CONCERTA® (methylphenidate HCl)
Dosing - Dosing of CONCERTA Over 72 mg Per Day in Adolescents

SUMMARY

- Daily dosages above 72 mg in adolescents have not been studied and are not recommended.[1]
- An open-label, smoking prevention study of CONCERTA in adolescents with attention-deficit/hyperactivity disorder (ADHD) reported the mean daily Dose to be 67.2±24.3 mg, with 50% of subjects receiving doses greater than 72 mg daily.[2]
- One naturalistic study of CONCERTA in adolescents with ADHD utilized a range of CONCERTA doses between 126 and 270 mg/day (mean Dose, 169 mg/day).[3]

PRODUCT LABELING

Please refer to the following section of the enclosed Full Prescribing Information that is relevant to your inquiry[1]: DOSAGE AND ADMINISTRATION, Dose Titration.

CLINICAL DATA

Long-term, open-label study

Hammerness et al (2009)[2] evaluated the Cardiovascular Effects of OROS methylphenidate (MPH) from a smoking prevention study in adolescents with ADHD (N=114).

Study Design/Methods

- Long-term, open-label, smoking prevention study
- A physical examination, including blood pressure and heart rate measurements, as well as an ECG was conducted prior to starting OROS MPH.
- During week 1, subjects began taking OROS MPH at a Dose of 0.5 to 0.75 mg/kg/d which was increased to 0.75 to 1.0 mg/kg/d during week 2, and finally to 1.5 mg/kg/d in week 3.
- Doses were titrated according to tolerability and symptom improvement, based on ADHD-specific Clinical Global Impression Scale-Improvement score.
- Blood pressure, heart rate measurements, and adverse events were collected at each study visit, which occurred weekly for the first 6 weeks and monthly thereafter for a total of 6 months. ECG's were obtained at week 6 and then monthly thereafter.

Results

Patient Characteristics

- Adolescents with ADHD (aged 12-18 years)

Dose

- Fifty-seven (50%) of the subjects completed 6 months of treatment. At month 6, the mean total daily Dose of OROS MPH was 67.2± 24.3 mg, and 50% of subjects were taking doses greater than 72 mg daily.

Cardiovascular Effects

- Statistically significant increases in mean diastolic blood pressure (DBP) and heart rate (HR) were noted at week 6 compared to baseline (DBP, 65.4 vs. 62.5 mm Hg, respectively and HR, 86.0 vs. 81.7 bpm, respectively; $p<0.05$ for both), while changes in systolic blood pressure (SBP) were not statistically significant.
- At 6 months, only SBP was significantly increased compared to baseline (117.3 vs. 112.8 mm Hg, respectively; $p<0.05$), and a trend towards baseline values was observed

for DBP measurements. At 6 months, the change in HR from baseline was not statistically significant.
- There were no statistically or clinically significant changes in mean ECG values at study endpoint compared to baseline.
- No serious cardiovascular adverse events were reported by any subject.
- Ten subjects reported one or more cardiovascular adverse events during the study, four of which reported events on more than one occasion. One of these subjects discontinued study treatment because of reoccurring heart palpitations.
- The remaining events were isolated, occurred most commonly in the short term portion of the study, and did not reoccur with continued treatment.

Authors' Conclusion

- The authors concluded that after 6 months of treatment, OROS MPH at doses up to 1.5 mg/kg/d resulted in small, but statistically significant increases in SBP and HR consistent with previous studies of stimulants at lower doses.

Naturalistic Study

Stevens et al (2010)[3] described a Naturalistic Study in adolescents with ADHD (N=18).

Results

Patient Characteristics

- Seventeen adolescent patients (mean age, 16 years) with ADHD
- Treated by a single psychiatrist in Oregon between December 2006 and August 2007.

Dose

- Patients were administered a mean total daily dose of OROS MPH of 169 mg/day (range, 126–270 mg/day).

Safety

- There were no serious adverse effects or changes in cardiovascular parameters observed during the retrospective study period.

LITERATURE SEARCH

A literature search of MEDLINE®, EMBASE®, BIOSIS Previews®, DERWENT® (and/or other resources, including internal/external databases) pertaining to this topic was conducted on 25 October 2023.

REFERENCES

1. CONCERTA (methylphenidate HCl) [Prescribing Information]. Titusville, NJ: Janssen Pharmaceuticals, Inc; https://imedicalknowledge.veevavault.com/ui/approved_viewer?token=7994-edb60a5a-a794-4ed6-b7ab-758d0aa94194.
2. Hammerness P, Wilens T, Mick E, et al. Cardiovascular effects of longer-term, high-dose OROS methylphenidate in adolescents with attention deficit hyperactivity disorder. *J Pediatr*. 2009;155(1):84-89.
3. Stevens JR, George RA, Fusillo S, et al. Plasma methylphenidate concentrations in youths treated with high-dose osmotic release oral system formulation. *Journal of Child and Adolescent Psychopharmacology*. 2010;20(1):49-54.