

**ALERT: TOPAMAX® (topiramate) AND TOPROL-XL® (metoprolol succinate)
DISPENSING ERRORS**





September 2005

Dear Pharmacist:





Ortho-McNeil Neurologics, Inc. and Johnson & Johnson Pharmaceutical Research & Development, L.L.C. have become aware of reports of drug dispensing errors involving TOPAMAX® (topiramate) tablets and TOPROL-XL® (metoprolol succinate) extended-release tablets, a product of AstraZeneca LP, leading to patient exposure to the wrong drug.

Based on a review of spontaneous reports submitted to the Food and Drug Administration, World Health Organization, and the United States Pharmacopoeia, prescriptions for TOPAMAX® and TOPROL-XL® have been incorrectly written, interpreted, labeled, and/or dispensed. Possible explanations for these medication errors include similarity in names between TOPAMAX® and TOPROL-XL®, proximity of the two products on pharmacy shelves and/or in computerized listings, and identical dose strengths in the tablet formulations. Additionally, during the dispensing process, use of mnemonic abbreviations in computerized listings incorporating the first three letters and dose of both names, (e.g., “TOP25”), may be a contributing factor.

TOPAMAX® Tablets are available as debossed, coated, round tablets with the following characteristics:

Tablet	Color	Engraving	Sample
25 mg	White	“TOP” on one side, “25” on the other	
50 mg	Light-Yellow	“TOPAMAX” on one side, “50” on the other	
100 mg	Yellow	“TOPAMAX” on one side, “100” on the other	
200 mg	Salmon	“TOPAMAX” on one side, “200” on the other	

TOPROL-XL® extended release tablets are available as white, biconvex, film-coated, and scored tablets, with the following characteristics:

Tablet	Shape	Engraving	Sample
25 mg*	Oval	A β	
50 mg	Round	A mo	
100 mg	Round	A ms	
200 mg	Oval	A my	

*The 25 mg tablet is scored on both sides.

Another similarity between TOPAMAX® and TOPROL-XL® is dose titration, which is recommended for both products when initiating therapy. The TOPAMAX® starting dose may be administered once or twice daily, maintenance dosing is twice daily; and the TOPROL-XL® starting and maintenance dosing is once daily.

We recognize that medication errors have multiple causes and the pharmacist's role in avoiding such errors is pivotal. We urge you to maintain a high level of vigilance when verifying and accurately dispensing oral and written prescriptions for these two products to avoid future errors. Your role is critically important in correctly dispensing prescriptions to ensure that all patients receive their intended treatment. Patients who receive incorrect medications are at risk of experiencing potentially serious health consequences associated with unintended exposure or the lack of a needed therapy (e.g., patients with epilepsy without their TOPAMAX® therapy can experience seizures or increased seizure frequency).

WHAT YOU CAN DO TO REDUCE THE POTENTIAL FOR DISPENSING ERRORS

For pharmacists, we offer the following suggestions to help decrease the potential for future errors:

- Place TOPAMAX® and TOPROL-XL® apart from each other on the shelf; we advise use of the enclosed “shelf talker” described below
- Confirm the brand and generic names prescribed on written and oral prescriptions
- Use both brand and generic names when communicating drug names within the pharmacy
- Counsel patients about the brand name, indication, and proper use of each medication

For drug database content providers, we suggest the following error reduction strategies:

- Install sound-alike/look-alike name alert warnings to the name pair confusion with TOPAMAX® and TOPROL-XL®
- Use “tall man” lettering highlighting the end of each name (i.e., topAMAX and topROL-XL)
- Use both brand and generic names when communicating the drug names
- Avoid the use of confusing drug mnemonics such as “TOP25”

MATERIALS TO HELP PREVENT DISPENSING ERRORS

Ortho-McNeil Neurologics, Inc. has developed the enclosed “shelf talker” that can be used to help you differentiate TOPAMAX® from other stocked merchandise in your pharmacy. This tactic is just one in a broad range of activities the company is undertaking to raise awareness of the issue in the pharmacy community and with patients taking TOPAMAX®.

INDICATIONS for TOPAMAX®

Monotherapy Epilepsy- TOPAMAX®¹ is indicated as initial monotherapy in patients 10 years of age and older with partial onset or primary generalized tonic-clonic seizures. Effectiveness was demonstrated in a controlled trial in patients with epilepsy who had no more than 2 seizures in the 3 months prior to enrollment. Safety and effectiveness in patients who were converted to monotherapy from a previous regimen of other anticonvulsant drugs have not been established in controlled trials.

Adjunctive Therapy Epilepsy- TOPAMAX® is indicated as adjunctive therapy for adults and pediatric patients ages 2 – 16 years with partial onset seizures or primary generalized tonic-clonic seizures, and in patients 2 years of age and older with seizures associated with Lennox-Gastaut syndrome.

Migraine- TOPAMAX® is indicated for adults for the prophylaxis of migraine headache. The usefulness of TOPAMAX® in the acute treatment of migraine headache has not been studied.

IMPORTANT SAFETY INFORMATION FOR TOPAMAX®

TOPAMAX® has been associated with serious adverse events including: hyperchloremic, non-anion gap metabolic acidosis (lowering of serum bicarbonate levels)—measurement of baseline and periodic serum bicarbonate levels is recommended; acute myopia and secondary angle closure glaucoma—patients should seek medical attention if they experience blurred vision or ocular pain; oligohidrosis and hyperthermia—occurs most often in hot weather and in children; cognitive/psychiatric side effects, including somnolence and fatigue,

cognitive dysfunction, and psychiatric/behavioral disturbances; hyperammonemia with or without encephalopathy—associated with the concomitant use of valproic acid; and kidney stones—patients should maintain an adequate fluid intake to minimize the risk of renal stone formation.

Epilepsy

In combination with other antiepileptic drugs (AEDs), the most common side effects of TOPAMAX® in adults (200 to 400 mg/day) were somnolence, dizziness, nervousness, ataxia, fatigue, speech disorders and related problems, psychomotor slowing, abnormal vision, difficulty with memory, paresthesia, and diplopia; and in children (5 to 9 mg/kg/day), fatigue, somnolence, anorexia, nervousness, difficulty with concentration/attention, difficulty with memory, aggressive reaction, and weight decrease.

As monotherapy, the most common side effects of TOPAMAX® (in the 400 mg/day group and at a rate higher than the 50 mg/day group) in adults were: paresthesia, weight decrease, somnolence, anorexia, dizziness, and difficulty with memory; and in children: weight decrease, upper respiratory tract infection, paresthesia, anorexia, diarrhea, and mood problems.

Migraine

Most common adverse events associated with TOPAMAX® 100 mg vs placebo were paresthesia, anorexia, fatigue, nausea, diarrhea, weight decrease, and taste alteration.

INDICATIONS for TOPROL-XL®

TOPROL-XL®² is indicated for the treatment of hypertension, long-term treatment of angina pectoris, and heart failure NYHA Class II or III.

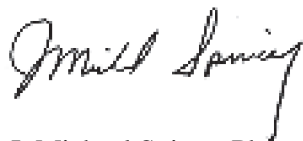
IMPORTANT SAFETY INFORMATION FOR TOPROL-XL®

TOPROL-XL® has a boxed warning against abrupt cessation of therapy.

If you become aware of any medication errors involving TOPAMAX®, report them immediately to us at 1-800-682-6532, and if TOPROL-XL® is involved, also report the error to AstraZeneca at 1-800-236-9933. Medication errors should also be reported to the USP Medication Error Reporting Program in cooperation with the Institute for Safe Medication Practices (1-800-23ERROR; 1-800-FAIL-SAF) or FDA's MedWatch Adverse Event Reporting Program (1-800-FDA-1088).

Thank you for your attention to this matter. For additional medical information about TOPAMAX®, please call 1-800-682-6532 from 9AM to 5PM EST, Monday through Friday.

Sincerely,



J. Michael Spivey, Pharm.D.
Director, Medical Communications - Neurology
Ortho-McNeil Janssen Scientific Affairs, LLC



Joseph Hulihan, M.D.
Vice President, Medical Affairs
Ortho-McNeil Neurologics, Inc.

PLEASE CONSULT ENCLOSED COMPLETE PRESCRIBING INFORMATION FOR TOPAMAX®¹.

1. Package Insert – TOPAMAX® (topiramate) Tablets and TOPAMAX® (topiramate capsules) Sprinkle Capsules. Ortho-McNeil Neurologics, Inc. Titusville, NJ 08560. REVISED JUNE 2005.

2. Package Insert – TOPROL-XL® (metoprolol succinate) Extended-Release Tablets. AstraZeneca LP. Wilmington, DE 19850. REVISED 2/05.