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Richard Kahn, PhD
Chief Medical and Scientific Officer
American Diabetes Association
1701 N. Beauregard St.
Alexandria, VA 22311

RE: Consensus Development Conference on Antipsychotic Drugs and Diabetes

Dear Dr. Kahn:

We wish to commend the ADA for convening the consensus conference on this important topic. As the company that originally sought to partner with the ADA to hold a workshop on this topic, Eli Lilly and Company appreciates the ADA's commitment to developing guidelines for clinicians and identifying the potential impact these recommendations may have on treatment outcomes in patients with severe mental illness.

We appreciated the opportunity to attend the conference and to briefly present highlights of the extensive studies that have been conducted by Eli Lilly and Company. We hope the material we forwarded to you prior to the conference was informative and contributed to the writing panel's evaluation of this topic.

After reflecting on the content and tone of the presentations, we would like to share with you several concerns about the proceedings and their potential outcomes:

We do not believe that adequate consideration was given to the epidemiology of diabetes in patients with severe mental illness, and the relevance of risk factors for diabetes in this population irrespective of antipsychotic treatment choice. Although mounting evidence indicates that the prevalence of diabetes is substantially greater among patients with severe mental illness, this important topic was left largely unaddressed during the conference.

2. With the exception of the Lilly presentation, little or no consideration was given to data that indicate a significant association between the development of diabetes and overall risk factor load. Rather, the proceedings focused more exclusively on weight gain or drug assignment as potential determinants of diabetes risk. This focus was not consistent with our understanding of the primary purpose of the conference, and resulted in less attention being paid to other elements critical to the understanding of antipsychotic drugs and diabetes. This includes the vulnerability of schizophrenic patients to development of diabetes and the importance of evaluating overall risk factor load, irrespective of treatment assignment. In fact, the Canadian Diabetes Association has recently published guidelines that specify schizophrenia as a risk factor for diabetes, illustrating the increasing recognition that the increased prevalence of diabetes in patients with schizophrenia represents a significant public health concern.

3 Many of the non-industry speakers at the conference presented unpublished data that did not have adequate description of methodology, nor benefit of peer review. The Lilly presentation was given less time than other industry sponsors, which limited our ability to fully address all of the data relevant to this issue.

4. Although not the purpose of this conference, the topic of differential efficacy and overall side-effect profiles of antipsychotic drugs was not discussed. These are critically important points of discussion, as antipsychotic drug choice is predicated on the balance of multiple facets of each drug's attributes as they relate to specific patients. A comprehensive benefit-versus-risk assessment should not be based solely on one criterion, such as potential to induce weight gain.

We would like to take this opportunity to reassert Lilly's conclusion that the available data are insufficient to provide reliable estimates of differences in hyperglycemia-related adverse-event risk among patients treated with different atypical antipsychotics. This conclusion is consistent with FDA's determination that labeling for all atypical antipsychotics should be updated to include a warning regarding hyperglycemia and diabetes mellitus.

Further, risk factors for diabetes characterized in the general population appear to overlap the risk in patients with schizophrenia, and multiple lines of evidence support a higher prevalence of diabetes in patients with serious mental illness. Finally, antipsychotic drug choice must be made by considering *all* relevant data relative to the efficacy and side-effect profile of each agent.

We hope the Consensus Statement, which clinicians will use to guide their evaluation of patients with severe mental illness, will emphasize the need to screen for baseline diabetes risk factors irrespective of choice of antipsychotic therapy, and will provide guidelines for appropriate monitoring once a therapy is selected. Should the Consensus Statement lack this emphasis, patients treated with some antipsychotic agents may be viewed as not having an increased risk of development of diabetes, while concern about patients treated with other agents – disproportionate to the currently available evidence – may lead to inappropriate withdrawal of treatment. Both scenarios have the potential for inadequate clinical evaluation and monitoring, adverse patient care decisions, and deleterious clinical outcomes in a patient population at high risk for diabetes.

Through its established record of excellence in neuroscience and diabetes research, Lilly is committed to its continuing partnership with ADA to provide answers to clinicians and patients. We believe that recommendations that may influence clinicians' antipsychotic treatment choices and patient outcomes should be based on in-depth, objective evaluation of the totality of the data currently available.

Given the importance of these issues, we request the opportunity to further discuss our concerns prior to publication of the Consensus Statement. The ADA may wish to extend this same opportunity to the other sponsors.

Sincerely,

Alan Breier, MD
Chief Medical Officer and Vice President, Medical
Eli Lilly and Company

Patrizia Cavazzoni, MD
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Global Product Safety
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cc: Nathaniel Clark, MD, Vice President, Clinical Affairs, ADA
Darrel A. Regier, MD, MPH, Director, Office of Research, APA
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