



Isotretinoin Updates



One of the best studied medications for treating acne, isotretinoin can deliver high rates of lasting cures with predictable side effect profiles. Here's an update on the latest in patient management.

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>> Isotretinoin (13-cis-retinoic acid) has been a highly effective medication for treating acne since its release in 1982. Because of its relative safety and efficacy, it remains among the top prescribed medications for treating severe grades of acne or acne that is refractory to other topical and/or oral medications. Furthermore, with expert guidelines recommending limiting courses of systemic antibiotics for acne therapy to three to four months because of concerns about emerging antibiotic resistance, dermatologists may frequently need isotretinoin as an alternative treatment for what is often a long-term condition. Alternative acne treatments, including a variety of topical products, hormonal based therapies, and photodynamic therapies, often have limitations or limited efficacy or insurance coverage. Isotretinoin remains among the most effective, time-honored products capable of producing durable remissions and dramatic response rates, and dermatologists increasingly need to be aware of the latest information about it to control the narrative when advising patients about this medication.

TERATOGENICITY AND MOOD EFFECTS

Isotretinoin has been used by millions of patients both in the US and internationally for many years and has a generally predictable side effect profile that has been well known by dermatologists. The most pressing concern since its release continues to be the “black box warning” about teratogenicity and need for pregnancy prevention with committed abstinence and/or highly effective forms of contraception for female patients of reproductive potential or transgender patients with a uterus. Prescribers of isotretinoin must adhere to the FDA-mandated iPledge risk-management program guidelines for pregnancy prevention both during and for up to one month after completion of therapy. Unintended pregnancy exposures still occur despite this extensive program and multiple preceding similar pregnancy prevention programs and specific prescriber-, pharmacist-, and patient-directed warnings.

Allegations and case reports of isotretinoin causing psychosocial mood disorders, depression and suicidal behavior, and inflammatory bowel disease have been well publicized and often cause fear and concern about this medication. In 2006, Chicago dermatologist Dr. David Cornbleet was murdered by a former patient who alleged that a few doses of isotretinoin aggravated depression and sexual issues. In 2000, former Michigan Congressman Bart Stupak's son committed suicide with a gun shortly after completing a course of isotretinoin, leading to congressional hearings and increased package warnings about this. A 2002 incident inspired by the events of 9/11 involving a suicidal teenager who crashed a stolen small aircraft into a Miami skyscraper was blamed by his mother on his isotretinoin use, although a lawsuit against the manufacturer was later dropped.

Isotretinoin remains one of our best studied medications for treating acne that can deliver high rates of lasting cures with predictable side-effect profiles. Prescribers of isotretinoin must adhere to the FDA mandated iPledge risk-management program guidelines for pregnancy prevention both during and for up to one month after completion of therapy. Unintended pregnancy exposures still occur despite this extensive program. Isotretinoin treatment for acne does not appear to be associated with an increased risk for depression, and treatment of acne appeared to ameliorate depressive symptoms. It has been suggested to decrease standard blood test monitoring to baseline and one to two months after therapy for otherwise healthy young patients. Culturally sensitive prescribing is an important aspect of patient care.

thebottomline

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These and other cases of depression and suicide attempts and completed suicides have led to specific product warnings about these psychiatric disorders. It is well known that there is an appreciable rate of depression among teens and young adults. According to the National Institute of Mental Health, an estimated 13.3 percent of the adolescent population, age 12-17, had at least one major depressive episode; and 9.4 percent of that population had a major depressive episode associated with severe impairment. Suicide remains the second leading cause of death for ages 10-34 and has been increasing in frequency in recent years. It is well known that acne negatively affects self esteem, which puts those affected with severe grades of acne at higher risk of developing depression.

A recent published meta-analysis of 31 qualified studies looking at the relationship between isotretinoin and depression found that the change in depression scores from baseline was not significantly different between patients receiving isotretinoin and other alternative acne treatments and that the prevalence of depression after isotretinoin treatment significantly declined. Mean depression scores also significantly decreased from baseline. The authors concluded that isotretinoin treatment for acne does not appear to be associated with an increased risk for depression and that, indeed, the treatment of acne appeared to ameliorate depressive symptoms quite probably as a result of the improvement in the acne.

LABORATORY MONITORING

The clinical utility of laboratory monitoring during isotretinoin therapy has also been questioned. A recently published meta-analysis of 61 studies showed that while abnormalities of white blood cell counts, hepatic, and lipid panels did occur, the proportion of patients with what were considered high risk abnormalities was very low. Another large single center study of 515 patients undergoing 574 courses of isotretinoin over eight years found infrequent and largely insignificant abnormalities of white blood cell, platelet, and liver transaminase levels and significant abnormalities of serum cholesterol and triglyceride levels with a majority being mild to moderate in significance.

The American Academy of Dermatology Guidelines of Care for the management of acne vulgaris specifically no longer advise checking complete blood counts during isotretinoin therapy because of their low incidence of clinical utility. It has been suggested to decrease blood test monitoring to baseline and one to two months after therapy for otherwise healthy young patients. Consideration of reduced blood testing during isotretinoin therapy can significantly reduce cost, increase convenience, and eliminate fear of blood drawing that can be obstacles to therapy for many patients.

CULTURALLY COMPETENT PRESCRIBING

The issue of prescribing isotretinoin to transgender or non-binary

patients in a culturally competent manner has gained more attention. Unfortunately, gender-neutral categories are not an option for the iPledge program at this time. Transgender male patients receiving testosterone hormonal therapy often get troublesome acne for which treatment with isotretinoin may well be an appropriate option. Patients with a uterus, however, must still comply with appropriate iPledge requirements, and this should be discussed in a manner with non-maleficence and respect for patient autonomy.

PROTECTING ACCESS

In conclusion, isotretinoin remains one of our best studied medications for treating acne that can deliver high rates of lasting cures with predictable side effect profiles. Dermatologists should be willing to minimize obstacles to care and address exaggerated and unsubstantiated risk concerns so that patients can get access to this highly efficacious medication. ■

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