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Skin Deep

Doctors Fear Acne Drug Rules Go Too Far

By LAUREL NAVERSEN GERAGHTY

JANINE CARPENTER arrived at Columbia University in September with a complexion as clear as her bright blue eyes. But during her first month of college, her face began breaking out in pimples and deep, inflamed nodules, the same symptoms that had plagued her early in high school in San Jose, Calif. "My acne just immediately started to come back at a really rapid rate," Ms. Carpenter, 18, said. So her doctor gave her the potent acne drug isotretinoin, best known as Accutane.

The prescription came with a bright yellow label assuring the pharmacist that Ms. Carpenter was not pregnant, because Accutane can cause severe birth defects. She agreed to also have a pregnancy test each month before refilling her prescription, even though she takes birth control pills. These precautions were part of a program organized by the makers of Accutane and other brands of isotretinoin (Amnesteem, Claravis and Sotret) meant to prevent pregnancy in women taking the drug.

But voluntary programs like this, which have existed since the drug became available in 1982, were not entirely successful. Two to three out of 1,000 women taking isotretinoin still became pregnant, a survey of nearly 450,000 patients, conducted at Boston University from 1989 to 2003, found.

So, as of the beginning of this year, the companies that make isotretinoin, together with the Food and Drug Administration, have imposed mandatory prescribing rules. Any woman of childbearing age who is given the drug must meet several requirements. Before starting the medication she must have negative pregnancy tests two months in a row. While taking it, she must either promise in writing to abstain from sex with a man or else use two forms of contraception, one of which must be a highly effective kind like birth control pills or the injectable Depo-Provera. Each month during her treatment (usually five months) she must take a pregnancy test. And she must document every step she takes by logging onto iPledge, a national online database.

The new rules are meant to prevent isotretinoin-related birth defects once and for all. But the rules are so strict, some doctors say, they might discourage or even prevent many patients from using the drug, the only treatment that can erase severe acne. Many dermatologists say the iPledge program is overkill.

"It's one of the worst things that's happened to our specialty," said Dr. Ranelia Hirsch, a Boston dermatologist who is the vice president of the American Society of Cosmetic Dermatology & Aesthetic Surgery. "We're taking a very good drug that is for many people the only real choice out of reasonable access."



USER PLEDGE REQUIRED
Prescriptions for the anti-acne drug Accutane require that users adhere to rules intended to prevent pregnancy, like using two types of birth control or promising to abstain from sex.

Acne is the most common skin disease in the United States, affecting as many as 85 percent of people from 12 to 24 years old, according to the National Institutes of Health. Nearly 17 million people have it, most of them under 30. Many acne sufferers are satisfied with simple, over-the-counter treatments like benzoyl peroxide cream. But isotretinoin has been the undisputed gold standard for extreme cases, and even for many moderate ones. (The F.D.A. has approved the drug only for severe acne, but doctors may use it off-label to treat milder problems.)

Roche, the maker of Accutane, estimates that nearly seven million Americans have taken its drug. Hundreds of thousands more have taken other brands of isotretinoin since they came on the market after Roche's patent expired in 2002. "It is perhaps the most revolutionary drug in dermatology ever," said Dr. Lee Zane, the director of the Acne Specialty Practice at the University of California, San Francisco. "The number of people walking around with really severe scarring acne has diminished significantly with the advent of isotretinoin."

The most commonly reported side effects are dry skin and chapped lips, but the drug has also been linked to fatigue, severe joint pain, headache, upset stomach and blurred vision. Some suspect that isotretinoin may also cause depression or even suicide, although scientific studies have not demonstrated a connection.

But the importance of avoiding pregnancy is undisputed. Isotretinoin causes the most severe birth defects if an expectant mother takes it during her first trimester, when she is least likely to know she is pregnant.

"There's something that's known as Accutane embryopathy," said Margaret Honein, an epidemiologist at the National Center on Birth Defects and Developmental Disabilities. Exposed fetuses, she said, "often have a pattern of several major malformations," including those of the head, ears, eyes, face and heart, as well as brain abnormalities.

Yet some doctors say that rare preg-

A drug can cause severe birth defects if taken during the first trimester.

nancies should not limit drug access for the millions who get acne. "If the use of Accutane goes down 75 percent, in my mind, the program will be a failure, because there will be tens of thousands of people who will have been hurt," said Dr. Noah Scheinfeld, a dermatologist at St. Luke's-Roosevelt Hospital Center in Manhattan.

Dr. Scheinfeld advocates returning to a voluntary pregnancy-prevention program. "I would have patients certify on a written statement at each visit that they are not sharing pills, know the risks and are using birth control pills," he said.

Dr. Sidney M. Wolfe, the director of Public Citizen's Health Research Group, a consumer advocacy organization, argued that doctors have overprescribed isotretinoin to people whose acne is not severe enough to need it. Strengthening voluntary precautions, he added, has done nothing to reduce pregnancies in women taking the drug. "The only alternative is really to have some imposed restriction," Dr. Wolfe said.

Dr. Nancy Green, the medical director of the March of Dimes, which supports research and education to prevent birth defects, said: "We've been advocating since 2000 for F.D.A. to take this kind of step. Is this the perfect solution? We'll have to wait and see. We are cautiously optimistic that this is the right way to go." The new rules require that men who are prescribed isotretinoin, as well as women who have had hysterectomies or are otherwise unable to become pregnant, register with iPledge, though they are not required to use contraception or have pregnancy tests.

As of March 1 physicians and pharmacists will also be required to register each isotretinoin prescription with iPledge to verify that they have done their part to ensure against pregnancy.

Doctors say the new rules may force them to raise the price of treatment to cover the time and testing required. The drugs alone cost about \$600 a month.

Some doctors are expected to avoid the trouble by turning to less effective treatments. Dr. Ronald G. Wheeland, the chief of dermatology at the University of Arizona Health Sciences Center in Tucson, said it is "almost inevitable" that isotretinoin will be prescribed mainly in academic medical centers in major cities and in practices that specialize in acne treatment. He said he is "fearful that a lot of legislators don't understand the severity of this devastating, scarring, horrible disease."

The iPledge rules are comparable to those that apply to thalidomide, the medicine once used to treat morning sickness that became known in the 1960's for causing severe birth defects. Thalidomide, now used to treat blood cancer, can be prescribed to women only if they promise either to avoid sex or to use two forms of birth control, and to have regular pregnancy tests.

But doctors say that because acne is so widespread, the restrictions on isotretinoin are more onerous.

Dr. Zane, of the University of California, said some patients may be encouraged to seek the drug from foreign sources, forgoing supervision by a physician and any education about the risks of pregnancy.

Most troubling to dermatologists is the possibility that a few pregnancies may still occur, causing the F.D.A. to ban isotretinoin altogether. This, Dr. Zane said, "will send us back essentially to the dark ages of acne treatment, where there will be many, many, many people walking around with severe, scarring, debilitating and psychologically-devastating acne."



Chang W. Lee/The New York Times

'LIKE A TANNING BOOTH' Pauline Muzyka receives a blue-light treatment for acne.

Light or Heat Treatments As Alternatives to Drug

By LAUREL NAVERSEN GERAGHTY

WITH new restrictions on prescribing Accutane and other forms of isotretinoin now in effect, light and heat treatments for pimples may become more popular, doctors say. Although they cannot banish severe acne completely, as the drug can, lasers and other lights can wipe out at least some blemishes, prevent many more and minimize scarring.

Most effective are high-intensity lasers, which heat, and thus shrink, the oil-producing glands in the skin. Lasers are not effective at treating blackheads. But "they work pretty well for the inflammatory type of acne, which is the papules and the pustules," said Dr. Roy G. Geronemus, a Manhattan dermatologist who is the president of the American Society for Laser Medicine and Surgery.

The Smoothbeam laser worked for Tonya Carter, 26, a sixth-grade teacher in Lugoff, S.C. After applying a numbing cream to her face, Ms. Carter's dermatologist would inch the laser across her skin, making targeted blasts. "It's like a little sting, like a little rubber band prick at you," Ms. Carter said.

Each treatment left her face covered with tiny red dots, which lasted less than a day. Even her first session brought noticeable improvement, and after six treatments, she said, her acne was "pretty much wiped out."

Dermatologists also zap pimples with intense pulsed light, which is less penetrating than a laser and works by reducing inflammation, and with Thermage, a radio-frequency-emitting device that heats the skin deep down. Thermage, which is more often used to reduce wrinkles or sagging skin, can disable overactive oil glands and also lessen the appearance of acne scars.

So-called blue-light treatments work as sun exposure does to destroy bacteria in the skin that contributes to acne. The blue light, which has a wavelength slightly longer than ultraviolet light, does not damage the skin as sun exposure can.

"It's kind of like a tanning booth on your face," said Pauline Muzyka, 30, a dental assistant in the Bronx whose recent twice-a-week blue-light treatments helped clear up her skin.

Another acne treatment, Levulan-PDT (for photodynamic therapy), involves using a laser or blue light after coating the face in a cream that makes the skin more light-sensitive. This helps the light destroy bacteria and disable overactive oil glands. But because the photosensitizing cream leaves the skin vulnerable to sunlight, patients must avoid the sun for a day or two after each treatment.

Levulan-PDT can also be used with low-intensity light emitting diodes — the same sort of beams found in remote controls — to treat acne by killing bacteria. For a minute or two the patient sits in front of a light source that is about the size of a computer monitor. A new type of

Doctors say limits on one remedy could make others more popular.

L.E.D. device appears to be effective even when used without Levulan-PDT, Dr. Geronemus said.

The prices of light treatments range widely, from \$250 to \$600 per session. Other acne remedies include some birth control pills, which lower testosterone, a hormone that helps make skin oily. Prescription antibiotic pills or creams can help kill bacteria. And chemical peels and retinoids like adapalene (brand name Differin) and tretinoin (Retin-A) help too, by preventing dead skin cells from clogging pores.

Over-the-counter treatments — washes, cleansing pads, creams and gels — often use either benzoyl peroxide or salicylic or glycolic acid, which slough off dead skin cells. Benzoyl peroxide also kills bacteria. Doctors say these remedies bring about mild improvement.