Part IC 3

Clinical Expert Report

Ritalin® (methylphenidate)

10 mg tablets

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or isolated undesired effects not foreseen in the Summary of Product Characteristics whose causes are likely to be other than the drug.

Of the 11 fatal cases reported, some are insufficiently documented to allow a causal relationship to be established, others involved the simultaneous administration of other drugs or the reported disease was already present before the start of therapy, and some were due to an intentional overdose.
There were no reports of hepatoblastoma, indicated in the previous PSUR as a subject of specific interest. The incidence of hepatoblastoma during the course of Ritalin® treatment has been revised and there is so far only one case, a number that falls well inside the expected incidence in the population as a whole.
The following possible and previously unidentified adverse drug effects have been noted:

1) Hypersensitivity reactions (Schoenlein-Henoch purpurea and angioedema), for which Ritalin® will be continuously observed in the future.
2) Suicide: it is known that Ritalin® therapy and its sudden discontinuation may cause depression in some patients. The use of Ritalin® in the treatment of depressed patients is contraindicated. A search of the Novartis international safety data base allowed the identification of 21 cases of attempted suicide and six suicides, in addition to 25 reports of suicidal ideations in patient aged 6-48 years, 56% of whom were children aged less than 16 years.
3) Hypoglycemia: four cases of hypoglycemia were reported during the 3-year period, and a search of the Novartis data base identified a further seven cases that were poorly documented in terms of the medical history of the patients and concomitant therapies.
4) Pharmacological interactions: in addition to the 12 cases of lack of efficacy included in the PSUR3, there have been 17 cases of pharmacological interactions classified as "unlisted". However, the majority of these are already included in the package leaflet of Ritalin® or the concomitant drug and are poorly documented. In the absence of plasma drug level determinations, it is more probable that these effects were additive rather than true pharmacological interactions.

5. OTHER INFORMATION

5.1 Therapeutic alternatives

According to numerous authors, psychostimulants in general and methylphenidate in particular represent the treatment of choice for pure ADHD syndrome (Losier,1996; Mervyn Fox,1993; MTA Cooperative Group,1999; Spencer,1996;). In general the therapeutic approach also includes other measures, such as