

MEMORANDUM

DATE: May 6, 2004

FROM: Steven Galson, MD, MPH
Acting Director, Center for Drug Evaluation and Research

TO: NDA 21-045

SUBJECT: Review of NDA for Rx to Over the Counter Switch for Plan B

I have read and carefully considered all of the reviews in the action package for this application. I do not concur with the recommendation by the Office of New Drugs to approve Barr's application to switch Plan B to over-the-counter (OTC) status. My decision is based on the lack of available data relevant to OTC use of the product by adolescents younger than 14 and very limited data in the 14-16 age group. Without data in the application on OTC use in this age group, and lacking confidence that data from older adolescents can be confidently extrapolated to this age group, I find the proposal to switch Plan B from Rx to OTC use — thus making it available to very young adolescents — to be unsupported. Specific concerns regarding the application include the following:

- Sexual activity among 11- to 14-year-old females in the United States is well documented.¹ Despite the urgent need to prevent pregnancy in these young adolescents, the application contained no data in subjects under 14 years of age.
- In making decisions about pediatric use, it is often possible to extrapolate data from one age group to another, based on knowledge of the similarity of the condition. However, in this case, adolescence is known to be a time of rapid and profound physical and emotional change. For example, during early adolescence (10-13), this age group experiences the emergence of impulsive behavior without the cognitive ability to understand the etiology of their behavior. During mid-adolescence (14-16), youth begin to develop the capacity to think abstractly; however, their ability to integrate their emerging cognitive skills into their real-life experiences is immature and incomplete. The capacity to understand complex concepts, which develops during middle adolescence, allows adolescents to modulate their impulsive behavior.² Because of these large developmental differences, I believe that it is very difficult to extrapolate data on behavior from older ages to younger ages. I am uncomfortable with our current level of knowledge about the potential differential impact of OTC availability of Plan B on these age subsets.

¹ "14 and Younger: The Sexual Behavior of Young Adolescents," The National Campaign to Prevent Teen Pregnancy, May 2003).

² *Rudolph's Pediatrics*, 21st edition, Chapter 3.1, Growth and Development, Psychological Development During Adolescence.

I also have the following concerns:

- The additional studies cited in the Office of New Drugs reviews do not approximate actual OTC use sufficiently to support approval. Although the studies are relevant, none tests the hypothesis that typical adolescent consumers with no extra information will use the product correctly. The studies are either not conducted in the general population or they provide product education assistance beyond what adolescents would receive in an OTC situation, where no contact with a health care professional is expected. Likewise, the literature review submitted to address questions of important potential behavioral changes associated with availability of an emergency contraceptive (e.g., substitution of the product for routine and more effective contraception, or increased medically risky sexual behavior) did not contain studies that mimic what would be actual OTC availability.
- The number of adolescent participants in the actual use study is too small to generalize to the U.S. population of adolescents. I do not believe the data set on this age group is large enough to reach valid conclusions from the study.

Some staff have expressed the concern that this decision is based on non-medical implications of teen sexual behavior, or judgments about the propriety of this activity. These issues are beyond the scope of our drug approval process, and I have not considered them in this decision.

The need for data on young adolescent behavior discussed in this memo does not apply to prescription contraceptive products because use of prescription products involves monitoring by health care practitioners and, most-likely in this age group, parents.

I will be working toward the expeditious evaluation of Barr's proposed access plan when we receive a complete version. If it is approved, this plan would dramatically increase access of this product and will represent an important incremental step forward in contraceptive availability in the United States.

Wider availability of safe and effective contraceptives is important to public health. I look forward to supporting CDER's important continued role in ensuring improved availability of these products.

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/s/

Steven Galson
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MEDICAL OFFICER
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