

## ▼ Guanfacine for ADHD in children and adolescents

### Question 1

Prolonged-action guanfacine is licensed in Europe for the management of ADHD in children and adolescents. What is the pharmacological mechanism of action of guanfacine?

- Guanfacine is a selective noradrenaline re-uptake inhibitor
- Guanfacine is a selective  $\alpha_{2A}$ -adrenergic receptor agonist**
- Guanfacine is a selective dopamine- $D_1$  receptor agonist
- Guanfacine is a selective serotonin reuptake inhibitor
- Guanfacine is a selective gamma-aminobutyric acid B agonist

**Answer: b.** Guanfacine is a selective  $\alpha_{2A}$ -adrenergic receptor agonist. In ADHD, its mode of action has not been fully established.

### Question 2

Which one of the following does not need to be assessed before starting treatment with guanfacine?

- Blood pressure
- Height
- Weight
- Heart rate
- Blood glucose**

**Answer: e.** The summary of product characteristics (SPC) states that before starting treatment with guanfacine, a baseline evaluation is required to identify patients at increased risk of QT-prolongation-related arrhythmia, hypotension, bradycardia, somnolence, sedation and weight gain. This should include assessment of cardiovascular status (including blood pressure and heart rate), concomitant medications, past and present medical and psychiatric disorders or symptoms, family history of sudden cardiac/unexplained death and pretreatment height and weight.

### Question 3

The recommended starting dose of guanfacine is 1mg daily. The dose may be adjusted in increments and should be individualised according to response. What is recommended as the usual dose range for guanfacine in children and adolescents?

- 0.01–0.07mg/kg/day
- 0.05–0.12mg/kg/day**
- 0.2–0.48mg/kg/day
- 0.4–0.96mg/kg/day
- 1.0–1.6mg/kg/day

**Answer: b** The initial dose is guanfacine 1mg daily, given either in the morning or the evening, titrated according to response in increments of not more than 1mg a week to a maximum of 4mg daily in children 6–12 years and up to 7mg daily, depending on body weight, in adolescents 13–17 years, corresponding to a usual dose range of 0.05–0.12mg/kg/day.

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### Question 4

Two phase III flexible-dose double-blind studies compared guanfacine (dose range 1–7mg/day) with placebo using the change in ADHD-RS-IV from baseline as the primary outcome. What was placebo-adjusted mean difference in score for both studies?

- a. –24.6 and –23.9
- b. –18.5 and –15.0
- c. –6.1 and –8.9
- d. –3.8 and –4.4
- e. –2.5 and –8.1

Answer: c. In one study involving 314 adolescents (minimum ADHD-RS-IV score of 32 at baseline) the mean decrease in ADHD-RS-IV from baseline was –24.6 with guanfacine compared with –18.5 for placebo (placebo-adjusted mean difference –6.1; effect size 0.52;  $p < 0.001$ ) after 13 weeks. In the other study of 338 children and adolescents, the mean change in ADHD-RS-IV total score (from a baseline of 43) was –23.9 for guanfacine and –15.0 for placebo (placebo-adjusted mean difference of –8.9 [ $p < 0.001$ ]).

### Question 5

Which one of the following adverse effects is very common ( $\geq 1/10$ ) with guanfacine?

- a. Weight gain
- b. Syncope
- c. Hypotension
- d. Somnolence
- e. Bradycardia

Answer: d. The SPC states that the most frequently reported very common ( $\geq 1/10$ ) adverse reactions in controlled double-blind and open-label clinical studies included somnolence (40.6%), headache (27.4%), fatigue (18.1%), upper abdominal pain (12.0%) and sedation (10.2%).