ToxTidbits

Maryland Poison Center
UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY

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The Maryland Poison Center's Monthly Update: News, Advances, Information

Bupropion

Bupropion is unique monocyclic antidepressant and smoking cessation agent that is also used off-label for anxiety, bipolar disorder, and attention deficit/hyperactivity disorder. It is available generically in immediate release(IR) , sustained release (SR) and extended release (XL, ER) formulations as well as under the trade names Wellbutrin®, Budeprion®, Zyban®, Aplenzin® and Forfivo XL®. Its mechanism of action as an antidepressant is unclear; however, it blocks dopamine and norepinephrine reuptake and antagonizes acetylcholine at nicotinic receptors. It is structurally similar to stimulants such as amphetamine. Although generally recognized as having low abuse potential, bupropion abuse by crushing the tablets and snorting or injecting the drug has been reported.

Bupropion is often involved in unintentional and deliberate poisonings reported to poison centers and is one of the most common causes of drug-induced seizures. It has a narrow therapeutic index; seizures have occurred at therapeutic doses but mainly at doses greater than 450 mg/day. In a 3-year multi-poison center observational study, seizures occurred in 31.6% of patients 12 years and older who ingested 600 mg or more of extended-release bupropion *(AJEM 2009;27:911-5).* Children who ingest ≥10 mg/kg are at risk for toxicity and should be evaluated in a health care facility *(J Emerg Med 2010;38:332-6).*

Seizures usually occur within 6 hours of an overdose or therapeutic error but can be delayed up to 24 hours after the ingestion of extended release formulations *(AJEM 2009;27:911-5).* Seizures are usually self-limited and single, but status epilepticus can occur with severe toxicity. Seizures may occur suddenly without any preceding toxic effects. Other signs and symptoms of bupropion toxicity include vomiting, hypokalemia, agitation, slurred speech, lethargy, confusion, hallucinations, tremors, and coma. Cardiovascular effects include tachycardia, hyper– or hypotension, and rarely QRS widening, QTc prolongation and ventricular dysrhythmias. Deaths following overdoses of bupropion without coingested drugs are rare.

Patients who ingest SR or XL/ER formulations should be admitted for observation as the onset of seizures may be delayed. Benzodiazepines for seizures, vasopressors, and antiarrhythmic agents may be given as needed. Activated charcoal may be considered for large ingestions of bupropion being managed in the emergency department, only if the patient is awake and is capable of protecting his/her airway. Bupropion is a lipid-soluble drug, and as such, intravenous lipid emulsion has been reported to be successful in reversing cardiovascular toxicity and status epilepticus along with good supportive measures *(Basic Clin Pharm Tox 2011; 109:418-22. Ann Emerg Med 2008; 51:412-5).*

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Did you know?

Bupropion (Wellbutrin®) was first approved by the FDA in 1985 and withdrawn in 1986 due to the incidence of seizures.

The risk of seizures was determined to be associated with doses as low as 400-600 mg/day and primarily in certain populations (e.g. seizure disorders, eating disorders). Wellbutrin® was reintroduced in 1989 with a lower maximum daily dose of 450 mg/day and added contraindications to minimize the risk of seizures.