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:	Concerta	Volume: n/a	
Name of Active Ingredient:	OROS-Methylphenidate hydrochloride	Page: n/a	
Title of Study:		**42603ATT3003/CON-CAN-4, An Open-Label study evaluating the safety and effectiveness of OROS* Methylphenidate (CONCERTA*) in adults with Attention Deficit Hyperactivity Disorder**	
Investigators:		A. Fallu, Sherbrooke, Quebec	
Study centre(s):			
Publication (reference)		Curr Med Res Opin. 2006 Dec;22(12):2557-66.	
Studied period (years):		Phase of development:	Phase III b)
	(date of first enrolment)	March 2005	
	(date of last completed)	October 2005	
Objectives:		To evaluate the safety, tolerability and potential effectiveness of CONCERTA® for the treatment of adults with Attention Deficit Hyperactivity Disorder (ADHD)	
Methodology:		Approximately 30 subjects will be enrolled in this 38 day, open-label study. Subjects cannot have been treated with any methylphenidate or amphetamine containing medication within 4 weeks of the screening visit. Once deemed eligible, subjects will be started on 18 mg of CONCERTA® daily for 3 days and titrated up on Day 4 to 36 mg daily for 7 days. Depending on response, tolerability and clinician's discretion, the dose of CONCERTA® can continue to be titrated up, every 7 days thereafter, first to 54 mg and then to a MAXIMUM of 72 mg (2 x 36 mg tablets) per day, in order to achieve the optimal dose for each subject.	
Number of patients (planned and analyzed):		30/32 enrolled, 2 misdiagnosed patients removed from PP analysis	

Diagnosis and main criteria for inclusion:		1. Male or female outpatients. 2. Age must be between 18 and 65 years, inclusive. 3. Diagnosis of ADHD according to the Diagnostic and Statistical Manual of Mental Diseases, Fourth Edition (DSM-IV)[1,50] obtained via clinical interview and confirmed by the Wender Utah Rating Scale (WURS) 4. Described chronic course of ADHD symptomatology from childhood to adulthood, with some symptoms present before age 7 years which continue to meet DSM-IV criteria at the time of assessment. ADHD is not diagnosed if the symptoms are better accounted for by another psychiatric disorder [e.g. mood disorder (especially bipolar disorder),anxiety disorder, psychotic disorder, personality disorder]. 5. Investigator-rated CAARS **baseline** score of >=24 6. CGI-Severity **baseline** score >=4 (at least "moderate" severity) 7. Total MADRS score at **baseline** of <= 16 8. signed consent
Test product, dose and mode of administration, batch number:		Once daily, PO CONCERTA® 18 mg LOT # 0422606 CONCERTA® 36 mg LOT # 0424620 CONCERTA® 54 mg LOT # 0432377
Duration of treatment:		38 days
Reference therapy, dose and mode of administration, batch number		N/A
Criteria for evaluation:		
	Efficacy:	The primary efficacy criterion will be the change vs. baseline of the inattention and hyperactivity/impulsivity subscale scores of the investigator-rated CAARS at the end of treatment. Secondary end points will include changes from baseline to the end of the treatment in: • CGI-S • CGI-I • Conners' Adult ADHD Self-Report Short Version (CAARS-S:S) • Montgomery-Asberg Depression Rating Scale (MADRS) • Stroop Colour Word test • WAIS-III Working Memory Sub-scale • Controlled Oral Word Association Test (COWAT) • Sheehan Disability Scale (SDS) • Patient Satisfaction with Treatment
	Safety:	Vital signs and physical examination, laboratory assessment, body weight, height, Adverse Event (AE) and Concomitant Medication (C-MED) surveillance, ECG, urine pregnancy tests for females of childbearing potential.

Statistical Methods:		This is a pilot trial to evaluate safety, tolerability and potential trends in effectiveness. No formal sample size calculation was performed. No hypotheses are specified for statistical testing. Safety and effectiveness endpoints will be summarized by descriptive statistics. All subjects who take at least one dose of CONCERTA® will be included in the safety analysis. The percentage of subjects with treatment-emergent adverse events will be provided. Changes in vital signs, ECG, physical examination will be summarized. All subjects who take at least one dose of CONCERTA® and have both baseline and at least one post-baseline effectiveness assessment will be included in the intent-to-treat effectiveness analysis. Descriptive statistics will be provided for the changes in all effectiveness endpoints from baseline to each post-baseline visit. The primary analysis will utilize the last available observations.
SUMMARY – CONCLUSIONS		
	EFFICACY RESULTS	N=26/30. Mean age=36.5+/-10.5 years. Mean OROS*Methylphenidate dose was =51.2 +/- 14.1 mg with a mean treatment duration of 36.3 +/- 5.7 days. Mean baseline investigator-rated CAARS score=32.5+/-6.0 with a mean endpoint improvement = -17.0+/-11.7. ($p<0.0001$). Mean baseline CAARS self report total score=46.3 +/-10.3 with a mean improvement observed at endpoint = -19.4+/-17.9 ($p<0.0001$). Mean endpoint CGI-I improvement= -2.2+/-1.1 ($p<0.0001$) and 75% of patients were "completely" or "somewhat satisfied" with treatment at endpoint. At endpoint, mean improvements were observed in Stroop Colour-Word, ($p=0.0001$), COWAT Letter T-score ($p<0.0001$), COWAT Object T-score ($p=0.001$), WMI percentile ($p<0.0001$), Sheehan Disability Scale.
	SAFETY RESULTS	OROS-MPH was well tolerated. 31/32 (97%) of subjects reported at least one adverse event during the study. The most common adverse events were headache (17/32, 53%), decreased appetite (12/32, 38%), and insomnia (10/32, 31%) There were no serious adverse events and study medication was not discontinued in any subject due to an adverse event. Adverse events were of mild to moderate severity with the exception of two events rated as severe: one report of headache considered probably related to study medication and one report of fatigue considered not related to study medication. Both subjects recovered from these events while still in study. There were no clinically significant changes in ECG, physical examination or blood pressure results from baseline to last observation. A mean body weight decrease of 2.2 +/- 1.8 kg was observed over the course of the study (baseline mean = 76.4+/- 23.8 kg, $P < .0001$); maximum weight lost was 5.4 kg and maximum weight gain was 2.9 kg. OROS*-MPH was associated with small but statistically significant increases in heart rate ($P=.003$). Reductions in absolute systolic and diastolic blood pressure were observed. (systolic mmHg, $P=0.16$; diastolic mmHg, $P=0.27$).
	CONCLUSION:	OROS*- Methylphenidate is a well tolerated and effective treatment for adult ADHD. The results also suggest that OROS*-MPH offers an additional benefit of improvement in executive function, in the areas of response inhibition, verbal/category fluency and working memory, previously identified in the literature as having a critical role in adult ADHD.
Date of this report:		July 26th, 2006

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