AMERICAN
EPILEPSY
SOCIETY

December 5, 2008

Russell Katz, M.D.
Food And Drug Administration
10903 New Hampshire Avenue
Room 4332
Silver Spring, MD 20993-0002

Dear Dr. Katz,

The Board of Directors of the American Epilepsy Society has examined carefully the results of the meta-analysis conducted by your office on the potential relation between the use of antiepileptic drugs (AED) and an increased suicidality risk. The Board has taken this matter very seriously. I have created a task force to examine the data very carefully, to follow on any new findings from the meta-analysis and to recommend specific steps that clinicians and patients need to follow to minimize any suicidality risk.

I understand that the data of the meta-analysis were reviewed by an Advisory Board that met in June of this year at the offices of the FDA. The Board recommended that warnings on this potential risk be included in the insert packages of AEDs, but voted against the inclusion of a black box. The Board members agreed with this recommendation.

I am writing this letter to express the unanimous concern of our Board's members regarding a potential misinterpretation by patients, families and physicians of the warnings to be included in the package insert of AEDs. In our opinion, such warnings may result in serious consequences with devastating results for the following reasons:

1) The warnings may cause significant worry and confusion in patients with epilepsy and their families, because they may misinterpret the magnitude of the suicidal risk identified in the meta-analysis. Indeed, they may construe such risk as being very high, when in fact the data suggested an extremely low risk (0.2%). This may lead patients to discontinue their AEDs without discussing it with their physician causing self-harm and including death. As you know, a recent study has demonstrated a greater than three-fold increase in mortality risk associated with non-compliance to AEDs (Faught E et al, Neurology 2008).

2) Physicians who do not specialize in epilepsy may be concerned about prescribing AEDs for fear of being sued. As you know such a precedent already exists in the way SSRIs were prescribed following the black box warning. Indeed, a significant drop in the prescription of SSRIs in children and adolescents with depression followed the inclusion of a black box warning in the package insert.

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In addition, an increased refusal by parents to have their children take these medications was also identified.

3) The members of the Board were also concerned about the committee's recommendation to extend the warning to *all* AEDs. While we understand their rationale for such recommendation, (a concern that clinicians would limit their prescription of

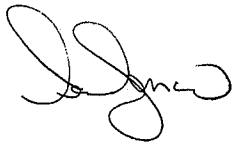
AEDs to those not included in the meta-analysis), we think that it is inappropriate for an official warning not be supported by actual data.

Our Board recognizes the importance of screening patients with epilepsy for comorbid psychiatric disorders and suicidal risk at the time of their initial evaluation and throughout their treatment. Yet, our members consider that the inclusion of a warning in the package insert of AEDs may cause more harm than good.

Therefore, we encourage you to seriously consider these concerns in the formulation of the warnings you plan to include in the package inserts of AEDs. Our Society will work very closely with our members and with other professional societies to provide the necessary education to help clinicians screen patients for comorbid mood, anxiety disorders and suicidal risks prior to and throughout their treatment with AEDs. We are also eager to work with your office on this matter for the benefit of patients.

Please do not hesitate to contact me if you have any questions. I appreciate your attention to this matter.

Sincerely,



Dennis Spencer, MD
President,
American Epilepsy Society