

**MEMORANDUM      DEPARTMENT OF HEALTH AND HUMAN SERVICES  
PUBLIC HEALTH SERVICE  
FOOD AND DRUG ADMINISTRATION  
CENTER FOR DRUG EVALUATION AND RESEARCH**

**DATE:**      **January 2, 2004**

**FROM:**      Susan Cummins, M.D., M.P.H.  
Medical Team Leader  
Division of Pediatric Drug Development  
HFD-960

and

Thomas P. Laughren, M.D.  
Team Leader, Psychiatric Drug Products  
Division of Neuropharmacological Drug Products  
HFD-120

**SUBJECT:**    Overview for February 2, 2004 Meeting of Psychopharmacological Drugs Advisory Committee (PDAC) and Pediatric Subcommittee of the Anti-Infective Drugs Advisory Committee (Peds AC)

**TO:**          Members of PDAC and Peds AC

On February 2<sup>nd</sup>, the PDAC and Peds AC will meet to consider the emergence of suicidality in the course of treatment of pediatric patients with various antidepressants, in particular, those patients being treated for major depressive disorder (MDD). At the meeting, we will present background information on this issue, data from the Adverse Event Reporting System (AERS) database, and preliminary data from placebo-controlled clinical trials in pediatric MDD. We have two goals for this meeting: to provide both committees with background information on these issues and to obtain advice from you about how to best address the methodological issues involved in the further evaluation and interpretation of these data so that you can help us to move forward in addressing this concern. We anticipate that we will hold a second meeting in the summer of 2004 to seek further advice on these issues.

To prepare you for these deliberations, you will first hear presentations by experts in adolescent suicidality. Dr. Cynthia Pfeffer, from the Weill Medical College of Cornell University, will address adolescent depression and suicidality, and its treatment generally. Dr. David Shaffer, from the College of Physicians and Surgeons at Columbia University, will discuss the epidemiology of adolescent depression and suicidality.

Dr. Solomon Iyasu, Medical Team Leader with the Division of Pediatric Drug Development will report on adverse events, including treatment emergent suicidality, for the first year of marketing

following the granting of exclusivity for the following two drugs that were granted market exclusivity under 505A of the Federal Food, Drug, and Cosmetic Act: Paxil (paroxetine) and Celexa (citalopram). These reports are required under section 17 of the Best Pharmaceuticals for Children Act. Importantly, his talk will be followed by presentations from staff of the Office of Drug Safety on spontaneous reports of treatment emergent suicidality for the first three years of marketing for all antidepressant drugs in order to place the findings Dr. Iyasu will be presenting into perspective.

Dr. Laughren will provide an overall clinical and regulatory perspective on the evolution of concerns about suicidality associated with antidepressant drug treatment, with a particular focus on the recently emerging suicidality data from various drug development programs involving the use of antidepressant drug products in pediatric patients with MDD. Dr. Kelly Posner, from Columbia University, will provide a brief perspective on the plans for a blinded reclassification of the events identified in these trials as possible representative of suicidality. Finally, Dr. Tarek Hammad, from the Safety Group in the Division of Neuropharmacological Drug Products, will briefly discuss our plans to analyze patient level data sets that we have recently obtained from the sponsors of these various pediatric studies.

There will be two open public sessions during the Feb 2<sup>nd</sup> meeting, one in morning, and one in the afternoon, to provide an opportunity for others in the community to make statements pertinent to this concern about a possible causal association between antidepressant drug treatment and emergent suicidality in pediatric patients.

While we will not be seeking specific votes from the committees on any definitive regulatory actions regarding this concern, we will seek your guidance on various methodological issues pertinent to our continuing review of the clinical trials data. These methodological questions are presented in Dr. Laughren's separate background memo for the committees.

The background package for this meeting will include the following documents in addition to this cover memo:

- Four guidance documents/review papers on pediatric depression and suicidality:
  - American Academy of Child and Adolescent Psychiatry (AACAP) Practice Parameter for the Assessment and Treatment of Children and Adolescents With Suicidal Behavior (J. Am. Acad. Child and Adolesc. Psychiatry, 40 (7):24S-51S, 2001)
  - A summary of the AACAP guideline the assessment and treatment of pediatric depression from the Agency for Health Care Research and Quality Clinical Guidelines clearinghouse website: [http://www.guideline.gov/summary/summary.aspx?ss=15&doc\\_id=1531&nbr=757](http://www.guideline.gov/summary/summary.aspx?ss=15&doc_id=1531&nbr=757)
  - American Academy of Pediatrics, Committee on Adolescence, Policy Statement on Suicide and Suicide Attempts in Adolescents (Pediatrics, 105(4): 871-874, 2000)
  - Youth Suicide Risk and Preventive Interventions: A Review of the Past 10 Years (Gould, Greenberg, Velting, and Shaffer; J. Am. Acad. Child and Adolesc. Psychiatry, 42 (4):386-405, 2003)

- A background memo by Dr. Laughren providing an overall clinical and regulatory perspective on the evolution of concerns about suicidality associated with antidepressant drug treatment, with a particular focus on the recently emerging suicidality data from various drug development programs involving the use of antidepressant drug products in pediatric patients with MDD;
- A summary of Pediatric Exclusivity statistics, associated labeling changes for pediatric major depressive disorder for fluoxetine, and the sample Written Request template for the study of antidepressants in pediatric patients; and
- Product labeling for all 7 antidepressants that have been studied in pediatric MDD in these pediatric development programs.

The FDA relies on the knowledge, judgement, experience and wisdom of scientists and practitioners like you to help determine how to move forward and address newly emerging issues related to drug development. We thank you for your time and effort, and we look forward to seeing and hearing from you on Feb 2<sup>nd</sup>.

cc:

HFD-120/TLaughren/RKatz/JRacoosin/PDavid

HFD-960/SCummins/DMurphy

HFD-040/RTemple

HFD-020/JJenkins

**DOC:** PDAC\_Memo\_Feb2004\_Cover01.doc