



AMERICAN
PSYCHOLOGICAL
ASSOCIATION

**Statement of Ronald T. Brown, PhD, ABPP, on behalf of the
American Psychological Association
Before the U.S. Food and Drug Administration**

Psychopharmacologic Drugs Advisory Committee

June 9, 2009

Good afternoon. I'm Dr. Ronald T. Brown, Professor of Public Health and Dean of Public Health at Temple University. Thank you for the opportunity to address you today on behalf of the American Psychological Association (APA) on the matter of the New Drug Applications filed for Geodon, Seroquel, and Zyprexa.

Three years ago, I chaired the APA Working Group on Psychotropic Medications, which surveyed the complex landscape related to the treatment of childhood mental health disorders. At the time, the Working Group delineated significant reasons for caution regarding the use of psychotropic medications in children and youth. Despite advances since 2006 in the knowledge base, the thrust of this important report remains entirely applicable: families and health care providers must act as partners in considering treatment plans to address mental health disorders among children and adolescents, and they must consider the real tradeoffs between the psychological benefits and serious risks associated with psychotropic medications.

Today, fundamental concerns persist about the research on the use of psychopharmacological treatments during childhood. First principles for treatment of children and youth are extrapolated from the adult literature, and for many reasons, few randomized controlled trials exist that involve subjects under the age of 18. Of the few pediatric studies that do exist, many include small samples sizes and attendant methodological weaknesses. Also, ecologically valid effectiveness studies often fail to reflect the gains demonstrated in controlled clinical trials. Finally, adverse side effects and safety issues exist for all drugs examined in the report, and we found a great need for more information on the long-term benefits and particularly the long-term risks associated with psychotropic medications used to treat childhood disorders.

The APA Working Group also specifically examined the literature on childhood bipolar and schizophrenia spectrum disorders and their treatment. Fortunately, these disorders occur at a very low frequency in the pediatric population, but this fact impedes quick advances in research and treatment. No studies on bipolar or schizophrenia spectrum

disorders found in the course of our literature review attempted to address long-term safety and effectiveness issues for children and adolescents.

For bipolar disorders, the Working Group included in its review ten studies on the use of psychopharmacological interventions for children and adolescents. A double-blind, placebo-controlled trial established the efficacy of Seroquel as an adjunct to valproate, but no studies specifically examined the efficacy or safety of Seroquel itself. Open trials supported the use of Zyprexa but included no control group and yielded results that our Working Group labeled “no evidence” of effect. We found no studies on Geodon.

The profile looked similar for diagnoses in the schizophrenia spectrum. For Zyprexa, we reviewed one randomized double-blind study that yielded results we labeled “no evidence” of effect, and additional studies of this drug used no control group and yielded results we labeled “no evidence” or “small evidence” of effect. Case studies, valuable as an early stage of the treatment research process, show benefits from Geodon in the treatment of psychosis. We found no studies on Seroquel.

The recent literature continues to bear out consistently the same adverse side effects associated with atypical antipsychotics that the Working Group found. These include:

- Weight gain that potentially can lead to type 2 diabetes, lipid level changes, and liver transaminase elevation;
- The less-common problem of tardive dyskinesia (abnormal involuntary movement);
- Sustained tachycardia;
- Somnolence, difficulty concentrating, and others.

Despite these findings, the reality stands: bipolar disorders and schizophrenia present serious and significant impediments to quality of life for young sufferers and their families, and first-line treatments depend heavily on psychopharmacological agents. Be assured that the APA understands the benefits gained from the use of atypical

antipsychotics and believes earnestly in the rights of families, children, and youth to the best available treatment. It is APA's sincere hope, though, that the deployment of such drugs to treat childhood disorders would be a choice made under the best of conditions, represented by a collaborative approach between families and health care providers armed with the most comprehensive information possible.

In closing, I respectfully ask that the Advisory Committee consider these three points during tomorrow's votes: first, that over the three years since APA released the findings of the Working Group, serious questions have not been answered regarding the long-term effectiveness and, more importantly, safety of atypical antipsychotics in treating childhood disorders; second, that continued, strong development of the research and knowledge base related to serious emotional disturbance and its treatment during childhood should be of the highest priority; and finally, that physicians may continue prescribing Geodon, Seroquel, and Zyprexa off-label to children, as we continue to grow this knowledge base.

Thank you very much for the opportunity to present this statement.