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Letters

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Isotretinoin and Pregnancy

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To the Editor: Since 1983, when the teratogenicity of isotretinoin was first documented in humans,[1] the Dermatologic and Ophthalmic Drugs Advisory Committee of the US Food and Drug Administration (FDA) has met frequently to make recommendations to balance the needs of patients with severe cystic acne to receive isotretinoin with the need to protect fetuses from exposure.[2] Central to these efforts has been a sponsor-developed pregnancy prevention program (PPP). Unfortunately there has been suboptimal participation in the PPP, and noncompliance with aspects of the program has been documented.[2] Most importantly, pregnancies have continued to occur in women receiving this drug. In fact, since the drug was approved in 1982, the sponsor has documented 1995 isotretinoin-exposed pregnancies–clearly this is an underrepresentation of the total number of exposed pregnancies as the enrollment in the PPP has been low.[2] On September 18, 2000, the FDA's Advisory Committee recommended new restrictions on prescribing and dispensing of isotretinoin that included the following:

(1) Improvements in educating the public, as well as physicians, about the PPP and changes to the informed consent process. Both of these recommendations represent revisions suggested by the sponsor.

(2) Mandatory, not voluntary, registration in the PPP by all female patients.

(3) Continued monitoring of the impact of the PPP through the isotretinoin pregnancy registry administered by the Slone Epidemiology Unit (SEU) at Boston University. In addition, the sponsor will be required to use independent surveillance systems to identify pregnancy exposures.

(4) Limits on the prescription of isotretinoin to a 30-day supply, as is the case in the current program.

(5) The requirement that before dispensing an isotretinoin prescription, the pharmacist must confirm that a negative result of a pregnancy test has been documented.

The Teratology Society enthusiastically endorses these recommendations. While we recognize the efforts made by the manufacturer through the current PPP, participation in this voluntary program has been suboptimal, enrolling an estimated 40% to 50% of women receiving isotretinoin at its peak, and falling to an estimated 25% enrollment over the past few years.[2] During this same time period, the number of new isotretinoin prescriptions to reproductive-aged women has tripled, from around 70 000 per year in 1989 to estimates of nearly 210 000 in 1999. The recommendations made by the FDA Advisory Committee represent

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recommendations made by the FDA Advisory Committee represent appropriate additional interventions to decrease the devastating structural and neurological defects associated with prenatal exposure to this drug.[3]

We remain concerned, however, about the marked increase during the 1990s in prescribing isotretinoin to reproductive-aged women. Data from the PPP indicate that the probability of becoming pregnant while taking isotretinoin in women who take the drug and who enroll in the PPP is 3 in 1000, which is likely an underestimate. Any programmatic interventions to reduce the frequency of fetal exposures to isotretinoin must acknowledge that this medication appears to be overprescribed and that an appropriate strategy to reduce fetal exposures would be to limit the availability of this drug to only those women who truly meet the clinical criteria for severe recalcitrant cystic acne.

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1. Rosa FW. Teratogenicity of isotretinoin. *Lancet.* 1983;2:513. MEDLINE

2. Dermatologic and Ophthalmic Drugs Advisory Committee. Sept. 18-19, 2000. Briefing Information. Available at: http://www.fda.gov/ohrms/dockets/ac/00/backgrd/3639b1.htm. Accessed March 30, 2001.

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In Reply: The PPP was first developed in 1988 to assist physicians in