[Docket Number 2005N-0345] RIN 0910-AF72

Date: September 1, 2005
To: Food and Drug Administrators
From: Anne Kisly
Regarding: Agency Request for Information pertaining to levonorgestrel, Plan B
Note: My comments are in italics and follow each question.

1. A. Should FDA initiate a rule making to codify its interpretation of section 503(b) of the act regarding when an active ingredient can be simultaneously marketed in both a prescription drug product and an over-the-counter (OTC) drug product?
I think the text and examples provide clear examples of when a drug product may be marketed as both prescription and OTC. Examples should not be interpreted to mean that they cover all situations. They are after all, examples.

B. Is there significant confusion regarding FDA's interpretation of section 503(b) of the act?
The interpretation of it may be confusing because, as in the case in question, the safety data for levonorgestrel is different from the safety data in the examples and the past regulatory decisions. I would expect decisions regarding prescription(RX) and OTC access to be made on a case-by-case basis. Not all drugs will fit the examples provided. The regulatory interpretation of section 503(b) will never explicitly address all the different possible situations.

C. If so, would a rule making on this issue help dispel that confusion?
I think a sentence could be added to clarify that decisions are made on a case-by-case basis. I doubt that any rule is hard and fast and will cover all submissions.

2. A. If FDA limited sale of an OTC product to a particular subpopulation, eg, by making the product available to the subpopulation by prescription only, would FDA be able to enforce such a limitation as a matter of law?
Someone would have to act in the role of the enforcer. In the case of the OTC availability of levonorgestrel, the pharmacist would have to check the consumer's age by asking for personal identification. The pharmacist would have to assume the person, if of legal age, is buying it for herself or for someone who is of legal age. The assumption is the problem.

B. If it could, would it be able to do so as practical matter and, if so, how?
No. I do not think it is practical. We know that minors have friends who are of legal age who buy restricted items for them. The situation with levonorgestrel is no different. Consider the motivation level of a young woman who does not want to handle an unwanted pregnancy. The motivation to acquire and take emergency contraception (EC) would be high. While a licensed medical practitioner could still prescribe and counsel the younger patient on the safe use of EC, I'm not convinced this is an absolute necessity. ***If*** *there are data, from a randomized controlled study, that show a younger woman is at risk if her access to EC is not limited by prescription and she does not receive counseling, I would challenge the extrapolation of the findings from the sample of study participants in the study to the population at large. I expect a highly-motivated young woman would read and follow the instructions on an OTC product.*

3. A. Assuming it is legal to market the same active ingredient in both a prescription and OTC product, may the different products be legally sold in the same package?

Do you mean the same products (not different in terms of strength, route of administration, indication, etc) or the same package? Is less information required on an RX package because someone assumes the licensed practitioner provides counseling, than an OTC package? The patient or consumer information, regarding dosing instructions and safety risks provided in the package, should be the same for a product available OTC or RX. An OTC package should list the following in large font size: (1) specific situations in which levonorgestrel should NOT be used; (2) the side effects to be expected; (3) information for special groups, possibly diabetics? The choice of words should be carefully selected, eg, side effects not adverse events, specific situations in which levonorgestrel should NOT be used, not contraindications.

B. If the 2 products may be lawfully sold in a single package, under what circumstances would it be inappropriate to do so?

This must be determined on a case-by-case basis. All possible scenarios can't be foreseen. As soon as we agree, this circumstance or that circumstance requires different packages, another circumstance will arise to be an exception.

The question we have been asked to address is whether Plan B should be available without a prescription on a pharmacy shelf, similar to the way other OTC medicines like some cough syrups and allergy pills are sold, for women age 16 and older, and remain prescription-only for those under the age of 16.

How severe are the side effects (nausea and vomiting) if taken incorrectly, enough to meet the criteria for a serious adverse event, or are they mild, transient events that occur in isolation (without other events)? Are the proposed dosing instructions in the package provided by the drug company clearly written, such that counseling by a licensed practitioner is not necessary?

Can age be used as a criterion on which we decide whether a drug should be prescription or OTC, as has been proposed in this case?

I would question if factors other than age comprise the real underlying basis for restricting access to a medication. In the case of EC, age, in and of itself, is not a valid criterion for ethical reasons. I don't think the majority of women should have restricted access to EC, because a few women are at greater risk from of a lack of understanding dosing requirements, dosing limitations, lack of understanding the potential safety issues, etc.

In the case of levonorgestrel, the decision to restrict access by younger women sends a message to young women that they can't read and understand instructions on a package that describes dosing instructions, safety warnings, etc. Limiting access to EC to younger women is not ethical and is discriminatory, because it assumes low intellectual abilities and poor judgment on the part of the younger women.

My 12-year-old son, with his 7th grade education, can walk into a store, buy, and take aspirin or Tylenol following the dosage chart on the bottle. Am I supposed to be convinced that young women are less intelligent than he is in understanding how to take an OTC drug?

The FDA's drug center, the Center for Drug Evaluation and Research or CDER, completed its review of this application, as amended, and has concluded that the available scientific data are sufficient to support the safe use of Plan B as an over the counter product, but only for women who are 17 years of age and older.

The decision to restrict access by younger women sends a message to young women that they can't read and understand instructions on a package that describes dosing instructions, safety warnings, etc.

I have a question for you. Is this really about concern for the safety of younger women, or is it about preventing legal problems if young women acquire the drug OTC, take the drug incorrectly, develop safety issues then sue the pharmaceutical company and accuse the FDA representatives of not doing their jobs? *A prescription is no guarantee that the patient received the necessary counseling from the licensed practitioner on the specifics of how to use the medicine correctly, regardless of age. A prescription is no guarantee that the patient will be compliant, regardless of age.*

I commend you on your extensive safety review. Please continue. Since when was Congress staffed by anyone who knows anything about evaluating the safety of drugs?