Accutane Program Remains a Work in Progress

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Contributing Writer

Dermatologists and their patients taking isotretinoin are entering the second year of the iPLEDGE mandatory risk management program aimed at preventing isotretinoin-related teratogenicity, and the specialty's leaders on the issue are anticipating further improvement in a system they say remains poorly designed.

"It's safe to say that within the first half of 2007, probably in later spring, there should be additional program improvement. … More improvement is coming," said Dr. Diane Thiboutot, former chair of the American Academy of Dermatology task force on isotretinoin.

What is not clear, however—and won't be for at least another year—is the impact the program is having on the prevention of pregnancies in women taking the teratogenic drug.

Both Dr. Thiboutot, who will continue serving on the task force, and Dr. Susan Walker, who became the director of the Food and Drug Administration's Division of Dermatology and Dental Products last June, said for the first time in February that there is "preliminary" evidence that the program is reducing the number of women who are pregnant at the time they start isotretinoin therapy.

But they offered no details, and Dr. Thiboutot explained that the manufacturers now plan to use data from the first full year of iPLEDGE "as baseline data" for comparison with pregnancy data collected during the entire second year. Before iPLEDGE was implemented, the pregnancy rate in women taking isotretinoin (Accutane) was about 4 per 1,000 women, she said.

"In the interim, some sort of methodology [for evaluating success of the program] will be determined," said Dr. Thiboutot, professor of dermatology at Pennsyvania State University, Hershey.

The most significant change to come this year, in the meantime, will likely be an elimination of the 23-day lockout period for women of childbearing potential. With such a rule change, women who do not have their prescriptions filled within 7 days could undergo another pregnancy test and office visit and then get a refill without having to wait 23 days.

The FDA eliminated this lockout period last October for males and females of nonchildbearing potential, while promising

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DR. DEL ROSSO

that a change in this rule for females of childbearing potential would be "rolled out" in 2007 (INTERNAL MEDICINE NEWS, Dec. 1, 2006, p. 11).

A spokesperson for Covance, the Princeton, N.J.–based company that manages iPLEDGE, confirmed that the firm is "working on eliminating [the lockout]."

Dr. Thiboutot said she and other AAD leaders have been pushing for other changes as well—for instance, the incorporation of specific dates rather than time windows in the iPLEDGE online program—based on input from dermatologists who have communicated with the academy as well as a survey of 400 dermatologists taken this summer. The poll showed that 95% were prescribing isotretinoin and that 90% of them were having difficulty with the iPLEDGE program.

Dr. Stephen Stone, who recently assumed the chairmanship of the academy's task force on isotretinoin, said the academy has a "seat at the table" that it did not have as iPLEDGE was being designed and implemented.

"The FDA is definitely listening to us," said Dr. Stone, immediate past president of the AAD and professor of clinical medicine at Southern Illinois University, Springfield. "My understanding is that iPLEDGE will be improved, at least in its ease of application."

Even with the elimination of the 23-day lockout period for men and women of nonchildbearing potential, "participation of these patients in the system is still overly complicated," he said. "There still [needs to be] some liberalization of rules."

Dermatologists still are debating the program's effects on prescribing. Dr. Noah

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Scheinfeld, of the dermatology department of Columbia University, New York, estimated last spring that prescribing in his region had dropped by at least 50%. That estimate still holds true, he said.

Dr. Elaine Siegfried, a dermatologist at St. Louis University who chairs the AAD's Environment and Drugs Committee, said, on the other hand, that the number of isotretinoin prescriptions dropped after implementation of iPLEDGE but now appears to be back up to approximately where it was under the voluntary SMART (System to Manage Accutane-Related Teratogenicity) program.

(The total number of prescriptions dispensed in the United States in the year after SMART was implemented had declined 23% from the previous year.)

According to Covance's data, while the number of prescribers and pharmacies activated has remained about the same in the last 6 months, the number of patients activated in the program has risen significantly, from 140,000 patients last June to more than 244,000 in December.

Calls to the AAD office, meanwhile, have continued to decline—a trend that AAD leaders say likely reflects changes made by Covance in the spring (the company added staff to its call center and made changes to its Web site, for instance, resolving some of the program's operational difficulties), as well as time needed to learn the system and delegate responsibility.

The average wait time for getting help from the iPLEDGE call center in December was 2 minutes, according to Covance spokesperson Laurene Isip.

"The program is definitely running light-years better" than it did at the start, said Dr. James Del Rosso, of the department of dermatology at University of Nevada, Reno, and immediate past chairman of the AAD's Environment and Drugs Committee.

Dr. Sharon Gardepe, who has a solo practice in general dermatology in Huntsville, Ala., called her legislators and the AAD soon after implementation about her concerns and experience with iPLEDGE. She also created a handout listing local legislators to give to her patients who complained about the program. "Giving them the list underlined the fact that it wasn't me," she said.

One year into the program, Dr. Gardepe said her hour-long phone calls to Covance are a thing of the past, but the requirement that prescriptions be picked up within 7 days and the rule that lab tests be conducted no sooner than 1 day before the office visit still result in "a lot of time spent troubleshooting.

"Some people are optimistic that we might be better able to work with [FDA and Covance], but I'm still skeptical" about the extent of future change, she said.

Dr. Siegfried said such skepticism is understandable. "I really am optimistic. I do think that Dr. Walker [at the FDA] wants to build bridges," she said. "But in the end it's not her call—it's Congress."

Dr. Siegfried and other AAD leaders urge physicians to remain vigilant and active. Isotretinoin, they caution, will likely be in the limelight this year, since Rep. Bart Stupak (D-Mich.) has announced that he wants to hold a congressional hearing on the FDA's management of the drug.

Dr. Siegfried said that she believes the decision to collect a full year of baseline data and then another year of comparison data before reporting pregnancy rates—rather than releasing iPLEDGE data quarterly, as was first anticipated—reflects the realization that "if the data were made public [along the way], and there's been one pregnancy, it will haunt us and we won't have the drug [at all]."

Dr. Stone said he too is concerned, saying that iPLEDGE "will minimize the number of pregnancies by forcing people to go through the hoops, but I don't think we'll ever eliminate pregnancies." ■

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