

## **FDA Psychopharmacologic Drugs Advisory Committee Hearings April 7 – 8, 2009**

On Tuesday, April 7, the Advisory Committee reviewed the request from Lundbeck, USA, that Seroquel (quetiapine) be granted FDA indication approval for the treatment of schizophrenia for adult patients. Lundbeck, USA and the FDA presented data from clinical trials on the efficacy and safety of this medication for the treatment of schizophrenia and the treatment of suicidal behavior in schizophrenia. After thorough discussion, the Committee held the following votes regarding efficacy: 1) they found that Seroquel had been shown to be effective for the treatment of schizophrenia (unanimous vote); and 2) they voted against (12 – No, 1- Yes) the statement that Seroquel was an effective treatment of suicidal behavior in schizophrenia. The Committee determined that the study trials were not developed to address this issue and the data did not meet efficacy standards. Additionally, the Committee voted no (12 – No, 1 – Yes) to the question regarding the overall safety of this medication for the purposes of broad treatment and voted yes (8 – Yes, 2 – No, and 3 Abstention) that the medication could be acceptably safe for certain patient populations. The members of the Committee who had voted yes explained that they believed there were some patients who had failed first line treatments that may find a benefit from Seroquel. Safety concerns noted with this medication included sudden cardiac death, suicide attempts, and QT prolongation factors. Two individuals provided public comments encouraging the Committee to ensure an adequate array of treatment options are available to the many individuals suffering from this disorder. AACAP members serving on the Committee included **Robert Hendren, D.O. (AACAP President)**, Chief of Child and Adolescent Psychiatry at the University of California, Davis and Executive Director of the M.I.N.D. Institute, **Richard Malone, M.D.**, Professor of Psychiatry, Drexel University College of Medicine, **Daniel Pine, M.D.**, Chief of Child Adolescent Research, National Institute of Mental Health, Mood and Anxiety Disorders Program, and **Marcia Slattery, M.D., M.S.**, Associate Professor of Psychiatry, University of Wisconsin School of Medicine and Public Health.

The same Advisory Committee (with some Committee member changes) met on Wednesday April 8, 2009, to review Astra Zeneca Pharmaceuticals LP request for FDA approval of Seroquel XR (quetiapine maleate extended release) for two new additional indications for adult major depressive disorder (MDD) and generalized anxiety disorder (GAD). (Seroquel XR is already approved for adult schizophrenia and bipolar disorder.) In the morning, the Committee listened to five presentations from Astra Zeneca Pharmaceuticals LP and two different presentations organized by the FDA --including one from external consultant Wayne Ray, Ph.D. author of the *New England Journal of Medicine* article “Atypical Antipsychotics and the Risk of Sudden Cardiac Death” which included Seroquel XR clinical trial data. The FDA presented a fascinating discussion about the doubtful validity of reports of sudden cardiac death.

At Noon, fourteen non-committee public representatives spoke for 3 minutes each. Several speakers represented families of loved ones who had experienced a fatal side effect while taking Seroquel so they advised disapproval of the extended indications. Several of the deceased family members were veterans returning from war being treated with Seroquel for post traumatic stress disorder. Three individuals represented health

organizations including the National Research Center for Women and Families (urging the Committee to carefully review the data and safety concerns) and the National Council for Community Behavioral Healthcare (requesting the Committee consider the need for additional treatment options for patients). AACAP was represented by **Laurence Greenhill, M.D.**, President-elect, who expressed concern about the probable increased use of Seroquel XR off-label in children and adolescents if new indications were granted and the need for more research to identify safe new treatment options for pediatric patients. ([Click here to review the oral comments provided by AACAP.](#))

At the end of the meeting, the Committee voted on the efficacy and on the safety of Seroquel XR in a series of votes. They voted *Yes* (9 – Yes, 1 – No) in regards to Seroquel XR being an effective adjunct treatment for major depressive disorder; *Yes* (8 – Yes, 1 – No and 1 Abstention) in regards to it being an effective treatment for major depressive disorder; and *Yes* (7-Yes, 2 – No and 1 Abstention) in regards to it being an effective treatment for generalized anxiety disorder. They also voted *Yes* (6 – Yes, 3 – No) indicating that it had been shown to be acceptably safe as an adjunctive treatment for major depressive disorder. They unanimously voted *No* to both questions regarding its safety for the monotherapy treatment of major depressive disorder or generalized anxiety disorder; and voted *No* concerning its safety as monotherapy in certain special populations that either have major depressive disorder (4-Yes, 4-No, and 1-Abstention) or generalized anxiety disorder (2-Yes, 6-No, and 1 Abstention).

What were the reasons for the lack of agreement among the Committee? Those who voted “no” indicated there were no data to support the long-term use of these medications and no data on its long-term risks. There were safety concerns about the reports of those taking Seroquel XR experiencing sudden cardiac death, suicidality, long-term metabolic safety, and Tardive dyskinesia. The studies provided by the sponsor were based on inclusion criteria of those individuals who had previously had an inadequate response to an antidepressant, but no data were provided on the use of the indication as an add-on or adjunctive treatment.

AACAP members serving as voting members on the Psychopharmacologic Drugs Advisory Committee included **Richard Malone, M.D.**, Professor of Psychiatry, Drexel University College of Medicine, and **Daniel Pine, M.D.**, Chief of Child Adolescent Research, National Institute of Mental Health, Mood and Anxiety Disorders Program. (*Please note one member departed the meeting early changing the voting member number from ten to nine.*)

To view copies of the data and presentations provided during the hearings, please visit the FDA website.

<http://www.fda.gov/ohrms/dockets/ac/cder09.html#Psychopharmacologic>

It is anticipated that another FDA Psychopharmacologic Drugs Advisory Committee hearing will be held June 9-10, 2009 to review additional data on the use of antipsychotic medications.