Dermatology Times®
Clinical Analysis for Today's Skincare Specialists
February 2014 VOL. 35, NO. 2

In This Issue

February 2014
VOL. 35, NO. 2

Data points to new disease concerns

How to recognize & manage formerly rare infections

Now, Therapy That's Always Close at Hand

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INDICATIONS FOR USE: Eletone® Cream is indicated for the management and relief of burning, itching, and redness associated with various types of dermatoses, including atopic dermatitis, allergic contact dermatitis, and radiation dermatitis (post-radiation treatment).

CONTRAINDICATIONS: THIS PRODUCT SHOULD NOT BE USED DURING THE PERIOD OF TIME WHEN RADIATION TREATMENT IS OCCURRING BECAUSE OF THE INCREASED RISK OF SKIN TOXICITY WHEN RADIATING THROUGH PETROLATUM AND OIL. Eletone® Cream is contraindicated in patients with a known hypersensitivity to any of the components of the formulation.

PRECAUTIONS: Eletone® Cream is for external use only.
Eletone® Cream does not contain a sunscreen and should always be used in conjunction with a sunscreen in sun exposed areas.

INSTRUCTIONS FOR USE: Apply liberally to the affected areas three times daily or as needed. If skin is broken, cover Eletone® Cream with a dressing of choice.

INGREDIENTS: Eletone® Cream contains petrolatum, purified water, mineral oil, cetostearyl alcohol, ceteth-20, citric acid, sodium citrate, propylparaben, and butylparaben.

HOW SUPPLIED: Eletone® Cream is available in a 100 gram tube **NHRIC** 0178-0368-01.

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In This Issue

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VOL. 35, NO. 2

Many products make what sound like medical claims about the efficacy of these agents. Zoe Draelos, M.D., discussed the issues surrounding cosmeceuticals with Norman Levine, M.D.

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Clinical

IS THERE A CLINICAL CASE FOR A LOW-DOSE APPROACH?

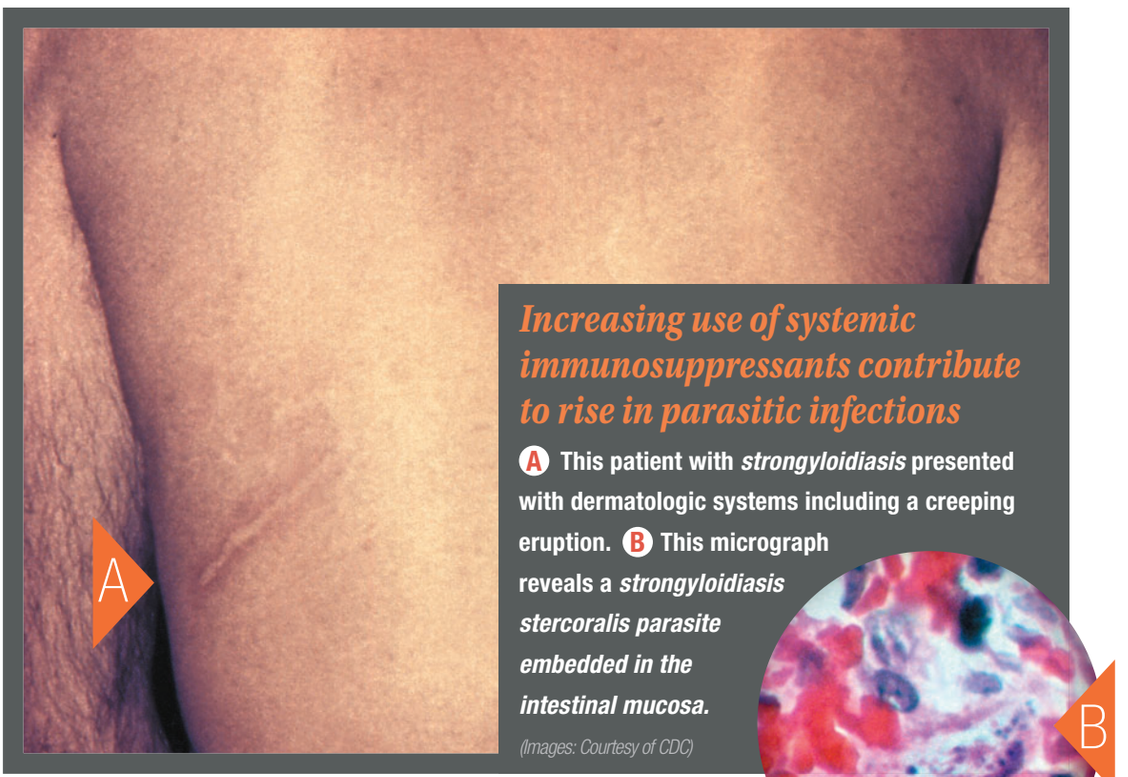
John Jesitus | Senior Staff Correspondent

DERMATOLOGISTS might slash the development of resistance to antibiotics by embracing lower, subantimicrobial doses for acne cases that require only anti-inflammatory activity, experts say. However, they add, getting the majority of dermatologists to accept this message likely will prove challenging.

LOW DOSE see page **34**

Data points to new disease concerns

How to recognize & manage formerly rare infections



Increasing use of systemic immunosuppressants contribute to rise in parasitic infections

A This patient with *strongyloidiasis* presented with dermatologic systems including a creeping eruption. B This micrograph reveals a *strongyloidiasis stercoralis parasite embedded in the intestinal mucosa.*

(Images: Courtesy of CDC)

John Jesitus | Senior Staff Correspondent

Key concerns regarding infectious diseases with cutaneous manifestations include the expanding reach of infections formerly thought rare and exotic, experts say. Meanwhile, they add, some infections rarely seen stateside in recent years are resurging.

Expanding global travel fuels the spread of many of these diseases, say Stephen K. Tyring, M.D., Ph.D., M.B.A., and Casey Carlos, M.D., Ph.D. Dr. Tyring is clinical professor of dermatology, microbiology/molecular genetics and internal medicine at the University of Texas Health Science Center, and medical director of the Center for Clinical Studies in Houston. Dr. Carlos is assistant professor of internal medicine in the division of dermatology, University of California, San Diego.

GOING VIRAL

Dr. Tyring also blames complacency. With fewer parents getting their children vaccinated for measles, for example, he says that 2013 saw more measles cases in the United States (175 as of Dec. 6) than any prior year of the 21st century.

Accordingly, he says, "Infectious diseases of the 20th century such as measles are not eradicated. And some diseases that were very rare in the United States at the beginning of the 21st century are coming back with a vengeance." Therefore, he says that for every disease for which there is a vaccine, "It's important that people get vaccinated."

Somewhat similarly, Dr. Carlos says, "Hepatitis B is emerging in the United States," fueled largely by immigrants and refugees who grew up in areas where the disease is endemic and developed chronic infections.

"Many of the medications we use for conditions

RESURGING INFECTIONS see page **30**

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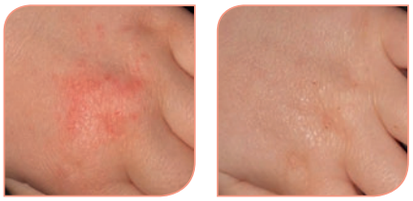

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[1]Results from 32 subjects (ages 7 months to 9 years). Application of XeraCalm A.D Lipid-Replenishing Cream twice daily for 4 weeks.
[2]Results from 55 subjects (ages 1 to 4 years). Application of XeraCalm A.D Lipid-Replenishing Balm twice daily for 28 days.

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Dermatology Times is the only clinical news resource serving a readership of more than 14,000 dermatologists and other professionals focused on skincare. Through unbiased reporting, we strive to help practitioners put into perspective developments that affect their business. Our goal is to provide practical information that will help them to better understand clinical, regulatory and financial issues, as well as chart business growth.

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ONLINE Exclusive

Listen to an expert panel discuss which injectable products they prefer to use, in what way and why. Many agree that it's wonderful to have so many tools and that each one serves a purpose for enhancing different features and areas of the face. Hear more about their tips and techniques.
Video credit: xMedica/2013 Vegas Cosmetic Surgery and Aesthetic Dermatology
dermatologytimes.com/palette

resources in dermatology

Symptoms of psoriatic arthritis include inflammation in the joints and excessive production of skin cells. Learn about treatment options to help reduce these symptoms in your patients. dermatologytimes.com/psoriaticarthritis

Botulinum toxin has a variety of medical uses, including smoothing frown lines and treating pain. Use these resources to stay informed on the latest in neurotoxins. dermatologytimes.com/injections

Smartphone technology provides patients a way to submit information from anywhere, and the option to receive diagnoses quickly and conveniently. Learn how: dermatologytimes.com/onlineconsult

Trending FROM JANUARY

Study reveals side effects of methotrexate
DermatologyTimes.com/methotrexate

Case Western researcher gets $1.9M grant for psoriasis studies
DermatologyTimes.com/psoriasisgrant

Valeant joins with Living Proof to create aesthetic product
DermatologyTimes.com/LivingProof

Derm practice pays $150K settlement for stolen patient data
DermatologyTimes.com/settlement

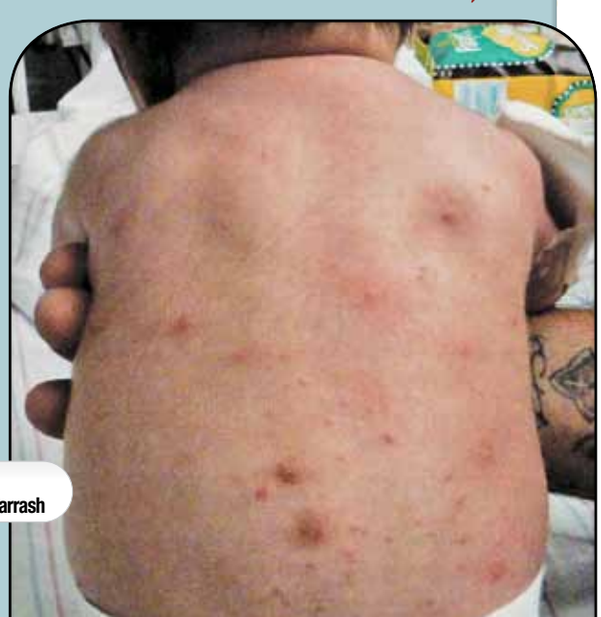
Clinically relevant advances in 2013
DermatologyTimes.com/2013

Future of dermatologic innovation has bright spots
DermatologyTimes.com/futureofderm

Study: Benefits of sun exposure may outweigh risks
DermatologyTimes.com/UVbenefits

WHAT'S YOUR DIAGNOSIS?

The worried mother of a 4-week-old boy brings her son to you for evaluation of a rash that started 3 weeks ago on his left eyebrow and chest, then spread to his back, arms, and legs despite treatment with topical steroids. What's your diagnosis?



Comment at dermatologytimes.com/discussrash
Read about this case at dermatologytimes.com/nodularrash

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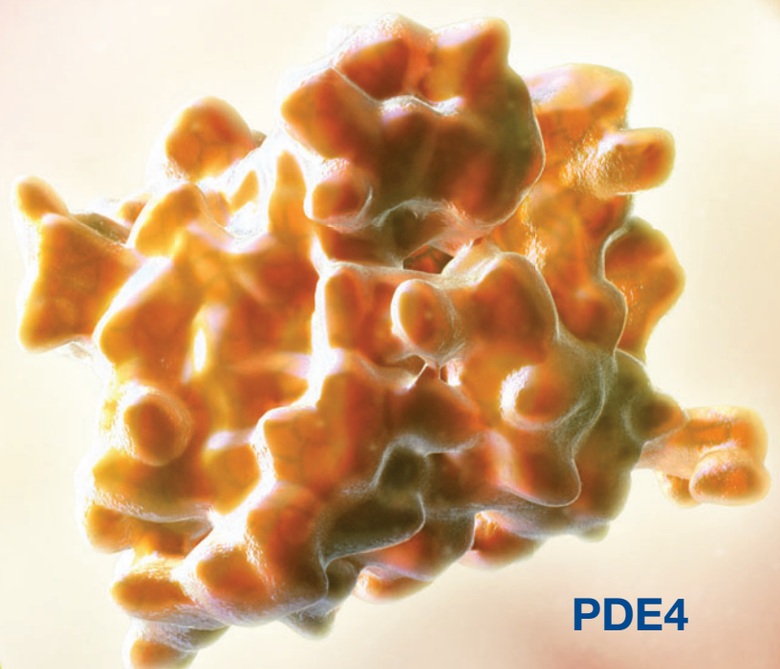
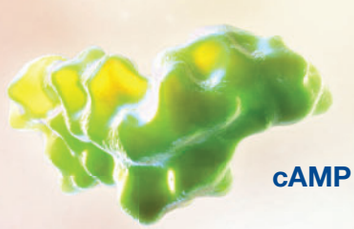
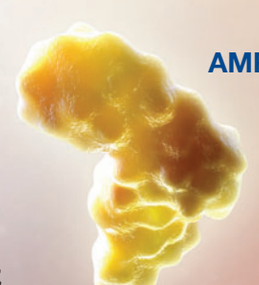
LOOK INSIDE THE CELL[1]

DISCOVER THE ROLE OF PDE4

PDE4 promotes the dysregulation of pro- and anti-inflammatory mediators thought to occur in inflammatory disease[2,3] and is present in key inflammatory cells.[1]







AMP=adenosine monophosphate; cAMP=cyclic AMP; PDE4=phosphodiesterase 4.

References: 1. Baumer W, Hoppmann J, Rundfeldt C, Kietzmann M. *Inflamm Allergy Drug Targets.* 2007;6(1):17-26. **2.** Houslay MD, Schafer P, Zhang KYJ. *Drug Discov Today.* 2005;10(22):1503-1519. **3.** Press NJ, Banner KH. In: Lawton G, Witty DR, eds. *Progress in Medicinal Chemistry.* Amsterdam, The Netherlands: Elsevier; 2009:37-74.

Celgene

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Dermatologists are feeling the squeeze

Are you a squeezed dermatologist? I am afraid many of us are entering this uncomfortable position with little space for relief. What do I mean by being squeezed? I am alluding to the place where dermatology has been relegated in the new modern order of medical care. A place where we will need to blaze new territory in order to continue to deliver the best we have to offer in skin, hair and nail care.

Dermatology is being squeezed as medically necessary clauses are being inserted into insurance contracts with the provision that the physician can be removed from the plan if guidelines are violated. While cosmetic procedures have not been covered for quite some time, the definition of "medically necessary" is not clear in most patient's minds.

Medically necessary to the patient is the unsightly appearance of skin tags around the neck; however, benign skin tags do not meet the insurance perception of medically necessary. Hence, the dermatologist is squeezed trying to explain to the patient why she or he will need to pay for skin tag removal in addition to paying a copay for the medical treatment of their psoriasis.

Pricey medications

Dermatology is being squeezed as the best medications for treating a given condition are $400-$800 a tube, and many brand name medications are now off formulary. This creates challenges when patients expect to see excellent treatment results, which the dermatologist can deliver, but not without the best medications. Dermatologists are only as good as their ability to prescribe, given the correct diagnosis.

Dermatologists are only as good as their ability to prescribe, given the correct diagnosis.

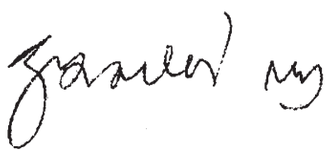
Patients frequently call back wanting more affordable medications, only to call back again, stating the provided alternative was ineffective. The dermatologist is being squeezed, as less effective treatments must be used due to tremendous medication inflation.

Dermatology is being squeezed as medical care in this country moves toward only covering procedures that save lives rather than improving the quality of life. Dermatologists are fortunate to take care of one of the most adaptable and rapidly healing organs of the body. Problems are visually recognized early and treated efficiently prior to the onset of severe issues. This means that skin disease is rarely fatal and one could argue that the only condition that should be covered is malignant melanoma. Thus, the dermatologist is squeezed, as the efficient early cost-effective care that is delivered results in little mortality.

Avoiding the squeeze

How do dermatologists avoid the squeeze? We need to be cohesive and creative. First, we need to be sure that patients are educated on what constitutes a medically necessary procedure and dermatologists should deliver uncovered services for a fair cash price. Second, dermatologists should familiarize themselves with available cost effective formulary medications and encourage patients to do the same.

Finally, dermatologists should be sure to recognize those insurance plans that do not cover dermatologic care. I think part of avoiding the squeeze is helping patients better understand healthcare issues. With proper education, patients will want to give their dermatologist a hug and a squeeze! **DT**



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SANDY JOHNSON, M.D.,
is in private practice in Fort Smith, Ark.

Antibiotic dialogue needs to continue

I thoroughly enjoyed the lead article about "antimicrobial stewardship" in the October edition of **Dermatology Times** (Antimicrobial stewardship: How dermatologists can be part of the solution, Vol. 34, No. 10). It succinctly and effectively detailed that for healthcare providers in general and dermatologists in specific, it is our duty to utilize antimicrobials appropriately. It appears to me that the ability of bacteria to outsmart our antibacterials is outpacing the generation of new antibacterials. We need to save the tools (antibiotics) in our tool bag for when we really need them (to treat infection).

I think the article stopped short and I ask you to consider a part two of "Antimicrobial stewardship." Ideally, it would include a call to action plan encouraging all of us to find ways to save the antibiotics. One way I try to judiciously use antibiotics is to limit their use for acne. Acne is probably the dermatological condition for which we use (misuse) antibiotics the most.

There was an interesting study that looked at *P. acnes* reaction to doxycycline 100 mg twice a day versus benzoyl peroxide. Surprisingly, the doxycycline had none to minimal effect on the *P. acnes*, while benzoyl peroxide was very effective in eradicating the bacteria. So, I deduce that the doxycycline benefit for acne really is from its anti-inflammatory properties and not from its antibacterial effects.

> The pit in my stomach grows a little bigger every time I prescribe oral antibiotics to healthy, athletic teenagers for their acne.

Therefore, my oral agent of choice for acne is sub-antimicrobial Oracea (doxycycline, Galderma). Oracea is also my agent of choice for other inflammatory diseases such as rosacea, periorificial dermatitis, hand eczema and bullous pemphigoid. During my residency, for inflammatory conditions we commonly used tetracycline ... until it was no longer available. Then we (the dermatology community) switched to doxycycline 100 mg twice a day. Why the convention became to use the antibacterial dose of doxycycline when lower sub-antimicrobial doses had similar anti-inflammatory benefit in research still eludes me.

The main hurdles to prescribing Oracea are the cost and insurance coverage. This is distressing to me because the cost to society of prescribing (sometimes) less expensive antibiotics for acne is causing an increased financial burden to society by creating more resistant bacteria. It is easier to prescribe antimicrobial doses of doxycycline for our clinic team with fewer callbacks, letters from insurance carriers, and prior authorizations to complete. But even though it is easier in the short term, I know it is not what is best for the long term.

The pit in my stomach grows a little bigger every time I prescribe oral antibiotics to healthy, athletic teenagers for their acne knowing I am increasing their risk of contracting MRSA (methicillin resistant *Staphylococcus aureus*) from the locker room, classroom, or anywhere in the community. Would it be better to prescribe isotretinoin instead of oral antibiotics when an oral medication is warranted if I am not able to prescribe sub-antimicrobial medications?

I do not know what the answers are when it comes to proper antibiotic usage by dermatologists, but I appreciate you for bringing this issue to light and continuing the dialogue. I hope you follow through and interview people who are considered expert in this area. **DT**

Read the follow-up article this month on page 1, "Is there a clinical case for a low-dose approach?"

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VALCHLOR is contraindicated in patients with known severe hypersensitivity to mechlorethamine. Hypersensitivity reactions, including anaphylaxis, have occurred with topical formulations of mechlorethamine.

DOSING AND APPLICATION

VALCHLOR is for topical dermatologic use only. Apply a thin film once daily to affected areas of the skin. Caregivers must wear disposable nitrile gloves when applying VALCHLOR. Patients and caregivers must wash hands thoroughly after handling or applying VALCHLOR.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

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- **Secondary Exposure:** VALCHLOR is a cytotoxic drug. Avoid direct skin contact with VALCHLOR in individuals other than the patients due to risk of dermatitis, mucosal injury, and secondary cancers
- **Dermatitis:** Monitor patients for redness, swelling, inflammation, itchiness, blisters, ulceration and secondary skin infections. Stop treatment or reduce dose frequency.
- **Non-melanoma skin cancer:** Monitor patients during and after treatment.
- **Embryo-fetal toxicity:** Women should avoid becoming pregnant or nursing while using VALCHLOR due to the potential hazard to the fetus.
- **Flammable gel:** VALCHLOR is an alcohol-based gel. Avoid fire, flame, and smoking until the gel has dried.

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The most common adverse reactions (≥ 5%) are dermatitis, pruritus, bacterial skin infection, skin ulceration or blistering, and hyperpigmentation. These reactions may be mild to severe. Elderly patients may be more susceptible. Depending on severity, dosing changes or discontinuation may be required.

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Please see **Brief Summary of Prescribing Information** on adjacent page.

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This brief summary does not include all the information needed to use VALCHLOR safely and effectively. See Full Prescribing Information for VALCHLOR.

- **INDICATIONS AND USAGE**

  VALCHLOR is an alkylating drug indicated for the topical treatment of Stage IA and IB mycosis fungoides-type cutaneous T-cell lymphoma in patients who have received prior skin-directed therapy.

- **CONTRAINDICATIONS**

  The use of VALCHLOR is contraindicated in patients with known severe hypersensitivity to mechlorethamine. Hypersensitivity reactions, including anaphylaxis, have occurred with topical formulations of mechlorethamine.

- **WARNINGS AND PRECAUTIONS**

  >> Mucosal or Eye Injury

  Exposure of the eyes to mechlorethamine causes pain, burns, inflammation, photophobia, and blurred vision. Blindness and severe irreversible anterior eye injury may occur. Advise patients that if eye exposure occurs, (1) immediately irrigate for at least 15 minutes with copious amounts of water, normal saline, or a balanced salt ophthalmic irrigating solution and (2) obtain immediate medical care (including ophthalmologic consultation).

  Exposure of mucous membranes such as the oral mucosa or nasal mucosa causes pain, redness, and ulceration, which may be severe. Should mucosal contact occur, immediately irrigate for at least 15 minutes with copious amounts of water, followed by immediate medical consultation.

  >> Secondary Exposure to VALCHLOR

  Avoid direct skin contact with VALCHLOR in individuals other than the patient. Risks of secondary exposure include dermatitis, mucosal injury, and secondary cancers. Follow recommended application instructions to prevent secondary exposure.

  >> Dermatitis

  The most common adverse reaction was dermatitis, which occurred in 56% of the patients. Dermatitis was moderately severe or severe in 23% of patients. Monitor patients for redness, swelling, inflammation, itchiness, blisters, ulceration, and secondary skin infections. The face, genitalia, anus, and intertriginous skin are at increased risk of dermatitis. Follow dose modification instructions for dermatitis.

  >> Non-Melanoma Skin Cancer

  Four percent (4%, 11/255) of patients developed a non-melanoma skin cancer during the clinical trial or during one year of post-treatment follow-up: 2% (3/128) of patients receiving VALCHLOR and 6% (8/127) of patients receiving the mechlorethamine ointment comparator. Some of these non-melanoma skin cancers occurred in patients who had received prior therapies known to cause non-melanoma skin cancer. Monitor patients for non-melanoma skin cancers during and after treatment with VALCHLOR. Non-melanoma skin cancer may occur on any area of the skin, including untreated areas.

  >> Embryo-fetal Toxicity

  Based on its mechanism of action, case reports in humans, and findings in animals, VALCHLOR can cause fetal harm when administered to a pregnant woman. There are case reports of children born with malformations in pregnant women systemically administered mechlorethamine. Mechlorethamine was teratogenic and embryo-lethal after a single subcutaneous administration to animals. Advise women to avoid becoming pregnant while using VALCHLOR. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus.

  >> Flammable Gel

  Alcohol-based products, including VALCHLOR, are flammable. Follow recommended application instructions.

- **ADVERSE REACTIONS**

  In a randomized, observer-blinded, controlled trial, VALCHLOR 0.016% (equivalent to 0.02% mechlorethamine HCl) was compared to an Aquaphor®-based mechlorethamine HCl 0.02% ointment (Comparator). The maximum duration of treatment was 12 months. Sixty-three percent (63%) of patients in the VALCHLOR arm and 67% in the comparator arm completed 12 months of treatment.

  The body system associated with the most frequent adverse reactions was skin and subcutaneous tissue disorders. The most common adverse reactions (occurring in at least 5% of the patients) are shown in Table 1.

Table 1. Most Commonly Reported (≥5%) Cutaneous Adverse Reactions

	VALCHLOR N=128 % of patients		Comparator N=127 % of patients	
	Any Grade	Moderately-Severe or Severe	Any Grade	Moderately-Severe or Severe
Dermatitis	56	23	58	17
Pruritus	20	4	16	2
Bacterial skin infection	11	2	9	2
Skin ulceration or blistering	6	3	5	2
Skin hyperpigmentation	5	0	7	0

In the clinical trial, moderately-severe to severe skin-related adverse events were managed with treatment reduction, suspension, or discontinuation. Discontinuations due to adverse reactions occurred in 22% of patients treated with VALCHLOR and 18% of patients treated with the comparator. Sixty-seven percent (67%) of the discontinuations for adverse reactions occurred within the first 90 days of treatment. Temporary treatment suspension occurred in 34% of patients treated with VALCHLOR and 20% of patients treated with the comparator. Reductions in dosing frequency occurred in 23% of patients treated with VALCHLOR and 12% of patients treated with the comparator.

Reductions in hemoglobin, neutrophil count, or platelet count occurred in 13% of patients treated with VALCHLOR and 17% treated with Comparator.

- **DRUG INTERACTIONS**

  No drug interaction studies have been performed with VALCHLOR. Systemic exposure has not been observed with topical administration of VALCHLOR; therefore, systemic drug interactions are not likely.

- **USE IN SPECIFIC POPULATIONS**

  >> Pregnancy

  Pregnancy Category D

  Risk Summary

  Mechlorethamine can cause fetal harm when administered to a pregnant woman. There are case reports of children born with malformations to pregnant women systemically administered mechlorethamine. Mechlorethamine was teratogenic in animals after a single subcutaneous administration. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus.

  Animal Data

  Mechlorethamine caused fetal malformations in the rat and ferret when given as single subcutaneous injections of 1 mg/kg. Other findings in animals included embryolethality and growth retardation when administered as a single subcutaneous injection.

  >> Nursing Mothers

  It is not known if mechlorethamine is excreted in human milk. Due to the potential for topical or systemic exposure to VALCHLOR through exposure to the mother's skin, a decision should be made whether to discontinue nursing or the drug, taking into account the importance of the drug to the mother.

  >> Pediatric Use

  Safety and effectiveness in pediatric patients have not been established.

  >> Geriatric Use

  A total of 79 patients age 65 and older (31% of the clinical trial population) were treated with either VALCHLOR or the comparator in the clinical trial. Forty-four percent (44%) of patients age 65 or older treated with VALCHLOR achieved a Composite Assessment of Index Lesion Severity (CAILS) response compared to 66% of patients below the age of 65. Seventy percent (70%) of patients age 65 and older experienced cutaneous adverse reactions and 38% discontinued treatment due to adverse reactions, compared to 58% and 14% in patients below the age of 65, respectively. Similar differences in discontinuation rates between age subgroups were observed in the comparator group.

Manufactured for:
Actelion Pharmaceuticals US, Inc.
South San Francisco, CA 94080, USA

ACTELION

David J. Goldberg, M.D., J.D., *is director of Skin Laser & Surgery Specialists of New York and New Jersey; director of laser research, Mount Sinai School of Medicine; and adjunct professor of law, Fordham Law School.*

I violated HIPAA. Now what?

Dr. Doe has a 25-year-old dermatology practice in a quiet suburban area. Although he loves practicing dermatology, he finds himself overwhelmed with government regulation. HIPAA, EMR, meaningful use, ACA — he does not know where to begin.

One year ago, his practice administrator received a request for medical records from a female patient seemingly on behalf of her husband who was also a patient in the practice. What the administrator did not realize is the husband had not authorized release of the records that contained documentation of his several sexually transmitted diseases. What the administrator also did not know was the couple was in the process of a bitter matrimonial dispute.

The wife gave the records to her divorce attorney, who submitted them to the court as proof of the husband's infidelity. The husband filed suit against Dr. Doe for a HIPAA violation — he never would have authorized release of his medical records to his estranged wife. Dr. Doe knows that this is a HIPAA violation and is now frightened about the consequences of this act. Should he be?

HIPAA's impact widespread

The Affordable Care Act (ACA), or "Obamacare," gets most of the front-page headlines in healthcare right now. However, an earlier and perhaps equally sweeping piece of healthcare legislation still consumes much of the healthcare industry's time and concern behind the scenes. The Health Insurance Portability and Accountability Act (HIPAA) can be felt in almost every corner of the healthcare industry.

Like Obamacare, HIPAA covers a great deal of legislative and regulatory ground, and both cause significant confusion and anxiety for healthcare professionals. In HIPAA's case, however, only one small part of the original law in particular is responsible for this frustration.

> The Privacy Rule is structured such that consent from the individual is always required to use or disclose an individual's PHI.

HIPAA's Administrative Simplification Rules turned out to be one of the most important parts of the law's legal legacy. The Simplification Rules now dominate how each and every patient experiences healthcare. Whether they realize it or not, almost every person who receives care in this country sees some version of a HIPAA authorization stating their rights under the statute and the terms on which their personal health information (PHI) can be disclosed. Healthcare providers who transmit any health information electronically are termed "covered entities" (CEs).

The Privacy Rule of HIPAA sets out the terms on which health information may be transferred and disclosed without any additional or special consent from the individual, and what rights the individual has regarding their health information. The Privacy Rule is structured such that consent from the individual is **always** required to use or disclose an individual's PHI, but most of the routine uses of PHI in the healthcare industry, such as treatment or payment activities, are exempted from the authorization requirement. Disclosure of medical records to others is generally not exempt.

What are the consequences?

Besides being required to get the individual's consent, CEs must, upon request, allow individuals to amend their PHI records, provide them with an accounting of all the disclosures of their PHI, and provide them a full copy of their PHI records. These terms may seem like innocuous services that should be provided as a common sense courtesy to the individual, but come to form the meat and potatoes of the Simplification Rules. They control how and when information can flow.

The big question in today's healthcare industry is how this law affects actual practice. The amount of actual enforcement of the Simplification Rules under the original Enforcement Rule was not significant. It has been hard for CEs to take HIPAA seriously when they saw what the statistics showed.

From July 2003 — when the complaints system was set up — to Aug. 31, 2007, there were a total of 29,994 submitted complaints. Over those four years and almost 30,000 complaints, however, there were no civil fines whatsoever levied for a violation of HIPAA. It seemed clear that CEs and others affected by HIPAA had little to fear from the Privacy Rule or other Simplification Rules based on these numbers. However, the Department of Justice has had slightly more luck in enforcing the criminal (non-civil) aspects of HIPAA. Yet by 2006, there were only three HIPAA criminal cases against individuals.

Dr. Doe's staff seems to have clearly committed a HIPAA violation. However, the consequences, in reality, may lead to nothing. **DT**

Share your experience: How has your practice been impacted by HIPAA regulations? Tell us at **editor@dermatologytimes.com**.

INDICATION

XEOMIN® (incobotulinumtoxinA) for injection, for intramuscular use is indicated for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients.

IMPORTANT SAFETY INFORMATION, INCLUDING BOXED WARNING

WARNING: DISTANT SPREAD OF TOXIN EFFECT

Postmarketing reports indicate that the effects of XEOMIN and all botulinum toxin products may spread from the area of injection to produce symptoms consistent with botulinum toxin effects. These may include asthenia, generalized muscle weakness, diplopia, blurred vision, ptosis, dysphagia, dysphonia, dysarthria, urinary incontinence and breathing difficulties. These symptoms have been reported hours to weeks after injection. Swallowing and breathing difficulties can be life threatening and there have been reports of death. The risk of symptoms is probably greatest in children treated for spasticity but symptoms can also occur in adults treated for spasticity and other conditions, particularly in those patients who have underlying conditions that would predispose them to these symptoms. In unapproved uses, including spasticity in children and adults, and in approved indications, cases of spread of effect have been reported at doses comparable to those used to treat cervical dystonia and at lower doses.

CONTRAINDICATIONS

XEOMIN is contraindicated in patients with a known hypersensitivity to the active substance botulinum toxin type A or to any of the components in the formulation and in the presence of infection at the proposed injection site(s), as injection could lead to severe local or disseminated infection.

WARNINGS AND PRECAUTIONS

- The potency units of XEOMIN are not interchangeable with other preparations of botulinum toxin products. Therefore, units of biological activity of XEOMIN cannot be compared to or converted into units of any other botulinum toxin products.
- Hypersensitivity reactions have been reported with botulinum toxin products (anaphylaxis, serum sickness, urticaria, soft tissue edema, and dyspnea). If serious and/or immediate hypersensitivity reactions occur further injection of XEOMIN should be discontinued and appropriate medical therapy immediately instituted.
- Treatment with XEOMIN and other botulinum toxin products can result in swallowing or breathing difficulties. Patients with pre-existing swallowing or breathing difficulties may be more susceptible to these complications. When distant effects occur, additional respiratory muscles may be involved. Patients may require immediate medical attention should they develop problems with swallowing, speech, or respiratory disorders. Dysphagia may persist for several months, which may require use of a feeding tube and aspiration may result from severe dysphagia *[See Boxed Warning]*.
- **Glabellar Lines:** Do not exceed the recommended dosage and frequency of administration of XEOMIN. In order to reduce the complication of ptosis the following steps should be taken:
  - » avoid injection near the levator palpebrae superioris, particularly in patients with larger brow depressor complexes;
  - » corrugator injections should be placed at least 1 cm above the bony supraorbital ridge.
- Individuals with peripheral motor neuropathic diseases, amyotrophic lateral sclerosis, or neuromuscular junctional disorders (e.g., myasthenia gravis or Lambert-Eaton syndrome) should be monitored particularly closely when given botulinum toxin. Patients with neuromuscular disorders may be at increased risk of clinically significant effects including severe dysphagia and respiratory compromise from typical doses of XEOMIN.
- XEOMIN contains human serum albumin. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases and Creutzfeldt-Jakob disease (CJD). No cases of transmission of viral diseases or CJD have ever been reported for albumin.

ADVERSE REACTIONS

Glabellar Lines: The most commonly observed adverse reaction (incidence ≥ 2% of patients and greater than placebo) for XEOMIN was Headache (5.4%).

DRUG INTERACTIONS

Concomitant treatment of XEOMIN and aminoglycoside antibiotics, spectinomycin, or other agents that interfere with neuromuscular transmission (e.g., tubocurarine-like agents), or muscle relaxants, should be observed closely because the effect of XEOMIN may be potentiated. The effect of administering different botulinum toxin products at the same time or within several months of each other is unknown. Excessive neuromuscular weakness may be exacerbated by administration of another botulinum toxin prior to the resolution of the effects of a previously administered botulinum toxin.

USE IN PREGNANCY

Pregnancy Category C: There are no adequate and well-controlled studies in pregnant women. XEOMIN should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

PEDIATRIC USE

The safety and effectiveness of XEOMIN in patients less than 18 years of age have not been established.

Please see Brief Summary of full Prescribing Information on the following pages.

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XEOMIN (incobotulinumtoxinA) for injection, for intramuscular use
BRIEF SUMMARY. Visit www.XEOMIN.com for full Prescribing Information.

WARNING: DISTANT SPREAD OF TOXIN EFFECT

Postmarketing reports indicate that the effects of XEOMIN and all botulinum toxin products may spread from the area of injection to produce symptoms consistent with botulinum toxin effects. These may include asthenia, generalized muscle weakness, diplopia, blurred vision, ptosis, dysphagia, dysphonia, dysarthria, urinary incontinence and breathing difficulties. These symptoms have been reported hours to weeks after injection. Swallowing and breathing difficulties can be life threatening and there have been reports of death. The risk of symptoms is probably greatest in children treated for spasticity but symptoms can also occur in adults treated for spasticity and other conditions, particularly in those patients who have underlying conditions that would predispose them to these symptoms. In unapproved uses, including spasticity in children and adults, and in approved indications, cases of spread of effect have been reported at doses comparable to those used to treat cervical dystonia and at lower doses *[see Warnings and Precautions]*.

CONTRAINDICATIONS

Hypersensitivity-Use in patients with a known hypersensitivity to the active substance botulinum neurotoxin type A, or to any of the excipients (human albumin, sucrose), could lead to a life-threatening allergic reaction. XEOMIN is contraindicated in patients with known hypersensitivity to any botulinum toxin preparation or to any of the components in the formulation *[see Warnings and Precautions]*.

Infection at Injection Site-Use in patients with an infection at the injection site could lead to severe local or disseminated infection. XEOMIN is contraindicated in the presence of infection at the proposed injection site(s).

WARNINGS AND PRECAUTIONS

- **Spread of Toxin Effect-**Postmarketing safety data from XEOMIN and other approved botulinum toxins suggest that botulinum toxin effects may, in some cases, be observed beyond the site of local injection. The symptoms are consistent with the mechanism of action of botulinum toxin and may include asthenia, generalized muscle weakness, diplopia, blurred vision, ptosis, dysphagia, dysphonia, dysarthria, urinary incontinence, and breathing difficulties *[see Boxed Warning (above)]*.
- **Lack of Interchangeability between Botulinum Toxin Products-**The potency Units of XEOMIN are specific to the preparation and assay method utilized. They are not interchangeable with the other preparations of botulinum toxin products and, therefore, Units of biological activity of XEOMIN cannot be compared to or converted into Units of any other botulinum toxin products assessed with any other specific assay method.
- **Hypersensitivity Reactions-**Hypersensitivity reactions have been reported with botulinum toxin products (anaphylaxis, serum sickness, urticaria, soft tissue edema, and dyspnea). If serious and/or immediate hypersensitivity reactions occur further injection of XEOMIN should be discontinued and appropriate medical therapy immediately instituted.
- **Dysphagia and Breathing Difficulties in Treatment of Cervical Dystonia-**Treatment with XEOMIN and other botulinum toxin products can result in swallowing or breathing difficulties. Patients with pre-existing swallowing or breathing difficulties may be more susceptible to these complications. In most cases, this is a consequence of weakening of muscles in the area of injection that are involved in breathing or swallowing. When distant effects occur, additional respiratory muscles may be involved. Deaths as a complication of severe dysphagia have been reported after treatment with botulinum toxin. Dysphagia may persist for several months, and require use of a feeding tube to maintain adequate nutrition and hydration. Aspiration may result from severe dysphagia and is a particular risk when treating patients in whom swallowing or respiratory function is already compromised. In general, limiting the dose injected into the sternocleidomastoid muscle may decrease the occurrence of dysphagia. Patients treated with botulinum toxin may require immediate medical attention should they develop problems with swallowing, speech or respiratory disorders. These reactions can occur within hours to weeks after injection with botulinum toxin *[see Warnings and Precautions and Adverse Reactions in Full Prescribing Information for more information]*.
- **Pre-existing Neuromuscular Disorders and other Special Populations-**Individuals with peripheral motor neuropathic diseases, amyotrophic lateral sclerosis, or neuromuscular junctional disorders (e.g., myasthenia gravis or Lambert-Eaton syndrome) should be monitored particularly closely when given botulinum toxin. Patients with neuromuscular disorders may be at increased risk of clinically significant effects including severe dysphagia and respiratory compromise from typical doses of XEOMIN *[see Adverse Reactions]*.
- **Corneal Exposure, Corneal Ulceration, and Ectropion in Patients Treated with XEOMIN for Blepharospasm-**Reduced blinking from injection of botulinum toxin products in the orbicularis muscle can lead to corneal exposure, persistent epithelial defect and corneal ulceration, especially in patients with VII nerve disorders. Careful testing of corneal sensation in eyes previously operated upon, avoidance of injection into the lower lid area to avoid ectropion, and vigorous treatment of any epithelial defect should be employed. This may require protective drops, ointment, therapeutic soft contact lenses, or closure of the eye by patching or other means. Because of its anticholinergic effects, XEOMIN should be used with caution in patients at risk of developing narrow angle glaucoma. To prevent ectropion, botulinum toxin products should not be injected into the medial lower eyelid area. Ecchymosis easily occurs in the soft tissues of the eyelid. Immediate gentle pressure at the injection site can limit that risk.
- **Risk of Ptosis in Patients Treated with XEOMIN for Glabellar Lines-**Do not exceed the recommended dosage and frequency of administration of XEOMIN. In order to reduce the complication of ptosis the following steps should be taken:
  - » Avoid injection near the levator palpebrae superioris, particularly in patients with larger brow depressor complexes.
  - » Corrugator injections should be placed at least 1 cm above the bony supraorbital ridge.
- **Human Albumin and Transmission of Viral Diseases-**This product contains albumin, a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases. A theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD) is also considered extremely remote. No cases of transmission of viral diseases or CJD have ever been reported for albumin.

ADVERSE REACTIONS

The following adverse reactions to XEOMIN are discussed in greater detail in other sections of the labeling:

- » Hypersensitivity *[see Contraindications and Warnings and Precautions]*
- » Spread of Effects from Toxin *[see Warnings and Precautions]*

Glabellar Lines In three placebo-controlled trials in 803 subjects with glabellar lines, 535 subjects received a single dose of 20 Units XEOMIN and 268 subjects received placebo. XEOMIN treated subjects were 24 to 74 years old, and were predominantly female (88%). The most frequent adverse reactions in XEOMIN treated subjects were: headache 29 (5.4%), facial paresis 4 (0.7%), injection site hematoma 3 (0.6%) and eyelid edema 2 (0.4%). Four serious adverse events occurred in two placebo-treated subjects. Six XEOMIN treated subjects experienced six serious adverse events. All serious adverse events were assessed as unrelated to study drug. The adverse reactions below reflect exposure to XEOMIN with glabellar lines in placebo-controlled studies. Adverse reactions are adverse events in which there is some basis to believe there is a causal relationship between the drug and the occurrence of the adverse event. Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Table 4: Adverse Reactions in Placebo-Controlled Trials

Adverse reactions	XEOMIN (N=535) (%)	Placebo (N=268) (%)
Nervous system disorders	**33 (6.1)**	**6 (2.2)**
Headache[1]	29 (5.4)	6 (2.2)
Facial paresis (brow ptosis)	4 (0.7)	0
General disorders and administration site conditions	**5 (0.9)**	**2 (0.7)**
Injection site hematoma	3 (0.6)	0
Injection site pain	1 (0.2)	0
Facial pain	1 (0.2)	0
Injection site swelling	0	1 (0.4)
Sensation of pressure	0	1 (0.4)
Eye disorders	**5 (0.9)**	**0**
Eyelid edema	2 (0.4)	0
Blepharospasm	1 (0.2)	0
Eye disorder	1 (0.2)	0
Eyelid ptosis	1 (0.2)	0

In open label, multiple dose trials, adverse reactions were reported for 105 of the 800 subjects (13.1%). Headache was the most common adverse reaction, reported for 57 subjects (7.1%), followed by injection site hematoma in 8 subjects (1.0%). Adverse reactions reported in less than 1% of subjects were: facial paresis (brow ptosis), muscle disorder (elevation of eyebrow), injection site pain, and eyelid edema.

Immunogenicity-As with all therapeutic proteins, there is a potential for immunogenicity.

Postmarketing Experience-The following adverse reactions have been reported during post-approval use with XEOMIN. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure: eye swelling, eyelid edema, dysphagia, nausea, flu-like symptoms, injection site pain, injection site reaction, allergic dermatitis, localized allergic reactions like swelling, edema, erythema, pruritus or rash, herpes zoster, muscular weakness, muscle spasm, dysarthria, myalgia and hypersensitivity.

DRUG INTERACTIONS

No formal drug interaction studies have been conducted with XEOMIN. Coadministration of XEOMIN and aminoglycoside antibiotics or other agents interfering with neuromuscular transmission, e.g., tubocurarine-type muscle relaxants, should only be performed with caution as these agents may potentiate the effect of the toxin. Use of anticholinergic drugs after administration of XEOMIN may potentiate systemic anticholinergic effects. The effect of administering different botulinum toxin products at the same time or within several months of each other is unknown. Excessive neuromuscular weakness may be exacerbated by administration of another botulinum toxin prior to the resolution of the effects of a previously administered botulinum toxin. Excessive weakness may also be exaggerated by administration of a muscle relaxant before or after administration of XEOMIN.

USE IN SPECIFIC POPULATIONS

Pregnancy-Pregnancy Category C: There are no adequate and well-controlled studies in pregnant women. XEOMIN should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers-It is not known whether botulinum toxin type A is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when XEOMIN is administered to a nursing woman.

Pediatric Use-Safety and effectiveness of XEOMIN in patients less than 18 years of age have not been established *[see Warnings and Precautions]*.

Geriatric Use-Glabellar Lines There are limited clinical data with XEOMIN in subjects over 65 years of age and over in clinical studies with glabellar lines. Of the total number of subjects in the placebo-controlled clinical studies GL1 and GL2, 21 (4%) subjects were 65 and over. Efficacy was observed in 20% (3/15) of XEOMIN subjects 65 years and over. For the entire safety database of geriatric subjects, there was no increase in the incidence of adverse events related to treatment with XEOMIN.

OVERDOSAGE

Excessive doses of XEOMIN may be expected to produce neuromuscular weakness with a variety of symptoms. Respiratory support may be required where excessive doses cause paralysis of the respiratory muscles. In the event of overdose, the patient should be medically monitored for symptoms of excessive muscle weakness or muscle paralysis *[see Warnings and Precautions].* Symptomatic treatment may be necessary. Symptoms of overdose are not likely to be present immediately following injection. Should accidental injection or oral ingestion occur, the person should be medically supervised for several weeks for signs and symptoms of excessive muscle weakness or paralysis. In the event of overdose, antitoxin raised against botulinum toxin is available from the Centers for Disease Control and Prevention (CDC) in Atlanta, GA. However, the antitoxin will not reverse any botulinum toxin-induced effects already apparent by the time of antitoxin administration. In the event of suspected or actual cases of botulinum toxin poisoning, please contact your local or state Health Department to process a request for antitoxin through the CDC. If you do not receive a response within 30 minutes, please contact the CDC directly at 770-488-7100. More information can be obtained at http://www.cdc.gov/ncidod/srp/drugs/formulary.html#1a.

Please visit www.xeomin.com for full Prescribing Information.

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FDA approves combo treatment for melanoma

MEKINIST (trametinib, GlaxoSmithKline) in combination with Tafinlar (dabrafenib) has been approved by the Food and Drug Administration for use as a possible treatment for patients suffering from inoperable melanoma and certain types of metastatic melanoma.

The combination of drugs was approved through the FDA's Accelerated Approval program and given Priority Review status. The approval is dependent on the results of an ongoing trial (referred to as MEK115306 or COMBI-d), which is designed to determine the benefit of the drug combination among this patient population.

The combination of drugs is approved for metastatic melanoma with BRAF V600E or V600K mutations, which must be detected via testing. Use of Tafinlar is contraindicated for patients with wild-type BRAF melanoma. The combination acts to inhibit both BRAF and MEK, while lessening the side effects of only inhibiting MEK. The combination also can increase the efficacy of BRAF inhibitors, which alone lasts about six months.

"The main efficacy endpoint of investigator-assessed overall response rate was 76 percent for dabrafenib in combination with trametinib, and 54 percent for dabrafenib alone," Kiran Patel, M.D., GSK's vice president and medicine development leader for oncology, tells Dermatology Times. "This is an important finding because it suggests that two drugs can work better together. In terms of dermatologists' routine monitoring of patients for cutaneous squamous cell carcinoma (including squamous cell carcinomas of the skin and keratoacanthomas), the trial's primary safety endpoint, the incidence rate was 7 percent for dabrafenib in combination with trametinib and 19 percent for dabrafenib alone."

The accelerated approval is positive news for those patients with some of the most difficult cases of melanoma, says dermatopathologist Ronald Wheeland, M.D., who practices in Tucson, Ariz.

"Unresectable and metastatic melanoma represent the most serious and difficult to manage forms of melanoma," says Dr. Wheeland, who was not involved in the studies. "For this reason, it is great news that the FDA has granted an accelerated approval for the combination treatment of these forms of melanoma using trametinib and dabrafenib based on the results of clinical trials. While additional follow-up and study are needed to evaluate the clinical benefit of this combination therapy, early evidence suggests that this combined treatment may provide successful management of appropriate melanoma patients." **DT**

FDA looking at safety of antibacterial hand soaps

THE FOOD AND DRUG ADMINISTRATION has proposed a rule that would require manufacturers of antibacterial hand soaps to demonstrate that their products are safe and effective.

The FDA is conducting an ongoing review of the active ingredients in antibacterial soaps to ensure they are safe for long-term daily use and whether they are more effective than plain soap and water for preventing illnesses and the spread of germs, according to a news release.

"Some data suggest that long-term exposure to certain active ingredients used in antibacterial products — for example, triclosan (liquid soaps) and triclocarban (bar soaps) — could pose health risks, such as bacterial resistance or hormonal effects," the FDA stated.

The proposed rule does not impact hand sanitizers, wipes or antibacterial products used in healthcare settings. The FDA noted that nearly all soaps labeled as "antibacterial" or "antimicrobial" contain at least one of the antibacterial ingredients addressed in the proposed rule.

"Due to consumers' extensive exposure to the ingredients in antibacterial soaps, we believe there should be a clearly demonstrated benefit from using antibacterial soap to balance any potential risk," Janet Woodcock, M.D., director of the FDA's Center for Drug Evaluation and Research, said in the news release. **DT**

Cancer may trigger scleroderma

Science
December 2013

dermatologytimes.com/scleroderma

RESULTS of a Johns Hopkins study suggest that cancer triggers the autoimmune disease scleroderma.

Patients with scleroderma often make immune proteins or antibodies to another protein, RPC1, according to a news release. These antibodies are believed to cause the organ damage characteristic of scleroderma, though it's not known what causes the production of these antibodies.

Using blood and tumor tissue samples from 16 patients with scleroderma and different kinds of cancer, the research team found that cancers from most patients with severe scleroderma had a mutation in the gene POLR3A, which codes for RPC1. These alterations created a "foreign" form of the RPC1 protein, which the researchers say appears to trigger an immune response.

"The most significant finding is that specific mutations in autoantigens in cancer initiate the immune response in a subset of scleroderma patients, suggesting that cancer is an initiator of scleroderma in some patients," study investigator Antony Rosen, M.D., tells Dermatology Times. "This may have broader implications for other autoimmune diseases, and for understanding the role of the immune system in controlling cancer."

Dr. Rosen, vice dean for research at Johns Hopkins University School of Medicine, says the team's findings should spur research into the possible cancerous origins of other autoimmune diseases, including lupus and myositis, and whether immune responses to antigens other than RPC1 are involved. **DT**

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Standard wound treatments may still be best

Johns Hopkins Evidence-Based Practice Center
Johns Hopkins Wound Healing Center

dermatologytimes.com/woundstudy

AN ANALYSIS of 60 papers related to skin ulcer treatment suggests that the research presented in the majority of the papers is flawed, leading to unreliable results.

The analysis also suggested that those papers that were scientifically rigorous in their research methods pointed to weak or inconclusive evidence that there are more successful treatments than standard procedures.

The analysis was led by researchers from the Johns Hopkins Evidence-Based Practice Center and the Johns Hopkins Wound Healing Center. The research team began the analysis in 2011, after receiving a grant from the Agency for Healthcare Research and Quality.

The study examined treatment options for chronic venous ulcers. The treatments examined were wound dressings, antibiotics and venous surgery. The standard treatments are compression therapy or stockings.

According to the study there was some data that dressings using living cells increased wound healing. Data also suggest that cadexomer iodine and collagen possibly increase healing.

Despite this, compression therapy should still be considered the standard treatment for chronic venous ulcers, according to Gerald Lazarus, M.D., director of Bayview Dermatology and one of the study's leaders.

"Almost all dressings applied to venous wounds have similar efficacy with the exception that biological dressings containing viable cells demonstrated significantly enhanced wound healing," Dr. Lazarus tells Dermatology Times. "Iodosorb and collagen/connective tissue component preparations had more efficacy than controls. Venous surgery did not convincingly enhance healing, but did appear to maintain more durable healing after the wound was healed. There was no evidence that routine use of systemic antibiotics was of value in promoting the healing of venous ulcers.

"This does not mean that these interventions do not work; rather, there is insufficient evidence to prove their therapeutic efficacy," he adds. "Our studies of this easily diagnosable entity of venous ulcers demonstrates the need for better evidence to ensure reimbursement in a growingly cost-conscious financial environment."

Dr. Lazarus also notes that only 60 of 10,066 papers focusing on therapeutic interventions could be analyzed, because of design or implementation failures.

"This observation should alert all dermatologists to carefully analyze the quality of clinical research," he says. **DT**

Skin creams cause reactions in patients with atopic dermatitis

Journal of the American Academy of Dermatology
November 2013

dermatologytimes.com/topicalsensitivity

PATIENTS with atopic dermatitis are more likely than those without the condition to have allergic reactions to formaldehyde releasers found in skin creams, according to a recent study.

Researchers with the University of Louisville conducted patch testing on 2,453 people for allergic reactions, and 342 of those tested had eczema.

"Compared with nonatopic patients, patients with AD (atopic dermatitis) were statistically more likely to have positive patch tests," the study states. "AD was associated with contact hypersensitivity to quaternium-15, imidazolidinyl urea, DMDM hydantoin, and 2-bromo-2-nitropropane-1,3-diol but not to parabens, formaldehyde, or diazolidinyl urea."

The test patients were limited to the metropolitan areas of Kansas City, Mo., and New York City, and only those suspected of having allergic contact dermatitis were tested.

"Patients with AD should avoid the use of skincare products preserved with formaldehyde releasers," study authors concluded. **DT**

Formaldehyde concentrations in hair straightening products may be health threat

Journal of the American Academy of Dermatology
February 2014

dermatologytimes.com/folliclestimulation

FORMALDEHYDE concentrations in Brazilian keratin hair straightening products may be high enough to serve as a health hazard, a recent study reports.

Researchers in South Africa measured formaldehyde concentrations in seven commercial Brazilian keratin treatments marketed in South Africa in 2012 using a high-performance liquid chromatography with ultraviolet light detection after derivatization with dinitrophenylhydrazine.

While the maximum safe concentration set by the U.S. Cosmetic Ingredient Review Expert Panel is less than 0.2 percent, the researchers found that six of the brands studied, five of which were labeled "formaldehyde free", actually had levels ranging five times higher than this recommended level (0.96 to 1.4 percent).

The authors tested each brand three times.

"Industry monitoring is needed to improve compliance and protection of hairdressers and consumers," the authors concluded. **DT**


WHEN ACNE HAS
YOUR PATIENTS
LOOKING DOWN...
Turn the page to see
how you can help.

Important Safety Information

Indication: EPIDUO® Gel is indicated for the topical treatment of acne vulgaris in patients 9 years of age and older. **Adverse Events:** In controlled clinical studies, the most commonly reported adverse events (≥1%) in patients treated with EPIDUO® Gel were dry skin, contact dermatitis, application site burning, application site irritation and skin irritation **Warnings/Precautions:** Patients taking EPIDUO® Gel should avoid exposure to sunlight and sunlamps and wear sunscreen whensun exposure cannot be avoided. Erythema, scaling, dryness, stinging/burning, irritant and allergic contact dermatitis may occur with use of EPIDUO® Gel and may necessitate discontinuation.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit *www.fda.gov/medwatch* or call 1-800-FDA-1088.

*A phase 3, randomized, multicenter, double-blind, active- and vehicle-controlled, parallel-group study evaluating the efficacy and safety of adapalene 0.1%–BPO 2.5% fixed-dose combination gel relative to adapalene 0.1% monotherapy, BPO 2.5% monotherapy, and gel vehicle in a large population for the treatment of acne vulgaris (N=1670).

†A multicenter, randomized, vehicle-controlled, double-blind study evaluating the efficacy and safety of adapalene 0.1%—BPO 2.5% fixed-dose combination gel in subjects 9 to 11 years of age with acne vulgaris (N=285).

Please see brief summary of full Prescribing Information on next page.

Epiduo®
(adapalene and benzoyl peroxide) Gel 0.1%/2.5%

IMPORTANT INFORMATION ABOUT

EPIDUO® GEL

(adapalene and benzoyl peroxide) Gel, 0.1% / 2.5%

BRIEF SUMMARY

This summary contains important information about EPIDUO (EP-E-Do-Oh) gel. It is not meant to take the place of your doctor's instructions. Read this information carefully before you start using EPIDUO gel. Ask your doctor or pharmacist if you do not understand any of this information or if you want to know more about EPIDUO gel. For full Prescribing Information and Patient Information please see the package insert.

WHAT IS EPIDUO GEL?

EPIDUO gel is a prescription medicine for skin use only (topical) used to treat acne vulgaris in people 9 years of age or older. Acne vulgaris is a condition in which the skin has blackheads, whiteheads, and pimples.

WHO IS EPIDUO GEL FOR?

EPIDUO gel is for use in people 9 years of age and older. It is not known if EPIDUO gel is safe and effective for children younger than 9 years old.

Do not use EPIDUO gel for a condition for which it was not prescribed. Do not give EPIDUO gel to other people, even if they have the same symptoms you have. It may harm them.

WHAT SHOULD I TELL MY DOCTOR BEFORE USING EPIDUO GEL?

Before you use EPIDUO gel, tell your doctor if you:

- have other skin problems, including cuts or sunburn.
- have any other medical conditions.
- are pregnant or planning to become pregnant. It is not known if EPIDUO gel can harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if EPIDUO gel passes into your breast milk and if it can harm your baby. Talk to your doctor about the best way to feed your baby if you use EPIDUO gel.

Tell your doctor about all of the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

- Especially tell your doctor if you use any other medicine for acne. Using EPIDUO gel with topical medicines that contain sulfur, resorcinol or salicylic acid may cause skin irritation.
- Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

WHAT SHOULD I AVOID WHILE USING EPIDUO GEL?

- You should avoid spending time in sunlight or artificial sunlight, such as tanning beds or sunlamps. EPIDUO gel can make your skin sensitive to sun and the light from tanning beds and sunlamps. You should wear sunscreen and wear a hat and clothes that cover the areas treated with EPIDUO gel if you have to be in the sunlight.
- You should avoid weather extremes such as wind and cold as this may cause irritation to your skin.
- You should avoid applying EPIDUO gel to cuts, abrasions and sunburned skin.
- You should avoid skin products that may dry or irritate your skin such as harsh soaps, astringents, cosmetics that have strong skin drying effects and products containing high levels of alcohol.
- You should avoid the use of "waxing" as a hair removal method on skin treated with EPIDUO gel.
- EPIDUO gel may bleach your clothes or hair. Allow EPIDUO gel to dry completely before dressing to prevent bleaching of your clothes.

WHAT ARE THE MOST COMMON SIDE EFFECTS OF EPIDUO GEL?

The most commonly reported side effects when using EPIDUO gel include erythema, scaling, dryness, application site irritation, stinging and burning.

Depending upon the severity of these side effects, patients should be instructed to use a moisturizer, reduce the frequency of the application of EPIDUO gel, or discontinue use.

Tell your doctor right away if these side effects continue for longer than 4 weeks or get worse, you may have to stop using EPIDUO gel. Tell your doctor if you have any side effect that bothers you or that does not go away.

These are not all of the possible side effects of EPIDUO gel. For more information, ask your doctor or pharmacist.

You are encouraged to report negative side effects of prescription drugs to the FDA at *www.fda.gov/medwatch* or call 1-800-FDA-1088. You may also contact GALDERMA LABORATORIES, L.P. at 1-866-735-4137.

HOW SHOULD I USE EPIDUO GEL?

- Use EPIDUO gel exactly as your doctor tells you to use it. EPIDUO gel is for skin use only. Do not use EPIDUO gel in or on your mouth, eyes, or vagina.
- Apply EPIDUO gel 1 time a day.
- Do not use more EPIDUO gel than you need to cover the treatment area. Using too much EPIDUO gel or using it more than 1 time a day may increase your chance of skin irritation.

APPLYING EPIDUO GEL:

- Wash the area where the gel will be applied with a mild cleanser and pat dry.
- EPIDUO gel comes in a tube and a pump. If you have been prescribed the:
  - Tube: Squeeze a small amount (about the size of a pea) of EPIDUO gel onto your fingertips and spread a thin layer over the affected area.
  - Pump: Depress the pump to dispense a small amount (about the size of a pea) of EPIDUO gel and spread a thin layer over the affected area.

WHERE SHOULD I GO FOR MORE INFORMATION ABOUT EPIDUO GEL?

- Talk to your doctor or pharmacist
- Go to **www.epiduo.com** or call **1-866-735-4137**

GALDERMA LABORATORIES, L.P., Fort Worth, Texas 76177 USA
Revised: February 2013

References: 1. Gollnick HPM, Draelos Z, Glenn MJ, et al; Adapalene–BPO Study Group. Adapalene–benzoyl peroxide, a unique fixed-dose combination topical gel for the treatment of acne vulgaris: a transatlantic, randomized, double-blind, controlled study in 1670 patients. *Br J Dermatol.* 2009;161(5):1180-1189. **2.** Czernielewski J, Michel S, Bouclier M, Baker M, Hensby C. Adapalene biochemistry and the evolution of a new topical retinoid for treatment of acne. *J Eur Acad Dermatol Venereol.* 2001;15(suppl 3):5-12. **3.** Tenaud I, Khammari A, Dréno B. In vitro modulation of TLR-2, CD1d and IL-10 by adapalene on normal human skin and acne inflammatory lesions. *Exp Dermatol.* 2007;16:500-506. **4.** Thiboutot D, Gollnick H, Bettoli V, et al; Global Alliance to Improve Outcomes in Acne. New insights into the management of acne: an update from the Global Alliance to Improve Outcomes in Acne group. *J Am Acad Dermatol.* 2009;60(5)(suppl):S1-S50. **5.** Eichenfield LF, Draelos Z, Lucky AW, et al. Preadolescent moderate acne vulgaris: a randomized trial of the efficacy and safety of topical adapalene-benzoyl peroxides. *J Drugs Dermatol.* 2013;12(6):611-618.

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Report identifies opportunities in psoriasis research

Journal of the American Academy of Dermatology
January 2014

dermatologytimes.com/psoriasisresearch

A NEW REPORT identifies areas in psoriasis research that provide opportunities for additional study in the future. The report outlined areas in clinical features, genetics and pathophysiology, environmental factors, subpopulations, comorbidities, treatment, and health care economics of psoriasis.

"Data sharing and the rapid dissemination of new findings between research groups will be essential to facilitate further advances in psoriasis research at a global level," The report authors concluded. "Despite revolutionary advances in psoriasis therapy, our long-term experience of newer targeted treatment is still limited and robust evidence of long-term safety data is essential to safeguard our patients."

Specifically, these areas require more psoriasis research attention, according to the authors:

1. Genetics
2. Immunology
3. Angiogenesis
4. Neurogenic inflammation
5. Pediatric psoriasis
6. Pregnancy
7. The elderly
8. Psoriatic arthritis
9. Cardiometabolic comorbidities in psoriasis
10. Management of cardiometabolic risk
11. Psychological comorbidities
12. Topical therapies
13. Phototherapy
14. Methotrexate
15. Combination treatment
16. Personalized medicine
17. Safety

"To this end, it is critical that dermatologists become actively involved in accruing these data by enrolling patients in drug registries and continuing to report adverse events and safety concerns at the earliest stage," the authors stated. **DT**

iPhone app may make referrals easier for dermatologists

JAMA Dermatology
January 2014

dermatologytimes.com/dermapp

THE USE OF a skin disease advocacy iPhone app among dermatologists leads to an increase of physician awareness and patient referrals to the advocacy organizations, recent study findings show.

Although there are numerous skin disease advocacy groups in existence, physician study respondents reported the most common reasons for not referring their patients were lack of awareness of the organizations and how time-consuming it is to make a referral, according to the study.

A survey conducted during the study found that 85 percent of physicians reported they would use an iPhone app that made making referrals easier, and 85 percent reported use of an iPhone app would probably increase their referrals.

The app, called The Skin Advocate, gave physicians contact information for advocacy organizations in the Coalition of Skin Diseases, as well as the ability to quickly and anonymously share the information with patients by way of email.

After three months of app use, several organization reported an increase in referrals, and the National Eczema Association saw a 10-fold monthly registration increase. **DT**

AD-associated staphylococci biofilms may block sweat ducts

JAMA Dermatology
January 2014

dermatologytimes.com/staphbiofilms

THE BLOCKAGE, inflammation and itching of sweat ducts could be caused by biofilm formation of atopic dermatitis-associated staphylococci, according to a new study.

According to the findings, various staph bacteria found in normal skin tissues are capable of producing biofilms and extracelluar polysaccharide biomass material, most of which showed multidrug resistance. The biofilms play a role in the blockage of sweat ducts.

"These findings support the hypothesis that AD lesional areas have strong biofilm-producing staphylococci and that those biofilms occlude sweat ducts, whereas nonlesional areas do not (or at least do it to a much lesser, nonrecognizable, extent)," the study authors stated in the abstract. "They also support the concept that subclinical miliaria is an important feature of AD, whereby the biofilms occlude the sweat ducts."

The study was conducted with 40 patients, between the ages of 3 months and 85 years old who have atopic dermatitis. Routine skin swabs from lesional and nonlesional skin were scraped, biopsied and processed. **DT**

twitter.com/DermTimesNow

What area of dermatologic research do you think needs more attention? Tweet us.

29 BIOLOGICS EFFECTIVE FOR HS
Non-antibiotic options can help to manage hidradenitis suppurativa

Early treatment of severe psoriasis could curb comorbidities

Louise Gagnon | Staff Correspondent

MONTREAL — There is a suggestion that early treatment of severe psoriasis will decrease the risk of cardiovascular comorbidities that have been associated with severe psoriasis such as stroke and heart attack, according to a clinical professor dermatology at the State University of New York Buffalo School of Medicine.

Discussing the systemic impact of psoriasis at a dermatology symposium here, Robert Kalb, M.D., F.A.A.D., a dermatologist at the Buffalo Medical Group in Buffalo, N.Y., said six different meta-analyses published within the last year demonstrate that psoriasis is an independent risk factor for cardiovascular disease.

But it remains to be determined if initiation of therapy as early as possible will diminish the likelihood of appearance of comorbidities.

QUICK READ

Cutaneous adverse events may occur with biologic therapy in nondermatologic conditions, but should not be a reason to stop using the treatments.

"The current evidence is suggestive but not definitive," Dr. Kalb tells **Dermatology Times**. "If you treat early, you may decrease the systemic inflammation and thereby decrease the chance of arthritis developing or decrease the chance of having a heart attack or stroke.

"The state of the art is to aggressively manage the comorbid factors that are present such as decreasing weight, lowering blood pressure, controlling diabetes, lowering of lipids, cessation of smoking, and promoting exercise," he says.

The impact of treatment on comorbidities is not limited to biologic treatments, Dr. Kalb says, noting the effect has been observed with methotrexate.

CUTANEOUS COMPLICATIONS

Patients who are on a regimen of biologic therapies to treat nondermatological conditions can develop cutaneous complications, but the development of these side effects should not be a signal for ceasing biologic therapy, according to Christina Han, M.D.

"In most cases, patients can continue with their biologics," says Dr. Han, clinical instructor at the University of British Columbia department of dermatology, Vancouver. She spoke in Montreal at a dermatology symposium. "If patients are considering discontinuing their (biologic) therapy, we should collaborate with

PSORIASIS see page **26**

Quotable

"We know (finasteride) is effective in the pediatric setting."

John Kraft, M.D.
Markham, Ontario

On non-antibiotic options for treating hidradenitis suppurativa

See story, page 29

DTExtra

New research indicates that outer skin cells are able to unite to form a bridge during wound healing. Investigators found that skin cells can move over areas without support from the extracellular matrix. The study, published in the journal *Natural Materials*, revealed that keratinocytes can create suspended multicellular bridges over regions with poor cell adhesion. The keratinocytes comprise a homogeneous group that forms a barrier over a wound. The cell sheet is formed by the build-up of large-scale tensions activated by actomyosin, a motor protein that causes cellular contraction.

READ MORE: DERMATOLOGYTIMES.COM/WOUNDBRIDGE

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The *first* and *only* FDA-approved filler for the midface[1]

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INDICATION

JUVÉDERM VOLUMA™ XC injectable gel is indicated for deep (subcutaneous and/or supraperiosteal) injection for cheek augmentation to correct age-related volume deficit in the mid-face in adults over the age of 21.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

JUVÉDERM VOLUMA™ XC is contraindicated for patients with severe allergies, manifested by a history of anaphylaxis or history or presence of multiple severe allergies, and a history of allergies to gram-positive bacterial proteins or lidocaine.

WARNINGS

- JUVÉDERM VOLUMA™ XC injectable gel must not be injected into blood vessels and should not be used in vascular-rich areas. Use in these areas, such as glabella and nose, has resulted in cases of vascular embolization, occlusion of the vessels, ischemia or infarction, or blindness. Symptoms of vessel occlusion and embolization include pain that is disproportionate to the procedure or remote to the injection site, immediate blanching extending beyond the injected area, and color changes that reflect ischemic tissue such as a dusky or reticular appearance
- Product use at specific sites in which an active inflammatory process (skin eruptions such as cysts, pimples, rashes, or hives) or infection is present should be deferred until the underlying process has been controlled

PRECAUTIONS

- The safety and effectiveness for the treatment of anatomic regions other than the mid-face have not been established
- As with all transcutaneous procedures, dermal filler implantation carries a risk of infection. Follow standard precautions associated with injectable materials
- The safety for use during pregnancy, in breastfeeding females, and in patients with very thin skin in the mid-face region has not been established
- The safety for use in patients under 35 years or over 65 years has not been established
- The safety in patients with known susceptibility to keloid formation, hypertrophic scarring, and pigmentation disorders has not been studied
- JUVÉDERM VOLUMA™ XC injectable gel should be used with caution in patients on immunosuppressive therapy
- Patients who are using products that can prolong bleeding (such as aspirin, nonsteroidal anti-inflammatory drugs, and warfarin) may experience increased bruising or bleeding at treatment sites
- Patients who experience skin injury near the site of JUVÉDERM VOLUMA™ XC implantation may be at a higher risk for adverse events
- Patients may experience late onset nodules with use of dermal fillers including JUVÉDERM VOLUMA™ XC
- Patients should be limited to 20 mL of JUVÉDERM VOLUMA™ XC per 60 kg (130 lbs) body mass per year. The safety of injecting greater amounts has not been established
- JUVÉDERM VOLUMA™ XC should only be used by physicians who have appropriate experience and who are knowledgeable about facial anatomy and the product for use in deep (subcutaneous and/or supraperiosteal) injection for cheek augmentation

ADVERSE EVENTS

Side effects in > 5% of subjects were temporary injection-site tenderness, swelling, firmness, lumps/bumps, bruising, pain, redness, discoloration, and itching. They were predominantly moderate in severity, with a duration of 2 to 4 weeks.

To report an adverse reaction, please call Allergan Product Surveillance at 1-877-345-5372.

For more information, please see the About Safety page at www.juvederm.com or call the Allergan Medical Information line at 1-800-433-8871.

JUVÉDERM VOLUMA™ XC injectable gel is available by prescription only.

1. JUVÉDERM VOLUMA™ XC Directions for Use, 2013. **2.** Data on file, Allergan, Inc.

THE NEXT DIMENSION

Juvéderm

VOLUMA™ XC

voice of the dermatologist

"When treating very dense, dark pigment, we must be more careful because patients can get bulk heating, which can lead to scarring."

George Hruza, M.D.
See story, page 44

PSORIASIS:

Researchers examine ways to curb comorbidities from page 24

our colleagues in gastroenterology and rheumatology."

Some of the complications include the paradoxical development of psoriasis induced by tumor necrosis factor (TNF)-alpha blockers, notes Dr. Han, citing a patient with ulcerative colitis who developed psoriasis while taking TNF-alpha blockers.

"This paradoxical phenomenon of anti-TNF-alpha-induced psoriasis is fairly well-documented in the literature," Dr. Han says. "We are trying to elucidate why this happens."

"If patients are considering discontinuing their (biologic) therapy, we should collaborate with our colleagues in gastroenterology and rheumatology."

Christina Han, M.D.
Vancouver

One of the theories has been unopposed interferon alpha production, which stimulates T-cells, Dr. Han says. But since the vast majority of users of TNF-alpha blockers do not develop such a paradoxical response, there is likely more at play, such as genetics, she says.

Eczema is another cutaneous adverse event that has developed in an ulcerative colitis patient taking infliximab, Dr. Han notes.

Another possible complication of anti-TNF-alpha agents is the development of herpes zoster. A study in 2012 found that one-third of patients with herpes zoster who were receiving TNF-alpha blockers had severe herpes zoster. Another finding was an elevated risk of herpes zoster with monoclonal anti-TNF-alpha antibodies than with soluble TNF-alpha receptor (Serac G, Tubach F, Mariette X, et al. *J Invest Dermatol*. 2012;132(3 Pt 1):726-729).

But Dr. Han also notes a large cohort study published this year suggested that patients who are started on anti-TNF agents are at an equivalent risk of herpes zoster as patients who use non-biologic therapies (Winthrop KL, Badley JW, Chen L, et al. *JAMA*. 2013;309(9):887-895).

BIOLOGIC REGISTRIES

A decade of use of biologic agents has led to the development of registries which offer longer-term information that supplements the evidence that comes from randomized, controlled trials (RCTs), which are typically short in duration, according to Melinda Gooderham, M.D., F.R.C.P.C., medical director, Skin Centre for Dermatology, Peterborough, Ontario, and assistant professor at Queen's University, Kingston, Ontario.

"Registries, particularly biologic registries, offer us a lot of information that we don't get from RCTs, and they provide us with information on patients who may not be included in RCTs," Dr. Gooderham says, discussing the value of biologic registries. "We can put the two (registries and RCTs) together to get more information."

"Biologic registries, offer us a lot of information that we don't get from RCTs, and they provide us with information on patients who may not be included in RCTs."

Melinda Gooderham, M.D.
Kingston, Ontario

There are many factors that may confound the data that come from registries such as options for flexible dosing, physician preferences and patient preferences, Dr. Gooderham says.

Still, many of the registries look at the retention of patients, which can serve as a proxy for variables like safety, efficacy, and tolerability of a medication, she says. **DT**

Disclosures: Dr. Kalb is an investigator and consultant for AbbVie, Janssen and Amgen. Dr. Han has been a consultant, advisory board member and speaker for Amgen, Ortho Janssen, AbbVie, and LEO Pharma. Dr. Gooderham is an investigator for the Psoriasis Longitudinal Assessment and Registry.

Finacea® (azelaic acid) Gel, 15% is a topical prescription medication used to treat inflammatory papules and pustules of mild to moderate rosacea.

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It's true. Rosacea is complex and it's with them for life. Finacea® treats the papules and pustules with associated erythema of mild to moderate rosacea. Although some reduction of erythema which was present in patients with papules and pustules of rosacea occurred in clinical studies, efficacy for treatment of erythema in rosacea in the absence of papules and pustules has not been evaluated.

You have made Finacea® the #1 Dermatologist-prescribed topical rosacea brand.[1]

Finacea®
(azelaic acid) Gel, 15%

INDICATION & USAGE

Finacea® (azelaic acid) Gel, 15% is indicated for topical treatment of inflammatory papules and pustules of mild to moderate rosacea. Although some reduction of erythema which was present in patients with papules and pustules of rosacea occurred in clinical studies, efficacy for treatment of erythema in rosacea in the absence of papules and pustules has not been evaluated.

IMPORTANT SAFETY INFORMATION

Skin irritation (e.g. pruritus, burning or stinging) may occur during use with Finacea®, usually during the first few weeks of treatment. If sensitivity or severe irritation develops and persists during use with Finacea®, discontinue use and institute appropriate therapy. There have been isolated reports of hypopigmentation after use of azelaic acid. Since azelaic acid has not been well studied in patients with dark complexion, monitor these patients for early signs of hypopigmentation.

Avoid contact with the eyes, mouth, and other mucous membranes. In case of eye exposure, wash eyes with large amounts of water. Wash hands immediately following application of Finacea®.

Avoid use of alcoholic cleansers, tinctures and astringents, abrasives and peeling agents. Avoid the use of occlusive dressings or wrappings.

In clinical trials with Finacea®, the most common treatment-related adverse events (AE's) were: burning/stinging/tingling (29%), pruritus (11%), scaling/dry skin/xerosis (8%) and erythema/irritation (4%). Contact dermatitis, edema and acne were observed at frequencies of 1% or less.

Finacea® is for topical use only. It is not for ophthalmic, oral or intravaginal use. Patients should be reassessed if no improvement is observed upon completing 12 weeks of therapy.

Please see Brief Summary of full Prescribing Information on adjacent page.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

1. According to IMS NPA™ (National Prescription Audit) July 2010-October 2013

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Rx only

BRIEF SUMMARY
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1 INDICATIONS AND USAGE
FINACEA® Gel is indicated for topical treatment of the inflammatory papules and pustules of mild to moderate rosacea. Although some reduction of erythema which was present in patients with papules and pustules of rosacea occurred in clinical studies, efficacy for treatment of erythema in rosacea in the absence of papules and pustules has not been evaluated.

5 WARNINGS AND PRECAUTIONS
5.1 Skin Reactions
Skin irritation (i.e. pruritus, burning or stinging) may occur during use of FINACEA Gel, usually during the first few weeks of treatment. If sensitivity or severe irritation develops and persists, discontinue treatment and institute appropriate therapy.

There have been isolated reports of hypopigmentation after use of azelaic acid. Since azelaic acid has not been well studied in patients with dark complexion, monitor these patients for early signs of hypopigmentation.

5.2 Eye and Mucous Membranes Irritation
Avoid contact with the eyes, mouth and other mucous membranes. If FINACEA Gel does come in contact with the eyes, wash the eyes with large amounts of water and consult a physician if eye irritation persists *[see Adverse Reactions (6.2)]*.

6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In two vehicle-controlled and one active-controlled U.S. clinical trials, treatment safety was monitored in 788 subjects who used twice-daily FINACEA Gel for 12 weeks (N=333) or 15 weeks (N=124), or the gel vehicle (N=331) for 12 weeks. In all three trials, the most common treatment-related adverse events were: burning/stinging/tingling (29%), pruritus (11%), scaling/dry skin/xerosis (8%) and erythema/irritation (4%). In the active-controlled trial, overall adverse reactions (including burning, stinging/tingling, dryness/tightness/ scaling, itching, and erythema/irritation/redness) were 19.4% (24/124) for FINACEA Gel compared to 7.1% (9/127) for the active comparator gel at 15 weeks.

Table 1: Adverse Events Occurring in ≥1% of Subjects in the Rosacea Trials by Treatment Group and Maximum Intensity*

	FINACEA Gel, 15% N=457 (100%)			Vehicle N=331 (100%)		
	Mild n=99 (22%)	Moderate n=61 (13%)	Severe n=27 (6%)	Mild n=46 (14%)	Moderate n=30 (9%)	Severe n=5 (2%)
Burning/ stinging/ tingling	71 (16%)	42 (9%)	17 (4%)	8 (2%)	6 (2%)	2 (1%)
Pruritus	29 (6%)	18 (4%)	5 (1%)	9 (3%)	6 (2%)	0 (0%)
Scaling/ dry skin/ xerosis	21 (5%)	10 (2%)	5 (1%)	31 (9%)	14 (4%)	1 (<1%)
Erythema/ irritation	6 (1%)	7 (2%)	2 (<1%)	8 (2%)	4 (1%)	2 (1%)
Contact dermatitis	2 (<1%)	3 (1%)	0 (0%)	1 (<1%)	0 (0%)	0 (0%)
Edema	3 (1%)	2 (<1%)	0 (0%)	3 (1%)	0 (0%)	0 (0%)
Acne	3 (1%)	1 (<1%)	0 (0%)	1 (<1%)	0 (0%)	0 (0%)

* Subjects may have >1 cutaneous adverse event; thus, the sum of the frequencies of preferred terms may exceed the number of subjects with at least 1 cutaneous adverse event.

In patients using azelaic acid formulations, the following adverse events have been reported: worsening of asthma, vitiligo, depigmentation, small depigmented spots, hypertrichosis, reddening (signs of keratosis pilaris) and exacerbation of recurrent herpes labialis.

Local Tolerability Studies
FINACEA Gel and its vehicle caused irritant reactions at the application site in human dermal safety studies. FINACEA Gel caused significantly more irritation than its vehicle in a cumulative irritation study. Some improvement in irritation was demonstrated over the course of the clinical trials, but this improvement might be attributed to subject dropouts. No phototoxicity or photoallergenicity were reported in human dermal safety studies.

6.2 Post-Marketing Experience
The following adverse reactions have been identified post approval of FINACEA Gel. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate the frequency or establish a causal relationship to drug exposure:

Eyes: iridocyclitis upon accidental exposure of the eyes to FINACEA Gel

7 DRUG INTERACTIONS
There have been no formal studies of the interaction of FINACEA Gel with other drugs.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Teratogenic Effects: Pregnancy Category B
There are no adequate and well-controlled studies in pregnant women. Therefore, FINACEA Gel should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Dermal embryofetal developmental toxicology studies have not been performed with azelaic acid, 15% gel. Oral embryofetal developmental studies were conducted with azelaic acid in rats, rabbits, and cynomolgus monkeys. Azelaic acid was administered during the period of organogenesis in all three animal species. Embryotoxicity was observed in rats, rabbits, and monkeys at oral doses of azelaic acid that generated some maternal toxicity. Embryotoxicity was observed in rats given 2500 mg/kg/day [162 times the maximum recommended human dose (MRHD) based on body surface area (BSA)], rabbits given 150 or 500 mg/kg/day (19 or 65 times the MRHD based on BSA) and cynomolgus monkeys given 500 mg/kg/day (65 times the MRHD based on BSA) azelaic acid. No teratogenic effects were observed in the oral embryofetal developmental studies conducted in rats, rabbits and cynomolgus monkeys.

An oral peri- and post-natal developmental study was conducted in rats. Azelaic acid was administered from gestational day 15 through day 21 postpartum up to a dose level of 2500 mg/kg/day. Embryotoxicity was observed in rats at an oral dose of 2500 mg/kg/day (162 times the MRHD based on BSA) that generated some maternal toxicity. In addition, slight disturbances in the post-natal development of fetuses was noted in rats at oral doses that generated some maternal toxicity (500 and 2500 mg/kg/day; 32 and 162 times the MRHD based on BSA). No effects on sexual maturation of the fetuses were noted in this study.

8.3 Nursing Mothers
It is not known whether azelaic acid is excreted in human milk; however, *in vitro* studies using equilibrium dialysis were conducted to assess the potential for human milk partitioning. The studies demonstrated that, at an azelaic acid concentration of 25 µg/mL, the milk/plasma distribution coefficient was 0.7 and the milk/buffer distribution was 1.0. These data indicate that passage of drug into maternal milk may occur. Since less than 4% of a topically applied dose of 20% azelaic acid cream is systemically absorbed, the uptake of azelaic acid into maternal milk is not expected to cause a significant change from baseline azelaic acid levels in the milk. Nevertheless, a decision should be made to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

8.4 Pediatric Use
Safety and effectiveness of FINACEA Gel in pediatric patients have not been established.

8.5 Geriatric Use
Clinical studies of FINACEA Gel did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

17 PATIENT COUNSELING INFORMATION
Inform patients using FINACEA Gel of the following information and instructions:

Use only as directed by your physician.

- For external use only.
- Before applying FINACEA Gel, cleanse affected area(s) with a very mild soap or a soapless cleansing lotion and pat dry with a soft towel.
- Avoid use of alcoholic cleansers, tinctures and astringents, abrasives and peeling agents.
- Avoid contact with the eyes, mouth and other mucous membranes. If FINACEA Gel does come in contact with the eyes, wash the eyes with large amounts of water and consult your physician if eye irritation persists.
- Wash hands immediately following application of FINACEA Gel.
- Cosmetics may be applied after the application of FINACEA Gel has dried.
- Avoid the use of occlusive dressings or wrappings.
- Skin irritation (e.g., pruritus, burning, or stinging) may occur during use of FINACEA Gel, usually during the first few weeks of treatment. If irritation is excessive or persists, discontinue use and consult your physician.
- Report abnormal changes in skin color to your physician.
- To help manage rosacea, avoid any triggers that may provoke erythema, flushing, and blushing. These triggers can include spicy and thermally hot food and drinks such as hot coffee, tea, or alcoholic beverages.

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Biologics may be effective alternative for treating hidradenitis suppurativa

Louise Gagnon | Staff Correspondent

MONTREAL — A variety of treatments aside from antibiotics have shown some efficacy in managing hidradenitis suppurativa (HS), according to a clinician speaking at the Dermatology Update 2013 meeting.

John Kraft, M.D., F.R.C.P.C., a dermatologist at the Lynde Centre for Dermatology, Markham, Ontario, reviewed data on the evidence for numerous medical therapies that have been employed to manage a chronic condition that is not uncommon in premenopausal women.

HS is caused by a defect of the follicular epithelium, leading to follicular occlusion and subsequent follicular rupture in areas rich in apocrine glands. Clinicians make the diagnosis by recognizing typical lesions at typical sites where there is recurrence, Dr. Kraft notes.

"First-line therapy for mild-to-moderate disease is antibiotics," Dr. Kraft says.

NON-ANTIBIOTIC OPTIONS

Given the hormonal involvement of the condition, one of the non-antibiotic options for treating hidradenitis suppurativa is the anti-androgen finasteride. There have been more studies in adults to support its evidence, but recent data suggest it can be administered to teenagers as well, Dr. Kraft says.

"We know it's effective in the pediatric setting," he says.

A case series of three pediatric patients published in June 2013 demonstrated reduced frequency and severity of disease flares without any serious side effects (Randhawa HK, Hamilton J, Pope E. *JAMA Dermatol.* 2013;149(6):732-735).

Biologic agents have also been used to treat HS. A study looked at the efficacy of infliximab in a randomized, placebo-controlled crossover trial of patients with moderate-to-severe HS. Patients who received infliximab showed a 50 percent decline from baseline HS Severity Index score (Grant A, Gonzalez T, Montgomery MO, et al. *J Am Acad Dermatol.* 2010;62(2):205-217).

QUICK READ

There is evidence for numerous non-antibiotic therapies to manage hidradenitis suppurativa, and when patients do not respond to most therapies, clinicians should consider cyclosporine.

The investigators of that infliximab study conducted a post-hoc analysis confirming the benefit of using infliximab, Dr. Kraft adds.

Etanercept, another biologic agent, has been used to treat HS, Dr. Kraft notes, pointing to a 2010 investigation that showed that after therapy, there was no benefit in using etanercept compared to placebo (Adams DR, Yankura JA, Fogelberg AC, Anderson BE. *Arch Dermatol.* 2010;146(5):501-504).

"They found no statistically significant difference in any of the outcomes at 12 and 24 weeks," Dr. Kraft says. "The authors even said to look at other treatment options rather than pursue etanercept for hidradenitis suppurativa."

ADDITIONAL STUDIES

Adalimumab is likely one of the therapies that is the most well-studied for the treatment of HS, he says.

Dr. Kraft points to a prospective, randomized study in which patients who were administered adalimumab by injection every two weeks experienced a decrease in Sartorius score after six weeks and at 12 weeks, had close to a significant reduction in that score compared to patients who received placebo (Miller I, Lynggaard CD, Lophaven S, et al. *Br J Dermatol.* 2011;165(2):391-398).

50%

Percentage of decline from baseline HS Severity Index score in patients receiving infliximab

Another study examining the impact of adalimumab involved three arms of patients, involving two different dosing regimens of adalimumab and placebo. It found 17.6 percent of patients dosed weekly achieved a HS Physician Global Assessment of clear, minimal or mild disease (Kimball AB, Kerdel F, Adams D, et al. *Ann Internal Med.* 2012;157(12):846-855).

"This is not a high percentage, but the finding is valid," Dr. Kraft says. "It was significant for the 40 mg per week (group), but not (the group dosed) every other week."

There have been variable results in the use of ustekinumab to manage HS. One investigation of three patients found complete remission in one patient, some improvement in another patient, and no response in the third patient (Gulliver WP, Jemec GBE, Baker KA. *J Eur Acad Dermatol Venereol.* 2012;26(7):911-914).

Colchicine has been studied to manage HS, with one study finding no improvement in disease severity (Van der Zee HH, Prens EP. *Dermatology.* 2011;223(2):169-173). A retrospective review found a small positive impact with colchicine, but no bigger an effect than antibiotics such as clindamycin or rifampin, Dr. Kraft says.

When patients with HS prove unresponsive, dermatologists should keep a therapy such as cyclosporine in their back pockets, he says.

Because of the large variability in design of studies looking at the management of HS, it can be a challenge to establish which therapies will be effective for a given patient, Dr. Kraft says. **DT**

Disclosures: Dr. Kraft is a speaker, adviser and investigator for AbbVie and Janssen. He is an adviser and investigator for Amgen.

RESURGING INFECTIONS:

Growing prevalence of formerly rare infections raises concern among experts

from page 1

like psoriasis and pemphigus are more difficult to use in patients with chronic hepatitis B," Dr. Carlos says. Examples include rituximab and the tumor necrosis factor (TNF) inhibitors, which she says physicians must use cautiously in these patients because they can reactivate the disease.

As for hepatitis C, Dr. Tyring says that the Food and Drug Administration approvals of boceprevir and telaprevir — for use with pegylated interferon plus ribavirin — ushered in a new approach. Most recently, he adds, "Sofosbuvir and simeprevir were approved for treatment of hepatitis C. It is notable that sofosbuvir is given without interferon, which eliminates many of the side effects of combination therapies. When we talk about the viral diseases we commonly see in dermatology, such as papillomaviruses and herpes viruses, we're talking about treatments, not cures. And now the hepatologists are talking about cures for hepatitis C."

For treating herpes simplex, he adds, a new helicase primase inhibitor has shown promise in a phase 2 clinical trial (Tyring S, Wald A, Zadeikis N, et al. *J Infect Dis*. 2012;205(7):1100-1110).

"The point of developing a new drug is for those who develop resistance to the available medications — particularly people with AIDS and other immunocompromised individuals. This works when other drugs fail due to resistance," Dr. Tyring says.

NEW VIRUS STRAINS

Other threats include new strains of existing viruses. In this regard, says Jason Lott, M.D., M.S.P.H., hand, foot and mouth disease (HFMD) typically arises from coxsackievirus A16, which generally causes mild, limited disease in children and immunocompromised adults. However, he says, the coxsackievirus A6 (CVA6) that he and others first reported in the United States may affect both children and immunocompetent adults.

Additionally, "It can be far more severe," he says. Many patients require hospitalization due to severe stomatitis or acral involvement, says Dr. Lott, who is a Robert Wood Johnson Foundation Clinical Scholar in the departments of dermatology and internal medicine at Yale University School of Medicine, New Haven, Conn.

CVA6 often presents with an atypical distribution and seasonality (e.g., late fall and winter), he adds.

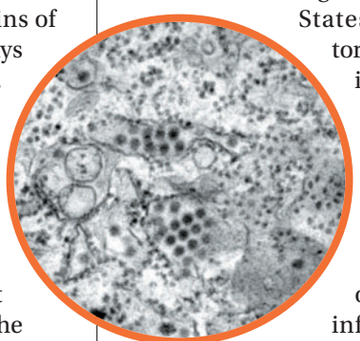
"Frequently, it will colocalize to areas of prior cutaneous inflammation or injury, including skin areas affected by atopic dermatitis (Mathes EF, Oza V, Frieden IJ, et al. *Pediatrics*. 2013;132(1):e149-e157). Also unlike typical HFMD, Dr. Tyring says, CVA6 typically causes patients to shed their fingernails and toenails.

With no vaccine available, Dr. Tyring says, battling CVA6 requires awareness. But with supportive care, Dr. Lott adds, "It resolves on its own, usually in a couple weeks." A recent review counted 80 cases worldwide (Oza V, et al. American Academy of Dermatology Annual Meeting. Presented March 2, 2013. Miami Beach, Fla.).

TROPICAL TOPICS

Among tropical infections with cutaneous components, Dr. Carlos says, "Dengue was fairly well controlled in the Americas until about 1970." Then many governments in afflicted areas stopped their efforts to control the population of the responsible Aedes mosquito, she says.

Perhaps not surprisingly, the first 10 months of 2013 saw more cases of dengue in the United States (7,802 laboratory-confirmed, all in Puerto Rico) than the similar period in 2012, Dr. Tyring says. "Everyone should have dengue fever on their list of infections to worry about for the future," Dr. Lott says. In this regard, he says he's especially concerned about the potential spread of dengue consequent to the World Cup soccer tournament scheduled for mid-2014 in Brazil.



This transmission electron micrograph (TEM) depicts a number of round, Dengue virus particles that were revealed in this tissue specimen.

Photo credit: CDC

Of greatest concern with dengue, Dr. Lott says, is that infection with one of its four serotypes does not confer lifelong immunity against the other three.

> "New antibiotics **are not coming out nearly as fast as we need them** for the resistant strains of *Staphylococcus* and other bacteria."
>
> **Stephen K. Tyring, M.D., Ph.D., M.B.A.**
> Houston

Dr. Carlos says if a patient clears one serotype, then catches another, "The patient has a high risk of developing dengue-associated hemorrhagic fever, which can be fatal. It's something for clinicians to be aware of, especially in returning travelers or people from other areas who are traveling, because they may only present on their way back into their home country."

Mosquitoes from the same *Aedes* genus (*A. aegypti, A. albopictus*) also can carry the chikungunya virus, the causative agent of chikungunya fever. Though it mainly affects southeast Asia and countries surrounding the Indian Ocean, Dr. Lott says, the World Health Organization recently confirmed 10 cases on the French side of St. Martin in the Caribbean. *A. albopictus* furthermore can range as far north as Connecticut, he adds.

Like dengue, chikungunya fever has a three- to seven-day incubation period and presents with a similar rash that includes islands of sparing, Dr. Carlos says.

RESURGING INFECTIONS see page 33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Brief Summary (For full Prescribing Information and Patient Information, refer to package insert.)

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- Systemic absorption of topical corticosteroids has produced reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, manifestations of Cushing's syndrome, hyperglycemia, and glucosuria in some patients.
- Conditions which augment systemic absorption include the application of the more potent steroids, use over large surface areas, prolonged use, and the addition of occlusive dressings.
- Children may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic toxicity. Parents of pediatric patients should be advised not to use tight-fitting diapers or plastic pants on a child being treated in the diaper area, as these garments may constitute occlusive dressings.
- Administration of topical corticosteroids to children should be limited to the least amount compatible with an effective therapeutic regimen. Chronic corticosteroid therapy may interfere with the growth and development of children.
- This medication is to be used as directed by the physician. It is for dermatologic use only. Avoid contact with the eyes.
- Patients should be advised not to use this medication for any disorder other than for which it was prescribed.
- The treated skin area should not be bandaged or otherwise covered or wrapped as to be occlusive unless directed by the physician.
- Patients should report any signs of local adverse reactions especially under occlusive dressing.
- **Pregnancy Category C:** Topical corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Drugs of this class should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time.
- Systemically administered corticosteroids are secreted into breast milk in quantities **not** likely to have a deleterious effect on the infant. Nevertheless, caution should be exercised when topical corticosteroids are administered to a nursing woman.

ADVERSE REACTIONS

The following local adverse reactions are reported infrequently with topical corticosteroids, but may occur more frequently with the use of occlusive dressings (reactions are listed in an approximate decreasing order of occurrence): burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae, and miliaria.

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RESURGING INFECTIONS:

Growing prevalence of formerly rare infections raises concern among experts

from page 30

"Chikungunya is Makonde for 'that which bends,' and afflicted patients may develop severe lumbar back pain," Dr. Lott says.

Treatment for chikungunya and dengue addresses symptoms until the illness resolves, according to Dr. Tyring. Additional tropical skin infections on the rise include the following:

- **Myiasis** — It's marked by furuncles that form after the botfly lays eggs upon the skin. First-line treatment involves topical therapies that induce the larvae to exit the skin, or surgical removal, he says.
- **Leishmaniasis** — With this infection, Dr. Tyring says, "Patients can present with large ulcers on the skin, or large erythematous plaques that don't quite fit any other diagnosis." Because leishmaniasis progresses relatively slowly, "It's necessary to biopsy to confirm the diagnosis." Treatment for leishmaniasis can include pentavalent antimonial compounds or miltefosine, he says.

Also occurring more commonly, due partly to increased use of systemic immunosuppressants, is the parasite *Strongyloides*, Dr. Carlos says. Severe illness can increase abdominal pressure, leading to the appearance of "thumbprint" purpura in the area as the parasites breach the gastrointestinal tract and enter the skin.

Typical markers for *Strongyloides* infections include eosinophilia, she says. Fortunately, oral anti-helminthic medications tend to resolve these infections. But for serious cases involving immunosuppression, she says, patients may need to take these medicines for years.

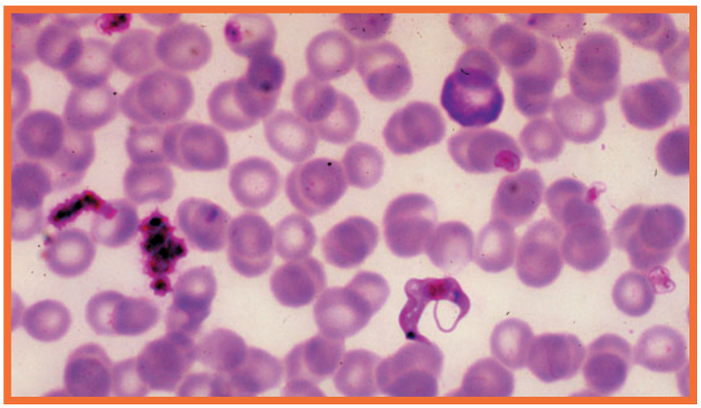
BACTERIAL BUGS

Among bacterial infections, according to Dr. Lott, American tick bite fever (a.k.a. maculatum disease) is a relatively new rickettsial illness to reach dermatologists' radar.

The *Amblyomma maculatum* tick, which lives in the Southeast, Mid-South and Mid-Atlantic regions, transmits American tick bite fever, through the *Rickettsia parkeri* bacterium, Dr. Lott says. As with rickettsial pox, the initial tick bite can cause an eschar, he says, followed by an ill-defined papular eruption.

"That's important to distinguish these and select other rickettsial infections from Rocky Mountain spotted fever," he says.

Simultaneously, Dr. Lott says, "Chagas disease (a.k.a. American trypanosomiasis) is becoming a tremendous problem," especially in the Southwestern and Western United States. "Many people are monitoring that disease, partly because its vector — the so-called 'kissing bug' — is hard to control. Furthermore, there are no highly effective therapies for it, especially once it moves from its acute phase to the chronic phase," which can lead to severe cardiomyopathy, megaesophagus, megacolon and other complications.



This is a micrograph of *Trypanosoma cruzi* in a blood smear using Giemsa staining technique. *T. cruzi* is the causative agent for Chagas disease.

Photo credit: CDC

DRUG-RESISTENT DISEASES

Dermatologists also should watch for multi-drug-resistant gonorrhea, say Drs. Carlos and Lott. Dr. Carlos says it has been described mostly in Asia to date. However, Dr. Lott adds, it's already appeared in the Western United States and may be spreading toward the rest of the country.

"It's scary," Dr. Carlos says, "because there are no effective medications for some of the strains that have been cultured." In such cases, she says, using multiple antibiotics simultaneously appears to have prevented any fatalities.

However, Dr. Carlos says, "The real worry is that many of these people carry it in their tonsils," a location that physicians perhaps previously overlooked. As these patients take antibiotics for other health problems over time, more resistance may develop.

Overall, "New antibiotics are not coming out nearly as fast as we need them for the resistant strains of *Staphylococcus* and other bacteria," Dr. Tyring says. Therefore, he says that presently, prevention — through standard infection-control measures — represents the best strategy for methicillin-resistant *S. aureus*. Physicians also must continue eliminating unnecessary antibiotic use, Dr. Carlos adds.

Antibiotic development efforts relaxed for years, she says, because most major bacterial threats appeared to be under control. But with antibiotic resistance growing and new bacterial strains emerging yearly, "We need to devote more resources to treating these illnesses — and not just what we see in the United States." With global travel ever increasing, "We can't ignore what's going on in other parts of the world." **DT**

For more information: www.CDC.gov

Disclosures: Drs. Carlos and Lott report no relevant financial interests. Dr. Tyring has received research support from Astellas, Epiphany, Catalyst, GlaxoSmithKline, Novartis, 3M, VaxGen, Merck, BMS, Amgen, Biogen, Genentech, Corixa, Abbott, Graceway, LEO and the National Institutes of Health. He serves on speakers' bureaus for GlaxoSmithKline, Amgen, Abbott and Warner Chilcott and is a consultant for GlaxoSmithKline, Merck, Astellas, Novartis, Epiphany and Catalyst.

Chikungunya information for clinicians at www.cdc.gov/chikungunya/pdfs/CHIKV_Clinicians.pdf

LOW DOSE:

Lower anti-inflammatory antibiotic doses may improve resistance problem from page 1

BY THE NUMBERS

Dermatologists have long used antibiotics to reduce inflammation in acne, says Sandra Johnson, M.D., a dermatologist in private practice in Fort Smith, Ark. In fact, she says, "Maybe 60 percent to 70 percent of the general dermatology practice's use of antibiotics is not for antibiotic purposes, but for inflammatory purposes in conditions such as acne and rosacea. So I would bet that we could improve the resistance problem by using lower anti-inflammatory doses" in acne cases that are predominantly inflammatory.

Neal D. Bhatia, M.D., says that based on dermatologists' acceptance of extended-release minocycline for acne, dermatologists might reduce their overall antibiotic use by 30 percent if they embraced the low-dose approach in appropriate acne cases. He is a dermatologist in private practice in Long Beach, Calif., and an associate professor of dermatology at Harbor-UCLA Medical Center, Los Angeles.

If dermatologists accepted extended-release minocycline for acne, their overall antibiotic use could be REDUCED BY 30%

Typical doxycycline doses for antimicrobial activity in acne are 100 mg to 200 mg daily. Doxycycline 20 mg BID, however — approved for periodontitis in 2006 — also has shown utility and safety in treating inflammatory acne. Additionally, extended-release minocycline (in doses starting at 45 mg daily) gained approval for inflammatory acne in 2006.

But dermatologists have not widely accepted the subantimicrobial dose (SD) concept, Dr. Johnson says, because most were not trained to do so.

"In training, we were taught to use antibacterial doses of antibiotics to treat inflammatory conditions such as acne. But now we have more data, especially regarding doxycycline," she says.

She says that her "aha" moment came with the first small study of low-dose doxycycline in acne (Skidmore R, Kovach R, Walker C, et al. *Arch Dermatol.* 2003;139(4):459-464). After six months of treatment, inflammatory lesion counts in patients randomized to receive doxycycline 20 mg twice daily fell 50 percent, versus 30 percent for placebo-treated patients (p=0.04), with no significant changes in normal skin flora.

In another study, investigators gave 11 subjects eight weeks of doxycycline 100 mg daily. Those whose inflammatory lesion counts fell 50 percent then got either eight weeks of SD doxycycline or placebo. The six subjects who got SD doxycycline maintained their improvements through the trial's conclusion, while the placebo group did not (Parish LC, Parish JL, Routh HB, Witkowski JA. *Acta Dermatovenerol Croat*. 2005;13(3):156-159).

"This study is intriguing," says Hilary Baldwin, M.D., "because it shows you can start with a full-dose antibiotic, get your bang for your buck, and then back off to the low dose and maintain clinical improvements, while having less concerns about development of resistance." Dr. Baldwin is associate professor and vice chair of dermatology at the State University of New York Downstate Medical Center, Brooklyn, N.Y.

DOSING VERSUS CHRONICITY

In larger patients or for more severe cases, Dr. Bhatia says, "Dosing and duration are paradoxical." Minimizing the duration of therapy demands dosing patients properly for their weight, he says. "It also requires making sure that their topical program is optimized. That's where we lose out a lot. Without a proper topical program, patients are wasting their time with oral antibiotics. A good topical program will penetrate better to the comedones, as well as the papular component."

Drs. Bhatia and Johnson agree that for those concerned with antibiotic resistance, dose levels ultimately matter less than treatment duration.

"But you could argue that if you use a low, non-antibiotic dose, then you can use it for as long as you wish" without stoking antibiotic resistance, Dr. Baldwin says. As such, "There's no need to discontinue Oracea (doxycycline, Galderma) rapidly, because we have nine-month data showing that no antibiotic resistance occurs during that time (Preshaw PM, Novak MJ, Mellonig J, et al. *J Periodontol*. 2008;79(3):440-452)."

However, Dr. Bhatia says, another study shows that resistance can develop within two to four weeks (Walker C, Bradshaw M. Poster presented at: Fall Clinical Dermatology Meeting; Oct. 18-21, 2007; Las Vegas).

"This should affect our prescribing decisions," he says.

Other factors to consider in prescribing oral antibiotics include acne patterns.

"For example," Dr. Bhatia says, "if there's secondary folliculitis, or a diffuse presentation of acne, it's different than rosacea, which has no bacterial target — the anti-inflammatory dose won't help." In such cases, he recommends adding topical treatments and tapering oral antibiotics as soon as possible.

'TOO MANY REFILLS'

Occasionally, Dr. Bhatia says, a patient needs six months on standard-dose oral antibiotics. For patients who

LOW DOSE see page 36

> "No study shows conclusively that doxycycline or minocycline is better than the other. So it's basically a judgment call."
>
> **Hilary Baldwin, M.D.**
> Brooklyn, N.Y.

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LOW DOSE:

Lower anti-inflammatory antibiotic doses may improve resistance problem from page 34

don't, "That's where people tend to get too many refills. Some of that also comes from dermatologists maybe waiting too long between visits to taper patients down." When this happens, "We're seeing a little more resistance developing."

To avoid this, Dr. Bhatia sees patients monthly (insurance permitting), usually starting the tapering process during the second month.

Other key considerations for Dr. Bhatia include the risk of scarring.

"If there's a secondary infection, he adds, "That's going to lead to longer treatment. Also, acne can be pretty painful," which provides another rationale for standard-dose oral antibiotics — and lowers the threshold for isotretinoin, he says. Similarly, Dr. Johnson considers acne duration, previous treatments and patient expectations when she chooses medications for acne.

Regarding efficacy, "No study shows conclusively that doxycycline or minocycline better than the other. So it's basically a judgment call" based not on data, but on a dermatologist's experience, Dr. Baldwin says. In this regard, "I believe most people feel that minocycline is a bit more effective. Because it's more lipophilic, you can use a lower dose. And there is less risk of antibiotic resistance developing with minocycline, for some reason, and less phototoxicity. Also, minocycline can be taken with food, including dairy products," while doxycycline cannot.

Conversely, she says, "Doxycycline has more short-term side effects in terms of gastrointestinal issues, but fewer long-term or severe side effects." Long-term minocycline use is associated with hyperpigmentation, a possible lupus-like drug reaction and other immune hypersensitivity, she says.

Dermatologists also must consider patients' ability to comply with treatment regimens, say Drs. Bhatia and Johnson.

"Teenagers may take their antibiotic dose one day, but then skip a day or two, just out of forgetfulness. And if their acne clears up, they may stop taking their medication for a while. Then they may flare, and start up again. It's that chronic, intermittent use that concerns me most for antibiotic resistance," Dr. Johnson says.

Such usage can foster unusual resistance patterns that don't appear in studies, which use consistent dosing, she explains. To avoid this problem, Dr. Johnson generally gives teenagers SD antibiotics, and switches to isotretinoin if the antibiotic isn't working after three months.

> "**Changing our beliefs** and thought process is an **uphill battle**."
>
> **Sandra Johnson, M.D.**
> Fort Smith, Ark.

'RESISTANCE HIT PARADE'

As resistance to tetracyclines grows, dermatologists' lack of other options represents the "elephant in the room. If the tetracycline family is next on the resistance hit parade, then what do we do?" Dr. Bhatia says.

"Development of resistance in *P. acnes* is not the most pressing issue that we face," Dr. Baldwin says. "Once antibiotics are discontinued, *P. acnes* often returns to the wild type, and concurrent use of benzoyl peroxide can prevent the development of resistance or reduce resistant strains." A much bigger worry, she says, is whether resistant *P. acnes* will pass along resistance to other organisms such as *Staphylococcus aureus* or *Streptococcus*.

To prevent such problems, Dr. Bhatia says, "We must go back to looking at prescribing patterns, with an eye toward minimizing antibiotic dosage and duration and maximizing topical regimens."

He traces dermatologists' slow acceptance of SD antibiotics partly to the way the manufacturer of SD doxycycline introduced the product.

"There haven't been any new studies on the use of doxycycline at that dose for acne," since the product debuted, he says. At press time, however, a study of doxycycline 40 mg daily was ongoing, according to Galderma.

Without pharmaceutical funds supporting such research and publications, Dr. Johnson says, "Changing our beliefs and thought process is an uphill battle."

Going forward, Dr. Bhatia says he believes dermatologists' use of extended-release minocycline will decline mainly due to the reduced support for the drug from manufacturer Valeant as compared to Medicis.

"There are many doubters who don't believe SD doxycycline works for acne. Many dermatologists must get into the habit of using it. But that's really up to us, because we must get into the mind-set of incorporating more of the low dose, especially for facial, perioral or perimenstrual acne, where we don't believe there's a huge infectious component. We can probably use it more first-line to reduce the rate of exposure to unnecessary antibiotics," he says.

To nudge dermatologists along, opinion leaders must synthesize existing data for clinical application, and ultimately they may have to perform more investigator-initiated studies, according to Dr. Bhatia.

Dr. Johnson adds that shifting dermatologists' habits will require peer discussions in settings ranging from small groups to national conferences. Likewise, she says, "Media coverage can make people think about a problem that they may not be aware is a problem." **DT**

For more information: www.cdc.gov/drugresistance/index.html

Disclosures: Dr. Johnson is a speaker for Galderma. Dr. Bhatia is a consultant and/or investigator for Galderma, Valeant, Onset Therapeutics, Ferndale, Promius and Quinnova. Dr. Baldwin is a speaker for Allergan, Galderma, Valeant Dermatology, Medicis and Onset Therapeutics.

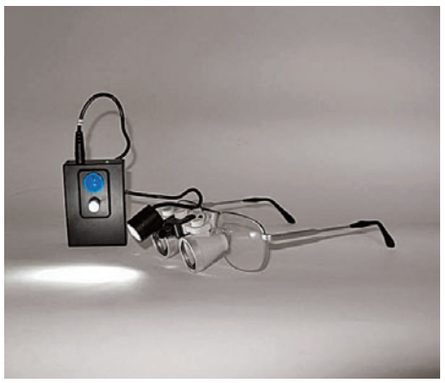
NIA 24

Company offers loyalty rewards program

NIA 24 has introduced its Priority Club for dermatologists and other clinicians, a loyalty club that rewards participants with additional support, free shipping and "sneak previews" of products.

Upon joining the program, members will gain the benefits as they grow their business. Four levels make up the Priority Club, with rewards including credit on orders for support tools, free testers, free shipping and sneak peeks of new NIA 24 products.

FOR MORE INFORMATION:
www.NIA24.com



VISION USA

Waterproof loupes include clip-on LED headlight

Vision USA's new loupes are waterproof, dust-resistant, and include a clip-on LED headlight. The Task Vision Platinum Frame has a side shield and can be made in prescription strengths. The loupe, which is fully adjustable, is available in 2.5x and 3.5x, the company states. The headlight has a variable intensity control (0-100 percent) 50,000 LUX.

FOR MORE INFORMATION:
www.visionusasupplies.com
800-257-5782

OCUSOFT

Cream reduces postprocedural bruising

Zoria Recovery Bruise and Scar Cream is formulated to minimize the effects of facial and eyelid procedures and bruising from infections, and to promote healing, according to the company.

The formula contains ingredients such as arnica and vitamin K to help promote the skin's healing process and to minimize skin discoloration. Escin, from horse chestnut, helps to improve circulation, while moisturizers hydrate dry, delicate skin. The cream can be applied to the affected areas both prior to and immediately after procedures, including injections, and can be reapplied as needed.

The product will be available only through physician specialties at a discounted price, to encourage direct dispensing to patients, the company states.

FOR MORE INFORMATION:
www.zoriacosmetics.com
800-233-5469

RESTORATION ROBOTICS

Software generates 3-D model of patient's scalp

The new ARTAS Hair Studio is an expansion of the ARTAS Robotic System, designed to allow clinicians to create 3-D models of patients' heads and scalps to create hair recipient sites, the company states.

The physician takes photos of the patient to create 3-D images of the head and face on a computer. The image can then be manipulated, allowing the clinician to view all angles of the patient's balding pattern, according to the company. Using a stylus pen, the clinician then draws boundaries for where recipient site incisions will be made by the ARTAS Robotic System. The angles, direction, density, distribution and randomness of each recipient site can be defined with this process.

Current ARTAS Robotic Systems can be upgraded to add the Hair Studio, according to the company.

FOR MORE INFORMATION:
www.restorationrobotics.com
www.artashair.com

Dermatology Times

Pollution, stress take toll on skin aging

Ilya Petrou, M.D. | Staff Correspondent

DURHAM, N.C. — A new area of research may help in the development of more effective topical products to counteract polycyclic aromatic hydrocarbons, a result of air pollution which impacts skin aging.


Dr. Draelos

Many different factors beyond overexposure to ultraviolet (UV) radiation are in part responsible for intrinsic as well as extrinsic skin aging, such as various forms of air pollution and even stress, begging the need for dermatologists to appropriately address these factors in their patients in terms of treatment, avoidance and advice.

QUICK READ

Pollution and stress are two factors that have been proven to contribute to the premature aging of the skin, begging the need for dermatologists to appropriately address these issues in their patients.

Having a better handle on emotional stress and the role of psychological stress in aging is a new area of study, and although most dermatologists have considered their association, an expert says no one has actually been able to prove that there is a physiologic change associated with it, until now.

"One of the central factors that has been proven beyond any doubt to cause premature skin aging is overexposure to UV radiation. However, other potential contributors to this process can include smog, pollution, cigarette smoke as well as other particulates in the air, which behooves dermatologists to address these issues accordingly with their patients," says Zoe Draelos, M.D., consulting professor of dermatology at Duke University School of Medicine, Durham, N.C.

LOOKING BEYOND UV

According to Dr. Draelos, many dermatologists may often stop at sunscreen and photoprotection when advising their patients in how to better protect their skin. These other non-UV sources, however, can also negatively impact the skin, Dr. Draelos says, as they operate through the same mechanism of action, which is the creation of reactive oxygen species, resulting in the premature aging of the skin.

"I do not think that a lot of people fully understand or appreciate the effects of the nanoparticles that are generated from either internal combustion engines, cigarette smoke or byproducts of industrial processes," she says. "The truth is that these can have a profound effect on the skin in terms of premature skin aging, and we

AGING see page 43

Quotable

"Bruises due to minor trauma ... are shallower and are accompanied by less edema than those induced by facial plastic surgery."

Joely Kaufman, M.D., Jeremy Green, M.D., Kevin C. Smith, M.D.

On using light and laser devices to treat purpura
See story, page 50

DTExtra

Valeant Pharmaceuticals has partnered with beauty company Living Proof to create aesthetic products, beginning with a technology that reshapes the appearance of the skin. The first product development will be based on Living Proof's cross-linking polymer film technology, Strateris, which is a film-like substance that can be worn all day to reshape the texture and appearance of skin. The companies plan to officially launch the product at the annual American Academy of Dermatology meeting in March.

READ MORE: DERMATOLOGYTIMES.COM/LIVINGPROOF

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For plaque psoriasis

Topicort®
(desoximetasone)
Topical Spray 0.25%

0.25%
SPRAY

Important Safety Information

- Topicort® Topical Spray is a topical corticosteroid indicated for the treatment of plaque psoriasis in patients 18 years of age or older.
- Topicort® Topical Spray is a topical corticosteroid that has been shown to suppress the hypothalamic-pituitary-adrenal (HPA) axis.
- Systemic absorption of topical corticosteroids can produce reversible HPA axis suppression with the potential for glucocorticosteroid insufficiency. This may occur during treatment or upon withdrawal of the topical corticosteroid.
- Because of the potential for systemic absorption, use of topical corticosteroids may require that patients be periodically evaluated for HPA axis suppression.
- Local adverse reactions may be more likely to occur with occlusive use, prolonged use or use of higher potency corticosteroids. Reactions may include atrophy, striae, telangiectasias, burning, itching, irritation, dryness, folliculitis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, and miliaria. Some local reactions may be irreversible.
- Safety and effectiveness of Topicort® Topical Spray in patients younger than 18 years of age have not been studied; therefore use in pediatric patients is not recommended.

TaroPharma®

See brief summary of Prescribing Information on reverse side.

AD100-0033 July 2013

TOPICORT® (desoximetasone) Topical Spray, 0.25%
Rx Only

BRIEF SUMMARY

1 INDICATIONS AND USAGE
Topicort® Topical Spray is a corticosteroid indicated for the treatment of plaque psoriasis in patients 18 years of age or older.

4 CONTRAINDICATIONS
None

5 WARNINGS AND PRECAUTIONS

5.1 Effect on Endocrine System
Topicort® Topical Spray is a topical corticosteroid that has been shown to suppress the hypothalamic-pituitary-adrenal (HPA) axis.

Systemic absorption of topical corticosteroids can produce reversible HPA axis suppression with the potential for glucocorticosteroid insufficiency. This may occur during treatment or upon withdrawal of the topical corticosteroid.

In a study including 21 evaluable subjects 18 years of age or older with moderate to severe plaque psoriasis, adrenal suppression was identified in 1 out of 12 subjects having involvement of 10-15% of body surface area (BSA) and 2 out of 9 subjects having involvement of >15% of BSA after treatment with Topicort® Topical Spray twice a day for 28 days. [*see Clinical Pharmacology (12.2)*]

Because of the potential for systemic absorption, use of topical corticosteroids may require that patients be periodically evaluated for HPA axis suppression. Factors that predispose a patient using a topical corticosteroid to HPA axis suppression include the use of high potency steroids, larger treatment surface areas, prolonged use, use of occlusive dressings, altered skin barrier, liver failure and young age.

An ACTH stimulation test may be helpful in evaluating patients for HPA axis suppression.

If HPA axis suppression is documented, an attempt should be made to gradually withdraw the drug, to reduce the frequency of application, or to substitute a less potent steroid. Manifestations of adrenal insufficiency may require supplemental systemic corticosteroids. Recovery of HPA axis function is generally prompt and complete upon discontinuation of topical corticosteroids.

Cushing's syndrome, hyperglycemia, and unmasking of latent diabetes mellitus can also result from systemic absorption of topical corticosteroids.
Use of more than one corticosteroid-containing product at the same time may increase the total systemic corticosteroid exposure.
Pediatric patients may be more susceptible to systemic toxicity from use of topical corticosteroids. [*see Use in Specific Populations (8.4)*]

5.2 Local Adverse Reactions with Topical Corticosteroids
Local adverse reactions may be more likely to occur with occlusive use, prolonged use or use of higher potency corticosteroids. Reactions may include atrophy, striae, telangiectasias, burning, itching, irritation, dryness, folliculitis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, and miliaria. Some local adverse reactions may be irreversible.

5.3 Allergic Contact Dermatitis with Topical Corticosteroids
Allergic contact dermatitis to any component of topical corticosteroids is usually diagnosed by a failure to heal rather than a clinical exacerbation. Clinical diagnosis of allergic contact dermatitis can be confirmed by patch testing.

5.4 Concomitant Skin Infections
Concomitant skin infections should be treated with an appropriate antimicrobial agent.
If the infection persists, Topicort® Topical Spray should be discontinued until the infection has been adequately treated.

5.5 Flammable Contents
Topicort® Topical Spray is flammable; keep away from heat or flame.

ADVERSE REACTIONS

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In randomized, multicenter, prospective vehicle-controlled clinical trials, subjects with moderate to severe plaque psoriasis of the body applied Topicort® Topical Spray or vehicle spray twice daily for 4 weeks. A total of 149 subjects applied Topicort® Topical Spray.

Adverse reactions that occurred in ≥ 1% of subjects treated with Topicort® Topical Spray were application site dryness (2.7%), application site irritation (2.7%) and application site pruritus (2.0%).

Another less common adverse reaction (<1% but >0.1%) was folliculitis.

Table 1. Number (%) of Subjects with Adverse Reactions Occurring in ≥ 1%

	Topicort® Topical Spray, 0.25% b.i.d. (N = 149)	Vehicle spray b.i.d. (N = 135)
Number of Subjects with Adverse Reactions	13 (8.7%)	18 (13.3%)
Application site dryness	4 (2.7%)	7 (5.2%)
Application site irritation	4 (2.7%)	5 (3.7%)
Application site pruritus	3 (2.0%)	5 (3.7%)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Teratogenic Effects: Pregnancy Category C
There are no adequate and well-controlled studies in pregnant women. Topicort® Topical Spray should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Corticosteroids have been shown to be teratogenic in laboratory animals when administered systemically at relatively low dosage levels.

Desoximetasone has been shown to be teratogenic and embryotoxic in mice, rats, and rabbits when given by subcutaneous or dermal routes of administration at doses 3 to 30 times the human dose of Topicort® Topical Spray based on a body surface area comparison.

8.3 Nursing Mothers
Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in breast milk. Because many drugs are excreted in human milk, caution should be exercised when Topicort® Topical Spray is administered to a nursing woman.

If used during lactation, Topicort® Topical Spray should not be applied on the chest to avoid accidental ingestion by the infant.

8.4 Pediatric Use
Safety and effectiveness of Topicort® Topical Spray in patients younger than 18 years of age have not been studied; therefore use in pediatric patients is not recommended. Because of a higher ratio of skin surface area to body mass, pediatric patients are at a greater risk than adults of HPA axis suppression and Cushing's syndrome when they are treated with topical corticosteroids. They are therefore at greater risk of adrenal insufficiency during and/or after withdrawal of treatment. Adverse effects including striae have been reported with inappropriate use of topical corticosteroids in infants and children. [*see Warnings and Precautions (5.1)*]
HPA axis suppression, Cushing's syndrome, linear growth retardation, delayed weight gain, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include low plasma cortisol levels and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema. [*see Warnings and Precautions (5.1)*]

8.5 Geriatric Use
Clinical studies of Topicort® Topical Spray did not include sufficient numbers of subjects aged 65 years and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

10 OVERDOSAGE
Topicort® Topical Spray can be absorbed in sufficient amounts to produce systemic effects. [*see Warnings and Precautions (5.1)*]

17 PATIENT COUNSELING INFORMATION
See FDA-approved patient labeling (Patient Information and Instructions for Use)

Inform patients of the following:
- Use this medication as directed by the physician.
- Topicort® Topical Spray is for external use only. Avoid use on the face, axilla or groin.
- Do not use this medication for any disorder other than that for which it was prescribed.
- Do not bandage or otherwise cover or wrap the treated skin so as to be occlusive.
- Report any signs of local or systemic adverse reactions to the physician.
- Do not use other corticosteroid-containing products with Topicort® Topical Spray without first consulting with the physician.
- Discontinue therapy when control is achieved. If no improvement is seen within 4 weeks, contact the physician.
- This medication is flammable; avoid heat, flame, or smoking when applying this product.
- Discard this product 30 days after dispensed by pharmacist.

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Revised: April 2013

AD100-0030

AGING SKIN:

Understanding role of stress in skin aging is new area of research from page 40

as dermatologists need not only to be aware of their action but also appropriately advise our patients in how to best avoid them."

Cigarette smoke has long been thought to be associated with the breakdown of collagen and elastic fibers in the skin, resulting in the premature development of wrinkles and flaccid skin in individuals who smoke. Most recently, a study in Mexico City demonstrated that cigarette smoke reduces the facial blood flow in smokers, further underscoring the detrimental effects of cigarette smoke. In this yet to be published study, the perfusion between smokers and nonsmokers was compared using Doppler ultrasound and found that the test subjects who smoked demonstrated a prematurely aged microcirculation in terms of having reduced blood flow to the skin compared to those individuals who did not smoke.

"Smoking chronically deprives the skin of oxygen and arterially supplied nutrients. In my opinion, a prematurely aged microcirculation probably has just a big an effect on premature skin aging as do the nanoparticles that create reactive oxygen species that are inhaled or even touch the skin itself," Dr. Draelos says.

AIR POLLUTION IMPACT

In addition to cigarette smoke, Dr. Draelos says air pollution is also a major extrinsic contributing factor to premature skin aging. Research has shown that the polycyclic aromatic hydrocarbons (PAH) that are bound to the nanoparticles in the air from pollution are converted to quinones, according to Dr. Draelos. These quinones are the redox cycle chemicals that in turn produce reactive oxygen species (ROS), which result in the same type of skin aging that is seen with chronic exposure to UV light.

As air pollution will likely remain a major issue, particularly for those who reside in larger cities, Dr. Draelos says she often recommends that her patients regularly wash their face and consume antioxidants.

"Polycyclic aromatic hydrocarbons are inadvertently delivered to the skin via nanoparticles resultant from different forms of air pollution," she says. "Washing the skin is one effective way of reducing the nanoparticle content on the skin surface. More information is needed in topical formulation development to combat this newly recognized skin aging mechanism."

Quinones not only prematurely age the skin by creating ROS, Dr. Draelos says, but they are also thought to be a driving force behind pigmentation, which in and of itself can be considered another form of skin aging.

"Indeed, it has been shown that there is more facial dyspigmentation in individuals who dwell in high PAH environments (i.e. cities) compared to those who live in rural areas," Dr. Draelos says.

In a recent still to be published study sponsored by L'Oréal, Dr. Draelos says the effects of PAH on the skin of 93 individuals living in a rural area in Mexico was compared to that of 93 individuals living in Mexico City. Researchers analyzed both vitamin E and the squalene content in the facial sebum of all study participants, and found that there was a decreased vitamin E as well as a decreased squalene content in the individuals who lived in the city environment.

"Lipids of all substances in the entire body are the most prone to oxidation. Vitamin E and squalene become oxidized and subsequently, their levels decrease in facial sebum because of contact with environmental pollution," Dr. Draelos says.

NEW PRODUCT DEVELOPMENT

This is a new area of research, she says, that hopefully will bear fruit in terms of the development of more effective topical products that can counteract the harmful PAHs. Moreover, Dr. Draelos says one of the ways of showing just how much pollution is affecting someone's skin is to analyze and measure the squalene content in their sebum.

One of the problems in developing new topical products is that one needs to have an endpoint that can be measured, but quantifying the ROS on a patient's skin is not possible. According to Dr. Draelos, measuring the squalene content could be one approach, as it provides an endpoint that perhaps could be used to analyze different skin appearances in individuals who are exposed to this type of environmental change.

"Perhaps in the future, you could actually just do a sebum swab of a patient's face, analyze the squalene content, start an intervention with a topical formulation, and then look to see if more of the squalene is present in an oxidized state. If you had less oxidized squalene, that would tell you that there is less ROS being produced and that your product, if used over a lifetime, could reduce the oxidative burden of damage that prematurely ages people beyond their chronological years," Dr. Draelos says.

Chronic psychological stress is another factor that has been recently implicated as a contributor to accelerated cellular aging, Dr. Draelos says. In a recent study, researchers showed that in individuals who have premature aging possibly due to chronic psychological stress also have decreased leukocyte telomere length (O'Donovan A, Tomiyama J, Lin J, et al. *Brain Behav Immun*. 2012;26(4):573-579).

The shortening of telomeres basically reflects the time clock that is ticking, Dr. Draelos says, and indicates how many more cell replications are possible. Decreased leukocyte telomere length is important because the leukocytes play a crucial role in immune function, and when the telomere length is prematurely shortened, that shortens the number of replications that each leukocyte can undergo.

"We normally lose about 100-200 telomere bases with each cell division and when you add psychological stress to the formula, you lose the telomere bases more rapidly, and telomere shortening leads to premature aging," Dr. Draelos says. **DT**

Disclosures: Dr. Draelos is a researcher for L'Oréal.

Laser choices grow increasingly complex

John Jesitus | Staff Correspondent

ASPEN, COLO. — Successful laser treatment of pigmented lesions and tattoos requires choosing the right tool for the job, an expert says.


Dr. Hruza

Virtually any laser can target melanin, says George Hruza, M.D., a dermatologist in private practice in Chesterfield, Mo. "But some lasers work better than others."

In particular, he says that targeting melanosomes requires pulse widths under one µs, the thermal relaxation time of the dermis.

"On the other hand, targeting epidermal lesions requires pulse widths under 1 ms," because such pulses cause epidermal necrosis, he says.

Q-SWITCHED GETS RESULTS

The standard of care for pigmented lesions and tattoos generally involves Q-switched lasers, whether ruby, alexandrite or Nd:YAG, Dr. Hruza adds. "They all work quite well." Long-pulsed lasers also work for these indications, he says, but with a smaller safety margin. Somewhat similarly, he says that intense pulsed light (IPL) devices can lighten pigmented lesions. "However, I don't believe these are the best way to treat individual lesions," he says.

QUICK READ

Q-switched lasers work well for indications ranging from pigmented lesions to tattoo removal, an expert says. In the latter area, a color wheel can help one choose the right wavelength.

Ablative lasers remove pigment by removing the epidermis, Dr. Hruza says. Regarding fractional ablative lasers, he says, "I use them primarily for area treatments," to remove hundreds of lesions at once. But for individual lesions, he prefers Q-switched lasers. "They allow for very specific targeting — one or two treatments and you're done."

Regarding specific clinical entities, Dr. Hruza says he would not treat a benign melanocytic hyperplasia with a laser without first confirming via biopsy that it is not lentigo maligna (LM). For café au lait macules, Dr. Hruza says, several treatments with a laser such as the Q-switched Nd:YAG or Q-switched ruby laser can lighten them quite effectively.

"But at least 50 percent of the time, they return," Dr. Hruza says.

PIGMENTATION TREATMENTS

For dermal pigmented lesions such as nevi of Ota, he primarily uses Q-switched lasers with nanosecond pulsing, such as the 1,064 nm and occasionally the 532 nm Q-switched laser. For melanocytic dermal lesions, Dr. Hruza advises waiting four months between treatments to see the full results of the preceding session.

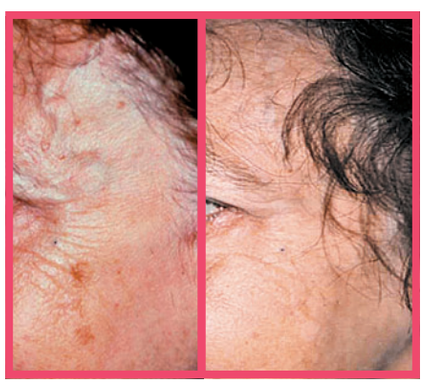
Additionally, "One can use a long-pulsed laser for compound nevi, provided one confirms that they are benign. Be somewhat careful," he says, because these treatments may leave patients with depressed scars created by bulk heating of the treatment area.

> "One can use a long-pulsed laser for compound nevi, provided one confirms that they are benign."
>
> **George Hruza, M.D.**
> Chesterfield, Mo.

Minocycline pigmentation also responds to treatment with any Q-switched laser, Dr. Hruza says. However, "The treatment hurts quite a bit because there's so much chromophore" to absorb the laser energy. Imipramine pigmentation also responds well to virtually any Q-switched laser (Atkin DH, Fitzpatrick RE. *J Am Acad Dermatol*. 2000;43(1 Pt 1):77-80).

Conversely, Dr. Hruza says he has never achieved long-term success in treating Becker's nevus with Q-switched or any other lasers. Even if one adds a nonablative fractionated laser, he says, "There's a dermal component that activates the pigmentation. So you don't really get rid of the whole problem."

As for melasma, "I still don't believe anything works very well." For this indication, Dr. Hruza says he prefers the Q-switched Nd:YAG laser operating at low fluences, rather than fractionated lasers. Even with the former, however, results are only temporary, he says. For freckles, Dr.


Solar lentigenes in a 78-year-old female patient, before and six months after one treatment with the Q-switched Nd:YAG 532 nm laser.

Source: Dr. Hruza

voice of the dermatologist

"It's very exciting that the top-line data demonstrate an excellent safety and effectiveness profile."

Derek H. Jones, M.D.

See story on ATX-101, page 46

Hruza generally treats the entire area with a fractional thulium laser, then has patients return for retreatment every year or so.

CLEARING TATTOOS

For tattoo treatments, Dr. Hruza says, many studies delineate which lasers work for which ink colors. He suggests, however, that simply choosing the opposite color (on a color wheel) of the one being treated usually suffices. For example, green lasers work for red tattoos, and vice versa, he says. Moreover, most tattoos require multiple lasers, or at least multiple wavelengths.

In his practice, tattoo treatments begin conservatively and increase fluence levels with each treatment. Conversely, "When treating very dense, dark pigment, we must be more careful because patients can get bulk heating, which can lead to scarring." Dr. Hruza generally spaces tattoo treatments at least six to eight weeks apart — and at least three months apart on the legs.

"It's important to give the body time to remove the particles of (treated) ink, and patients get more bang for the buck," he says.

On a practical note, Dr. Hruza says he never predicts how many tattoo or pigment treatments a patient will need. And he prices all laser treatments individually because selling packages would create the impression that the number of treatments in the recommended package would provide complete clearance.

In his experience, Dr. Hruza says, facial tattoos may require two to four treatments, versus up to 20 or more for tattoos on the legs. "For multicolored tattoos," he adds, "I generally try to talk patients out of treatment because treating every single color is very difficult." **DT**

Disclosures: Dr. Hruza reports no relevant financial interests.

ATX-101 studies yield favorable findings for reducing submental fat

Cheryl Guttman Krader | Staff Correspondent

CHICAGO — Top-line results from North American phase 3 clinical trials show that a series of injections with ATX-101 is safe, well-tolerated, and results in clinically meaningful and statistically significant reductions in submental fat or "double chin."

The findings from the two placebo-controlled, double-blind trials, REFINE-1 and REFINE-2, were presented by Jean D. Carruthers, M.D., F.R.C.S.C., F.R.C., REFINE-1 investigator and clinical professor, department of ophthalmology, University of British Columbia, Vancouver, at the annual meeting of the American Society for Dermatologic Surgery. She reported ATX-101 2 mg/cm^2 (purified synthetic version of deoxycholic acid, Kythera Biopharmaceuticals) demonstrated meaningful results in the population of study patients who were being treated with the drug for moderate-to-severe submental fat.

"There is currently no FDA (Food and Drug Administration)-approved injectable drug to reduce fat under the chin," says Derek H. Jones, M.D., associate professor of dermatology, University of California, Los Angeles, and founder and medical director or Skin Care and Laser Physicians of Beverly Hills. He was also a REFINE-1 investigator. "If approved, ATX-101 could address an unmet need in patients who desire a nonsurgical option to safely and effectively contour the area under the chin."

STUDY RESULTS

The two studies included more than 1,000 patients with moderate-to-severe submental fat enrolled at 70 centers in the U.S. and Canada. Eligibility was determined using three validated scales: the five-point Clinician-Reported Submental Fat Rating Scale (CR-SMFRS), the five-point Patient-Reported Submental Fat Rating Scale (PR-SMFRS), and the seven-point Subject Self Rating Scale (SSRS).

To be randomized to treatment, patients had to have a score of two or three on both the CR-SMFRS and PR-SMFRS and a score of 0 to 2 on the SSRS. Patients were allowed to receive up to six treatments, which were administered at about monthly intervals. Overall, about half of patients received the maximum number of injections.

Efficacy was evaluated at three months after the last treatment using a co-primary endpoint requiring a ≥1-grade improvement from baseline on both the CR- and PR-SMFRS scores. This clinically meaningful change was achieved in 70.3 percent of ATX-101 treated subjects in the REFINE-1 trial and 66.9 percent in REFINE-2, versus 18.7 percent and 22.4 percent in placebo, respectively ($p<0.001$).

A two-grade improvement in both rating scales — an FDA-preferred endpoint intended to drive the placebo responder rate very low — was achieved by 13.4 percent of ATX-101 treated subjects in REFINE-1 and 18.7 percent of ATX-101 treated subjects in REFINE-2 versus 0 percent and 3.2 percent for placebo, respectively ($p<0.001$).

Consistent with the subjective ratings, MRI measurements of the volume of submental fat also showed significantly higher responder rates in patients treated with ATX-101 compared with the controls ~44 vs. ~5 percent ($p<0.001$) in both REFINE-1 (46.6 vs. 5.4 percent) and REFINE-2 (40.0 vs. 5.1 percent).

Study subjects were asked to rate the visual and psychological impacts of their submental fat using the Patient-Reported Submental Fat Impact Scale (PR-SMFIS), and ATX-101 was associated with a statistically significant greater score improvement than placebo ($p<0.001$). Overall patient satisfaction with ATX-101 treatment approached 90 percent.

"We consider the ATX-101 phase 3 study results a real success and we could not be happier," says Frederick Beddingfield III, M.D., Ph.D., CEO of Kythera.

Analyses of the full data set are ongoing as Kythera prepares to submit its data to the FDA for product approval.

SAFETY ANALYSES

The safety analyses showed adverse events in both the ATX-101 and control groups, mostly representing the types of local reactions that would be expected with any injection. They included swelling, pain, bruising, numbness and redness. Adverse events were mostly transient, local to the treatment area and mild-to-moderate in severity, although rates of numbness and hard lumps, both temporary, were somewhat higher in the ATX-101 group. However, there were no serious adverse events, and less than 4 percent of patients withdrew from the study because of an adverse event.

Follow-up of patients in the phase 3 trials is continuing and will provide information about the durability of the treatment benefit. Available data from earlier studies indicate that more than 90 percent of treatment responders continue to show improvement at two years after their last ATX-101 injection while more than 80 percent sustain benefit after four years.

HOW IT WORKS

Histological studies from European investigators show that ATX-101 treatment results in targeted destruction of fat cells followed by removal of the cellular debris by normal host mechanisms and tissue remodeling. These observations are consistent with the durable results and data showing that submental skin laxity is improved or unchanged in 90 percent of treated patients.

Ongoing analyses of data collected in the phase 3 trials are expected to offer insight into how many monthly treatments patients will need to achieve acceptable improvement. Dr. Beddingfield says that while about half of patients in the studies received the maximum number of six injections, real-world practice represents a different situation.

"The goal of the clinical trials was to establish a treatment benefit and so investigators were encouraged to administer the maximum number of treatments as appropriate for each patient. In addition, patients generally had no reason to stop treatment before receiving all six injections," he says. **DT**

QUICK READ

ATX-101 demonstrates safety and efficacy for nonsurgical treatment of submental fat.

Disclosures: Drs. Carruthers and Jones are ATX-101 clinical trial investigators and consultants for Kythera.

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Q&A SKIN PORATION POPULARITY SPREADS TO U.S.

COSMETIC CONUNDRUMS

Zoe Diana Draelos, M.D., is a *Dermatology Times* editorial adviser and consulting professor of dermatology, Duke University School of Medicine, Durham, N.C. Questions may be submitted via email to zdraelos@northstate.net

Q. What is skin poration and how does it work?

A. Skin poration is a not a new concept, but rather the application of acupuncture techniques to skincare. In the Orient, rollers coated with sharp needles have been used for a variety of purposes from pressure point release for muscle pain to the rejuvenation of skin to a method of penetration enhancing topical products. This trend has now spread to the United States and I noted these rollers were offered for sale at the recent American Academy of Dermatology meeting.

The rollers typically are 1 to 2 inches in diameter and coated with sharp stainless steel needles. They are sold sterile for individual use and can be cleansed with alcohol, a disinfectant solution, or soap and water. The needles are conical with the point pressed into the skin to create a hole whose depth is dependent on the length of the needle and the pressure with which the roller is moved over the skin.

The minute holes are touted to increase collagen regeneration in the areas of wounding in columns similar to those created by a fractionated laser. The roller can also be applied after a topical product has been placed over the skin to allow the needles to carry the topical agent into the skin.

Perhaps the newest and most interesting use of poration is for the placement of hyaluronic acid into the skin. Instead of injecting hyaluronic acid based filler into the skin with a 30-gauge needle to correct folds and volumize the face, a thin hyaluronic acid serum is placed over the facial skin followed by use of the roller. The roller pushes the hyaluronic acid into the skin in small quantities on a daily basis. Over time, it is believed that the hyaluronic acid will build up in the skin to hydrate the superficial viable epidermis and possibly deeper. The roller is not intended to draw blood, thus it probably does not reach far into the dermis. More dramatic effects are said to occur when the roller is electrified to further modify the skin.

In Europe, many dermatologists are using the poration device over the skin that was treated with injectable filler. The theory is that the collagen regeneration plus the filler provide better anti-aging benefits. Others purport that the poration device more evenly distributes the injection hyaluronic acid droplets in the skin.

> The **spacing of the needles** is said to fit between the skin nerve bundles **allowing for reduced pain.**

Q. Does this technique work?

A. It depends. Hyaluronic acid is rapidly degraded in the skin unless it is crosslinked. Crosslinked hyaluronic acid is used in all currently marketed fillers to increase the longevity of the product in the skin, however it is not a thin liquid. Is it possible to put crosslinked hyaluronic acid into the skin with a poration device? I am not sure. Since these devices are sold in the over-the-counter market, no one really wanted to know because injection into the skin would technically make the rollers a device that would require Food and Drug Administration attention.

Q. Does the roller hurt?

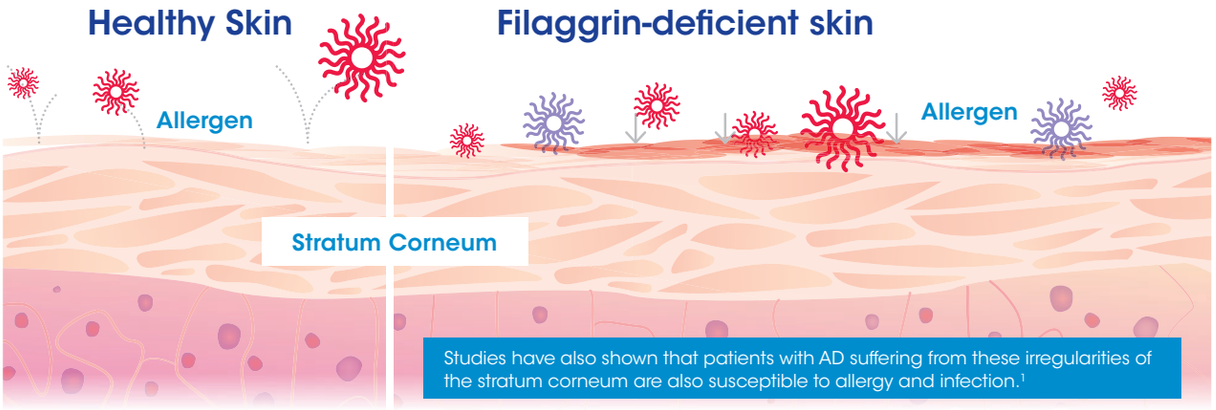
A. Not as much as you might expect. Good devices have very sharp well-engineered needles. Furthermore, the spacing of the needles is said to fit between the skin nerve bundles allowing for reduced pain. Certainly the discomfort of poration depends on the device construction and the pressure with which the device is rolled over the face. **DT**

Genetic breakthroughs are advancing the management of Atopic Dermatitis

Outcomes of numerous genetic studies suggest a strong association between the development of atopic dermatitis (AD) and a mutation in the filaggrin (FLG) gene. Filaggrin, an important protein found in the outer layers of the skin, plays a critical role in epidermal function, and up to 50% of AD sufferers may be positive for the mutation.[1,2] Since atopic dermatitis is a disorder of barrier dysfunction, these findings create an impetus for development of new barrier therapies.[3]

Filaggrin and epidermal function

Filaggrin proteins are important structural components of the epidermis. Within the skin, filaggrin becomes filaggrin breakdown products, which are amino acids that contribute to natural moisturizing factors (NMFs). NMFs help prevent water loss in the skin and maintain a normal skin pH.[1] A filaggrin deficiency in atopic skin results in water loss, decreased lipids, and elevated pH levels, all of which contribute to a compromised skin barrier.[1,3] Therefore targeting filaggrin deficiency in the skin may be an effective approach for regulating these defects.



Ceramides: A key component of the stratum corneum

Another important component of epidermal barrier function is the presence of lipids such as ceramides. The role of ceramides is to help maintain skin moisture. Atopic skin displays an abnormal lipid profile that contributes to barrier defect and increased water loss.[4]

The next evolution in atopic management is here

In light of research on filaggrin mutations and their role in AD, new innovations in barrier therapy are called for.

Only Galderma has formulated a nonprescription cleansing and moisturizing regimen containing both filaggrin breakdown products as well as advanced ceramides. Studies have shown these products to be gentle and effective in helping to restore skin barrier function for AD sufferers—including in the skin of infants as young as 3 months.[5]

As new research changes and informs the science of skincare, Galderma will continue to research, create and innovate new options and therapies to make a difference to patients, their healthcare providers and their families.

References: 1. Irvine AD, McClean WHI, Leung DYM. Filaggrin mutations associated with skin and allergic diseases. *N Engl J Med.* 2011;14:1315-1327. **2.** Brown SJ, McLean WHI. Eczema genetics: current state of knowledge and future goals. *J Invest Dermatol.* 2009;129:543-552. **3.** Elias PM, Schmuth M. Abnormal skin barrier in the etiopathogenesis of atopic dermatitis. *Curr Allergy Asthma Rep.* 2009;9:265-272. **4.** Castiel-Higounenc I, Chopart M, Ferraris C. Stratum corneum lipids: specificity role, deficiencies and modulation. *OCL.* 2004;11(6):401-406. **5.** Data on file. Galderma Laboratories.

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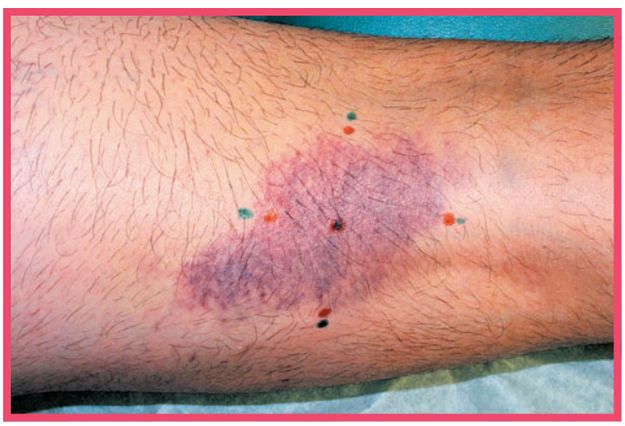
Laser, light treatment hasten resolution of purpura

PURPURA, WHETHER AFTER trauma or an aesthetic procedure, is undesirable to patients. The ecchymoses can last for up to two weeks, and dyspigmentation can persist even longer.

Fortunately, there are laser and light options that utilize the principle of selective photothermolysis to target hemoglobin within extravasated red blood cells and speed the resolution of purpura. Despite their widespread use, however, there is a paucity of published literature on the topic.

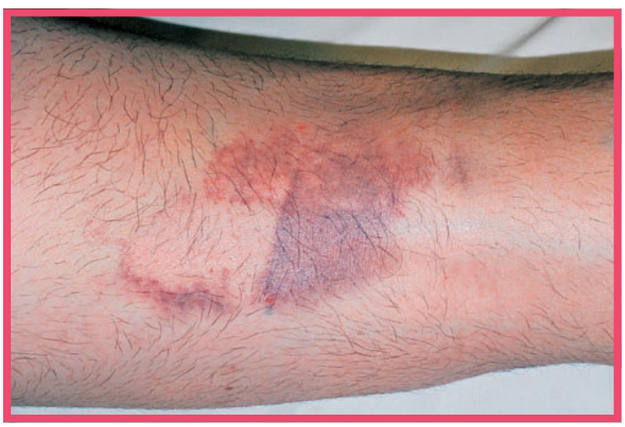
The earliest publication is from DeFatta and colleagues who reported their experience with the 595 nm yellow light pulsed dye laser (PDL) to treat the ecchymoses of 20 patients following facial plastic surgery (DeFatta RJ, Krishna Srinivasan, Williams EF. *Arch Facial Plast Surg.* 2009;11(2):99-103). At postoperative day (POD) five or six, the bruise was divided and part was treated with a PDL (V-beam, Candela) at 6 J/cm^2, 10 mm spot, 10 ms pulse duration, and cryogen 30 milliseconds with a 20 millisecond delay for three passes.

The patients returned 48 to 72 hours later for PDL of the untreated areas at the same parameters, and had a final follow-up 48 hours later. Three independent blinded observers graded photographs obtained using a purpura scale created by the investigators. There was a statistically significant 63 percent reduction in ecchymosis score, and it was found that the PDL performed earlier (POD five) was more efficacious. Minimal edema but no dyspigmentation was noted.



A five-day-old bruise (Figure 1) on the right popliteal fossa, pretreatment.

Photo: Kevin C. Smith, M.D.



The bruise (Figure 2) 24 hours post-treatment. Treatment types were, clockwise from upper left: 1064 nm Nd:YAG laser, intense pulsed light, control no treatment, and 532 nm KTP laser. Impressive clearing is evident in the KTP-treated quadrant.

Photo: Kevin C. Smith, M.D.

> Application of PDL light energy shortly after bruise induction may create an additive effect by disrupting hemostasis.

In their discussion the authors mentioned an unpublished pilot study where they treated the purpura as it started to appear on POD two or three. They found that the ecchymosis continued to worsen over the next two to three days, so they defined POD five as the time of initial treatment for this study. The authors theorized that the deeper dissection plane of facial plastic surgery combined with the postoperative tissue edema rendered the PDL less effective until swelling had reduced and the extravasated erythrocytes migrated more superficially and were lysed.

TREATING ECCHYMOSES

Geronemus and colleagues published their experience with the same PDL

PURPURA see page 52

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PURPURA:

Laser, light hastens treatment of bruises

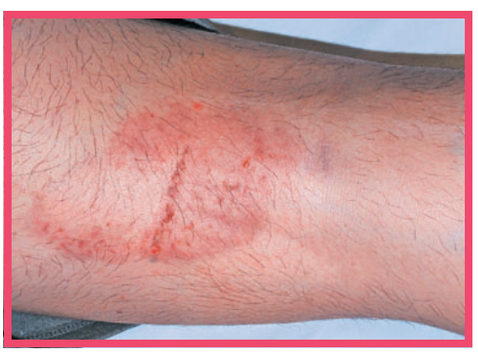
from page 50

in 10 patients who had ecchymoses from traumatic injury or a cosmetic procedure (Karen JK. *Dermatol Surg.* 2010). Six patients were treated 48 hours after the initial insult and the remaining four were treated at 72 hours at parameters more robust than the previous study: 7.5 J/cm^2, 10 mm spot, 6 ms pulse duration, and cryogen 30 milliseconds with a 20 millisecond delay for a single pass. They followed the patients 24, 48 hours and seven days after the procedure, and found that accelerated bruise resolution was evident as soon as six hours after laser treatment.

There are laser and light options that utilize the principle of selective photothermolysis to target hemoglobin within extravasated red blood cells and speed the resolution of purpura.

Utilizing a scale created by the investigators, they found at 24 hours the average improvement was 62 percent in treated and 13 percent in untreated bruises. At 48 hours the average improvement was 76 and 36 percent, respectively. Two patients experienced minor transient crusting.

In their discussion the authors noted that the yellow color change in bruises is due to the conversion of hemoglobin (one absorption peak near 595 nm) to bilirubin (broad absorption peak at 460 nm). For this reason they believe earlier violaceous to erythematous bruises respond better to PDL. They also theorize that the bruises due to minor trauma or nonsurgical cosmetic procedures (i.e. injectables) are shallower and are accompanied by less edema than those induced by facial plastic surgery. Therefore the laser energy is more readily absorbed by



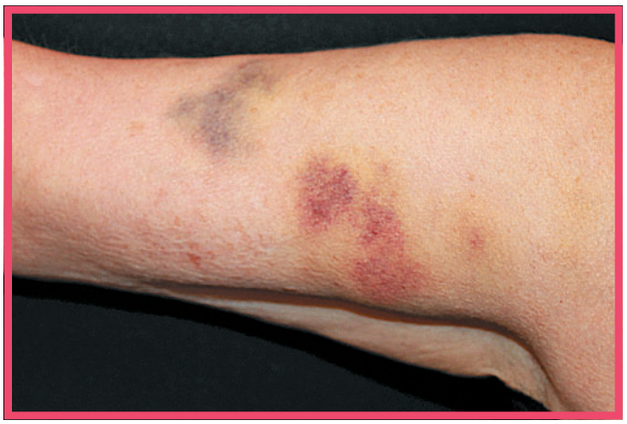
One hour after the entire bruise (Figure 3) was treated with 532 nm KTP laser, 24 hours after initial treatment.

Photo: Kevin C. Smith, M.D.

the target chromophore and these ecchymoses are more amenable to earlier PDL treatment.

The most recent report on lasers for bruise reduction comes from a group at Baylor University (Mayo TT, Khan F, Hunt C, et al. *Dermatol Surg*. 2013;39(10):1459-1464). The investigators used the same PDL as the previous two studies to induce purpura at 6.5 J/cm^2, 7 mm spot, 0.45 ms pulse duration cooling 30 ms/20 ms in 6, 2 x 2 cm zones on the lower abdomens of 17 patients. Each bruise was randomly treated with a cold compress, hydrogen peroxide soaked gauze, or a bruise serum for 10 minutes immediately after the bruise was induced or with a PDL (6.5 J/cm^2, 7 mm spot, 6 ms, 30/20) 30 minutes after purpura induction.

Two blinded evaluators graded the bruises at 30 minutes, three days and seven days. There was no significant reduction in bruise duration versus control in the three other interventions, whereas the authors actually found a statistically significant increase in bruise time to resolution in the PDL treated group. The authors hypothesized that the application of PDL light energy so shortly after bruise induction may actually create an additive effect by disrupting hemostasis.



A three-day-old traumatic bruise (Figure 4) on the right arm, pretreatment.

Photo: Jeremy Green, M.D.

The traumatic bruise (Figure 5) one day status post-treatment with KTP laser 7 J/cm^2 versus 14 J/cm^2. Clearing seen at both settings.

Photo: Jeremy Green, M.D.

EVALUATING TYPES OF LIGHT

It should be noted that visible light lasers and intense pulsed light devices with cut-off filters that cause the majority of light to be emitted in the visible light spectrum are safest when used in patients with Fitzpatrick skin types I to III. They can be used with caution in type IV, as melanin is a competing chromophore for short wavelength visible light.

The authors of this column prefer to treat post-procedural and traumatic purpura with a 532 nm green light potassium titanyl phosphate (KTP) laser (Excel V, Cutera Lasers). One author (KCS) recently treated a five-day-old traumatic ecchymosis of the popliteal fossa with three different types of light to further understand optimal treatment.

The bruise (Figure 1) was divided into quadrants and treated with KTP laser at 14 J/cm^2, 9 mm spot, 20 ms, 1064 nm neodymium yttrium aluminum garnet (Nd:YAG) laser at 60 J/cm^2, 9 mm spot, 40 ms, intense pulsed light (IPL) with a short-wavelength cut-off filter at 20 J/cm^2, 10 x 13 mm spot, program A (LimeLight, Cutera Lasers), versus an untreated control.

The following day (Figure 2), there was some minor improvement in the IPL- and Nd:YAG-treated sections, but considerable improvement in the KTP treated area. At that time all quadrants were treated with the KTP laser at the same settings, and only one hour later there was dramatic resolution of the treated areas (Figure 3).

The other authors (Dr. Green and Dr. Kaufman) sought to further ascertain optimal KTP parameters by treating a three-day-old traumatic bruise (Figure 4) with one half at the previously mentioned KTP settings, and the other half at the settings we had been using for bruises, 7 J/cm^2, 10 mm spot, 10 ms. There was slightly more procedural discomfort with the higher fluence, longer pulse duration setting. The following day both sides improved from the treatment but the higher fluence setting was more impressive (Figure 5). The authors look forward to additional investigations that study the optimum device, parameters and timing of laser/light treatment of purpura after initial insult to further enhance our abilities to hasten the resolution of this undesirable sequela. **DT**

Disclosures: Drs. Kaufman and Green have performed research and served on the speakers' bureau for Cutera Lasers.

GLYTONE

Product line addresses temporary, chronic hair loss

Glytone has introduced a product line that helps to alleviate thinning hair as the result of temporary and chronic hair loss. The Glytone by Ducray Hair Loss Range includes a shampoo, hair lotion spray, hair lotion concentrate and a dietary supplement.

The shampoo helps to strengthen and nourish weak, thinning hair and to prepare the scalp for hair loss treatments, according to the company. The lotion spray is formulated to promote nutritional exchanges in the hair bulb and to encourage reactivation of healthy hair growth. The lotion concentrate helps to stimulate the scalp and optimize the delivery of nutrients for strength, body and volume to the hair bulb. The dietary supplement contains vitamin B complex, vitamin P and E, methionine and cysteine, zinc and soybean extract.

FOR MORE INFORMATION:
www.glytone-usa.com

HOME SKINOVATIONS

At-home device stimulates collagen production

The Silk'n FaceFX is an at-home device that is cleared by the Food and Drug Administration for the treatment of wrinkles. The device is safe for all skin types and uses fractional red light therapy along with deep thermal heating to stimulate collagen production, according to the company. The Silk'n FaceFX also helps to reduce fine lines and wrinkles and promotes a clearer complexion. It can also make pores appear less visible. Some patients notice results as soon as immediately following the first use, the company states.

FOR MORE INFORMATION:
www.silkn.com/facefx/

NEOCUTIS

Cream reduces signs of photoaging, evens skin tone

The Nouvelle+ Retinol Correction Cream helps to minimize signs of photoaging and to correct uneven skin tone and smooth fine lines, according to the company. The cream contains 0.6 percent retinol — to fight skin aging — and Melaplex, a patent-pending skin brightener that is hydroquinone-free, according to the company.

The retinol is released over time at an optimal dose using µ-Bead technology, helping to intercept the signs of skin aging with minimal-to-low skin intolerabilities, the company states. Melaplex helps to reduce signs of skin discoloration and improve radiance and brightness when the product is used over the course of 12 weeks.

The cream is noncomedogenic and is free of color additives and fragrances.

FOR MORE INFORMATION:
www.neocutis.com

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Mask gives skin luminous complexion

The Snowise EX Brightening Mask is designed for those with dull, even skin tones, or those looking to combat photoaging and get a glowing complexion.

Formulated with Korean herbs and the Snowise Tri-White Complex, the mask helps to brighten skin. Each mask is also fermented with white ginseng for two weeks to help boost circulation, the company states, which also helps to prevent inflammation in the skin. The mask also helps to protect against collagen degradation and helps to minimize age spots.

The mask can be worn for 10-20 minutes, or longer for maximum absorption. When the mask is removed, the leftover serum does not need to be rinsed off, but instead can be massaged into the skin.

FOR MORE INFORMATION:
us.sulwhasoo.com

A NEW INNOVATION FOR THE MANAGEMENT OF HYPERPIGMENTATION

A Roundtable Discussion on Novel Management Strategies for Hyperpigmentation

Dermatologists have been challenged by the limits of existing treatments for hyperpigmentation. The unmet medical need has fueled research to develop more effective alternatives. Recently, a distinguished panel of dermatologists convened to discuss the potential of a novel addition to the various modalities available for treating the spectrum of hyperpigmentary disorders.

This exclusive supplement to the November 2013 issue of ***Dermatology Times*** summarizes the panel's discussion of their clinical experiences and variety of approaches to skin discoloration, including utilization of Lytera® Skin Brightening Complex—a nonprescription, hydroquinone-free topical cosmetic product which targets four key mechanisms involved in the development of hyperpigmentation.

Scan for more information

The panel's instructive exchange includes photo vignettes of some of their most challenging cases and reports the clinical data supporting the innovative Lytera® Skin Brightening Complex—both as monotherapy and in sequence with adjunctive topical and laser treatment regimens.

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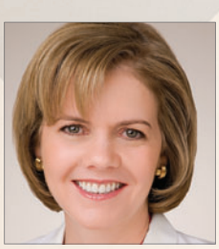

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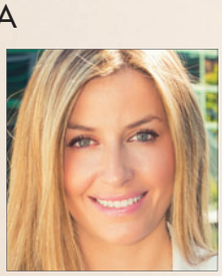

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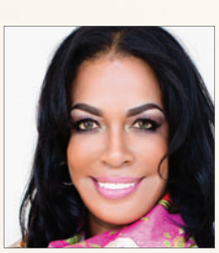

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Metastatic melanoma treatment enters new era

Cheryl Guttman Krader | Staff Correspondent

WAIKOLOA, HAWAII — Treatment for metastatic melanoma has begun a dramatic renaissance with the development of novel immunotherapy strategies and targeted therapeutic approaches.

Becoming knowledgeable about these advances is important for dermatologists as their referrals open the gate for affected patients to receive the best possible care, says Michael Postow, M.D., who spoke at the 38th Hawaii Dermatology Seminar held here.

"Until recently, chemotherapy and interleukin-2 were all that could be offered to patients with metastatic melanoma, but the efficacy of each of those approaches was limited. Therefore, metastatic melanoma was a fatal disease for most patients," says Dr. Postow, assistant attending physician, melanoma-sarcoma oncology service, Memorial Sloan-Kettering Cancer Center, New York.

"Thanks to increased understanding of the activity of the immune system in cancer and of the genetics of melanoma, new therapies have been developed that are extending survival in more patients with metastatic disease. As dermatologists are at the frontline of care for melanoma patients, they need to understand recent treatment advances so they can communicate to patients the existing promise and ensure they receive optimal available care."

QUICK READ

New and investigational treatments for advanced malignant melanoma that aim to boost the host immune system or target genetic mutations driving cancer growth and spread are bringing new hope for affected patients.

AVAILABLE IMMUNOTHERAPIES

Immunotherapies for metastatic melanoma are monoclonal antibodies designed to block signals that inhibit the ability of the host immune system to eradicate cancerous cells. Intravenous ipilimumab (Yervoy, Bristol-Myers Squibb), which targets cytotoxic T lymphocyte-associated antigen-4 (CTLA-4), is the first agent available in this class.

"Ipilimumab has shown benefit for prolonging survival of patients with metastatic melanoma, increasing the proportion of patients living for several years by about twofold compared with previously available therapy," Dr. Postow says. "Unfortunately, the numbers who have long-term survival are still just a fraction of the total patient population, and so current research is aiming to identify features that will predict response and ways to increase the proportion of patients who benefit."

Also within the immunotherapy category, there are several intravenous agents in development that are monoclonal antibodies targeting the programmed death-1 receptor (PD-1). The two farthest along in clinical trials are nivolumab (Bristol-Myers Squibb), and MK-3475 (Merck).

"Available data indicate that these treatments that target PD-1 result in sizeable tumor shrinkage in at least a third of patients with melanoma. In addition, the response to the anti-PD-1 agents seems to be durable, and this class appears to cause minimal side effects," Dr. Postow says.

"Results from phase 3 studies are needed to determine what effect the PD-1 inhibitors have on extending survival. However, based on the promising efficacy and safety observed so far, I would encourage dermatologists to refer their patients with metastatic melanoma to a center participating

MELANOMA see page **59**

Quotable

"One should be careful not to broadly implement screening without confidence in the trade-off between the benefits and harms."

Allan C. Halpern, M.D.
New York

On melanoma screening
See story, page 58

DTExtra

Dermoscopy can differentiate between superficial basal cell carcinoma (sBCC) and other basal cell carcinoma (BCC) subtypes, according to a study led by researchers in Italy. Investigators retrospectively examined dermoscopic images of histopathologically confirmed BCCs, looking for predefined criteria. Certain characteristics, including maple leaf-like areas, short, fine superficial telangiectasia, multiple small erosions, and shiny white or red structureless areas tended to predict sBCCs. The presence of these characteristics made diagnosis more than five times more likely.

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Melanoma screening efforts in flux

John Jesitus | Senior Staff Correspondent

NEW YORK — To document the value of melanoma screening, researchers in the United States continue to refine screening strategies, an expert says.

Allan C. Halpern, M.D., says he finds it surprising that in 2014, dermatologists don't routinely do melanoma screening. He is chief of dermatology, Memorial Sloan-Kettering Cancer Center, New York (MSKCC).

"There's a lot of public education regarding melanoma," he says.

There are also guidelines suggesting that people in "high-risk" groups should see a dermatologist, but these groups are poorly defined. A few examples include people with family histories of melanoma or with many atypical moles, Dr. Halpern says.

> "The United States Preventive Services Task Force has specifically concluded that there's not enough data to support population-based screening for melanoma."
>
> **Allan C. Halpern, M.D.**
> New York

However, "The United States Preventive Services Task Force (USPSTF) has specifically concluded that there's not enough data to support population-based screening for melanoma," he says. "So right now, if you're a primary care doctor with a patient over age 50, you know you're supposed to send the patient for a colonoscopy. But you're not supposed to send your patient for a skin cancer screening."

QUICK READ

Researchers in the United States are working to substantiate the benefits of routine melanoma screening, and to determine how to best conduct those efforts, an expert says.

WHO AND HOW TO SCREEN

Accordingly, he says, researchers are focusing on the questions of whether there should be population-based melanoma screening — and if so, who should be screened, and how. Complicating this task is the fact that "the general culture around cancer screening has been in flux for the last few years," Dr. Halpern says. "On the one hand, there's been increased recognition that while we've been pushing cancer screening as a bit of a panacea for decades, there are actually many potential harms associated with screening."

Physicians' use of prostate-specific antigen testing for prostate cancer screening, for example, has fueled a trend toward overtreatment. Therefore, the USPSTF recently recommended that PSA screening should not be done routinely, but at doctors' discretion.

Simultaneously, he says that although the benefits of preventive cancer screenings are real, stakeholders have realized that "They're not as dramatic as perhaps they've been made out to be."

The foregoing factors have created a climate in which, he says, "One should be careful not to broadly implement screening without confidence in the trade-off between the benefits and harms."

IMPACT OF SCREENINGS

In this regard, Dr. Halpern says, a large campaign underway in Germany may provide key evidence.

In 2003, the German government began an experiment to gauge the effect of skin cancer screening, performed once every two years for everyone over age 20 in the northernmost German state of Schleswig-Holstein.

"Over the next eight years, researchers saw a significant decrease in mortality from melanoma in that state (Breitbart EW, Waldmann A, Nolte S, et al. *J Am Acad Dermatol*. 2012;66(2):201-211)," he says.

> "Skin cancer screening should be a relatively low-cost, low-morbidity procedure that has the potential to save lives."
>
> **Allan C. Halpern, M.D.**
> New York

In 2008, the German government began offering skin cancer screenings for the entire German population over age 35, Dr. Halpern says. "We're waiting to see what effect that has on melanoma mortality in Germany as a whole. While this is not a formal clinical trial, it's a very large experiment that may support the fact that screening can save lives." The study also might help stakeholders determine the actual costs — in terms of both dollars and morbidity — associated with population-based screening, he says.

"Intuitively, skin cancer screening should be a relatively low-cost, low-morbidity procedure that has the potential to save lives. It's already happening very broadly, on a self-selected basis," Dr. Halpern says.

BOOST IN REQUESTS

Because dermatologists and groups including the American Academy of Dermatology have provided significant public education, he says, many people are requesting total-body skin examinations from their dermatologists.

"In that setting, it behooves us to begin to develop more efficient and effective ways of screening for skin

SCREENING see page **63**

MELANOMA:

New treatments aim to boost host immune system or target genetic mutations

from page 56

in one of the PD-1 inhibitor trials," he adds.

Targeted therapy for metastatic melanoma focuses primarily on patients with a BRAF mutation, who represent nearly 50 percent of the melanoma population. Currently, there are two approved BRAF inhibitors, vemurafenib (Zelboraf, Genentech) and dabrafenib (Tafinlar, GlaxoSmithKline). Trametinib (Mekinist, GlaxoSmithKline), which inhibits mitogen-activated protein kinase enzymes (MEK), is also approved for the treatment of metastatic melanoma in patients with a BRAF mutation. All three of these therapies are administered orally, and have been shown to be more effective than chemotherapy.

"These drugs have been game-changers for metastatic melanoma patients with a BRAF mutation. Unfortunately, the duration of benefit from BRAF inhibitor treatment is often limited," Dr. Postow says.

"Therefore, current research is investigating strategies for extending the longevity of the response, including by combining BRAF inhibitors (such as dabrafenib) with MEK inhibitors (such as trametinib).

PERSONALIZED APPROACH

Current decisions on treatment for metastatic melanoma first take into account whether the patient has a BRAF mutation. Those who don't are typically candidates for immunotherapy. In those with a BRAF mutation, consideration is given to symptom severity.

"In a patient with a BRAF mutation who is highly symptomatic, there may be a preference for initiating therapy with a BRAF inhibitor that will be most effective for shrinking the tumor, albeit at the expense of a less durable response," Dr. Postow says. "In contrast, a patient with an asymptomatic metastasis detected on CT scan might consider immunotherapy that likely would provide a more long-lasting benefit. However, the pros and cons of each modality are discussed with the patient in order to make an informed decision."

MAINTAINING SKIN HEALTH

Although treatment with the new immunotherapy agents and targeted therapies falls under the realm of medical oncologists, dermatologists are involved in the care of patients receiving these modalities due to their potential to cause dermatologic side effects. Skin rash can develop in patients treated with ipilimumab and the BRAF/MEK inhibitors. Patients treated with the BRAF inhibitors can also develop warty growths and are at increased risk for developing nonmelanoma skin cancers, particularly squamous cell carcinoma.

"As the use of these new strategies expands for the treatment of metastatic melanoma and other cancers, dermatologists can be expecting to see more patients on referral for adverse event management," Dr. Postow says. **DT**

Disclosures: Dr. Postow has received research grant support from Bristol-Myers Squibb.

Rising skin cancer rate spurs drive for new therapies

Louise Gagnon | Staff Correspondent

MONTREAL — The commercialization of ingenol mebutate (Picato, LEO Pharma) a medication that is currently approved in the United States and many other countries for the treatment of actinic keratosis, is an example of how enthusiasm and commitment can drive innovation, a LEO Pharma general manager says.

"It doesn't take a large, multinational pharmaceutical company to develop a new product," says Peter Welburn, Ph.D., general manager, Australia/New Zealand, LEO Pharma. He was based at GlaxoSmithKline in Brussels, and returned to his native country of Australia in 2000 to join a then-fledgling pharmaceutical firm known as Peplin. "It takes passion, and it takes dedication."

Speaking here at an update on therapeutics in dermatology, Dr. Welburn says it's a tremendous opportunity to be involved in taking a concept all the way to the pharmacy shelf. With the success of its flagship product ingenol mebutate, Peplin was acquired in 2009 by LEO Pharma.

STARTING SMALL

Dr. Welburn recounts that many challenges faced a small research and development team at Peplin, including securing a source of plant material from which the sap of the plant *Euphorbia peplus* could be extracted.

"Our research and development team in Australia never consisted of more than six people," Dr. Welburn says.

Dr. Welburn and other Peplin staff approached local farmers in Australia, asking them to grow this plant for the purposes of extraction and to use the plant on a commercial basis; several farmers initially agreed.

There has been documented use of *E. peplus* for skin cancer and solar keratosis with few side effects, Dr. Welburn notes. The anecdotal experience served to provide a foundation for clinical trials to examine the efficacy and safety of the compound in the treatment of nonmelanoma skin cancer.

"We needed to develop a clinical department, and needed to start doing clinical trials," Dr. Welburn says. "We had to draw on the experience of key opinion leaders."

QUICK READ

With its short course of treatment, ingenol mebutate represents an advance in the treatment of actinic keratosis, and a small pharmaceutical firm saw it through several stages of development before it was commercialized.

> "For long-term stability of the topical formulation, it needs to be refrigerated. It took us about six months to determine that."
>
> **Peter Welburn, Ph.D.**
> General manager, Australia/New Zealand, LEO Pharma

FOCUS ON STABILITY

Another challenge was attaining stability of the molecule, he says.

"We faced significant challenges in wondering how to stabilize this molecule and put it in an appropriate topical formulation," Dr. Welburn says. "For long-term stability of the topical formulation, it needs to be refrigerated. It took us about six months to determine that."

Many dose-ranging studies were conducted to determine the optimal dosing regimen, he says. The significant advantage of the therapy is the short course of treatment, anywhere from two to three days.

It is noteworthy that this therapy was developed in Australia, a jurisdiction where skin cancer represents a significant treatment burden for dermatologists, according to Dr. Welburn.

Skin cancers represent 80 percent of all newly diagnosed cancers in Australia, and the country has an incidence of skin cancer that is one of the highest in the world, two to three times the rates in the United States and the United Kingdom, according to the Cancer Council of Australia.

Innovative thinking is what has prompted the emergence of therapies such as Picato, which many maintain will improve adherence to treatment regimens, according to Stuart Maddin, M.D., F.R.C.P.C., clinical professor emeritus, department of dermatology and skin science, University of British Columbia, Vancouver.

TRUNCATED TREATMENT SPAN

"The major factor associated with this drug is that it is used over a period of two to three days, which truncates the treatment span, and this is most appreciated by patients," Dr. Welburn says. "I think it will go a long way to achieving enhanced compliance."

Other emerging skin cancer therapies include the BRAF-inhibitor dabrafenib (Tafinlar, GlaxoSmithKline), Dr. Maddin says. While there are numerous side effects for a drug like dabrafenib — such as kidney failure and fevers — Dr. Maddin points out that it is employed for very advanced cases of melanoma.

"The indication is for end-stage metastatic melanoma," Dr. Maddin says.

Trametinib, a MEK inhibitor, is a first in its class therapy, which also produces serious adverse events such as heart failure and loss of vision. Like dabrafenib, it is indicated for the treatment of metastatic melanoma and taken orally. The Food and Drug Administration on Jan. 10 approved trametinib (Mekinist, GlaxoSmithKline) in combination with dabrafenib for the treatment of patients with advanced melanoma that is either unresectable or metastatic. **DT**

Disclosures: Dr. Welburn is general manager, Australia/New Zealand, LEO Pharma.

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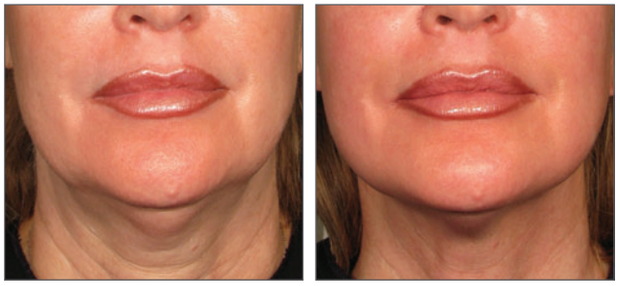

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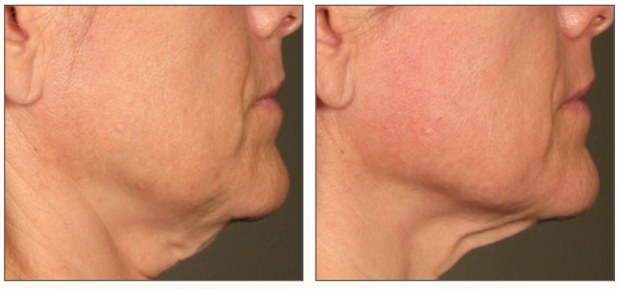

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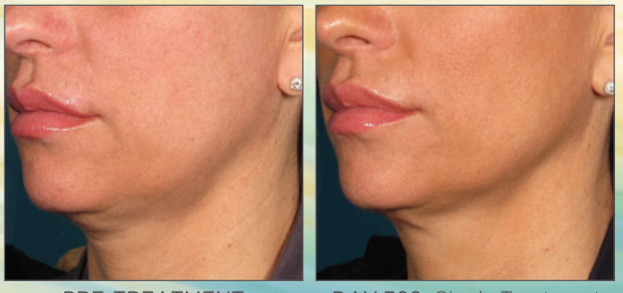

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SCREENING:

Experimental trial may support benefits of skin cancer screening

from page 58

cancer. That means doing a better job of educating both the public and physicians regarding the warning signs of skin cancer, as well as what benign spots on the skin look like, which will prevent many unnecessary visits," Dr. Halpern says.

Additionally, reducing unnecessary biopsies will require applying technologies effectively.

"The easiest technologies to bring to bear there include dermatoscopy in clinical practice, and prospective photographically assisted surveillance to monitor for changing lesions in high-risk patients," he says.

> Groups are working to help dermatologists more efficiently see their own high-risk patients through more effective triage strategies.

To simplify such surveillance, he says, MSKCC is working with the International Skin Imaging Collaboration to promote the development of standards for skin cancer imaging. Presently, MelaFind (MELA Sciences) is the only device approved by the Food and Drug Administration to help physicians diagnose atypical pigmented skin lesions. Other noninvasive devices under development range from a tape-stripping device that allows analysis of gene expression in individual lesions, to electrical impedance devices that may help diagnose individual lesions, Dr. Halpern says.

For now, some research groups based in the United States are attempting to replicate, on a smaller scale, the German model. Meanwhile, he adds, several groups are working to help dermatologists more efficiently see their own high-risk patients through more effective triage strategies. When patients call with worries about a lesion, Dr. Halpern says, it can be difficult to fit them into one's clinic. As such, he says that a small but growing body of research in the United States involves whether some of those visits can be avoided with teledermatology, or at least scheduled more appropriately based on some additional feedback from the patient or another healthcare provider. **DT**

Disclosures: Dr. Halpern serves as a scientific adviser to SciBase, DermTech and Canfield Scientific.

Dermatology Times

68 HOW TO USE TWITTER
Amplify your voice, accrue more influence, and extend your reach simply by leveraging this platform a few minutes each day

Q&A PRACTICE OWNERS MUST TALK WITH THEIR VENDORS NOW ABOUT ICD-10 UPDATES

Renee Stantz | Staff Correspondent

Q. We are worried that our vendor won't be ready for the ICD-10 updates by Oct. 1, 2014. What are some of the questions we can ask and how do we ensure that our vendor is ready?


Renee Stantz

A. This is a great question because most vendors will need to update their systems to be able to support the International Classification of Diseases, 10th edition, Clinical Modification (ICD-10-CM).

You'll first need to assess how the ICD-10-CM conversion will impact your practice. This means that you should list all your computer systems that currently include diagnosis coding, starting with your practice management system and electronic health record (EHR). Other systems that could be impacted include a disease management registry, e-prescribing module, and code selection software.

Once you've assessed your practice's software systems that need to be updated for ICD-10-CM, you can then contact your vendor(s) for each of these systems. The American Medical Association (AMA) suggests asking your vendor the following questions:

Q. Will you be doing updates to my system?

A. Some systems may be too old and the vendor may no longer support them.

Q. When will you be installing the updates to my system?

A. Vendors have many customers, and it may take time before the vendor can complete the work on your system.

Q. Will there be a charge for the updates to my system?

VENDOR COMPLIANCE see page 68

Quotable

"We are starting to see in dermatology the entry of substances that improve appearance but are truly drugs, which is one end of the spectrum of cosmeceuticals."

Zoe Diana Draelos, M.D.
Durham, N.C.

On cosmeceuticals
See story, page 70

DTExtra

The Maintenance of Certification (MOC) program's expense and time commitments continue to grow, producing greater complexity and more headaches, one physician says. What are your thoughts?

MOC Physician incentive statistics

Number of participating Eligible Professionals (EP)	Number of EPs who earned MOC incentive	Total amount of MOC incentive	Number of payments
1,683	964	$959,042.94	458

Source: Centers for Medicine and Medicaid Services, December 2011 data

READ MORE: DERMATOLOGYTIMES.COM/MOCVIEWPOINT

A Cure for Common ICD-10-dinitis

ICD-10-dinitis: A stress-related disease afflicting doctors and caused by inadequate solutions for ICD-10, resulting in lost reimbursements and time. Symptoms include number fatigue, extension nausea, crosswalk vertigo, laterality exhaustion, diagnosis pointer pain and superbill depression. Extremely contagious, ICD-10-dinitis can spread quickly and attack an entire medical practice.

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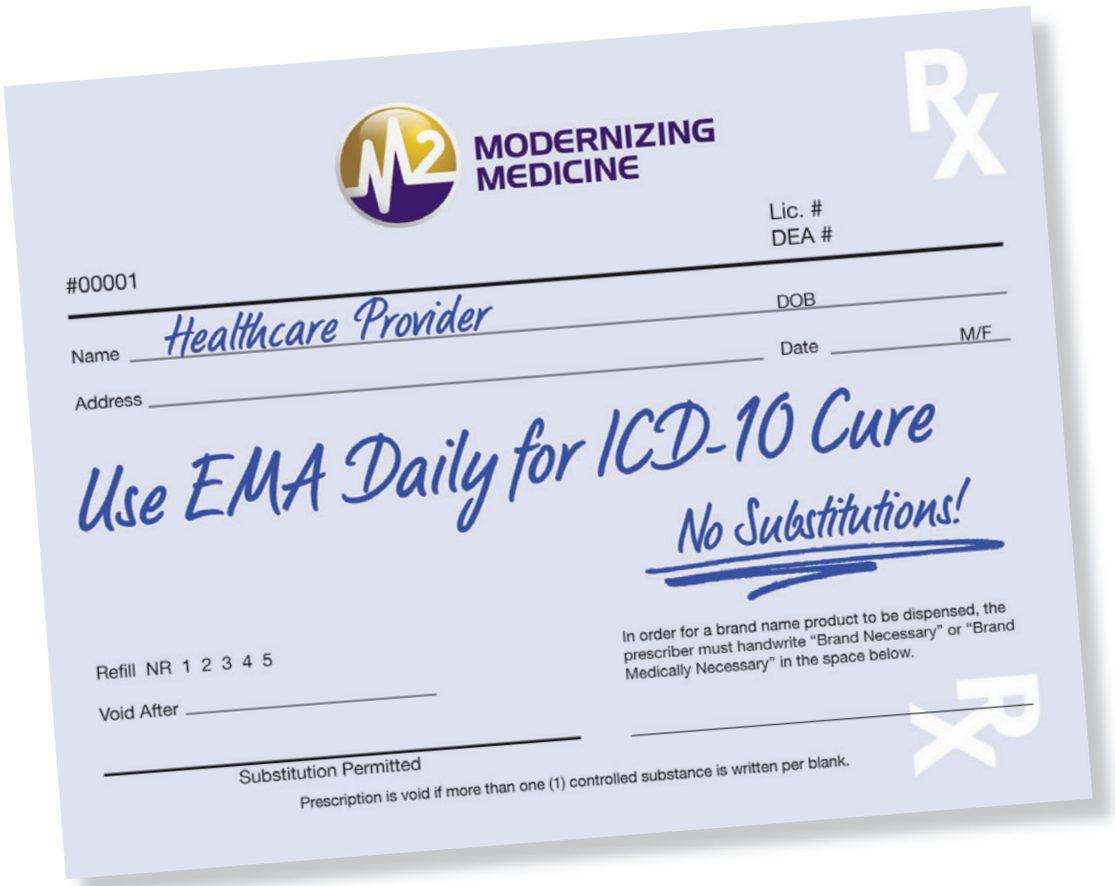

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Patricia Redsicker is a healthcare content marketing consultant and principal at Wordview Editing in Baltimore

How to promote your practice with Twitter

Patricia Redsicker | Staff Correspondent

ARE YOU INTERESTED in learning how to promote your dermatology practice on Twitter?

Compared to other social networks, Twitter is one of the simplest and most straightforward platforms you could ever use. The interface is simple and there are no privacy settings or new changes to deal with every few months. In fact Twitter is perceived by physicians to be a more relevant platform for medical conversations than, say, Facebook.

Even with a limitation of 140 characters per tweet, Twitter is a great place for dermatologists to amplify your voice, accrue more influence, and extend your reach simply by leveraging this platform a few minutes each day.

Here's how to get started on Twitter:

Create great content that engages your target audience.

PLANNING PHASE

1. DEFINE YOUR GOALS

Decide what you are trying to achieve with Twitter. Your objectives should be *specific, timely and measurable,* for example, to grow your email list by 10 percent each month.

2. DEFINE YOUR TARGET AUDIENCE

Apart from mere demographics you should have an in-depth understanding of your prospective patients' health needs, challenges, frustrations, life-style goals and even their content preferences. This knowledge (gained through research) will help you to develop interesting content that draws them to you as a trusted source of relevant content.

3. UNDERSTAND HOW HASHTAGS WORK

A hashtag is a word or phrase prefixed by the pound symbol (#), such as #melanoma or #acne. It is a form of metadata tag used to group Twitter conversations into specific categories. Hashtags are becoming increasingly popular on Twitter as evidenced by the creation of the Healthcare Hashtag Project.

CREATE YOUR ACCOUNT

1. Create a Twitter account using the name of your business domain. For example, if your domain is skindoctor.com, your Twitter profile should be @skindoctor.
2. Write up a short bio or description of your profile using keywords that are both "Google-friendly" and consistent with your practice (e.g., skincare, etc.)
3. Include your location
4. Add a link to your website
5. Upload a logo or photo that is consistent with the branding of your practice
6. Include an appealing Twitter background that complements your branding

DEVELOP YOUR TACTICS

1. Follow selectively — focus on people and brands that add value to your business. Use tools such as Twellow or Tweepi to help you find relevant followers on Twitter.
2. Use Twitter lists — A twitter list is a curated group of Twitter users that is based on specific characteristics. You may create your own list or subscribe to lists created by others. Here's a step-by-step guide for using Twitter lists.
3. Use time saving tools — Tools such as Hootsuite and Buffer are complementary to Twitter because they help you manage your account and save time.
4. Budget your time – allocate about 30 minutes each day to Twitter marketing. Within that time use your favorite tool (see No. 3) to schedule tweets, monitor conversations and "listen" to what others are saying about you.
5. Stay on-topic — It's easy to get distracted on Twitter if you're not focused. Stay on topic and ignore any conversations that are irrelevant to your practice. Lists and hashtags are effective in helping you stay on topic.
6. Engage in conversations with others by asking or answering questions, recognizing and thanking people who share your content and so on.
7. Add "Follow me on Twitter" buttons in the top-right corner of your website, newsletter, email signature lines and all other digital marketing properties.
8. Create great content that engages your target audience. And don't forget to share other people's content, too, particularly when it is consistent with your own brand's messaging.

MONITOR YOUR PROGRESS

1. Regularly check your mentions (@ mentions) to see what people are saying about you
2. Use Google analytics to see how much traffic is coming to your website from Twitter.
3. Learn, adjust, repeat — be prepared to experiment with new tactics to learn what works for your practice and what doesn't. If something isn't working, be prepared to let it go, modify your strategy and keep testing for new opportunities.

YOUR TURN

Twitter has become quite an impressive platform for promoting healthcare and medical brands. As a dermatologist what has been your experience so far? **DT**

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ICD-10 UPDATES:

Will your vendor be ready by the Oct. 1 deadline? from page 64

A. Check your contract, but also confirm costs with the vendor. Some regulatory updates are done at no charge, but the vendor may also have to make improvements to your system in order to be able to install the updates.

Q. How long will my system be down during the installation of the updates?

A. You will need to be prepared for how you will complete ongoing tasks while the system is down.

Q. Will my practice management system support entering the ICD-10 codes and then transmitting the code to my billing vendor, clearinghouse, and/or payer?

A. You will want to confirm that your system will support entry of the ICD-10 codes and transmission of the codes.

If your system will not support this, you will need to work with the organization(s) you are transmitting the data to and determine how you will send the ICD-10 codes to them. Your billing vendor or clearinghouse will be unable to convert an ICD-9 code to an ICD-10 code for you. You will have to be able to send the ICD-10 code for the claim and other transactions.

Q. Will you complete any testing of my system after you complete the updates?

A. Practices will want to complete "internal" testing of their systems to make sure they can enter and generate ICD-10 codes when appropriate. Your vendor may do this when they install the updates, but you will need to confirm this with them.

Q. What services or products are you providing to support ICD-10?

A. Ask your vendor what additional services or products they have available to support ICD-10 coding. While the services or products may add additional costs to your system, they may support easier and more efficient coding. **DT**

upcoming events

Dermatology Times lists meeting announcements for the following three months in our print issue.

17th Joint Meeting of the ISDP
www.intsocdermpath.org
March 19-20, 2014
Westin Denver Downtown
Denver

AAD 72nd Annual Meeting
www.aad.org
March 21-25, 2014
Colorado Convention Center, Denver

34th Annual ASLMS Conference
www.aslms.org
April 2-6, 2014
Phoenix Convention Center
Phoenix

State-of-the-Art in Facial Aesthetics 2014
www.ffasurg.org
April 9-13, 2014
Intercontinental Hotel Buckhead
Atlanta

South Carolina Dermatological Association Annual Meeting
www.scda-assn.org
April 11-12, 2014
DoubleTree Hotel
Charleston, S.C.

Icahn School of Medicine Advances in Facial Reconstruction & Cosmetic Surgery
cosmeticcadaverworkshop.com
April 12-13, 2014
Mount Sinai Medical Center
New York

ASDS - The Art & Science of Soft-Tissue Fillers and Neuromodulators
www.asds.net/Fillers
April 12-13, 2014
Loews Philadelphia Hotel
Philadelphia

European Workshop on Skin Immune Mediated Inflammatory Diseases
www.simid2014.org
April 24-26, 2014
Conference Centre Veronafiere
Verona, Italy

FSDDS 2014 Annual Meeting
www.fsdds.org
April 25-27, 2014
Disney's Contemporary Resort
Lake Buena Vista, Fla.

ad index

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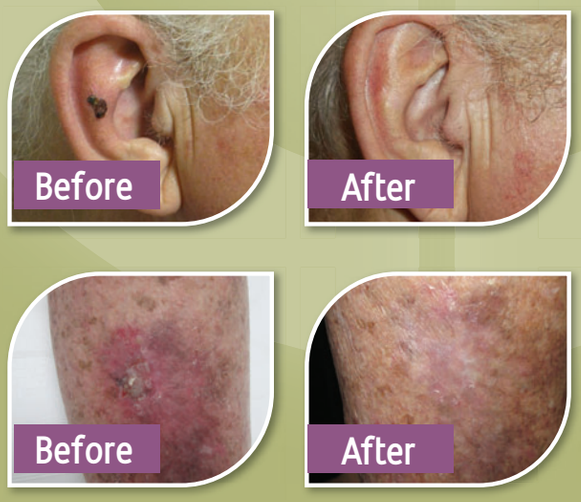

Visit the Xoft booth #416 at the American Academy of Dermatology Annual Meeting

1. Face, scalp, lower legs, ears, elbows

Images courtesy of Ajay Bhatnagar, MD, MBA, Cancer Treatment Services Arizona, Affiliate of 21st Century Oncology, DermeBx and Ken Gross, M.D., Skin Surgery Medical Group, Inc.

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THE VALUE OF COSMECEUTICALS

Q&A

NORMAN LEVINE, M.D.

Cosmetic concerns are important to many of our patients. Among the difficulties faced by consumers is the blitz of advertising of new and presumably revolutionary products that can rejuvenate and preserve the youthful appearance of the skin. Many products make what sound like medical claims about the efficacy of these agents. Norman Levine, M.D., asked Zoe Draelos, M.D. — the foremost authority on this subject — to discuss these issues with us.

Dr. Levine: There is a lot of misinformation out there about so-called cosmeceuticals, what they can do for our patients and how we should promote them. Can you explain what is a cosmeceutical, how is it different from a drug and how is it different from a cosmetic?

A. Actually, there is no such thing as a cosmeceutical. The FDA (Food and Drug Administration) does not recognize this term. The term cosmeceutical, in their eyes, is another word for cosmetics. I think if you ask the dermatologists what is a cosmeceutical, they would tell you that it's a product that enhances the skin in some manner, different from a cosmetic that traditionally is thought to only scent, color, and adorn the skin, but there is no such thing as a cosmeceutical from a regulatory standpoint.

There are three categories: there are prescription drugs; there are over-the-counter (OTC) drugs, which include such things as sunscreen, antiperspirants, and toothpaste; and then there are cosmetics. Cosmetics are a category that is currently unregulated. The over-the-counter drugs are regulated through a monograph and we are all familiar with how the FDA regulates pharmaceuticals.

Cosmeceuticals is a relatively new category. It's a contraction of the word cosmetic and pharmaceutical that was coined by Dr. Albert Kligman. There are countries around the world where cosmeceuticals are recognized, such as Japan. In Japan they call cosmeceuticals quasi-drugs. Cosmeceuticals are basically substances that perhaps might alter the skin, but the marketing claims that are used are identical to cosmetics and all ingredients that are used in cosmeceuticals must be considered GRAS (Generally Recognized As Safe) ingredients.

Dr. Levine: So by definition if these are cosmetics, my understanding is therefore they can have no medicinal value?

A. Exactly. If you look at the claims that are made for the efficacy of cosmeceuticals, they are all appearance claims. A drug claim would be "gets rid of wrinkles;" a cosmeceutical or cosmetic claim would be "improves the appearance of wrinkles." As you are reading packaging and trying to decide exactly what this particular formulation does, you will notice that it says "improves the appearance of fine lines," "improves the appearance of pores," "improves the appearance of facial redness," "smoothes the skin," "makes skin more radiant," "makes skin more luminous." Those are all referring to appearance changes that could be induced by the product when it's applied to the skin.

"If you look at the claims that are made for the efficacy of cosmeceuticals, they are all appearance claims."

Zoe Draelos, M.D.
Durham, N.C.

Dr. Levine: So does that mean that we as dermatologists have some obligation not to differentiate cosmeceuticals from cosmetics, or can we go beyond what FDA is interpreting as cosmetic?

A. I think we can go little bit beyond the FDA, because we are actually seeing the entry into dermatology of many substances that actually are cosmetic drugs. One of the first ones was approved by the FDA this year for a product that reduces facial redness. It is temporary, like a cosmetic. It reduces facial redness for several hours depending on the individual. It is given to the patient in a form of a prescription. It is purchased at the pharmacy, but instead of "curing or altering the disease process," it simply improves the appearance of facial redness.

We are starting to see in dermatology the entry of substances that improve appearance but are truly drugs, which is one end of the spectrum of cosmeceuticals. And then we also see products that are entering the marketplace, for example, things that are called line blurs or wrinkle reducers, and those are products that are also temporary, but they

are purchased over-the-counter and they contain silicone. The silicone base fills in the undulations of the skin surface where the wrinkles are present, and by filling those in, (it) improves skin smoothness and diminishes the appearance of wrinkles. So it's interesting that we have — in two very different categories — products to achieve the same thing, which is a temporary improvement in appearance.

Dr. Levine: So what do we as dermatologists do to find out which ones have some value and which ones do not?

A: There is actually a lot of testing that goes into cosmeceutical development. Companies test cosmeceuticals looking for an immediate benefit: that's the smoothness and the softness, because when a consumer purchases a product, she wants to see something immediate, which is something that pharmaceuticals traditionally do not deliver.

We usually tell a patient — for example, when they are using a topical rosacea medication — that one will need to use this product for four to six weeks before one will see a reduction in papules and pustules. But in the cosmeceuticals realm, people want to see immediate improvement. That's where the moisturizer comes in that makes the skin smooth and soft.

Then there are botanical anti-inflammatories that could be added into a cosmeceutical formulation that indeed over time might reduce redness, not perhaps to the degree that a pharmaceutical would, but it still has some beneficial effect. Most companies are looking for significant market share with their products and will build in short-term benefits and long-term benefits. The long-term benefits will not be to the level of a pharmaceutical, but still they are consumer perceivable benefits, which might result in some redness reduction because of a botanical anti-inflammatory, such as bisabolol, which is a chamomile extract with an anti-inflammatory topical effect.

Dr. Levine: Of all these hundreds of agents, can you pick out a few that you really think have value over and above the others?

A: Probably the most important one is sunscreen. Because the new sunscreen guidelines allow companies to make anti-aging claims based on the inclusion of sunscreen, we are going to see an increase in anti-aging claims because of sunscreen inclusion. The idea is that sunscreens prevent DNA damage, and when you prevent DNA damage, you prevent aging.

If a product contains a sunscreen, technically it does become an over-the-counter drug, but not only can SPF designations be placed on a label, companies can now make an anti-aging claim. You are going to see a whole new cadre of cosmeceuticals that have anti-aging claims, that may also contain sunscreen and mushroom extracts, but the sunscreen is the workhorse that's providing the anti-aging benefit and the mushroom extract is along just for the ride. The product will say that it reduces the appearance of wrinkles substantiated by sunscreen inclusion, and then it will say contains mushroom extract.

When you make a claim that says "contains something," that is basically a disclosure of the ingredient on the front of the package. They are not saying the mushroom extract does anything. But if you tell the consumer "this reduces the appearance of wrinkles and it contains mushroom extract," sometimes the consumer will think mushroom extract is reducing the wrinkles, not the inclusion of sunscreen. This is an interesting area.

The second interesting area of ingredients is the introduction of retinol into products. Retinol, as you remember, is the vitamin version of vitamin A. It is a precursor to retinoic acid, which we know of as tretinoin. Retinol is actually a precursor of tretinoin and since tretinoin has anti-aging benefits, so does retinol. There are some

COSMECEUTICALS see page **78**

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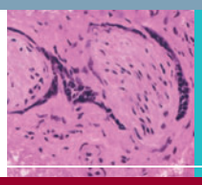

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Closure Course and Dermatologic Surgery: Focus on Skin Cancer

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May 21-22, 2014 - Closure Course
This intense learning experience will provide didactic instruction and practical demonstrations of multiple closure techniques, anatomic site-specific discussions, and valuable pearls, designed to take dermatologists to the next level of derm surgery practice. An elective lab session featuring realistic visco elastic models will allow registrants to practice new and more complex closures, proctored by highly experienced Mohs surgeons. The material presented in the Closure Course is unique and will nicely complement the topics and activities offered in Dermatologic Surgery: Focus on Skin Cancer (see below).

May 22-25, 2014 - Dermatologic Surgery: Focus on Skin Cancer
Top experts in Cutaneous Oncology, Dermatologic Surgery and Dermatopathology will provide updates on a wide range of surgical and Mohs topics. Interactive forum and panel participants will discuss appropriate repair strategies for different types of surgical wounds as well as innovative approaches to melanoma treatment and a variety of medicolegal controversies in dermatologic surgery. Both Mohs and non-Mohs histopathology cases provided by leading dermatopathologists will be featured in the microscope laboratory. Mohs technicians and nursing personnel are welcome to attend these sessions to further their understanding of skin cancer treatment and enhance their contributions to quality patient care and surgical efficiency.

Fundamentals of Mohs Pathology and Fundamentals of Mohs Surgery

DoubleTree Hotel San Diego, Mission Valley – San Diego, California

November 4-5, 2014 – Fundamentals of Mohs Pathology
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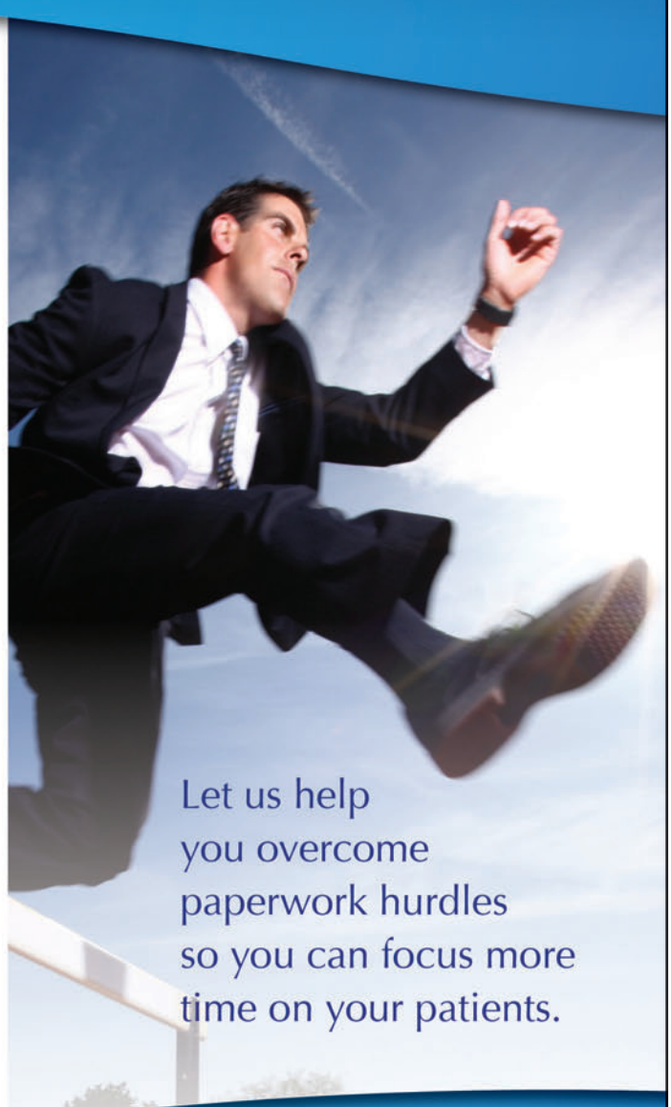

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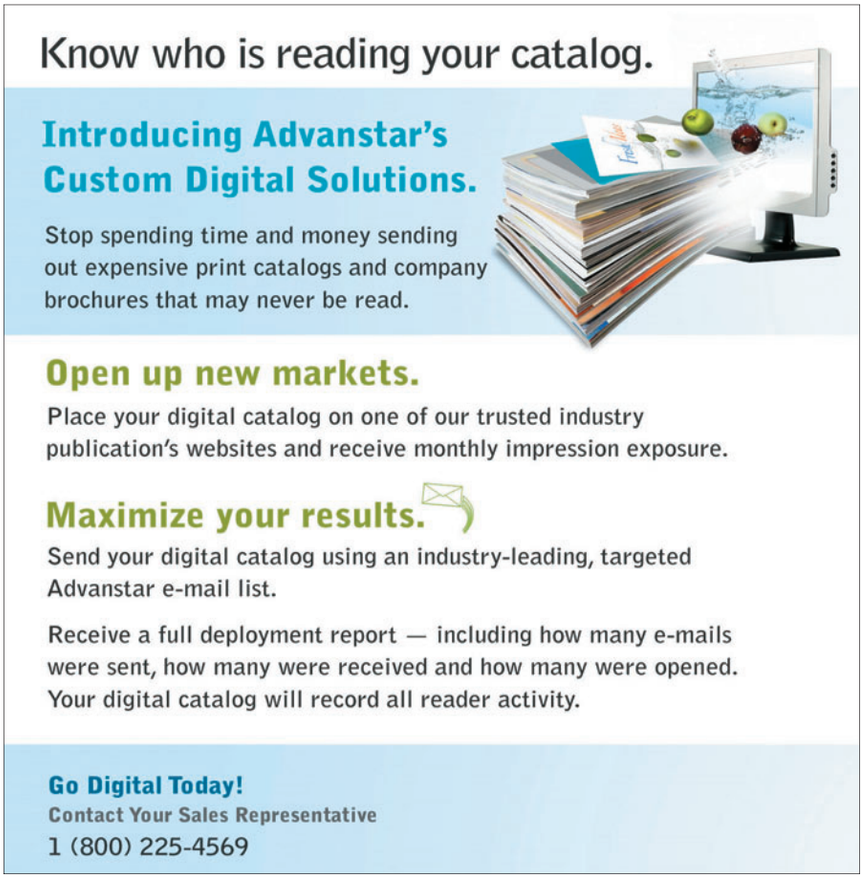

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COSMECEUTICALS:

Dr. Draelos sheds light on terminology and the value of cosmeceuticals

from page 71

studies that show that somewhere between 1 and 2 percent retinol can indeed improve the appearance of the skin by working through the retinoid receptor.

The third category to watch would be the anti-inflammatories. Now many of the new cosmetics that reduce redness and facial irritation actually contain 0.5 percent hydrocortisone, which makes them an over-the-counter drug. So it's interesting that cosmetic formulations are tapping into OTC drugs to deliver some of their claims, but there are some licorice extracts such as Licochalcone A. There are some camomile extracts like I mentioned earlier such as bisabolol. There are also other plant sterols that are being used as anti-inflammatory agents and so anti-inflammatories is another category.

Certainly these are not anti-inflammatory agents that will reduce disease, such as facial dermatitis, but they might reduce redness and they might reduce some of the itching and stinging. Many of those ingredients like bisabolol are used in sensitive skin formulations and the idea is to include an anti-inflammatory that will allow people with sensitive skin to be able to wear those products.

Dr. Levine: Could you comment on the current rage about the use of the word "natural" in many of these products. What does that mean and is that important?

A. The FDA actually has become very concerned about use of the word natural, because natural actually has no meaning whatsoever. "Natural" became a concern in food products because people were thinking that natural might somehow mean that these products didn't contain any chemicals, they didn't contain preservatives. In the cosmetics industry, people wanted to put "natural" on their products to imply that there weren't any chemicals that were toxic, irritating, or might induce some other type of damage, such as the generation of reactive oxygen species.

Everything that is found on the earth is natural to this earth, whether it will be a pesticide or preservative or a celery extract, but not all those substances are beneficial to the skin. For example, celery extract actually contains a carcinogen and that is an area of controversy where many plants, in order to protect themselves from overgrazing by animals, will contain toxins. Those toxins will poison the animal so to speak if it overeats that particular product and that's how the plant materials sustain themselves on the earth. There are many natural ingredients that could find their way into cosmetics that are not good for the skin.

For example, feverfew, which is an ingredient that is found in a number of facial products, actually has an allergen called parthenolide, The parthenolide had to be removed from the feverfew before it could be put in cosmetics. So, not everything that comes from plants is good for the skin. They are all natural, but natural is perhaps one of those words that doesn't have a lot of scientific meaning, just like the word radiance. You will see a lot of topical cosmeceuticals say they improve skin radiance. Well, what is radiance? No one really knows. We think that it's increased light reflection from the skin surface which is truly an optical effect, not implying any change in the skin itself, but if you tell someone you look natural and radiant, somehow those words have a connotation that make people feel they have an improved appearance.

Dr. Levine: Is there a way that we and consumers can sort out which manufacturers are reliable and which may not be reputable?

A. Sorting out quality products can be difficult, but many cosmetic companies are now publishing the results of their research and those results are being published in dermatology journals, such as the one I edit which is the *Journal of Cosmetic Dermatology.* If you Google a new ingredient, you should be able to pull up some articles that actually substantiate the value of that ingredient. So looking in the dermatology literature for supportive articles can be helpful.

You will also see many companies that will put their data with their packaging. For example, their data will say "dermatologist tested," and this is complemented by a bar graph that demonstrates efficacy. All cosmetic companies do some type of safety testing on their products, which is the Repeat Insult Patch Test (RIPT). This is done by the company or it could be done by the raw material supplier that provides the ingredients to the company.

Repeat Insult Patch Testing is where the product is applied to the back of volunteers to better understand if irritant contact dermatitis or allergic contact dermatitis might occur. RIPT testing is usually done not only on the raw materials that are put into the product, but also done on the final formulation. This type of testing is done routinely to prevent the introduction of products into the marketplace that could result in safety issues.

The second type of testing that is done is efficacy testing. Most of the large companies will do efficacy testing to prevent themselves from getting sued by the Federal Trade Commission over making false or misleading advertising claims. They will also do efficacy testing to prevent competitors from suing them and stating that they made false claims. So there are claims such as "dermatologist tested," that now mean that some dermatologist who is board-certified in dermatology tested that product. **DT**

IMPORTANT INFORMATION ABOUT

Mirvaso®

(Brimonidine) Topical Gel, 0.33%*

*Each gram of gel contains 5 mg of brimonidine tartrate, equivalent to 3.3 mg of brimonidine free base

BRIEF SUMMARY

This summary contains important information about MIRVASO (Mer-VAY-Soe) Gel. It is not meant to take the place of the full Prescribing Information. Read this information carefully before you prescribe MIRVASO Gel. For full Prescribing Information and Patient Information please see package insert.

WHAT IS MIRVASO GEL?

MIRVASO (brimonidine) Topical Gel, 0.33% is a prescription medicine that is used on the skin (topical) to treat facial redness due to rosacea that does not go away (persistent).

WHO IS MIRVASO GEL FOR?

MIRVASO Gel is for use in adults ages 18 years and older.

WHAT WARNINGS AND PRECAUTIONS SHOULD I BE AWARE OF?

MIRVASO Gel should be used with caution in patients that:

- have depression
- have heart or blood vessel problems
- have dizziness or blood pressure problems
- have problems with blood circulation or have had a stroke
- have dry mouth or Sjögren's Syndrome
- have skin tightening or Scleroderma
- have Raynaud's phenomenon
- have irritated skin or open sores
- are pregnant or plan to become pregnant. It is not known if MIRVASO Gel will harm an unborn baby.
- are breastfeeding. It is not known if MIRVASO Gel passes into breast milk. You and your female patient should decide if she will use MIRVASO Gel or breastfeed. She should not do both.

Ask your patient about all the medicines they take, including prescription and over-the-counter medicines, skin products, vitamins and herbal supplements. Using MIRVASO Gel with certain other medicines may affect each other and can cause serious side effects.

Keep MIRVASO Gel out of the reach of children.

If anyone, especially a child, accidentally swallows MIRVASO Gel, they may have serious side effects and need to be treated in a hospital. Get medical help right away if you, your patient, a child, or anyone else swallows MIRVASO Gel and has any of these symptoms:

- **Lack of energy, trouble breathing or stops breathing, a slow heart beat, confusion, sweating, restlessness, muscle spasms or twitching.**

WHAT ARE THE POSSIBLE SIDE EFFECTS OF MIRVASO GEL?

The most common side effects of using MIRVASO Gel include:

- redness, flushing, burning sensation of the skin, skin irritation

Skin redness and flushing may happen about 3 to 4 hours after applying MIRVASO Gel. Ask your patients to tell you if they get skin redness and flushing that is uncomfortable.

MIRVASO Gel can lower blood pressure in people with certain heart or blood vessel problems. See **"What warnings and precautions should I be aware of?"**

These are not all of the possible side effects of MIRVASO Gel. Remind your patients to call you for medical advice about side effects.

You are also encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

HOW SHOULD MIRVASO GEL BE APPLIED?

- Remind your patients to use MIRVASO Gel exactly as you instruct them. They should not use more MIRVASO Gel than prescribed.
- Patients should not apply MIRVASO Gel to irritated skin or open wounds.
- **Important**: MIRVASO Gel is for use on the face only. Patients should not use MIRVASO Gel in their eyes, mouth, or vagina. They should also avoid contact with the lips and eyes.
- Instruct your patients to see the detailed Instructions for Use that come with MIRVASO Gel for information about how to apply MIRVASO Gel correctly.

GENERAL INFORMATION ABOUT THE SAFE AND EFFECTIVE USE OF MIRVASO GEL

Remind your patients not to use MIRVASO Gel for a condition for which it was not prescribed and to not give MIRVASO Gel to other people, even if they have the same symptoms. It may harm them.

WHAT ARE THE INGREDIENTS IN MIRVASO GEL?

Active Ingredient: brimonidine tartrate
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References: 1. Fowler J Jr, Jackson JM, Moore A, et al; Brimonidine Phase III Study Group. Efficacy and safety of once-daily topical brimonidine tartrate gel 0.5% for the treatment of moderate to severe facial erythema of rosacea: results of two randomized, double-blind, vehicle-controlled pivotal studies. *J Drugs Dermatol.* 2013;12(6):650-656. **2.** Mirvaso [package insert]. Galderma Laboratories, L.P. Fort Worth, TX; 2013.

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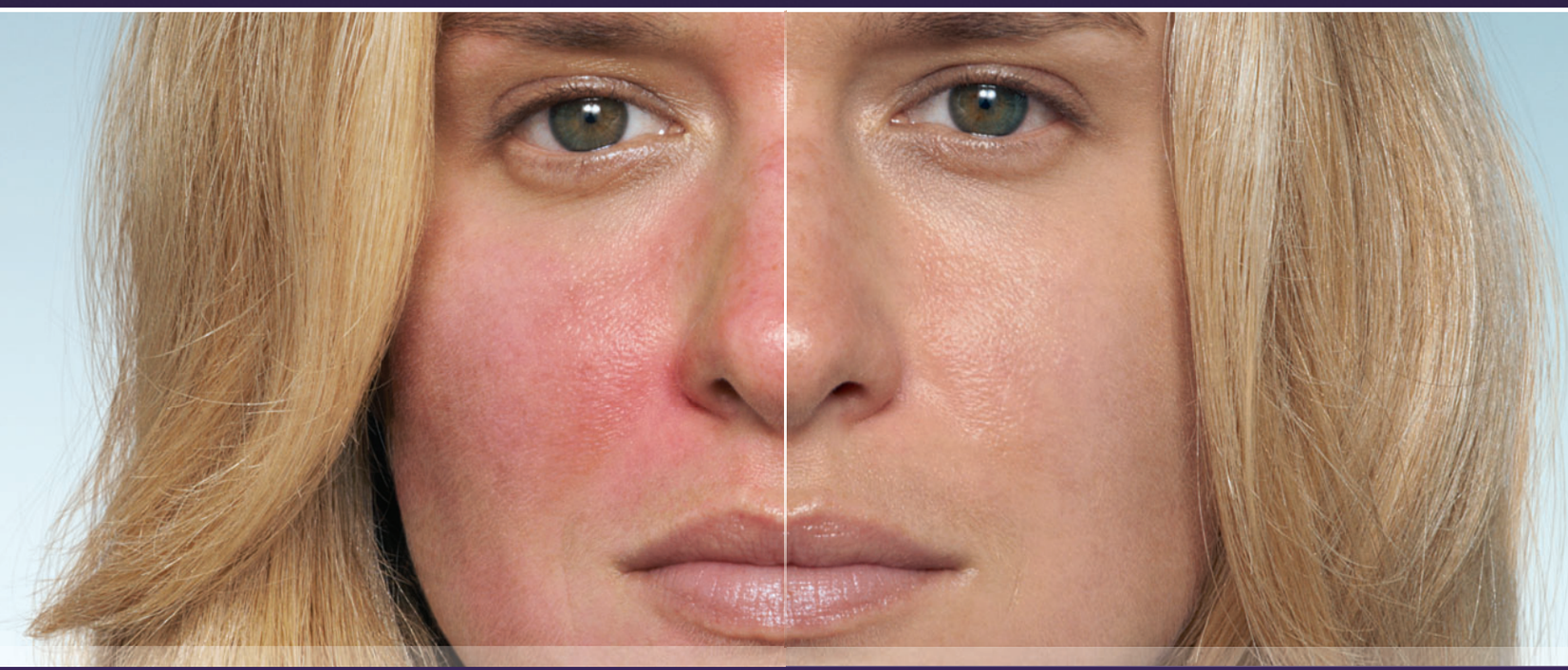

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*Phase 3 clinical studies of 553 subjects 18 and older. Subjects were randomized 1:1 to either Mirvaso Gel or vehicle for 29 days. Subjects and clinicians were asked to grade the improvement they saw at 30 minutes and hours 3, 6, 9, and 12 following application.

†Each gram of gel contains 5 mg of brimonidine tartrate equivalent to 3.3 mg of brimonidine free base.