

## Statement from the Regional HTA Centre of Region Västra Götaland, Sweden

**Treatment of ADHD (Attention-Deficit/Hyperactivity Disorder) in adults with central stimulants**Question at issue:

Are ADHD symptoms positively affected, in adult patients with ADHD, treated with methylphenidate or its derivatives, compared with placebo?

PICO (Patient, Intervention, Comparison, Outcome)

- P= Adults with ADHD.
- I= Methylphenidate (Concerta or Ritalin).
- C= Placebo, other pharmacological treatment, no treatment.
- O= Symptom alteration according to any validated scale.

**Summary of the health technology assessment:**Method and target group:

ADHD represents a symptom complex that involves a substantial risk of social dysfunction, substance abuse and reduced capacity to work. The HTA addresses short-term treatment with methylphenidate or derivatives thereof, in adult patients with diagnosed ADHD, according to current diagnostic criteria, compared with placebo treatment. The outcome variable was ADHD symptoms measured with validated symptom scales. Separate analyses were made for studies on unselected ADHD populations, as well as on abusing populations. Since there was a significant number of RCTs (randomized controlled studies) addressing the issued question, the analyses were limited to include only studies with RCT design. A detailed mapping of the adverse events was not included in the project, since these drugs already are registered for use in children and adolescents with ADHD diagnosis. The side effects that have been reported to the Medical Products Agency, Sweden (Läkemedelsverket) are listed in an enclosed document.

Level of evidence for studied patient benefit (ADHD symptoms measured with a validated scale):

12 out of 13 identified articles, that were based on unselected ADHD patients, reported a significant beneficial effect of methylphenidate (or its derivatives) on ADHD symptoms, compared with placebo. Effect size is considered as moderate. Six of these studies are considered of moderate quality, and seven of low quality. All studies of moderate quality showed unequivocal results in favor of methylphenidate. Level of evidence for the conclusion is thus in accordance with SBU's guidelines 2 (= **moderately strong scientific evidence**). The conclusion applies only to short-term studies (a few weeks) and for the outcome ADHD symptoms measured with validated scales. Scientific support is lacking regarding both long-term effects and objective, function-related outcome variables (social function, work, etc.).

With regard to isolated abusing populations, with outcome ADHD symptoms and/or relapse into abuse, three studies were identified. All of these studies were considered to be of low quality, and none of the studies revealed any effect of methylphenidate on relapse into abuse, compared with placebo. Only one of these three studies showed a significant favorable effect of methylphenidate on ADHD symptoms compared to placebo. The level of evidence for the effect of methylphenidate or its derivatives on abuse will therefore be 4, ie. **insufficient scientific evidence**.

Risks:

Risks have not been analyzed in detail within the framework of the current project, since these drugs are already approved for use in children and adolescents with ADHD. Reported side effects of the substances are appended to the report. When used in adults there is also a risk for abuse that is considered as low by psychiatric expertise.

Ethical aspects:

It is an ethical dilemma that a therapeutic approach is introduced into clinical practice without a prior assessment of the scientific evidence. Since the adult ADHD population is expected to be large (up to 4% of the population) a widespread use of these drugs may create significant displacement risks within psychiatric care.

Economical aspects

There is a great degree of uncertainty regarding the magnitude of the target population. Because data on long-term effects is missing, it is also uncertain how long the treatment should last. A conservative estimate is that with a target population to 10,000 individuals in the Västra Götaland Region, Sweden, continuous treatment with central stimulants would result in an annual drug cost of around 50 million SEK. To this amount should be added a substantial investigation cost to identify suitable patients.

Concluding remarks

Short-term treatment with methylphenidate or its derivatives has a significantly better effect than placebo on ADHD symptoms, in adult patients with ADHD diagnosis (evidence level 2, moderately strong scientific evidence). Effect size is considered moderate and data on long-term effects are lacking. Side effects are considered to be acceptable, with a question mark regarding abuse risk. The target population is considered to be large, and the drugs are relatively expensive. Moreover, the identification of the right patients for treatment will require an extensive and costly diagnostic workup. Introduction of the treatment is expected to generate an annual cost of 50-70 million SEK, which may create significant risks of displacement within psychiatry. There is a great need for long-term studies.

On behalf of the Regional HTA Centre of Region Västra Götaland, Sweden.

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