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Clinical Development

Ritalin® LA (methylphenidate-HCl/RIT124D)

[20, 30 and 40mg oral, hard gelatine capsules]

Expert report on the clinical documentation

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component, reproducing the pharmacokinetic profile of two doses of Ritalin administered four to five hours apart.

Ritalin LA administered as a single daily dose is an effective and safe therapy in the treatment of children with ADHD. The efficacy of Ritalin LA is apparent in both the normal school and home routines of the children as evaluated by teachers and parents and is independent of ADHD subtype. The safety profile of Ritalin LA is consistent with the known profile of Ritalin. No safety concerns unique to the new dosage form were observed.

8.2. Efficacy

The efficacy of Ritalin LA was demonstrated in two placebo-controlled clinical studies (Protocols 02 and 07) in 195 children aged 6 to 12 years with ADHD. This population represents the age group most frequently referred to clinics for treatment of ADHD. *2-115* *2-123* *6-001* *8-001*

- A single dose of Ritalin LA 20 mg was effective relative to placebo in improving behaviors of ADHD (Attention and Deportment) and measures of academic productivity (Math Tests) in a laboratory classroom setting. The improvement was statistically significant during both the morning and afternoon of a 9-hour evaluation period (Protocol 02)
- Ritalin LA administered once daily at individually titrated doses (optimal dose) in the range 10-40 mg/day was effective relative to placebo in improving symptoms of ADHD in a naturalistic setting (normal school and home settings) (Protocol 07). This study thus confirmed the clinical relevance of the statistically significant findings of the previous study.
- Ritalin LA was easy to titrate; an optimal dose was identified in the majority of patients (86%) who entered the Titration Period of Protocol 07. Response rates for stimulants have been reported in the literature to be similar (70-90%) [1-5].

In conclusion, the efficacy data collected in the Ritalin LA clinical program support the labelling of Ritalin LA as an effective once-daily treatment in the dose range of 10 to 40 mg in children with ADHD.

8.3. Safety

With decades of use, the safety of Ritalin is well established. The safety of Ritalin LA was demonstrated based on 195 children with ADHD (Protocols 02 and 07). A further 61 healthy adult volunteers in the clinical pharmacology studies contributed to the safety database.

- The AE profile of Ritalin LA was consistent with that associated with Ritalin use. In the placebo-controlled Double-blind Treatment Phase of Protocol 07, the proportion of patients reporting AEs was similar for Ritalin LA and placebo. Individual AEs were reported by few patients; the most frequently reported were anorexia, insomnia and headache, each reported by one to two patients in the Ritalin LA group and sore throat, headache and vomiting, each