



DERMATOLOGIST EVALUATES LATEST ISOTRETINOIN DEVELOPMENTS FOR TREATMENT OF SEVERE ACNE

Recent studies cast new light on reported side effects while new dosing and formulation could improve treatment outcomes

Denver
March 21, 2014

OVERVIEW:

Since its introduction in the early 1980s, isotretinoin has been the treatment of choice among dermatologists for patients with severe acne that has not improved with other acne therapies. This painful form of acne produces deep cysts, inflammation, and scarring, which can wreak havoc on the skin and severely impact a person's emotional well-being and overall quality of life.

While not for everyone, isotretinoin has proved to be the only therapy that can clear severe acne and provide long-lasting results. However, its reputation has been marred over the years by reported side effects and misconceptions of this potent drug. Now, new research disputes the link between isotretinoin use and inflammatory bowel disease (IBD) and provides evidence that suggests other medical conditions may be to blame for the drug's association with psychiatric conditions. In addition, high dose isotretinoin therapy and a new formulation could help some patients achieve even better results.

AMERICAN ACADEMY OF DERMATOLOGY EXPERT

Information provided by board-certified dermatologist William D. James, MD, FAAD, professor of dermatology at the University of Pennsylvania School of Medicine in Philadelphia.

ASSOCIATIONS WITH IBD, PSYCHIATRIC CONDITIONS EXAMINED

New Studies Dispute IBD Link

After isotretinoin was first introduced, there were some reports of IBD (which encompasses both Crohn's disease and ulcerative colitis) occurring or getting worse in patients using isotretinoin. Dr. James explained that by the mid-2000s, papers published in gastrointestinal journals reported that isotretinoin could cause IBD – resulting in several lawsuits stemming from this relationship. Interestingly, 88 percent of IBD-related cases reported on the Food and Drug Administration's (FDA) Adverse Event System were determined to be entered by attorneys rather than patients or physicians.¹

Two new studies published in 2013 closely examined the relationship between isotretinoin use and IBD.

- The most recent and statistically significant studies deny an association between isotretinoin and IBD and instead implicate a possible link between acne severity and IBD.^{2,3}
- Severe acne is seen in inflammatory diseases such as SAPHO syndrome (which includes a variety of inflammatory bone disorders that may be associated with skin changes) and PAPA syndrome (a rare genetic disorder characterized by its effect on the skin and joints), which were both found to be associated with IBD.⁴

News Release

American Academy of
Dermatology

930 East Woodfield Road
Schaumburg, Illinois 60173

Main: 847.330.0230

Fax: 847.330.8907

Website: www.aad.org

- On average, IBD begins at age 19, which is close to the same age when a patient might develop severe acne and be treated with isotretinoin.

Based on these new findings, Dr. James and other dermatologists believe severe acne itself might predispose a person to IBD, regardless of whether acne is treated with isotretinoin. Dr. James educates his patients about the scientific research concerning the possible association with IBD and monitors for it in patients taking isotretinoin. He recommends his colleagues follow this same course of action.

Acne, Attention Deficit Hyperactivity Disorder (ADHD) and Depression

Psychiatric side effects in patients taking isotretinoin – mainly depression – have been reported and studied for several years. A new observation includes an increased risk of Attention Deficit Hyperactivity Disorder (ADHD) in some patients with acne.⁵ Dr. James stressed that this association is not related to isotretinoin use, even though acne patients with ADHD may be taking this drug. Since ADHD is associated with an increased risk of suicide, Dr. James noted that a number of acne patients with ADHD may already be at a higher risk of depression regardless of whether or not they are taking isotretinoin.

- One recent study examining mood changes in a small group of patients taking isotretinoin found a marked improvement of psychiatric symptoms in conjunction with improved acne.⁶
- In a study that examined a large number of acne patients taking isotretinoin, Dr. James explained that there was a reported negative effect on mood in a small number of patients – likely about four per 1,000 in his estimates.

Despite the low risk of depression with isotretinoin use, Dr. James always checks for pre-existing mood disorders before prescribing isotretinoin and educates all patients taking this drug thoroughly about this controversy. He also insists that someone close to the patient – a roommate, parents, spouse – is made aware that the patient is taking isotretinoin so they can help monitor for any unexplained mood changes during the course of treatment.

NEW HIGHER DOSAGES, NEW FORMULATION

Benefits, Risks of High Dose Isotretinoin Examined

One of the key benefits of isotretinoin in patients with severe acne is that use of the drug has been shown to successfully treat acne and lead to long-term remission of the condition. While about half of all patients taking isotretinoin may relapse following treatment and require additional use of isotretinoin or a milder topical or oral acne therapy, new research suggests that using a higher dose of isotretinoin could provide longer lasting results.^{7,8}

- Dr. James cautioned that higher doses can increase the chance of side effects – primarily severely dry skin, nosebleeds, inflammation of the lips, triglyceride elevations, and psychiatric or mood disorders.
- In some cases where a high dose has been prescribed, a temporary worsening acne flare has been reported.
- Benefits of standard dose isotretinoin use include milder side effects and an increased likelihood that patients will take their medication as directed.

New Formulation Increases Absorption

A new isotretinoin formulation allows the medication to be better absorbed and circulated within the body – even without being taken with a fatty meal, a requirement in isotretinoin use that poses a challenge for some patients. Based on initial studies with this new formulation, Dr. James believes it is likely to enhance results as patients are absorbing more of the dosage.

- If a patient does not eat a fatty meal with isotretinoin, the patient only absorbs about 40 percent of the prescribed dose. With the new formulation, a patient will absorb about 70 percent of the prescribed dose even if the patient does not eat a fatty meal.⁹
- The higher cost of the new formulation could limit its use initially.
- Patients who are not responding to isotretinoin or eating fatty meals with the medication may be good candidates for the new formulation.

AMERICAN ACADEMY OF DERMATOLOGY EXPERT ADVICE:

“Isotretinoin remains the gold standard for treating severe acne, but there are many aspects that must be taken into consideration before it is prescribed,” said Dr. James. “It is important that dermatologists and patients who are good candidates for isotretinoin – along with friends or family and, in some cases, other physicians – work together to ensure the safest and most effective treatment outcome. It is encouraging that new studies continue to be conducted on the use of isotretinoin, and I expect more studies will further expand our knowledge of this powerful and effective medication in the future.”

#

Jennifer Allyn
(847) 240-1730
jallyn@aad.org

Nicole DiVito
(847) 240-1746
ndivito@aad.org

Kara Jilek
(847) 240-1701
kjilek@aad.org

Headquartered in Schaumburg, Ill., the American Academy of Dermatology (Academy), founded in 1938, is the largest, most influential, and most representative of all dermatologic associations. With a membership of more than 17,000 physicians worldwide, the Academy is committed to: advancing the diagnosis and medical, surgical and cosmetic treatment of the skin, hair and nails; advocating high standards in clinical practice, education, and research in dermatology; and supporting and enhancing patient care for a lifetime of healthier skin, hair and nails. For more information, contact the Academy at 1-888-462-DERM (3376) or www.aad.org. Follow the Academy on [Facebook](#) (American Academy of Dermatology) or [Twitter](#) (@AADskin).

1. Derrick J. Stobaugh, Parakkal Deepak, Eli D. Ehrenpreis Alleged isotretinoin-associated inflammatory bowel disease: Disproportionate reporting by attorneys to the Food and Drug Administration Adverse Event Reporting System. *J Am Acad Dermatol* 2013; 69(3): 393-398, DOI: 10.1016/j.jaad.2013.04.031)
2. Etminan M, Bird ST, Delaney JA, Bressler B, Brophy JM. Isotretinoin and Risk for Inflammatory Bowel Disease: A Nested Case-Control Study and Meta-analysis of Published and Unpublished Data. *JAMA Dermatol.* 2013;149(2):216-220. doi:10.1001/jamadermatol.2013.1344.
3. Alhusayen, Raed O, Juurlink, David N, Mamdani, Muhammad M, et al. Isotretinoin Use and the Risk of Inflammatory Bowel Disease: A Population-Based Cohort Study. *J Invest Dermatol.* 2013 April. 133: 907–912; doi:10.1038/jid.2012.387
4. Femia, Alisa N Ann Vleugels, Ruth Toward Improved Understanding of a Potential Association between Isotretinoin and Inflammatory Bowel Disease. *J Invest Dermatol* 2013 April. 133: 866-868; doi:10.1038/jid.2012.428
5. Gupta MA, Gupta AK, Vujcic B. Increased frequency of Attention Deficit Hyperactivity Disorder (ADHD) in acne versus dermatologic controls: analysis of an epidemiologic database from the US. *J Dermatolog Treat.* 2014 Apr;25(2):115-8. doi: 10.3109/09546634.2012.736021. Epub 2012 Dec 8.
6. Nevoralová Z, Dvořáková D. Mood changes, depression and suicide risk during isotretinoin treatment: a prospective study. *Int J Dermatol.* 2013 Feb;52(2):163-8. doi: 10.1111/j.1365-4632.2011.05334.
7. Blasiak RC, Stamey CR, Burkhart CN, et al. High-Dose Isotretinoin Treatment and the Rate of Retrial, Relapse, and Adverse Effects in Patients With Acne Vulgaris . *JAMA Dermatol.* 2013;149(12):1392-1398. doi:10.1001/jamadermatol.2013.6746.
8. Cyrulnik AA, Viola KV, Gewirtzman AJ, Cohen SR. High-dose isotretinoin in acne vulgaris: improved treatment outcomes and quality of life. *Int J Dermatol.* 2012 Sep;51(9):1123-30. doi: 10.1111/j.1365-4632.2011.05409
9. Webster GF1, Leyden JJ, Gross JA. Comparative pharmacokinetic profiles of a novel isotretinoin formulation (isotretinoin-Lidose) and the innovator isotretinoin formulation: a randomized, 4-treatment, crossover study. *J Am Acad Dermatol.* 2013 Nov;69(5):762-7. doi: 10.1016/j.jaad.2013.05.036. Epub 2013 Aug 13.