The recently partially updated NICE guideline on the diagnosis and management of attention deficit hyperactivity disorder (ADHD)\(^1\) recommends training and education for parents and carers of children and young people of school age with ADHD and moderate impairment, possibly with psychological treatment for younger children. Older children and young people may prefer individual psychological treatment.

Drug treatment is reserved for those with moderate impairment for whom nondrug interventions are unsuitable or have been unsuccessful; and as first-line treatment for those with severe ADHD and severe impairment. The recommended drugs are methylphenidate, atomoxetine and dexamfetamine (lisdexamfetamine has not been appraised), chosen according to co-morbidities, adverse effects, adherence, risk of diversion or misuse, and parent/carer or patient preference.

### Indications and dosage

Guanfacine (Intuniv) is an alpha 2A agonist indicated for the treatment of attention deficit hyperactivity disorder (ADHD) in children and adolescents for whom stimulants are not appropriate. This article discusses the indications, monitoring requirements and clinical trial results.

Not a stimulant but appears to act by modulating signalling in the prefrontal cortex and basal ganglia. It is licensed for the treatment of ADHD in children and adolescents aged 6–17 years old for whom stimulants are not appropriate, not tolerated or have been shown to be ineffective.

It must be used as a part of a comprehensive ADHD treatment programme that typically includes psychological, educational and social measures and must be initiated under the supervision of a specialist in childhood and/or adolescent behavioural disorders. Guanfacine is taken once daily in the morning or evening; it should not be taken with a high-fat meal or with grapefruit juice.

Treatment with guanfacine requires extensive pretreatment screening. The initial dosage of 1mg daily should be titrated over four to seven weeks according to age and body mass, during which time close monitoring for adverse effects is required. The maximum dosage is 4–7mg daily, depending on age and body mass. Further monitoring is required every three months in the first year of treatment and every six months thereafter.

### Key Points

- Guanfacine is a selective alpha 2A agonist for the treatment of ADHD in children and adolescents aged 6–17 years old for whom stimulants are not appropriate, for use as part of a programme that includes nonpharmacological interventions.
- Careful pretreatment screening, dose titration and monitoring during treatment are required.
- In clinical trials, guanfacine improved ADHD symptoms and functioning at school; it has not been directly compared with other drug treatments for ADHD.
- Adverse effects, notably somnolence and sedation, are common and adverse cardiovascular effects may occur.
- A month’s treatment at a dosage of 1–7mg daily costs £56.00–£141.68.
NEW PRODUCTS | Guanfacine

increase in blood pressure or pulse. The dose should be tapered to minimise any further increase. If guanfacine is discontinued, the dose should be titrated according to parent/carer assessments of functioning at school and in the family setting.

This study included the nonstimulant ADHD treatment atomoxetine “to provide reference data” and was not powered to compare this with guanfacine. The mean change in ADHD-RS-IV score for atomoxetine was -18.8 (p=0.017 vs placebo); 56.3 per cent of patients were rated improved/much improved on the CGI-I scale (see Figure 1).

Longer-term efficacy was evaluated in a randomised withdrawal study: children and adolescents (n=316) who responded during 13 weeks’ treatment were randomised to continue or discontinue treatment for a further 26 weeks.4 Treatment failure (≥50 per cent increase in ADHD-RS-IV total score and a two-point or more increase in CGI – Severity score) was less frequent with guanfacine than placebo (50 vs 65 per cent, p=0.006). In two nonblinded extension studies, efficacy was maintained for up to 24 months but overall discontinuation rates were 77 and 83 per cent.5,6

Adverse events

In clinical trials, the most frequently reported adverse events seen with guanfacine were somnolence (41 per cent), headache (27 per cent), fatigue (18 per cent), upper abdominal pain (12 per cent) and sedation (10 per cent). Serious adverse events included hypotension (3.2 per cent), weight increase (2.9 per cent), bradycardia (1.5 per cent) and syncope (0.7 per cent). Adverse events accounted for 13 per cent of premature discontinuations in long-term studies.7

Clinical trials

The pivotal clinical trial of guanfacine was a placebo-controlled, randomised study in 272 6–17-year-olds with moderately severe ADHD.3 The dose was titrated over four weeks (in those aged 6–12 years) or seven weeks (in those aged 13–17 years), to a mean of 3.6mg daily, followed by a six-week maintenance phase. The primary efficacy endpoint was change from baseline in ADHD Rating Scale IV (ADHD-RS-IV) at week 10 in the younger age group or week 13 in the older age group.

Mean ADHD-RS-IV score at baseline was approximately 43. The mean change at endpoint was -23.9 for guanfacine and -15.0 for placebo; this difference was statistically significant (p<0.001). There were also significant improvements in secondary endpoints such as the proportion of patients improved/very much improved on a Clinical Global Impression – Improvement (CGI-I) scale (67.9 vs 44.1 per cent with placebo; p<0.001) and according to parent/carer assessments of functioning at school and in the family setting.

This study included the nonstimulant ADHD treatment atomoxetine “to provide reference data” and was not powered to compare this with guanfacine. The mean change in ADHD-RS-IV score for atomoxetine was -18.8 (p=0.017 vs placebo); 56.3 per cent of patients were rated improved/much improved on the CGI-I scale (see Figure 1).

Longer-term efficacy was evaluated in a randomised withdrawal study: children and adolescents (n=316) who responded during 13 weeks’ treatment were randomised to continue or discontinue treatment for a further 26 weeks.4 Treatment failure (≥50 per cent increase in ADHD-RS-IV total score and a two-point or more increase in CGI – Severity score) was less frequent with guanfacine than placebo (50 vs 65 per cent, p=0.006). In two nonblinded extension studies, efficacy was maintained for up to 24 months but overall discontinuation rates were 77 and 83 per cent.5,6

Adverse events

In clinical trials, the most frequently reported adverse events seen with guanfacine were somnolence (41 per cent), headache (27 per cent), fatigue (18 per cent), upper abdominal pain (12 per cent) and sedation (10 per cent). Serious adverse events included hypotension (3.2 per cent), weight increase (2.9 per cent), bradycardia (1.5 per cent) and syncope (0.7 per cent). Adverse events accounted for 13 per cent of premature discontinuations in long-term studies.7

Clinical trials

The pivotal clinical trial of guanfacine was a placebo-controlled, randomised study in 272 6–17-year-olds with moderately severe ADHD.3 The dose was titrated over four weeks (in those aged 6–12 years) or seven weeks (in those aged 13–17 years), to a mean of 3.6mg daily, followed by a six-week maintenance phase. The primary efficacy endpoint was change from baseline in ADHD Rating Scale IV (ADHD-RS-IV) at week 10 in the younger age group or week 13 in the older age group.

Mean ADHD-RS-IV score at baseline was approximately 43. The mean change at endpoint was -23.9 for guanfacine and -15.0 for placebo; this difference was statistically significant (p<0.001). There were also significant improvements in secondary endpoints such as the proportion of patients improved/very much improved on a Clinical Global Impression – Improvement (CGI-I) scale (67.9 vs 44.1 per cent with placebo; p<0.001) and according to parent/carer assessments of functioning at school and in the family setting.

This study included the nonstimulant ADHD treatment atomoxetine “to provide reference data” and was not powered to compare this with guanfacine. The mean change in ADHD-RS-IV score for atomoxetine was -18.8 (p=0.017 vs placebo); 56.3 per cent of patients were rated improved/much improved on the CGI-I scale (see Figure 1).

Longer-term efficacy was evaluated in a randomised withdrawal study: children and adolescents (n=316) who responded during 13 weeks’ treatment were randomised to continue or discontinue treatment for a further 26 weeks.4 Treatment failure (≥50 per cent increase in ADHD-RS-IV total score and a two-point or more increase in CGI – Severity score) was less frequent with guanfacine than placebo (50 vs 65 per cent, p=0.006). In two nonblinded extension studies, efficacy was maintained for up to 24 months but overall discontinuation rates were 77 and 83 per cent.5,6

Adverse events

In clinical trials, the most frequently reported adverse events seen with guanfacine were somnolence (41 per cent), headache (27 per cent), fatigue (18 per cent), upper abdominal pain (12 per cent) and sedation (10 per cent). Serious adverse events included hypotension (3.2 per cent), weight increase (2.9 per cent), bradycardia (1.5 per cent) and syncope (0.7 per cent). Adverse events accounted for 13 per cent of premature discontinuations in long-term studies.7

References

2. Intuniv 1mg, 2mg, 3mg, 4mg prolonged-release tablets. Summary of Product Characteristics. www.medicines.org.uk/emc/medicine/31294

Declaration of interests

None to declare.

Steve Chaplin is a pharmacist who specialises in writing on therapeutics...