

## Bupropion (Zyban, Wellbutrin SR): reports of deaths, seizures, serum sickness

**Reason for posting:** In a letter to health professionals,<sup>1</sup> Health Canada and GlaxoSmithKline stated that 1127 reports of suspected adverse drug reactions for bupropion were received between May 1998 and May 28, 2001. Included were reports of 19 deaths (including 1 case of liver failure, 1 case of myocarditis, 3 cases of suicide), 172 reports of seizures or convulsions and 37 reports of serum-sickness-like reactions. Although cause-and-effect relations have not been established in the vast majority of the reports, it is important to remind physicians and warn patients of possible adverse effects of this medication.

**The drug:** Bupropion appears to block noradrenergic reuptake and dopaminergic reuptake in the brain. It is used as an antidepressant (marketed in Canada as Wellbutrin SR) and as a smoking cessation aid (marketed in Canada as Zyban). Common adverse events include dry mouth and insomnia, nausea, headache and rash.<sup>2</sup> Bupropion is known to reduce seizure thresholds, with a seizure rate of about 1 in 1000 subjects treated.<sup>3</sup> Anaphylactoid reactions, including dyspnea, angioedema, urticaria and pruritus, have been reported at a rate of 1 to 3 cases per 1000 patients enrolled in clinical trials.<sup>2</sup> Symptoms of arthralgias, myalgias and fever and rash resembling serum sickness have been reported rarely. For detailed descriptions of drug interactions and adverse effects, see the product monograph.

**What to do:** Patients should be warned of the risks of potential serious adverse effects of these medications, including seizures and allergic reactions. Zyban and Wellbutrin SR should not be administered concurrently, nor should they be prescribed to patients with a seizure disorder. Furthermore, bupropion should not be administered to patients with conditions altering the

seizure threshold, including anorexia nervosa or bulimia, patients with potential benzodiazepine or alcohol withdrawal, those with head trauma or central nervous system pathology, or patients taking antipsychotic drugs, systemic steroids, quinolone antibiotics or antimalarial drugs. Doses should be limited to no more than 150 mg per single dose and to no more than 300 mg per day. If a seizure or allergic reaction occurs, the medication should be discontinued and appropriate medical attention sought. To avoid prolonged QT intervals and ventricle arrhythmias secondary to thioridazine toxicity, bupropion should not be administered if a monoamine oxidase inhibitor or thioridazine antipsychotic drug has been given within the past 14 days. Bupropion is contraindicated in pa-

tients with severe hepatic impairment. A patient information sheet is now available online.<sup>4</sup>

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### References

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2. *Zyban, bupropion hydrochloride 150 mg sustained release tablets smoking cessation aid* [product monograph]. Mississauga (ON): GlaxoSmithKline; 2001 July 5.
3. Hurt RD, Sachs DPL, Glover ED, Offord KP, Johnston JA, Dale LC, et al. A comparison of sustained-release bupropion and placebo for smoking cessation. *N Engl J Med* 1997;337:1195-202.
4. Health Canada. Safety information for patients taking Zyban. Available: [www.hc-sc.gc.ca/hpb-dgpps/therapeut/zfiles/english/advisory/industry/zyban2\\_e.pdf](http://www.hc-sc.gc.ca/hpb-dgpps/therapeut/zfiles/english/advisory/industry/zyban2_e.pdf) (accessed 2001 Nov 29).