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:	Methylphenidate hydrochloride	Page: n/a	
Title of Study:		CR003112, A Randomized, Controlled, Effectiveness Trial of OROS-Methylphenidate compared to Usual Care with Immediate-Release-Methylphenidate in Attention-Deficit-Hyperactivity-Disorder	
Investigators:		T. Ahmed, N. Carrey, A. Stokes, Hlfx, NS; A. Carroll Edm,AB; L. Hechtman Mtl, QC:M. LeBlanc, Moncton NB;S. Malhotra PEI;D. Plante, Sherbrooke, QC:D. Quinn, Saskatoon, SK ;M. Steele, London, ON;A. Turgay, Scarborough, ON;U. Jain, Toronto, ON;M. Weiss, Vancouver, BC; T. Yates, Calgary, AB	
Study centre(s):			
Publication (reference)		Canadian Journal of Clinical Pharmacology	
Studied period (years):		Phase of development:	Phase 3
	(date of first enrolment)	March 2003	
	(date of last completed)	Feb 2004	
Objectives:		To evaluate the effectiveness and tolerability of OROS-MPH versus usual care with IR-MPH in children aged 6 to 12 years with ADHD.	
Methodology:		8 week, multicentre, open-label study randomized 147 subjects to either once-daily OROS-MPH or usual care with IR-MPH. Subjects were titrated to a clinically effective dose of either study medication over 4 weeks and maintained on that dose for an additional 4 weeks.	
Number of patients (planned and analyzed):		160/145 (143 for efficacy)	
Diagnosis and main criteria for inclusion:		-DSM-IV diagnosis of Attention Deficit Hyperactivity Disorder corroborated by the SNAP-IV, 26 item parent assessment (ADHD, any sub-type). - Male or females aged between 6 and 12 years, inclusive - CGI-Severity score at **baseline** of either "moderate", "marked", "severe", "extremely severe" -in the opinion of the parents/caregivers exhibit significant after-school/evening behavioural difficulties where 12 hour coverage is desired -signed consent	
Test product, dose and mode of administration, batch number:		Once daily CONCERTA® 18 mg F0009478 CONCERTA® 27 mg F0012202 CONCERTA® 36 mg F0009477 CONCERTA® 54 mg F0009989	
Duration of treatment:		8 weeks	

Reference therapy, dose and mode of administration, batch number		Methylphenidate 5 mg DIN#02234749 Methylphenidate 10 mg DIN#00584991 Per MD prescription of BID or TID.
Criteria for evaluation:		
	Efficacy:	The primary parameter for comparing the effectiveness of Concerta versus routine care with IR MPH was the SNAP-IV score. For each subject, analysis using the SNAP-IV score involved: a) average of total SNAP-IV score of the 26 items b) remission of symptoms between groups, defined as a score of ≤1 on every item of the standard 18 items of the SNAP-IV. Remission rates were analyzed by the Cochran-Mantel-Haenszel statistic with stratification by centre. Assumption of homogeneity of odds ratio across strata was verified. The secondary parameters were the Parenting Stress Index (PSI, short form), Conners Parent Rating Scale (short form), IOWA Conners Parent Rating Scale, VAS scale for homework and social play, Resource Use Questionnaire (RUQ), parent rating of satisfaction with treatment, and overall clinical global impression (CGI) of severity and improvement assessed by the physician.
	Safety:	Vital signs and physical examination, body weight, AE surveillance, urine pregnancy tests for females of childbearing potential.
Statistical Methods:		An intent-to-treat analysis was performed. All randomized subjects who took at least one dose of trial medication and had at least one post-baseline assessment were included in the analysis. The primary time point is end point, i.e. the last post-baseline observation during the treatment period for each patient. All statistical tests were interpreted at the 5% significance level (2-tailed). Parent rating of satisfaction with treatment and physician rating of CGI was analyzed by the Cochran-Mantel-Haenszel statistic (van Elteren test) with stratification by centre.
SUMMARY – CONCLUSIONS		
	EFFICACY RESULTS	OROS-MPH showed statistically significant superiority to IR-MPH in remission rate based on the 18 ADHD symptoms (p=0.0002, X^2=13.8, df=1) and severity of ADHD and ODD symptoms (p=0.004, F=8.4, df=1,127), as well as on the following secondary assessments: IOWA Conners, Conners Parent Rating Scale (short version), Parent Stress Index, (short version); Visual Analogue Scale for social play; Clinical Global Impression-Severity, Clinical Global Impression-Improvement and Parent Satisfaction with treatment.
	SAFETY RESULTS	OROS-MPH and IR-MPH were both well tolerated with a similar side effect profile. No serious adverse events were reported in either treatment group No statistically significant changes in either treatment group at endpoint in vital signs or weight N=6 (8%) of OROS-MPH patients discontinued due to an AE vs. N=2 (3%) of IR-MPH patients. In the OROS-MPH group, these events included 1 case of "emotionally over-reactive", "difficulty settling", "motor tics", "decreased appetite", "sedation", "racing heart" and 2 cases of "insomnia". In the IR-MPH group, these events included 1 case each of "pain in the back", "fever", "tics-full body" The most commonly reported AEs were decreased appetite (24% OROS-MPH and 32% IR-MPH), insomnia (17% OROS-MPH and 14% IR-MPH), headache (19% OROS-MPH and 16% IR-MPH) and abdominal pain (14% OROS-MPH and 12% IR-MPH)
	CONCLUSION:	Treatment with OROS-MPH, when compared with usual care with IR-MPH, results in a greater percentage of children that achieve remission of ADHD symptoms as well as a greater change (improvement) in average rating on the parent-completed SNAP-IV-26 scale.
Date of this report:		September 20, 2005

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