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A Review of the Rationale and Clinical Utilization of α 2-Adrenoceptor Agonists for the Treatment of Attention-Deficit/Hyperactivity and Related Disorders

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Journal of Child and Adolescent Psychopharmacology. June 2013, 23(5): 308-319.
doi:10.1089/cap.2013.0028.

Objective: Interest in the potential role for the α 2-adrenoceptor agonists clonidine and guanfacine as treatments for attention-deficit/hyperactivity disorder (ADHD) has driven additional clinical studies as well as development of new formulations of these agents. This article reviews the published data that supported United States Food and Drug Administration approval and subsequent clinical use of α 2-adrenoceptor agonists in the treatment of ADHD, and identifies promising directions for future research.

Methods: Electronic searches were performed in PubMed through October 2012 using the base terms ADHD or attention deficit hyperactivity disorder and alpha agonists, as well as the following limits: humans, clinical trial, meta-analysis, practice guideline, randomized controlled trial, review, English. The electronic searches were complemented with reference lists from the articles retrieved by informal search of the literature, producing a qualitative review of published, pertinent drug-class preclinical and clinical data. Articles were selected for greater exposition based on hierarchy of evidence (e.g., randomized controlled trials), relevance, and quality of individual studies, as well as generalizability to clinical practice.

Results: Results of clinical studies of immediate-release and extended-release formulations of α 2-adrenoceptor agonists and basic science investigations of cognitive effects of these drugs are discussed. Studies of both clonidine and guanfacine extended-release formulations as monotherapy and adjunctive therapy with psychostimulants for the treatment of ADHD are also reviewed.

Conclusions: Large, randomized, placebo-controlled clinical trials support the efficacy and safety of α 2-adrenoceptor agonists as monotherapy and adjunctive therapy with psychostimulants for the symptomatic treatment of ADHD. Future research could reveal whether there are cognitive

benefits associated with this drug class and thus further define the role of α 2-adrenoceptor agonists in the treatment of ADHD.