Guanfacine Extended Release: A Novel Treatment for Attention-Deficit/Hyperactivity Disorder in Children and Adolescents

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Background

Guanfacine extended release (GXR) has reported efficacy for the treatment of attention-deficit/hyperactivity disorder (ADHD) as monotherapy and adjunctive therapy to psychostimulant medications.

Objective

The objective of this article was to review the efficacy, safety profile, mechanism of action, pharmacokinetics, and appropriate dosing of GXR in children and adolescents with ADHD.

Methods

Pertinent English-language literature was identified from searches of MEDLINE (1950–February 2012), BIOSIS (1969–February 2012), and EMBASE (1974–February 2012). Search terms included guanfacine, guanfacine extended release, attention deficit disorder with hyperactivity, ADHD, nonstimulant, and alpha-2

adrenergic receptor. Of the 49 publications identified, 12 are reviewed herein. Citations from identified articles were reviewed for additional references. Abstracts and posters presented at recent scientific meetings and data included in the prescribing information were also reviewed.

Results

Studies of GXR have demonstrated efficacy as once-daily monotherapy as well as adjunctive therapy to psychostimulants for ADHD in short-term trials. The safety profile of GXR is consistent with that of a centrally acting α2A-adrenoceptor agonist. Somnolence, sedation, and hypersomnia adverse events (AEs), although frequent, are typically mild to moderate and tend to diminish with continued treatment. However, 1 long-term, open-label study found that 22 serious treatment-emergent AEs occurred in 16 (6.2%) of 259 subjects, and another found that 26% of subjects discontinued therapy due to AEs. The cardiovascular effects, of GXR are consistent with guanfacine's known effects, and are generally modest in nature. The mechanism of action of GXR in ADHD is unknown. Because the pharmacokinetics of immediate-release guanfacine differ from GXR, dose substitution on a milligram-for-milligram basis is inappropriate. Clinical trials analyzed according to weight-adjusted doses suggest a dose-response relationship for efficacy. Doses >4 mg/d cannot be recommended due to lack of study data at those doses.

Conclusions

Current evidence indicates that GXR is an effective treatment option for children and adolescents with ADHD. AEs are typically mild to moderate, although severe AEs and discontinuations due to AEs have been observed.

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