction (heart attack) have been noted, but the causal association to the use of bupropion is currently unknown.

Few cases of the urological emergency priapism (painful erection) have been seen. Immediate treatment is necessary, because the untreated patient may lose his possibility to have erections totally.

Interactions

Quite a great number of drugs show clinically significant interactions with bupropion. Study the packing insert carefully and ask your prescribing physician in any case of doubt.

Abuse liability

In animal studies and small studies with persons having experience with the use of amphetamines or cocaine, bupropion caused drug-seeking behaviour (animal experiments) and was recognized as an amphetamine-like drug by the humans. In a scale ranging from placebo on the lower side to benzedrine, it was given an intermediate score indicating moderate likelihood of abuse. In clinical practise, bupropion has been shown that the dose required for significant abuse would cause seizures in most patients. Abuse has not become a significant problem in clinical usage, but the drug should be given with caution to patients with a history of drug or alcohol abuse or dependence. Bupropion is not a controlled substance.

Additional warnings

Use in pediatric patients

Bupropion has been shown to increase the incidence of suicidal thoughts and attempts in children and adolescents with depression. When treating major depressive disorder in this group of patients, clinical benefits should be weighed carefully against therapeutic hazards. Usually, bupropion is not indicated for pediatric patients under age 18.

Risks in the treatment of tobacco withdrawal

In the UK, more than 5,000 reports of potentially hazardous side effects have been collected, among them more than 40 cases of death attributable to bupropion treatment. This study is questioning the benefit-risk-ratio in assisted tobacco withdrawal with bupropion. Also, 107 cases of serious side effects have been reported in Germany.

Dosage

- depression : usual dose is 300mg daily, starting with 200mg in the first few days

- tobacco withdrawal : 150mg initially, may be increased to 300mg if indicated and directed by physician. In patients also receiving Insulin, sympathomimetic anorectical drugs, or antimalaria agents, the daily dose of bupropion should not exceed 150mg.

Remarks

Limitation to tobacco withdrawal

In some countries bupropion is approved only as a smoking cessation aid and not for treatment of depression.

Influence on sexual function/libido

An advantage of bupropion over most conventional antidepressants is that it causes no sexual dysfunction in men and may even increase libido. According to a recent study, bupropion does also increase libido in women with "hypoactive sexual desire disorder" but without signs of depression. It is too early to come to conclusive evidence whether to treat these women or not. Further controlled studies are required.

Potential indications of bipolar and schizoaffective disorder

The effects of bupropion HCl in treating eleven patients with bipolar or schizoaffective disorder were examined in an open trial. Most patients had been intolerant of or showed minimal to moderate improvement on lithium, neuroleptics, antidepressants, or a combination of these drugs. All patients were maintained on bupropion alone or bupropion in combination with low-dose neuroleptics or anxiolytics for one year or more, with little or no relapse and few side effects. Although these results are encouraging, additional larger studies need to be conducted to confirm this indication (study conducted by G. Wright et al., 1985, published in : J Clin Psychiatry, 1985 Jan;46(1):22–5).