

SYNOPSIS

Name of Sponsor/Company: Janssen-Cilag EMEA	
Name of Finished Product: Concerta®	
Name of Active Ingredient(s): Methylphenidate HCl	
Protocol No.: CR002479_REF1	
Title of Study: A Multicentre, Randomized, Double-Blind, Placebo-Controlled, Parallel Group, Dose-Response Study to Evaluate Safety and Efficacy of Prolonged Release (PR) OROS® methylphenidate (18, 36 and 72 mg/day), With Open-Label Extension, in Adults with Attention Deficit/Hyperactivity Disorder [German Extension]	
Principal Investigator: Not applicable	
Publication (Reference): None	
Study Period: 28 November 2005 to 14 November 2006	Phase of development: 3
Objectives: The objective of this German extension treatment period was to keep eligible German subjects on treatment with PR OROS methylphenidate after completion of the 42603ATT3002 study 7-week open-label phase, and to continue safety and tolerability assessments until subjects could enter the planned long-term extension study 42603ATT3004. Safety and tolerability were assessed by means of adverse event reporting, vital signs, and clinical laboratory tests.	
Methodology: The international 42603ATT3002 study included 2 treatment phases: a double-blind placebo-controlled phase (5 weeks of treatment) and an open-label extension phase (7 weeks of treatment). Subjects entering the German extension study signed a new informed consent. Assessments performed at end of the 7-week open-label phase of the 42603ATT3002 study could have been used as Visit 1 assessments for this German extension. Subjects in the German extension phase received flexible dosages of PR OROS methylphenidate (18, 36, 54, 72, 90 mg/day). Subjects were asked to return every 3 months up to entrance into Study 42603ATT3004.	
Number of Subjects (planned and analyzed): 77 planned and analyzed.	
Diagnosis and Main Criteria for Inclusion: Eligible subjects were those who in Study 42603ATT3002 were treated at German centers, completed the open-label phase, and benefited from treatment.	
Test Product, Dose and Mode of Administration, Batch No.: PR OROS methylphenidate 18, 36, and 54 mg tablets; doses: 18, 36, 54, 72, or 90 mg/day; oral; batch numbers: 18 mg: 0009478/0410815, 0009478/0509369; 36 mg: 0009477/0413862, 0009477/0415973, 0009477/0522184; and 54 mg: 0009989/0412349, 0014585/0435317, 0009989/0520664, and 0009989/0533009.	
Reference Therapy, Dose and Mode of Administration, Batch No.: No reference	
Duration of Treatment: Up to 52 weeks	
Criteria for Evaluation: Efficacy: No analysis was planned for efficacy results. The following efficacy assessments (same assessments performed in the double-blind and 7-week open-label phase of Study 42603ATT3002) were performed at the Final Visit or Early Withdrawal Visit and at the Post-Study Visit; data obtained at the Final Visit could serve as baseline efficacy data for subjects rolling over into the 42603ATT3004 study: Conners' Adult ADHD Rating Scale (CAARS), Conners' Adult ADHD Rating Scale-Self Report: Short Version (CAARS-S:S), Clinical Global Impression (CGI) – Severity of Illness subscale (CGI-S) & Global Change Subscale (CGI-C), Sheehan's Disability Scale (SDS), Quality of Life Enjoyment and Satisfaction Questionnaire (Q LES Q): Short Form, and Global Assessment of Effectiveness (GAE). Safety: Adverse events, laboratory tests, vital signs, body weight, and physical examination	
Statistical Methods: Efficacy: Efficacy data were not analyzed. Safety: The incidence of adverse events was summarized. For laboratory values, descriptive statistics for each parameter at baseline and at scheduled time points were provided, changes from baseline were presented, and shift tables were generated. Descriptive statistics for vital sign data along with changes from baseline were presented.	

SYNOPSIS (CONTINUED)

SUMMARY - CONCLUSIONS

DEMOGRAPHIC AND BASELINE CHARACTERISTICS

A total of 77 German subjects (from 13 sites) participated in the German extension; 10 subjects (13%) prematurely discontinued the extension phase (6 subjects withdrew consent, 2 subjects were non-compliant, 1 subject was lost to follow-up, and 1 subject discontinued because of change in ADHD medication). The mean (SE) age was 33.8 (1.14) years and mean height and weight were 174 (1.18) cm and 76.6 (2.12) kg, respectively, resulting in a mean BMI of 25.26 (0.630). Ninety-seven percent of the subjects were Caucasian and 53% (41 subjects) were females. The mean (SD) duration of treatment was 145.2 (7.62) days (range: 34 – 329 days).

EFFICACY RESULTS:

No efficacy conclusions were drawn from this German extension of the 42603ATT3002 study.

SAFETY RESULTS:

There were no deaths. Two subjects experienced serious adverse events: tubo-ovarian abscess considered by the investigator to be not related to the study drug and psoriasis considered by the investigator to be possibility related to the study drug. There were no adverse events that led to study discontinuation.

Of the 77 subjects who participated in the German extension, 42 subjects (54.5%) reported at least one adverse event. The most frequently reported adverse events (reported by greater than 5% of the subjects) were nasopharyngitis (9 subjects), headache (6 subjects), back pain, insomnia (5 subjects each), and decreased weight (4 subjects). Tachycardia, initial insomnia, nervousness, and tubo-ovarian abscess were each reported as severe in 1 subject. All other adverse events were mild or moderate in severity.

A small number of subjects had laboratory data at the baseline and final visits; none of the laboratory values were identified as markedly abnormal.

Overall, small increases in mean diastolic and systolic blood pressure from baseline were noted. The changes from baseline in standing and supine pulse values were 3.4 bpm and 5.1 bpm, respectively.

Decreases in mean body weight and BMI from baseline were observed during this extension: -2.3 kg and -0.81 kg/m², respectively.

CONCLUSION:

The safety profile of PR OROS methylphenidate, administered as a flexible dose regimen between 18 mg and 90 mg daily to subjects continuing treatment in this German extension to the 42603ATT3002 study was consistent with that reported in other ADHD studies with methylphenidate in pediatric and adult subjects.

Date of the report: The 42603ATT3002 German Extension report was issued 13 September 2007.

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