

Optimizing Absorption of Oral Isotretinoin



An update on lidose-isotretinoin and the ability to enhance absorption in the absence of high-fat meals.

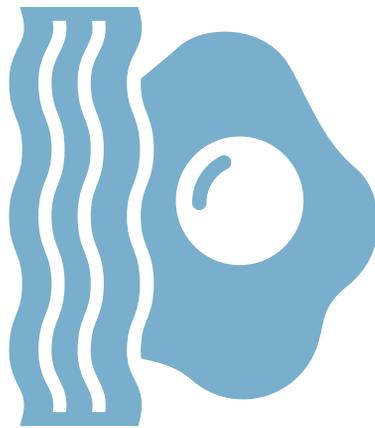
BY JOSHUA ZEICHNER, MD

>> Acne is the most common skin condition that dermatologists treat and is estimated to affect up to 50 million Americans annually.^{1,2} While mild to moderate acne may be controlled using topical medications alone or in combination with oral antibiotics or hormonal therapies in women, severe, nodular acne may require treatment with oral isotretinoin.^{3,4} In accordance with guidelines from the American Academy of Dermatology, oral isotretinoin is recommended as a first-line and highly efficacious option for patients with severe, recalcitrant, nodular acne.^{4,5}

Early, effective treatment of severe acne will minimize the risk of developing both physical and emotional scars. While scarring of the skin may occur in all acne patients, the frequency and severity of scarring generally correlates with the severity of the acne itself.^{6,7} Severe acne has been shown to affect the mental health of patients, resulting in impairments of self-esteem, social anxiety and anger, depression and suicidal thoughts, poor performance in school, withdrawal from social environments and sports activities, and higher rates of unemployment.⁸⁻¹⁰

ISOTRETINOIN FORMULATIONS

Like all vitamin A derivatives, isotretinoin is a lipophilic drug and best absorbed when taken with a



high-fat, high-calorie meal.^{3,11} In the clinical trials performed for FDA approval of isotretinoin, the drug was taken with an 800-1000 calorie meal, 50 percent of which was comprised of fat.¹² When isotretinoin is taken without a high-fat meal, fasting plasma levels of active drug were more than 60 percent lower than with fed conditions for conventional isotretinoin.³ Proper absorption of the drug is important to ensure that the effective dose of the isotretinoin is equivalent to the weight-based dose that is actually prescribed and taken.

Unlike conventional forms of isotretinoin, absorption of lidose-isotretinoin (Absorica, Sun Pharma) is less dependent on the amount and/or type of food intake than conventional isotretinoin. The capsule is comprised

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of a lipid matrix that solubilizes the medication, bypassing the need for food. This enhances absorption, even in the absence of a meal, and provides patients with greater flexibility in when they can take their medication. In a pharmacokinetic study, lidose-isotretinoin and conventional isotretinoin had equivalent plasma concentrations in the fed state. However, when the drugs were taken on an empty stomach, the plasma concentration of isotretinoin when taken in the lidose formulation was 83 percent greater than with the conventional form of the drug.¹³

It is estimated that more than 50 percent of teenage boys and more than 66 percent of teenage girls skip breakfast regularly.¹⁴ If patients are not taking their isotretinoin in the

Teen Acne Linked to Academic Success

Individuals who had acne during their teen years earned higher grades in high school and were more likely to complete their bachelor's degrees, according to a new study in *Journal of Human Capital*.

Researchers used data from the National Longitudinal Study of Adolescent to Adult Health to investigate the association between having acne in middle to high school and subsequent educational and labor market outcomes. In addition to its link to better grades and a greater likelihood of graduating college, acne was also associated with higher personal labor market earnings for women, the study showed.

Researchers speculate that students who had acne may have been more likely to study instead of socializing because they felt less attractive.

presence of food, it can significantly impact long-term treatment outcomes. It has been well documented that patients should be treated with isotretinoin until they reach a target cumulative dose of 120-150mg/kg total dose. Patients who do not reach the target cumulative dose appear more likely to relapse and require subsequent courses of therapy.¹⁵ Perhaps one of the reasons for disease relapse is that despite the target cumulative dose being prescribed, that target is not actually absorbed, due to a lack of concurrent fat when taking conventional isotretinoin.

NEW DATA

A recent Phase 4 study evaluating efficacy and relapse rates of patients taking lidose-isotretinoin in a fasting state was recently completed. The study was divided into two phases: a 20-week active treatment period (ATP) followed by a 104-week post-treatment period (PTP) follow-up. In this single-arm study, lidose-isotretinoin was taken without food, which was different than the requirements from the previous pivotal studies for conventional and lidose-isotretinoin. Clinical efficacy and quality of life were evaluated at week 20 compared to baseline, and relapse rates were observed in the 104-week PTP.¹⁶ In the PTP, non-isotretinoin re-treatment rates were found to be low (16.9 percent) in both male and female patients and across all age groups.¹⁶ Only 3.8 percent of patients who were clear and four percent of patients who were almost clear

at week 20 ultimately required isotretinoin re-treatment. Moreover, a higher percentage of male patients required isotretinoin re-treatment compared to female patients (5.8 percent and 1.6 percent, respectively). In addition, all male patients requiring re-treatment were between the ages of 14 and 18 years old.

REAL WORLD CARE

When prescribing isotretinoin to our patients, proper education on how and when to take the medication is as important as other aspects of patient counseling. We must discuss the requirement for a fatty meal for optimal absorption of isotretinoin. Our goal as dermatologists is to help our acne patients achieve clear skin and maintain it. However, in the real world, compliance to a regimen is a challenge, especially when it is diet-dependent. Given the recent data showing that lidose-isotretinoin demonstrated low relapse rates, even when taken without food throughout the duration of therapy, lidose-isotretinoin offers a flexible option for patients without compromising efficacy. Most patients have clear skin when they complete their initial course of isotretinoin, but our goal is to ensure that they stay clear in the long term, as well. ■

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