

Updated Safety Information Announced in Canada for Patients Taking TOPAMAX* (topiramate) Regarding Higher than Normal Blood Acid Levels.

Toronto, January 20, 2004 - Janssen–Ortho, following discussions with Health Canada, is alerting patients and healthcare professionals of emerging safety information in patients taking TOPAMAX.

Cases of persistent “metabolic acidosis” have been reported in patients taking TOPAMAX. Metabolic acidosis is a disruption of the normal acid/base balance of the body; TOPAMAX-related acidosis is due to decreased blood levels of bicarbonate, one of the substances in the body that regulates acid levels in the blood. Rates of acidosis in controlled clinical trials are substantially more frequent in patients given TOPAMAX than in patients given placebo (23-67% for TOPAMAX vs 1-10% for placebo). These decreases in bicarbonate blood levels are generally mild to moderate, and usually, though not always, occur early in treatment with TOPAMAX. In many cases there are no symptoms from the acid/base imbalance, but some patients may experience symptoms such as rapid breathing, persistent lack of energy, and loss of appetite. Some individuals may experience more serious symptoms such as heart problems, confused thinking, or reduced consciousness.

Patients with conditions that predispose them to acidosis include: those with underlying kidney disease; severe breathing disorders; multiple, severe seizures; diarrhea; those on a ketogenic carbohydrate diet (a diet high in fat and low in protein and sugar); and those who use other drugs. Patients on TOPAMAX or their caregivers should inform their doctors of their past medical history.

Do not discontinue TOPAMAX or reduce your dose without first consulting your doctor, who will be able to confirm if you have persistent acidosis and recommend treatment as appropriate.

As of September 30, 2003, information based on experience with more than 2.5 million patients worldwide shows that healthcare professionals have reported decreased serum bicarbonate in 76 patients treated with TOPAMAX, including 5 patients in Canada. TOPAMAX has been approved for use in Canada since 1997 for the add-on treatment of epilepsy; approximately 89,000 patients have been prescribed TOPAMAX in Canada.

Information about this safety update has been sent to doctors and pharmacists to ensure that they are aware of this new safety information. Janssen-Ortho is working with Health Canada to update the Canadian prescribing information for TOPAMAX. In the interim, all healthcare professionals are advised to review the letter recently received from the company.

A copy of this public advisory is available at <http://www.janssen-ortho.com/>

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