Janssen-Ortho Inc., Canada
MEDICAL AFFAIRS

SYNOPSIS

Name of Sponsor/Company:	Janssen Ortho Inc.	Individual Study Table Referring to Part of the Dossier **n/a**	(for National Authority Use only)
Name of Finished Product:	Topamax	Volume: n/a	
Name of Active Ingredient:	topiramate	Page: n/a	
Title of Study:		An open label study to evaluate the effect of topiramate on subject responsiveness to triptans used for symptomatic headache treatment.	
Investigators:		I. Werner Becker, Calgary, AB; Suzanne Christie, Ottawa, ON; Stephane Ledoux, Montreal, QC	
Study centre(s):			
Publication (reference)		Not yet accepted for publication	
Studied period (years):		Phase of development:	Phase 2
	(date of first enrolment)		
	(date of last completed)		
Objectives:		The objective of this pilot study was to determine if patients with migraine were more responsive to triptans taken for symptomatic headache treatment while on topiramate prophylactic therapy as compared to a baseline period without prophylaxis. As a measure of triptan responsiveness, the proportion of triptan treated migraine attacks in the patient group that were pain free at two hours after treatment was used. Our hypothesis was that topiramate prophylaxis would increase the responsiveness of migraine attacks to triptan therapy as measured by the proportion of attacks pain free two hours after triptan therapy.	

Methodology:	This was an open label, multicenter study to evaluate the ability of daily dosing of topiramate (maximum 200 mg/day) used as a migraine prophylaxis to improve the subject's response to triptans used as symptomatic migraine treatment for acute migraine attacks. Approximately 40 subjects were entered into the Prospective Baseline period. Subjects must have had an established history consistent with migraine for at least six months, with or without aura, based on International Headache Society (IHS) criteria.	
Number of patients (planned and analyzed):	40/40 (21 for efficacy)	
Diagnosis and main criteria for inclusion:	For inclusion, subjects must have used a triptan to treat at least 3 migraines per month. Entry criteria also included that patients had previously failed $\leq$ 2 prophylactic medications because of lack of efficacy. Excluded were patients whose migraines started after the age of 50, who were considered to overuse triptans (>14 days a month), opiates (>8 days/month) and non-opiates (>20 days/month) analgesics. Daily use of < 800 mg acetylsalicylic acid was permissible.	
Test product, dose and mode of administration, batch number:	Topiramate 25 mg: Product Number 2604-CA-11 or 46 or 6399030 Topiramate 100 mg Product Number 2604-CA-13-or 37 or 6419030 Oral medication: twice daily dosing	
Duration of treatment:	16 weeks	
Reference therapy, dose and mode of administration, batch number		
Criteria for evaluation:		
	Efficacy:	Efficacy evaluations were based on information recorded on the subject's headache diary. The following information was recorded in the diary: time of onset of headache and indication of type of headache, time headache stops, any symptomatic treatment taken, time that triptan medication is taken, headache intensity at time of triptan taken, half hour, one hour and 2 hours post triptan use, presence of nausea at time triptan is taken and half an hour,1 and 2 hours post dosing.
	Safety:	Laboratory assessments: hematology, chemistry, and urinalysis were performed at 3 time-points in the study. Vital signs (BP and pulse) were recorded and adverse events were collected

Statistical Methods:		The Primary Efficacy Sample will be the intent-to-treat sample; this sample will include those subjects who receive at least 10 weeks of topiramate as these subjects will have 6 weeks in the last 12 weeks of the topiramate treatment phase, and therefore will have evaluable data. The primary efficacy endpoint will be the difference for each patient in the proportion of triptan treated migraine attacks that are rendered pain free at two hours post dosing. Comparison between the last 12 weeks of the topiramate treatment trial and the 6 week prospective baseline period will be made using a paired t-test (if the data have approximate normal distribution) or a Wilcoxon signed-rank test (a nonparametric test) on the changes in the proportion. All statistical tests will be 2-sided tests performed at a significance level of 5%. All comparisons in the changes in proportion or changes in the number of migraine headaches or periods per month between the prospective baseline period and the last 12 weeks of topiramate treatment will be made using paired t-tests or Wilcoxon signed-rank tests
SUMMARY – CONCLUSIONS		
	EFFICACY RESULTS	In our study, we were unable to show an increased responsiveness of migraine attacks to triptan therapy while patients were on topiramate prophylaxis as measured by the proportion of attacks pain free two hours after triptan treatment. Other secondary endpoints including pain relief at two hours, and pain free at one hour also did not show any improvement. Our results, then, did not support the hypothesis that topiramate prophylaxis would improve the responsiveness of migraine attacks to acute triptan therapy.
	SAFETY RESULTS	The following adverse events (all events, related or unrelated to topiramate) were reported at an incidence rate of >= 10%: fatigue,paraesthesia, dizziness, nausea, anxiety, insomnia, thinking abnormal, amnesia, anorexia, emotional lability, taste perversion, vision abnormal.
	CONCLUSION:	Although topiramate prophylaxis does reduce migraine frequency, the data from this pilot study suggest that topiramate prophylactic treatment does not improve the responsiveness of migraine attack to symptomatic triptan therapy.
Date of this report:		September 28, 2005

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