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BEHAVIORAL NEUROLOGY
NEUROPSYCHIATRY
FUNCTIONAL MEDICINE

August 26, 2004

Division of Dockets Management (HFA-305)
Food and Drug Administration
5600 Fishers Lane, Room 1061
Rockville, MD 20852

Dear Sir/Madam,

I am a Clinical Nurse Specialist in Child and Adolescent psychiatry working with prescriptive privileges in Massachusetts in a Behavioral Neurology/Neuropsychiatry office. I am familiar with the ongoing discussion regarding the increased risk of suicidal behavior when treating pediatric and adolescent clients with SSRI medication.

I'd like to offer several ideas for your consideration that I have learned from my experience:

- 1) My colleague, Dr. Paul Hardy, and I long ago realized that all SSRI medications carry the risk of increased agitation, aggression, hypomanic states, and sometimes risky and suicidal behaviors when given to pediatric and adolescent clients. We use the term "activation" to describe the overall pattern we see. We always instruct our clients and their families to watch for increased sleep problems, especially difficulty falling asleep, restlessness, louder or more aggressive behavior, etc. This instruction generally keeps our clients from escalation to the point of danger. Sharing several scenarios that actually happened to my clients is usually helpful to the families trying to remember these side effects. I describe an uptight, very anxious 8 year old who "mooned" his classmates on the playground after starting Paroxetine, and a 5 year old on Fluoxetine for anxiety who told her mother to get her "fat face out of the way", this from a child who never addressed her mother this way before.
- 2) Many prescribing practitioners including local psychiatrists fail to inform families of these risks. As you already know, most general physicians and nurse practitioners have not known to give these warnings. We often hear stories of these children starting on the SSRIs and who respond with physical restlessness and become verbally fresh with their parents. The clinician response is to

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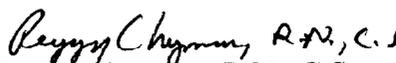
increase the dose and as a result and the story gets worse. Unfortunately, sometimes the initial depression or anxiety seems better so no one is recognizing the “activation” response.

- 3) As has been commented on by committee work already, the history of bipolar illness in the family dictates that more cautious instruction be conveyed to the family about this reaction occurring. Our experience is that activation absolutely occurs more in family members with this positive family history.
- 4) The drug companies, from what I am told, have carefully screened out potential candidates for antidepressant studies if there is a history of bipolar illness in the family. A Lilly drug representative told me that Lilly carefully screened out all subjects with any bipolar family history for their Strattera Phase 3 studies. When Strattera first came out I asked a very knowledgeable drug representative about activation side effects and we both noted that the drug literature states “aggression” and “anxiety” as reasons for some subjects not completing the study and “mood swings” were listed under common adverse reactions. If the antidepressant drug studies that you are reviewing have regularly screened out subjects with any family bipolar history then even the results of the reviews you are now undertaking will under report the agitated, aggressive and suicidal behaviors that will occur in the general population when given these medications. Since many parents and prescribers are going to rely on the results of your review, I feel that this screening information is paramount to factor into the review and comments that you will be making.
- 5) Although your mission is to study the trials of medication for antidepressants, I feel strongly that you need to comment on Strattera. It is psychopharmacologically an antidepressant. Hundreds of prescriptions are being written for this medication and these clients need the same instruction and warnings for this medication as with the antidepressants. We have seen the exact same activation response with Strattera as with SSRIs.
- 6) Because our office specializes in Behavioral Neurology and Neuropsychiatry we treat a large population of clients with neurologic problems, autism, mental retardation, etc. It is our experience that this population has a much higher risk, probably over 60%, of becoming activated on SSRI medication. The SSRI studies you are reviewing will not reflect this data at all. There are some published reports of SSRI use in this population and some of them comment on some patients worsening with these medications. This area needs further exploration and comment for future guidance to all practitioners.

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Thank you for your consideration of my comments. If you have further questions I can be reached at 781-740-8300.

Sincerely,


Peggy Chapman, R.N., C.S.