

December 18, 2003

Mark McClellan, M.D.  
Commissioner  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD 20857

Dear Dr. McClellan,

I am writing to you as an individual member of the Advisory Committee for Reproductive Health Drugs at the FDA. As I am sure you are aware, my appointment to this committee has been quite controversial. I am not writing to you out of concern about those controversial issues, but out of concern that, as always, the FDA carefully evaluate the data regarding a switch to over-the-counter availability of Plan B, which was addressed at our December 16, 2003 meeting.

My major concerns are related to the health and well-being of the women of this country, but especially adolescents. There was a great deal of discussion about the need for adolescents to be able to take medication that can prevent pregnancy. It is also important that these young women and their parents understand that there is the possibility that this medication may act on the endometrium to interrupt implantation, if they believe that pregnancy begins at fertilization. (See studies by Croxatto and Ugocsai, which are in our documents)

There were two major studies that were used as background in the decision to recommend the switch to OTC availability. The Label Comprehension Study (LCS) involved 656 women. Unfortunately, literacy evaluations were not done in women 18 years of age and younger. This is the group of young women who would be greatest at risk for not understanding the package insert and directions. This LCS indicated that 25% of women would take the medication in spite of undiagnosed vaginal bleeding (the sponsor wanted this eliminated as a risk factor), 33% did not understand that Plan B was only intended for backup contraception, and 19% did not understand the need to obtain a medical evaluation for severe abdominal pain.

In the Actual Use Study (AUS), comprising 665 women who were given one pack of Plan B, and were then followed for only four weeks, 94% of these women were enrolled in family planning clinics. Family planning clinics are not a typical OTC population. In addition, 84% had a high school education, which also may not adequately demonstrate the educational

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level of women who would obtain these products. My major concern is that only 29 (4.4%) of these women were 14-16 years of age. Thus, adolescents were not evaluated for literacy and very few were entered into the study.

We were told by the FDA staff that the "Pediatric Rule" would not be invoked in this situation and that this drug would be available to children and adolescents of all ages. Dr. McClellan, as a practicing obstetrician/gynecologist, I have great fears that approval of this OTC status will allow young women to have no medical evaluation or followup. In the Washington State data where pharmacists can dispense Plan B, we find that 81% of those subjects were felt to need medical followup. We are not told how many of them obtained medical followup.

The current national recommendations from the CDC are for us to screen sexually active adolescents for chlamydia and gonorrhea on an annual or semi-annual basis, and to do annual PAP smear screening to check for cervical pathology and HPV infection. In addition, many of these sexually active young people have HIV screening. One of the major reasons why they have seen us for such screening has been contraception. Now, these young people will have no incentive for annual screening.

I also have a great concern about those women of low socio-economic and educational status. The sponsor indicated that they would use pricing to prevent "repetitive dosing" of the product. Will this exclude lower socio-economic women from the availability of the drug? I don't think that we know that answer.

In England, where pharmacists have been able to dispense (since January 2001) levonogestrel, there has been an increase in sexually transmitted infections. In Scotland, there has been an increase in STIs as well as teen pregnancy. In Thailand, the most frequent purchasers are males who then dispense it to their female partners. In the Label Comprehension Study (LCS), fully one-third of the women did not understand that this medication was only for backup contraception.

It is with these grave concerns that I write as a practicing gynecologist to encourage you to consider asking that further data be obtained prior to approving this switch. We need longer term data among those who repetitively dose the medication. We also need more

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information among adolescents as to their ability to understand the package insert, use the medication correctly, not use it as their primary method of contraception, and continue to use contraceptive measures, as well as seek regular screening from their physicians. Thank you for your attention to these concerns. I look forward to hearing from you about this.

Sincerely,

A handwritten signature in black ink, appearing to read "W. David Hager". The signature is written in a cursive, somewhat stylized font.

W. David Hager, M.D., FACOG  
Professor (PT) and Consultant in Infectious Disease

WDH/tlb