Imagine this: A patient calls for her annual skin cancer check. A voice-activated artificial intelligence (AI) tied to your back-office operations answers, sets up the appointment or triages the call. The patient arrives to an appointment for total body imaging with an automated system, coupled with a machine learning system designed to identify suspicious skin lesions that need further single lesion assessment. Following individual lesion assessment, the decision to reassure the patient, monitor the lesion with close-up and dermoscopic images or perform a skin biopsy is rendered.

“This initial process of total body evaluation is performed in parallel with a dermatologist, followed by individual lesion examination by both AI-based devices and by clinical inspection, which are ultimately complementary,” says Clara N. Curiel-Lewandrowski, M.D., professor of dermatology at the University of Arizona (UA) and director of the Multidisciplinary Cutaneous Oncology Program, UA Skin Cancer Institute.

“This, Dr. Lewandrowski says, is a dynamic process upon which the human brain and computer systems continue to learn from one another. Some might view the use of non-human intelligence in dermatology as a threat. But we believe it’s a way for us to get to know each other better.”
DermatologyTimes is guided by a core group of trusted physician experts who review meetings; suggest topics & sources; & conduct interviews.

our MISSION
Provide practical analysis of recent studies, regulatory updates, techniques, devices and business solutions; and facilitate discussion to optimize practice and improve patient care.

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I've had a number of different interests and responsibilities during my dermatologic career, but it all began with treating general dermatology patients suffering from eczema, psoriasis, acne and warts. Following a fellowship in dermatopathology, I added pathology to my armamentarium of skills and interests. After another fellowship in Mohs, laser and cosmetic surgery, surgical procedures were added to my growing list of skills. Next, came clinical and basic research, academic medical administration and, finally, organizational dermatology. However, I found it somewhat surprising that I always returned to my roots of general dermatology. For, at every turn and junction, I saw patients with various general dermatologic skin diseases that required care. In all honesty, eczema was not my most favorite skin condition to treat. It was too difficult to determine causation in many cases and proved very difficult to treat. I found myself repeating daily to one or more patients what some of my trainees called my “eczema lecture.” However, despite those facts, I honestly believed until recently that I had offered those patients competent and compassionate care.

My new “insight” on eczema began one day when I awoke with an asymptomatic, solitary, round, scaly patch on my ankle. Even though I am an atopic, manifest by allergic rhinitis, except for some minor dryness during the winter, this was my first skin problem of any kind. After first ruling out a possible tinea infection with a simple negative KOH exam, I next went through a list of possible contactants to which I might have been exposed that could have been responsible. However, finding none, I decided to just “keep an eye on it.” This same advice I had given previously dozens of times to my eczema patients in the past. But this time was different as it made me start questioning just how competent and caring my treatment of eczema patients had been in the past. A few days later my solitary patch had been joined by a dozen others on my hands, antecubital fossae, legs and neck. The main difference with these new ones was that they were intensely pruritic. Despite how hard one tries, let me tell you that it is virtually impossible to stop scratching unless you are unconscious! This was my first of several new insights on eczema I had when dealing with my own “rash.” I can’t tell you how many times I heard the words to “STOP SCRATCHING!” from my loving wife. But unless you’ve walked a mile in my eczematous-laden shoes, you can’t know how hard it is to “NOT SCRATCH!” I’ve found myself in a checkout line or quietly listening to music and discovered one hand on the back of my neck subconsciously scratching away like a man possessed, completely unaware I was doing so. I remember that one of my faculty members when I was a resident made the comment that the uncontrollable scratching of a person with eczema was like a “cutaneous orgasm!” I can’t comment on the orgasmic part, but I can honestly say that it is truly impossible to stop.

So, finally, I came to my senses and did the right thing by taking my uncontrollably pruritic body to see my dermatologist where I got the definitive answer: “It’s just eczema.” After receiving the much-needed reassurance that my “rash” was not caused by an allergic reaction to food or chemicals and not due to some lurking internal malignancy or disease, I was told to apply emollients after a cool bath and steroid cream to the most pruritic areas twice daily. I was not told to “Stop scratching!” for he knew that was not within my power.

As expected, following a vigorous, multi-pronged attack using this combination of modalities, I started to improve and, slowly, I have become almost completely clear with only a rare bout of pruritus. This was the impetus of my thinking about the quality of care I provided as a dermatologist to my patients in the past with problems similar to mine.

Looking back now after having suffered with this dread disease, I’m sure that many times I did not show a proper level of concern about my patients’ problems. Nor did I likely answer all the questions that were going through their minds like those I had myself recently, such as: What caused this to come on? Is it related to some contact allergy? Do internal diseases play any role in its development? Why did it wait until now, at 71 years of age, to develop? What can I anticipate happening in the future?

My own personal battle with this whole problem has given me a new level of appreciation and respect for the complexity of eczema and how profoundly incapacitating it can be. I know I will be more understanding and caring the next time I see a patient with eczema than I was in the past, and I strongly urge those of you reading this to evaluate the quality your own past treatment of eczema patients, you might be surprised as to what you discover.
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- Depressed scars
Can I charge uninsured patients more?

by DAVID J. GOLDBERG, M.D., J.D.

Dr. Goldberg is director of Skin Laser and Surgery Specialists of New York and New Jersey, past director of Mohs and Laser Research, Icahn School of Medicine at Mt. Sinai; and, adjunct professor of law, Fordham Law School in New York City.

Dr. Fees has a large dermatology practice in an Appalachian community that, despite the ACA, has seen an increased number of people without health insurance. In fact, these patients have presented him with a unique economic advantage. He charges his uninsured patients double what he bills to contracted managed care insured patients.

Not only does he charge these patients more, but he also aggressively pursues them with collection agencies if they fail to pay. He thinks of himself as a quality physician and a smart business man. Much to his surprise, he is sued by one uninsured patient over his dual pricing.

Can Dr. Fees charge uninsured patients more?

In recent years, the United States has seen countless similar stories with regard to physician and hospital charges. Although patients with private or governmental insurances receive huge discounts for medical care, uninsured patients, who make up an ever increasing number of lower and middle income classes of Americans, pay higher prices for the same medical care. Apparently this pricing disparity has gone on for years, but over the last decade has been highlighted through stories in the Wall Street Journal and on CBS’s 60 Minutes. In one report, it was estimated that uninsured patients were charged two-and-a-half times more than a patient covered by one or more of the major insurance companies. The disparity is further accentuated by the fact that these inflated charges are not a voluntarily assumed debt, but rather, one that often cannot be avoided by the patient.

It is common knowledge that both not-for-profit and for-profit hospitals across the United States have policies of charging uninsured patients more. Some physicians have done the same. However, over the last decade, uninsured patients have increasingly sued hospitals for such policies. The claims have been based on several theories, one being that such differential billing policies violate state consumer protection statutes. Such lawsuits are based on the theory that uninsured patients have been subject to discrimination. The success of these claims depends on the state statutes where the litigation has been filed.

In Morrell v. Wellstar Health System, a patient argued the hospital violated the Georgia Uniform Deceptive Trade Practices Act because it charged unreasonable rates compared to those charged to insured patients. The Georgia statute at issue prohibited fraudulent misrepresentation, false advertising, or false and misleading statements. The court found nothing illegal about the hospital’s policies, because the hospital made patients aware of its fees. Despite this, similar decisions, some uninsured patients have been successful in their consumer protection claims.

In Servedio v. Our Lady of the Resurrection Medical Center, a lawsuit was brought by several uninsured patients who owed the hospital more than $60,000. The patients were unable to pay for their medical services and the hospital vigorously tried to collect the debt. The patients claimed they were charged inflated rates compared to insured patients, they were not considered for charity care, and excessive collection methods were used. In fact, Resurrection Medical Center had the highest charge-to-cost ratio of any Chicago hospital. The Illinois court ruled that medical services sold by a hospital were a form of trade or commerce, and that the hospital’s conduct was immoral, unethical, oppressive, and clearly against public policy.

Litigation entitled In re. Sutter Health Uninsured Pricing Cases, a group of uninsured patients of a California hospital alleged they were charged unreasonable rates compared to those charged to insured patients. The California Supreme Court noted that under the California Unfair Competition Law, any “unlawful, unfair, or fraudulent business act or practice” was a violation. Ultimately, Sutter agreed to a policy that provided discounts to uninsured patients.

Dr. Fees’ state statutes on unfair practices will determine whether he loses his lawsuit. He will likely need advice from a health law attorney. With today’s social media reach, one may question the long-term wisdom of such a practice.
Intellectual property: Technology transfer

by STEVE XU, M.D., FAAD

Dr. Xu is medical director of the Center for Bio-Integrated Electronics at the Simpson Querrey Institute for Bio-Nanotechnology, Northwestern University, and co-founder of the Advancing Innovation in Dermatology Accelerator Fund.

One of the key considerations for a new innovations center on intellectual property (IP). This is the first part of a two-part mini-series on IP with an initial focus on technology transfer. A big underappreciated question is who actually owns the IP. For innovators that are sole proprietors—you own any intellectual property along with your co-inventors (if any). The answer is rarely that simple. Inventors employed by a larger institution often have a duty to assign ownership back to the employer (e.g., a university). Thus, technology transfer must occur with clear documentation of transfer of ownership or control from one party to the commercializing entity. In this month’s column, we will discuss the scintillating technology transfer process.

For those of you working on an innovation and employed in a non-university setting, check your employment agreement first. Sometimes these agreements are favorable to you as the innovator—for instance, there are employer agreements that explicitly state that you own your invention completely if you develop your invention on your free time (nights and weekends), without the use of your employer’s resources or equipment. In the most relaxed agreements, there are no further stipulations. Often, employer agreements have an additional stipulation that inventions relevant to your scope of work (e.g., dermatology) are owned by the employer. For example, if you’re a dermatologist and you’ve invented a great new garden hose—you’re still in the clear. But, if your invention is a medical device, drug, or diagnostic in dermatology then you may be required to assign ownership of the patent to your employer. In many instances, you can also be proactive, especially if the language in your employer IP agreement is unclear. You can then reach out to your employer’s legal department and explain that on your free time you are working on an innovation and that it does not affect or impact your work performance. In these cases, you can ask for them to release or relinquish their rights to what you are working on. This may seem like a “big ask;” however, in truth, it is something that most employers would be happy to clarify or even release their right to. The earlier you do it the better, as the invention is harder to value at the earliest stages. Let’s assume that you’ve come up with a great medical device idea for acne and your employer’s IP agreement indicates you are required to assign the invention to your employer since the invention is within the scope of your work duties. In this case, you have several options. The best way to maximize your ownership and flexibility is for you to ask your employer to assign the patent back to you completely (e.g., relinquish rights)—this is an option when your employer decides that the cost of preparing a patent, which can easily cost $10,000 USDs or more, is not a worthwhile investment. If your employer decides to proceed in investing in a patent filing, then you will have to go through a licensing negotiation directly with your employer.

For academia-based innovators, universities also have employment agreements that may grant you sole ownership rights of inventions conceived and developed without university resources and outside of your work duties. Again, check the language of your agreement. Your first point of contact will be your university’s designated technology transfer office.

Being in an academic center, I have always believed fully that my university’s technology transfer office is one of my strongest allies. The university has an interest in ensuring that IP being developed by their faculty is adequately protected (e.g., by a well-written patent) and thus has the opportunity to return monetary value

HISTORICAL REFERENCE

THE UNIVERSITY TECHNOLOGY OFFICE was spawned after the 1980 passage of the Bayh-Dole Act. Prior to the Bayh-Dole act, all inventions patented as the result of government-sponsored research were assigned to the federal government—this led to tens of thousands of patents owned by the federal government that were not being licensed or commercialized. Neither the university nor the faculty inventor had a real incentive to pursue further commercialization. The new Act essentially transferred ownership of inventions from federally sponsored research back to the entity conducting the research—typically a not-for-profit university. The federal government only retained a license to the invention. This spawned a new era of technology transfer offices in universities where now there was direct financial value to the IP. Proper stewardship of this IP could then translate to hundreds of millions of recurring yearly revenue from royalties and payments — as in the case of new drugs. This has direct implications for academia based innovators.
Facial care fleshed out

by DR. ZOE DIANA DRAELOS

Dr. Draelos is a consulting professor of dermatology, Duke University School of Medicine, Durham, N.C.

**What is the medical value of the popular paper face masks?**

There is no medical value to paper face masks. Then, why are they so popular with consumers? Paper face masks are popular with consumers because of the aesthetic and temporary positive tactile benefits they provide. The masks consist of paper similar to that of diaper wipes, soaked with a solution and placed in a waterproof foil or plastic pouch. The masks sell for anywhere from $1 to $50 based on the place of purchase and the contents of the mask.

The most popular masks are the moisturizing masks that contain a thin serum. The mask is removed from the pouch and placed on the face with holes for the eyes, nose and mouth. The mask can be worn from 5 minutes to 30 minutes, or all day if the mask is elaborately decorated. Some are favored by youths as a party mask. The mask slightly impedes transepidermal water loss and allows the moisturizer to leave a thin film over the face. Many of these masks contain a polymer that creates a smooth film, leaving the skin very soft, however, the tactile assessment is the film and not the underlying skin. Thus, the softness is short lived, but enticing to the consumer.

More elaborate masks may contain rare ingredients, such as caviar, gold particles, or stem cells. While these ingredients add interest and marketing cache, the backbone benefit of the mask is the moisturizing film left behind on the skin. The mask can also be loaded with various fragrances for aromatherapy purposes and relaxation. The masks do not cause any problems unless the consumer has an irritant or allergic contact dermatitis to one of the ingredients.

**What is the role of skin care products that do not damage the microbiome?**

Microbiome has certainly become the buzzword of the moment in skincare! A new claim entering the cosmetic advertising vernacular is “does not damage the microbiome.” What exactly does this mean? All humans are covered in bacteria, primarily, and some fungus. These organisms are present on all surfaces of the body that interface with the environment and are obtained from the mother during the birthing process and controlled by the immune system. The microbiome is distinct for each human and possesses variations based on body location, sex, and age. It is clear that the microbiome is necessary for skin health and is very difficult to permanently alter.

Are there products that damage the microbiome? Well, the microbiome can be temporarily altered, but permanent changes are difficult to induce. The antibacterial ingredients triclosan and triclocarban were removed from the marketplace by the FDA based on health concerns and the fact that the cleansing industry could not support the antibacterial claim in microbiome studies. It is therefore easy to demonstrate that a skincare product does not damage the microbiome permanently.

Is there an effective cosmetic treatment for black dot follicles?

Black dot follicles are common on the nose of adolescents and mature individuals. In the case of adolescents, they represent retained oxidized sebum in the pores, but cannot be considered open comedones since the pore is not dilated. In mature individuals, the black dot follicle may contain both sebum and retained hairs. Black dot follicles do not respond well to acne treatment, and comedolytics, such as benzoyl peroxide, may cause excessive skin irritation. The best treatment for nasal black dot follicles are the pore strips that contain a glue that polymerizes on the skin. Once the pore strip has dried, it is pulled from the nose and, with it, the retained follicular debris. The pore strips must be pulled gently or the skin can be damaged and must be repeated weekly to prevent reaccumulation. Pore strips are a cosmetic temporary safe treatment for black dot follicles.
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ADVANCING WOMEN IN AESTHETICS

EARLIER THIS YEAR, Galderma announced a new multi-disciplinary group of advisory members that comprise The Women in Aesthetics Leadership Council. All current and future female leaders in the medical aesthetics specialty, their expressed purpose is to work together to empower women in the industry to succeed.

“Our goal is to accelerate the trend of women holding leadership roles in medical societies, conducting clinical research, supporting training organizations, and to foster support for female focused aesthetic business ownership,” according to Alisa Lask, Vice President and General Manager of the U.S. Aesthetic Business.

Galderma reports recently soliciting the council’s feedback to help guide the company’s development of programs and resources to support female-led practices, businesses and research projects.

As for the individual women on the advisory board, Dermatology Times is proud to be the first to acknowledge and congratulate those who fall under the dermatology specialty:

Glynnis Ablon, M.D., F.A.A.D.
Janet Allenby, D.O.
Kimberly Butterwick, M.D.
Elizabeth Callahan, M.D.
Caren Campbell, M.D.
Anne Chapon, M.D.
Jody Corstock, M.D.
Doris Day, M.D.
Dendy Engstrom, M.D.
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Dee Anna Glaser, M.D.
Elizabeth Hale, M.D.
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Anetta Reszko, M.D.
Heather Rogers, M.D.
Ava Shamban, M.D.
Robyn Sperber, M.D.
Lori Sklerer, M.D.
Susan Weinkle, M.D.
Kathleen Welsh, M.D.
Tina West, M.D.

COMPARING PHYSICIAN DEMAND & PAY GROWTH

NATIONALLY, PHYSICIAN JOBS grew by 7%, according to key findings from the 2018 U.S. Physician Employment Report published by Doximity. However, while physician job postings have grown significantly year-over-year in many large metropolitan areas, this demand does not always correlate to compensation changes.

Highest job growth

1. Fresno, Calif. 15%
2. New Haven, Conn. 12%
3. Fayetteville, Ark. 13%
4. Denver, Colo. 12%
5. Baltimore, Md. 12%
6. Boston, Mass. 7%
7. El Paso, Texas 8%
8. New Orleans, La. 15%
9. San Antonio, Texas 6%
10. Los Angeles, Calif. 6%
11. Little Rock, Ark. 6%

Highest compensation growth

1. Tucson, Ariz. 20%
2. Los Angeles, Calif. 19%
3. Chicago, Ill. 19%
4. St. Louis, Mo. 19%
5. Charlotte, N.C. 18%
6. Baltimore, Md. 17%
7. Virginia Beach, Va. 16%
8. Albuquerque, N.M. 16%
9. Little Rock, Ark. 16%
10. Phoenix, Ariz. 16%
FDA APPROVES RISANKIZUMAB FOR PLAQUE PSORIASIS

THE U.S. FOOD AND DRUG Administration (FDA) approved risankizumab-zaaq (SKYRIZI), an interleukin-23 antagonist, for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic or phototherapy on April 23.

“The eagerly anticipated approval of risankizumab... provides dermatology with a new treatment option with tremendous efficacy and excellent safety,” says George Martin, M.D., a dermatologist in Kihei, Hawaii, and member of the Medical Board of the National Psoriasis Foundation.

“After an initiation dose of 150 mg (two 75 mg injections) at weeks 0 and 4, the maintenance dosing schedule of 150 mg every three months also offers a level of convenience sought by many patients,” he adds.

In clinical trials, risankizumab-zaaq produced high rates of skin clearance — over 80% of people treated achieved PASI 100 within one year, whereas the majority (56-60%) achieved PASI 100. An integrated analysis of the two pivotal studies showed that most people who achieved PASI 90 and PASI 100 at week 16 maintained this response at one year (88% and 80%).

“Although not specifically approved for the treatment of generalized pustular psoriasis or erythrodermic psoriasis, risankizumab has also demonstrated efficacy in these patients and is approved in Japan for these two indications. Risankizumab is currently being studied in phase 3 clinical trials for the treatment of psoriatic arthritis,” Dr. Martin says.

The most common adverse events reported in clinical trials included upper respiratory infections, headache, fatigue, injection site reactions, and influenza. Prior to treatment, patients must be screened for tuberculosis and other infections.

— Drew Boxer, associate editor, Drug Topics
Immunotherapy studied as alternative for MRSA Tx

ILYA PETROU, M.D. | Staff Correspondent

One of the most common human bacterial skin pathogens, *Staphylococcus aureus*, has become a major public health threat because of the widespread emergence of virulent community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) strains caused, in part, by overuse of antibiotics. One of the central goals of current research and development in immunotherapy is to fulfill an unmet need for therapeutic options that could help minimize the use of antibiotics while exhibiting efficacy against *Staphylococcus aureus*.

“If immune-based therapies are to be an alternative to antibiotics then a greater understanding of the protective immune mechanisms and responses against *Staphylococcus aureus* skin infections is essential so that we can engage the host’s own immune system to help combat these infections. Our long-term goal is to uncover the mechanisms that serve as targets for immune-based therapies and vaccination strategies,” said Lloyd S. Miller, M.D., Ph.D., vice chair for research of dermatology and associate professor of dermatology, infectious diseases, orthopaedic surgery & materials science and engineering, Johns Hopkins Department of Dermatology, Baltimore, Md.

Previous research, including active (Staphvax, Nabi Biopharmaceuticals and V710, Merck, Inc.) and passive (Veronate, Inhibi-tex, Inc.) vaccines targeting capsular polysaccharides, iron surface determinant B or clumping factor A have all failed in clinical trials.

“Research on which mechanisms are mediating durable memory protection against the infection will be crucial to the development of effective immunotherapies.”

Both passive and active vaccines targeting capsular polysaccharides, iron surface determinant B or clumping factor A have all failed in clinical trials.

An immune response mediated by T cells or T lymphocytes is now being explored.

“Ideally, the immune system and the specific immune responses with T cells that can be targeted to promote immune clearance of *Staphylococcus aureus* is ongoing — results of which will hopefully soon translate to the clinic. According to Dr. Miller, the focus is to promote specific T cell immune responses directed against the bacteria instead of leading to nonspecific immune activation.

“It is critically important to understand the actual immune correlates that lead to protection against *Staphylococcus aureus* infections. This is likely the reason why most of the vaccines have failed in human trials, Dr. Miller added.

“I think if we learn more about the immune responses and really understand which mechanisms are mediating durable memory protection against the infection, we would be able to better target those immune responses for effective host immune clearance. I believe that understanding these immune mechanisms is crucial to the future development of effective immunotherapies and vaccines,” Dr. Miller concluded.

Disclosures:
Bioteringingenheim – (Grants/Research Funding); Medimmune – (Grants/Research Funding); Mederna Therapeutics – (Grants/Research Funding); Novocea (Biotherapeutics) – SHST, Pllcr Inc. – (Grants/Research Funding); Regeneron – (Grants/Research Funding);
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- OptumRx
- Prime Therapeutics
- UnitedHealthcare

*Indicates no DMARD or biologic step-edit required.

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*Basic, Standard, and Advanced Control Formularies.
†SaFeGuardRx® Program has 1 biologic step for patients on certain Otezla indications.

DMARD, disease-modifying antirheumatic drug.

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*Otezla® (apremilast) significantly increased PASI-75 response (n = 562) at week 16 (primary endpoint) vs placebo (n = 282) (33% vs 5%; P < 0.0001) in ESTEEM 1,2*

**ESTEEM® Study Design**

- Evaluated in 2 multicenter, double-blind, placebo-controlled trials of similar design. Patients with moderate to severe plaque psoriasis (N = 1257) were randomized 2:1 to Otezla 30 mg twice daily or placebo for 16 weeks after a 5-day titration

- Selected inclusion criteria: age ≥18 years, BSA ≥10%, sPGA ≥3, PASI ≥12, candidates for phototherapy or systemic therapy

**INDICATIONS**

Otezla® (apremilast) is indicated for the treatment of patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy. Otezla is indicated for the treatment of adult patients with active psoriatic arthritis.

**IMPORTANT SAFETY INFORMATION**

**Contraindications**

- Otezla® (apremilast) is contraindicated in patients with a known hypersensitivity to apremilast or to any of the excipients in the formulation

**Warnings and Precautions**

- Diarrhea, Nausea and Vomiting: Cases of severe diarrhea, nausea, and vomiting have been reported with the use of Otezla. Most events occurred within the first few weeks of treatment. In some cases patients were hospitalized. Patients 65 years of age or older and patients taking medications that can lead to volume depletion or hypotension may be at a higher risk of complications from severe diarrhea, nausea, or vomiting. Monitor patients who are more susceptible to complications of diarrhea or vomiting; advise patients to contact their healthcare provider. Consider Otezla dose reduction or suspension if patients develop severe diarrhea, nausea, or vomiting

- Depression: Treatment with Otezla is associated with an increase in depression. During clinical trials 1.3% (12/920) of patients reported depression, compared to 0.4% (2/506) on placebo. Suicidal behavior was observed in 0.1% (1/1308) of patients on Otezla, compared to 0.2% (1/506) on placebo. Carefully weigh the risks and benefits of treatment with Otezla for patients with a history of depression and/or suicidal thoughts/behavior, or in patients who develop such symptoms while on
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your patients on Otezla today

• Convenient oral dosing
• No required lab monitoring
• Samples available in office
• Bridge program offers 3 years for free
• $0 co-pay

Otezla. Patients, caregivers, and families should be advised of the need to be alert for the emergence or worsening of depression, suicidal thoughts or other mood changes, and they should contact their healthcare provider if such changes occur.

• Weight Decrease: Body weight loss of 5-10% occurred in 12% (96/784) of patients treated with Otezla and in 5% (19/382) of patients treated with placebo. Monitor body weight regularly; evaluate unexplained or clinically significant weight loss, and consider discontinuation of Otezla.

• Drug Interactions: Apremilast exposure was decreased when Otezla was co-administered with rifampin, a strong CYP450 enzyme inducer; loss of Otezla efficacy may occur. Concomitant use of Otezla with CYP450 enzyme inducers (e.g., rifampin, phenobarbital, carbamazepine, phenytoin) is not recommended.

Adverse Reactions

• Adverse reactions reported in ≥5% of patients were Otezla%, placebo%: diarrhea (17, 6), nausea (17, 7), upper respiratory tract infection (9, 6), tension headache (8, 4), and headache (6, 4).

Use in Specific Populations

• Pregnancy and Nursing Mothers: Otezla is Pregnancy Category C; it has not been studied in pregnant women. Use during pregnancy only if the potential benefit justifies the potential risk to the fetus. It is not known whether apremilast or its metabolites are present in human milk. Caution should be exercised when Otezla is administered to a nursing woman.

• Renal Impairment: Otezla dosage should be reduced in patients with severe renal impairment (creatinine clearance less than 30 mL/min); for details, see Dosage and Administration, Section 2, in the Full Prescribing Information.

*Following a 5-day titration, the recommended maintenance dosage is 30 mg twice daily.

†To receive a free bridge supply of Otezla, patients must have an on-label diagnosis and be denied or waiting for coverage.

‡Certain restrictions apply; eligibility not based on income, must be 18 years or older. This offer is not valid for persons eligible for reimbursement of this product, in whole or in part under Medicaid, Medicare, or similar state or federal programs. Offer not valid for cash-paying patients. People who are not eligible can call 1-844-4OTEZLA to discuss other financial assistance opportunities.

BSA, body surface area; ESTEEM, Efficacy and Safety Trial Evaluating the Effects of Apremilast in Psoriasis; PASI, Psoriasis Area and Severity Index; sPGA, static Physician Global Assessment.


Please turn the page for Brief Summary of Full Prescribing Information.
OTEZLA® (apremilast) tablets, for oral use

The following is a Brief Summary; refer to Full Prescribing Information for complete product information.

INDICATIONS AND USAGE
OTEZLA® (apremilast) is indicated for the treatment of patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

CONTRAINDICATIONS
OTEZLA is contraindicated in patients with a known hypersensitivity to apremilast or to any of the excipients in the formulation [see Adverse Reactions (6.1)].

WARNINGS AND PRECAUTIONS
Diarrhea, Nausea, and Vomiting: There have been postmarketing reports of severe diarrhea, nausea, and vomiting associated with the use of OTEZLA. Most events occurred within the first few weeks of treatment. In some cases patients were hospitalized. Patients 65 years of age or older and patients taking medications that can lead to volume depletion or hypotension may be at a higher risk of complications from severe diarrhea, nausea, or vomiting. Monitor patients who are more susceptible to complications of diarrhea or vomiting. Patients who reduced dosage or discontinued OTEZLA generally improved quickly. Consider OTEZLA dose reduction or suspension if patients develop severe diarrhea, nausea, or vomiting.

Depression: Treatment with OTEZLA is associated with an increase in adverse reactions of depression. Before using OTEZLA in patients with a history of depression and/or suicidal thoughts or behavior prescribers should carefully weigh the risks and benefits of treatment with OTEZLA in such patients. Patients, their caregivers, and families should be advised of the need to be alert for the emergence or worsening of depression, suicidal thoughts or other mood changes, and if such changes occur to contact their healthcare provider. Prescribers should carefully evaluate the risks and benefits of continuing treatment with OTEZLA if such events occur. During the 0 to 16 week placebo-controlled period of the 3 controlled clinical trials, 1.3% (12/920) of patients treated with OTEZLA reported depression compared to 0.4% (2/506) treated with placebo. During the clinical trials, 0.1% (1/1308) of patients treated with OTEZLA discontinued treatment due to depression compared with none in placebo-treated patients (0/506). Depression was reported as serious in 0.1% (1/1308) of patients exposed to OTEZLA, compared to none in placebo-treated patients (0/506). Incidences of suicidal behavior have been observed in 0.1% (1/1308) of patients while receiving OTEZLA, compared to 0.2% (1/506) in placebo-treated patients. In the clinical trials, one patient treated with OTEZLA attempted suicide while one who received placebo committed suicide.

Weight Decrease: During the controlled period of the trials in psoriasis, weight decrease between 5%-10% of body weight occurred in 12% (967/84) of patients treated with OTEZLA compared to 5% (19/382) treated with placebo. Weight decrease of ≥10% of body weight occurred in 2% (16/784) of patients treated with OTEZLA 30 mg twice daily compared to 1% (3/382) patients treated with placebo. Patients treated with OTEZLA should have their weight monitored regularly. If unexplained or clinically significant weight loss occurs, weight loss should be evaluated, and discontinuation of OTEZLA should be considered.

Drug Interactions: Co-administration of strong cytochrome P450 enzyme inducers, rifampin, resulted in a reduction of systemic exposure of apremilast, which may result in a loss of efficacy of OTEZLA [see Drug Interactions (7.1)].

ADVERSE REACTIONS
Clinical Trials Experience in Psoriasis: Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trial of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice. Diarrhea, nausea, and upper respiratory tract infection were the most commonly reported adverse reactions. The most common adverse reactions leading to discontinuation for patients taking OTEZLA were nausea (1.8%), diarrhea (1.0%), and headache (0.8%). The proportion of patients with psoriasis who discontinued treatment due to any adverse reaction was 6.1% for patients treated with OTEZLA 30 mg twice daily and 4.1% for placebo-treated patients.

Table 3: Adverse Reactions Reported in ≥2% of Patients on OTEZLA and With Greater Frequency Than in Patients on Placebo; up to Day 112 (Week 16)

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>Placebo (N=506) n (%)</th>
<th>OTEZLA 30 mg BID (N=920) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>32 (6)</td>
<td>160 (17)</td>
</tr>
<tr>
<td>Nausea</td>
<td>35 (7)</td>
<td>155 (17)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>31 (6)</td>
<td>84 (9)</td>
</tr>
<tr>
<td>Tension headache</td>
<td>21 (4)</td>
<td>75 (8)</td>
</tr>
<tr>
<td>Headache</td>
<td>19 (4)</td>
<td>55 (6)</td>
</tr>
<tr>
<td>Abdominal pain*</td>
<td>11 (2)</td>
<td>39 (4)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>8 (2)</td>
<td>35 (4)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>9 (2)</td>
<td>29 (3)</td>
</tr>
<tr>
<td>Decrease appetite</td>
<td>5 (1)</td>
<td>26 (3)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>4 (1)</td>
<td>21 (2)</td>
</tr>
<tr>
<td>Back pain</td>
<td>4 (1)</td>
<td>20 (2)</td>
</tr>
<tr>
<td>Migraine</td>
<td>5 (1)</td>
<td>19 (2)</td>
</tr>
<tr>
<td>Frequent bowel movements</td>
<td>1 (0)</td>
<td>17 (2)</td>
</tr>
<tr>
<td>Depression</td>
<td>2 (0)</td>
<td>12 (1)</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>2 (0)</td>
<td>12 (1)</td>
</tr>
<tr>
<td>Tooth abscess</td>
<td>0 (0)</td>
<td>10 (1)</td>
</tr>
<tr>
<td>Folliculitis</td>
<td>0 (0)</td>
<td>9 (1)</td>
</tr>
<tr>
<td>Sinus headache</td>
<td>0 (0)</td>
<td>9 (1)</td>
</tr>
</tbody>
</table>

* Two subject treated with OTEZLA experienced serious adverse reaction of abdominal pain.

Severe worsening of psoriasis (rebound) occurred in 0.3% (4/1184) patients following discontinuation of treatment with OTEZLA (apremilast).

DRUG INTERACTIONS

Strong CYP 450 Inducers: Apremilast exposure is decreased when OTEZLA is co-administered with strong CYP450 inducers (such as rifampin) and may result in a loss of efficacy [see Warnings and Precautions (5.3) and Clinical Pharmacology (12.3)].

USE IN SPECIFIC POPULATIONS

Pregnancy: Pregnancy Category C: OTEZLA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Pregnancy Exposure Registry: There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to OTEZLA during pregnancy. Information about the registry can be obtained by calling 1-877-311-8972. Nursing Mothers: It is not known whether OTEZLA or its metabolites are present in human milk. Because many drugs are present in human milk, caution should be exercised when OTEZLA is administered to a nursing woman.

Pediatric Use: The safety and effectiveness of OTEZLA in pediatric patients less than 18 years of age have not been established. Geriatric Use: Of the 1257 patients who enrolled in two placebo-controlled psoriasis trials (PSOR 1 and PSOR 2), a total of 108 psoriasis patients were 65 years of age and older, including 9 patients who were 75 years of age and older. No overall differences were observed in the efficacy and safety in elderly patients ≥65 years of age and younger adult patients <65 years of age in the clinical trials. Renal Impairment: Apremilast pharmacokinetics were characterized in subjects with mild, moderate, and severe renal impairment as defined by a creatinine clearance of 60-89, 30-59, and less than 30 ml per minute, respectively, by the Cockcroft–Gault equation. While no dose adjustment is needed in patients with mild or moderate renal impairment, the dose of OTEZLA should be reduced to 30 mg once daily in patients with severe renal impairment [see Dosage and Administration (2.2) and Clinical Pharmacology (12.3)].

Hepatic Impairment: Apremilast pharmacokinetics were characterized in patients with moderate (Child Pugh B) and severe (Child Pugh C) hepatic impairment. No dose adjustment is necessary in these patients.

OVERDOSAGE

In case of overdose, patients should seek immediate medical help. Patients should be managed by symptomatic and supportive care should there be an overdose.

Manufactured for: Celgene Corporation, Summit, NJ 07901

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Based on APRP1.006 OTZ_PsO_HCP_BSv.006 06_2017
**JAK inhibitors offer multiple applications**

JOHN JESITUS | Staff Correspondent

Unlike prior generations of dermatologic drugs, Janus kinase (JAK) inhibitors show potential for treating numerous dermatologic indications. “JAK inhibitors as a class are affecting treatment of vitiligo, alopecia areata, atopic dermatitis, psoriasis, connective tissue diseases and granulomatous diseases,” says Brett King, M.D., Ph.D., associate professor of dermatology at Yale University School of Medicine. “It’s a remarkable concept.”

TNF inhibitors were revolutionary when they debuted more than 14 years ago, says Dr. King. But to this day, he adds, they are only approved for two dermatologic indications — psoriasis and hidradenitis suppurativa.

Prednisone is probably history’s greatest example of a single drug that impacts innumerable pathways and disease mechanisms — and has many potential adverse effects, says Dr. King. More targeted drugs include the systemic immunomodulators methotrexate, azathioprine, mycophenolate mofetil and cyclosporine. “While they all have specific mechanisms, they still suppress broad switches of the immune system — T cell and, variably, B cell immunity.”

Dermatologists’ increasingly detailed understanding of psoriasis pathogenesis has paved the way for highly targeted biologic therapies. Following the TNF inhibitors, newer generation biologics for psoriasis target interleukin (IL)-12 and IL-23 (ustekinumab), IL-17 (secukinumab, ixekizumab, brodalumab) and IL-23 (guselkumab, risankizumab, tildrakizumab). Advances in the understanding of AD pathogenesis have led to dupilumab (which targets IL-4 and IL-13), the first FDA-approved targeted therapy for moderate to severe AD.

“Dermatologic diseases are sometimes driven by cytokines that course through the blood and tissues communicating signals to different cells. Sometimes those signals eventuate in disease. Our goal is to interrupt those signals when they are pathogenic.”

Strategies for interrupting or modulating cytokine signaling include developing antibodies to specific cytokines; for instance, IL-23 inhibitors. Alternatively, says Dr. King, one could block cytokine receptors, which are the docking sites on the cell surface where cytokines bind.

“Or you can disrupt cytokine signaling by giving a JAK inhibitor, which inhibits the first part of the signaling cascade on the inside of the cell.” Cytokine signaling can be thought of like a relay race, he notes. A pathogenic cytokine — for example, interferon-gamma or IL-23 — passes the baton to JAK enzymes, which pass the baton to STAT proteins. “STAT in turn passes the baton to the nucleus, where genes are transcribed, and disease happens,” he says. “I want to interrupt this relay race. I II can keep any one of the runners from taking the baton, the signal never makes it to the nucleus.”

The antibody and receptor-blocking strategies work on the outside of the cell, says Dr. King, while JAK inhibitors are small molecules that bind to and prevent activity of JAK family enzymes within the cell.

JAK inhibitors can variably target different JAK family enzymes and therefore can be more or less specific, he says.

More targeted JAK inhibitors potentially affect specific disease processes with less collateral impact, adds Dr. King.

More than 50 cytokines use the JAK-STAT pathway, he says, and many of these mediate dermatological diseases. “And so it is that JAK inhibitors will be effective for treating many of the diseases that we commonly see in dermatology.”

JAK inhibitors currently approved include tofacitinib (for rheumatoid arthritis/RA, psoriatic arthritis and ulcerative colitis), ruxolitinib (for myelofibrosis and polycythemia vera) and baricitinib (for moderate-to-severe RA). Experimental drugs, include PF-06651600 (Pfizer); drugs in development include BMS-986165 (Bristol-Myers Squibb) and PF-06700841 (Pfizer); and BMS-986165 is currently in phase 3 trials in psoriasis. Pfizer has initiated a phase 2b/3 trial of PF-06651600 in AA.

“There’s an opportunity here that we have not previously seen in dermatology.” The message for dermatologists: Get comfortable using JAK inhibitors for multiple indications.

References

Disclosures
Dr. King is a clinical trial investigator and received consulting fees and/or honoraria from Concert Pharmaceuticals, Eli Lilly, Pfizer. He is a speaker to Pfizer, Regeneron, Sanofi Genzyme, and has received honoraria and/or consulting fees from Adams Therapeutics and Dermotest Sciences.
A specific form of acne that is triggered when skin is pressed against heavy clothing or bulky protective gear, but dermatologists recently discovered a case of the condition caused by friction between the inner thighs of an obese teenager. Acne mechanica is defined as being any acneiform eruption in areas of friction, pressure, stretching, rubbing, pinching or occlusion of the skin in any individual, regardless of pre-existing acne. It presents as inflammatory papules and pustules that can progress to nodules and cysts. The condition occurs most often in very active people, such as athletes or soldiers. It seems to occur after intense activity causes heat and friction between sweaty skin and clothing, particularly if the person is wearing heavy or bulky protective gear. However, the condition has also been reported in relation to friction and pressure from other causes, such as prolonged rest against a seat or bed, and even pressure from a prosthetic limb. Now dermatologists in Washington, D.C. have reported what they believe is the first case of the condition occurring as a result of rubbing of the skin of the inner thighs. “Previously reported causes of acne mechanica have all been external factors, such as clothing. This patient’s presentation is unique because the lesions are caused by friction between cutaneous surfaces,” said Kalyani Marathe, M.D., M.P.H., a dermatologist from the Childrens National Medical Center and The George Washington University School of Medicine and Health Sciences, Washington, D.C. The patient presented for evaluation of facial acne but also complained of blackheads in her thigh area. She explained that these blackheads appeared during the summer when she wore shorts or dresses that allowed her legs to rub against each other. Comedones were extracted, patient was advised to wear cotton fabrics and change frequently, especially if hot and sweaty. Examination revealed that she had large bilateral collections of open comedones with black keratotic debris on inner thighs. She had no personal or family history of hidradenitis suppurativa, was not on any medications, and did not have any known allergies. "Antibiotics used to treat acne vulgaris are not as effective when used for acne mechanica," she added. To manage acne mechanica on the shoulders and upper trunk, sports physicians advise athletes to wear a clean absorbent cotton T-shirt worn under their kit and equipment to help diminish the four contributing factors to the condition: occlusion, heat, friction, and pressure. They are also encouraged to remove their kit and shower immediately after training and games. References


This patient’s presentation is unique because the lesions are caused by friction between cutaneous surfaces.”

Kalyani Marathe, M.D., M.P.H., The George Washington University School of Medicine and Health Sciences, Washington, D.C.
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SLEEP QUALITY SUFFERS IN MOTHERS OF CHILDREN WITH ATOPIC DERMATITIS

LISETTE HILTON

MOTHERS OF CHILDREN with atopic dermatitis are more likely than mothers whose children don’t have the skin condition to report problems sleeping, according to a study published online March 20, 2019 in JAMA Dermatology.1 U.S. researchers analyzed a cohort of 11,649 mother-child pairs from a town in Southwest England who were followed from birth for an average of 11 years. “Participants were asked annually about symptoms of atopic dermatitis, including whether disease was active and how severe it was,” says the study’s senior author Katrina E. Abuabara, M.D., M.A., M.S.C.E. The cohort also included data on multiple aspects of maternal sleep including sleep duration, difficulty falling asleep, early morning awakenings, subjectively insufficient sleep and daytime exhaustion.

They found that mothers with and without children with atopic dermatitis had similar reports on sleep duration and early morning awakenings. But mothers with children who had atopic dermatitis were 36% more likely to report difficulty falling asleep; 48% more likely to subjectively say they got insufficient sleep; and 41% more likely to report daytime exhaustion. That was independent of the child’s comorbid asthma and/or allergic rhinitis, according to the study.

Mothers’ sleep duration and sleep quality worsened with children who had more severe disease. Interestingly, children’s sleep disturbances didn’t fully explain maternal sleep disturbances. The authors point to research that suggests parental or caregiver stress, anxiety, distress and depression associated with caring for children with chronic diseases, including atopic dermatitis, could impact mothers’ sleep quality and duration. Mothers’ sleep problems could also impact children with atopic dermatitis, according to the authors.

“We have, for example, cyclosporin. But who wants to treat a child or adolescent with cyclosporin, which is documented to cause kidney damage after one year of use? Oral prednisone has deleterious effects. I never give it in children (and not even to adults), as patients will often immediately flare after it is stopped. And for phototherapy, children need to come two, three times a week. So, you can imagine that’s not feasible,” Dr. Guttman says. “Up to this approval, our hands were tied in treating pediatric patients with moderate-to-severe disease or eczema on significant parts of their bodies.”

Clinicians caring for children with atopic dermatitis should be aware of the potential for maternal sleep disturbances and fatigue. The authors suggest clinicians caring for children with AD screen caregivers for sleep disturbance, fatigue and emotional health, and consider offering support resources.

“We need additional research to develop recommendations for how dermatologists can best address this issue in clinical practice. The American Academy of Pediatrics recommends that pediatricians assess the health and wellbeing of parents, but the role for specialty providers is less clear. A first step might be to include data on the impact of atopic dermatitis on maternal/caregiver sleep in patient educational materials, to help bring awareness to the issue,” says Dr.
The need for a drug option like this is great because moderate-to-severe disease among children is not uncommon, according to Dr. Guttman. Without relief from treatment, these children often become withdrawn.

“Some of my patients with this disease are home schooled, as they are embarrassed to leave their homes due to the skin disease, and some parents and other children think they are infectious. You see terrible cases. It affects the entire family,” she says.

Regeneron reports that at 16 weeks in the phase 3 trial evaluating dupilumab monotherapy in adolescent patients with uncontrolled moderate-to-severe atopic dermatitis, average improvement in the Eczema Area and Severity Index (EASI) from baseline was about 66% compared with 24% for placebo. More than 40% of patients who received dupilumab achieved 75% (EASI-75) or greater skin improvement compared with 8% with placebo. And 37% of patients who received dupilumab achieved a clinically meaningful improvement in itch of at least four points on the Peak Pruritus Numerical Rating Scale (NRS) compared with 5% with placebo.

Among the most common adverse events: injection site reactions and eyelid edema, according to a company press release.

**DR. GUTTMAN’S EXPERIENCE**

Dr. Guttman says there is data to support dupilumab’s safety and efficacy in adults who are on it for up to five years. Among her patients on dupilumab, few adult atopic dermatitis patients have come off of it because it has lost its effect. The majority of patients, she says, have remained on the drug through five years.

“The FDA does not require bloodwork for dupilumab, which is unusual for a biologic. Most of them do require bloodwork. That tells you the FDA considers it safe,” Dr. Guttman says.

“To make the most impact for patients’ atopic dermatitis early on, Dr. Guttman says she starts most atopic dermatitis patients, including adolescents, with dupilumab and a topical steroid. She’ll then taper most patients off the topical and continue with dupilumab.

Most children, ages 12 to 17, are candidates for dupilumab if they have moderate-to-severe disease.

“I wouldn’t give this drug to children who only have a few body areas involved. For me, at least, I need to have a child that has significant involvement to prescribe the drug. For somebody that has less than 10% body surface area and is an adolescent, I will not use it unless they failed other treatments, and we can make a reasonable case for using a biologic,” she says.

**CLINICAL DEVELOPMENT**

Dermatologists and others treating these children should also consider that dupilumab might work to treat other allergic and type 2 inflammatory diseases, and dupilumab has recently been approved for asthma.

Another commonly associated disease, alopecia areata, also may respond to dupilumab, as a few case reports have shown. This indication is off label at this point, but it worked to treat Sun’s alopecia areata even though he got Dupixent to treat his eczema, according to Guttman.

In addition to the currently approved indications, Regeneron and Sanofi are also studying dupilumab in a broad range of clinical development programs for diseases driven by allergic and other type 2 inflammation, including: chronic rhinosinusitis with nasal polyps (phase 3 completed); pediatric, ages 6 to 11 years, atopic dermatitis (phase 3); pediatric, ages 6 months to 5 years, atopic dermatitis (phase 2/3); pediatric, ages 6 to 11 years, asthma (phase 3); eosinophilic esophagitis (phase 2/3), and food and environmental allergies (phase 2), according to the Regeneron press release.

Sun isn’t the only person in his family who is happy that dupilumab has worked for his atopic dermatitis. His mother, Tracy Wang, says the experience of her son’s flare at age 9 and subsequent years trying different treatments wasn’t easy. See also: Sleep quality suffers in mothers of children with atopic dermatitis, page 20 and Caregiver assessment tools, page 52.

She saw his struggle, so the family struggled to pay the nearly $4,000 a year it cost to get access to dupilumab before it was approved. Wang says she was worried about his being on cyclosporin, and the topicals did little to help with his symptoms and took a lot of time to apply.

“All these things don’t work that well. I would say [the experience is] very painful. Neither he nor I had a very good normal routine,” Wang says.

That all has changed. Sun administers his own injections every other week, and Wang hopes insurance will cover the drug now that it’s approved for patients Sun’s age.

“I’m so happy,” she says. “He’s a very active boy. He plays piano and is involved in all kinds of after-school activities. Totally, now his eczema is under control.”

---

**Abuabara, who is trained in dermatology, epidemiology, and sociology and is an assistant professor in the department of dermatology at the University of California San Francisco.**

The authors provide recommend ed screening tools for maternal sleep, depression and anxiety for providers who are interested in screening parents. These are: The Pittsburgh Sleep Quality Index for sleep problems; the Patient Health Questionnaire-9 for depression; and the Generalized Anxiety Disorder 7-item Scale for anxiety. See Table page 52 for more information.

**Disclosures**

Dr. Abuabara is on the academic steering committee for TARGET-DERM, a company developing an atopic dermatitis disease registry and driven by a need for better patient-care and outcomes research funding through his institution from Pfizer.

**Reference**


**Meet the INVESTIGATOR**

Dr. Katrina Abuabara

Take me to when you first knew that dermatology was the specialty you wanted to practice:

From a clinical perspective, I loved that dermatology patients could see the progress of their condition even better than I could. For me, this meant that patient care felt more like a partnership rather than a hierarchical relationship in which a physician would hand down lab test results.

From a research perspective, dermatology seemed like the perfect specialty to study the interplay between genetic and environmental factors. I have degrees in both biology and sociology, and I am fascinated by the ways in which our surroundings (both physical and social-cultural) affect our health.

Take me to the moment you knew you wanted to investigate the sleep disturbances of mothers of children with atopic dermatitis:

The National Eczema Association commissioned a burden of disease audit on quality of life and atopic dermatitis. I remember reading the paper by Aaron Drucker and colleagues and feeling amazed that there was a lack of population-based research on sleep and atopic dermatitis. It is well-established that sleep has profound impacts on multiple dimensions of health, and that children with severe atopic dermatitis seen in dermatology clinics have poor sleep quality, but there were little data on atopic dermatitis and sleep in the general population. Since atopic dermatitis is so common, I also felt there was an uncharacterized heterogeneous in terms of severity and activity. I thought it was important to examine sleep in kids with mild to severe disease throughout childhood. We were also able to obtain data on the mothers of children with atopic dermatitis, and as the mother of two small children, I was particularly interested in the effects of chronic illness and sleep depriva tion on families.

Take me to the proudest moment of your career so far:

Many of our research questions have come from clinical practice, and I find it incredibly satisfying when I can give a patient better prognostic information or treatment recommendations based on research I’ve participated in.
Examining the prejuvenation trend

LISETTE HILTON | Staff Correspondent

Youthful people are turning to botulinum toxin, fillers, peels and more to prevent signs of aging. But are they doing it for legitimate reasons or simply succumbing to marketing messaging and perceived pressure?

Sabrina Fabi, M.D., a dermatologist in San Diego, says it’s more about treating the signs of aging that are actually occurring than it is about “prejuvenating.”

“We start losing bone at age 25 and that bone loss becomes significant by 35. The reason people start to notice wrinkles — even though they’ve been frowning, laughing and lifting their foreheads all their lives — is because now every time they do that, the muscle doesn’t have bone to relax back onto. If you relax those muscles, then you’re able to minimize the appearance of lines and wrinkles,” Dr. Fabi says. “So, treating a 20- or 30-year-old is not inappropriate because they are already exhibiting the pathophysiologic signs of aging. It’s not that you’re pre-rejuvenating them, you’re treating them.”

There is evidence to suggest treating facial muscles that create significant lines with movement early might help people look younger as they age, according to Dr. Fabi, who was among the authors of a long-term study looking at patients whose glabellar lines were treated with onabotulinumtoxinA injections for an average 9.1 years.¹

“Among the 89.7% of patients who reported looking younger, the mean perceived age was 6.9 years younger,” according to the paper.

Prejuvenation is a term that’s being used for younger patients looking to prevent sun spots, wrinkles and skin sagging, according to dermatologist Noelani González, M.D., director of Cosmetic Dermatology-Mount Sinai West.

“We are seeing a trend where these services are being marketed to younger patients, starting with skincare including sun protection, antioxidants and retinoids, and ranging to the early use of neuromodulators, fillers and fractional resurfacing in their late 20s to early 30s, such as the non-ablative fractional resurfacing Clear and Brilliant [Solta Medical] laser, which is a favorite of mine for younger patients looking to improve their skin’s texture, tone and give it an overall nice glow,” Dr. González says.

“Skin tightening procedures, such as radiofrequency and ultrasound tightening devices, can be a great adjunct to other cosmetic procedures for patients looking to tighten and stim-
MINOVATION

MinoLira Tablets bring immediate- and sustained-release minocycline together for the first time ever in functionally scored tablets (105 and 135mg) for broad dosing options and safety similar to placebo.1

It’s the active ingredient you know – redefined.

INDICATION AND USAGE
MinoLira is indicated to treat only inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients 12 years of age and older.

MinoLira did not demonstrate any effect on non-inflammatory acne lesions. Safety of MinoLira has not been established beyond 12 weeks of use. This formulation of minocycline has not been evaluated in the treatment of infections. To reduce the development of drug-resistant bacteria as well as to maintain the effectiveness of other antibacterial drugs, MinoLira should be used only as indicated.

IMPORTANT SAFETY INFORMATION
- This drug is contraindicated in persons who have shown hypersensitivity to any of the tetracyclines.
- Minocycline, like other tetracycline-class drugs, can cause fetal harm when administered to a pregnant woman.

EPIHEALTH
(minocycline hydrochloride) extended-release tablets

- The use of MinoLira during the second and third trimesters of pregnancy, infancy, and childhood up to the age of 8 years may cause permanent discoloration of the teeth (yellow-gray-brown) and reversible inhibition of bone growth.
- If pseudomembranous colitis occurs, discontinue MinoLira.
- If renal impairment exists, MinoLira doses may need to be adjusted to avoid accumulations of the drug and possible liver toxicity.

- Minocycline may cause central nervous system side effects, including light-headedness, dizziness, or vertigo.
- Minocycline may cause intracranial hypertension and autoimmune disorders in adults and adolescents. Discontinue MinoLira if symptoms occur.
- Minocycline has been associated with anaphylaxis, serious skin reactions, erythema multiforme, and DRESS syndrome. Discontinue MinoLira immediately if symptoms occur.
- The most commonly observed adverse reactions are headache, fatigue, dizziness, and pruritus.

To report SUSPECTED ADVERSE REACTIONS, contact EPI Health, LLC at 1-800-499-4468 or FDA at 1-800-FDA-1088 or visit www.fda.gov/medwatch.

For Full Prescribing Information, please visit www.minolira.com


To learn more, please visit www.minolira.com
Dermatologists don’t let other dermatologists leave their offices without SPF. That’s essentially what Orlando, Fla.-based dermatologist, Allison Arthur, M.D., Sandlake Dermatology Center, Orlando, Fla., told me this year at the annual meeting of the AAD in Washington DC. Even more importantly, they shouldn’t ever let their post-skin treatment patients leave without proper sun protection either.

This entire conversation came about based on an experience that Dr. Arthur recently had herself as a patient. After having an undisclosed dermatologic treatment performed by a peer dermatologist, she found herself at the front desk and on her way out without being offered sun protection before her drive home. Did I mention that she lives in sunny Orlando?

Full disclosure: I met Dr. Arthur through the Colorescience team. Dr. Arthur is a consulting physician for the company. However, she had a really great message that’s worth sharing: Dermatologists live, breath and preach skin protection and should never send anyone out of their office unprotected.

In her practice, she uses a specific protocol that ensures her patients never leave without first protecting (and also beautifying) the skin. And, according to Dr. Arthur, there are many good reasons to do so:

- You just treated the skin to remove and/or repair damage. (OF COURSE, it needs to be protected.)
- The skin is even MORE susceptible to damage immediately following a treatment.
- You want your patient to see some of the immediate improvement, not just the redness, inflammation and other telltale post-procedure side effects.
- Your patient’s face is your calling card — it’s okay to recognize that it’s a work in progress, but you also don’t want to scare her (his) friends and family members from ever having a skin treatment.

Working with Colorescience, naturally, Dr. Arthur uses a protocol the company developed for physicians using their treatment line. It’s called the Finishing Touch Protocol, which is based on research published in late 2017 in the *Journal of Cosmetic Dermatology*.1

In the study, researchers examined the benefits of IPL treatment combined with skin care and UV protection products for eight weeks. They found synergistic effects that translated into better results, improved tolerability, fewer post-treatment side effects and the possibility of higher patient satisfaction.

“Importantly, patient questionnaires revealed the topical regimen improved the ability of patients to return to their daily lives by making them less self-conscious and their skin more comfortable, thereby optimizing patient outcomes,” report the study authors. “Better results and perceived experience may translate to higher patient satisfaction, resulting in increased patient retention.”

According to Dr. Arthur, the protocol can also be used post-laser (excluding ablative) treatment and post peel too.

You can go online to find out more about the specific Colorescience protocol itself, but it’s the overall approach and the philosophy that’s got real value for all dermatologists, no matter which products are your preference.

“It’s a great way to introduce products to patients without ‘selling’ products,” Dr. Arthur says. “And you send everyone out protected.”

Do you have a specific post-treatment skin protection protocol in place? Email me at ecabana@mmhgroup.com and we may also share yours.

Disclosures:
Dr. Arthur is a consulting physician for Colorescience.

References:
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Uses for micro-focused ultrasound (Ultherapy, Merz Aesthetics), the only FDA-cleared device with a nonsurgical skin lifting indication, are expanding, researchers are finding the device actually does make a difference to skin physiology and most patients give the treatment a thumbs up.

The keys, one expert says, are making sure patients have realistic expectations and using ultrasound visualization during treatment.

Ultherapy is FDA cleared for lifting of the brow, tightening the submental skin and improving wrinkles of the décolletage, according to Sabrina Fabi, M.D., a dermatologist in San Diego.

“But I also use it off-label for improving the laxity along the knees, which many women are bothered by, as well as the laxity that contributes the appearance of cellulite along the buttocks and posterior thighs. I also use it for the laxity of the abdomen and the posterior arms,” she says.

**SCIENCE & BEST PRACTICES**

Dermatologist researchers reported as early as 2012 that transcutaneous intense focused ultrasound was safe and effective when used to improve the clinical appearance, including texture and contour, of the upper arms, extensor knees and medial thighs. In 2014, researchers published a study suggesting, “Similar to its safety and efficacy for tightening facial skin and reducing wrinkles, [micro-focused ultrasound with visualization] MFU-V is an effective, noninvasive method for reducing skin laxity and improving the appearance of skin above the knee.”

Ultrasound visualization allows users to target tissue by visualizing where they’re applying the micro-focused ultrasound energy. That’s important because patients’ skin thickness and anatomical features vary, according to a paper published online October 30, 2017 in the journal *Clinical, Cosmetic and Investigational Dermatology*.

Providers can achieve optimal results by customizing Ultherapy treatment using visualization versus applying a standard protocol with no regard for the tissue being treated, Dr. Fabi says.

“That’s why [Ultherapy has] an indication for real-time visualization of tissue,” she says. “I think that people generally think that if you just deliver heat, you’ll get the result…. if you visualize the tissue that you’re intending to treat — not just fat or firing in air or firing in gel, but you actually can visualize superficial muscular aponeurotic system (SMAS) or any superficial fascial system, as well as dermis — you will get superior results.”

Those results do exist according to a recent basic science study showing that micro-focused ultrasound with visualization doesn’t change epidermal barrier function or skin physiology but does result in a significant increase in skin elasticity at 12 and 24 weeks after a single treatment.

And patient satisfaction with the Ultherapy is relatively high, according to RealSelf stats published March 8, 2019, showing that based on more than 1,100 reviews, people gave Ultherapy an 80% Worth It rating.

Researchers of a study published January 2019 in the *Journal of Drugs in Dermatology* surveyed 52 Ultherapy patients six months after treatment and found 41% thought the treatment outcome met or exceeded their expectations. By comparison, 52% needed to look at photos to be able see post-treatment changes. Half believed they looked years younger and nearly three-quarters would recommend Ultherapy to others.

**SETTING REALISTIC EXPECTATIONS**

Clinicians need to tell patients that Ultherapy is a medical treatment and therefore some type of analgesic is going to be required.

“Because you are delivering 65 degrees of Celsius worth of heat, patients will feel it,” Dr. Fabi says.

And results tend not to be immediate.

“Just as with any collagen stimulating procedure, whether it’s radiofrequency or nonablative fractionated lasers, it can take three months in order for enough collagen to be delivered for a patient to be able to appreciate the result,” Dr. Fabi says.

Until recently, there were no comparative clinical trials of the two major device categories for noninvasive skin tighten-
**Skin care moves from treatment to prevention**

It should be noted that studies still need to be done looking at the ‘preventive’ effects of most of these procedures. It is definitely better to prevent, rather than to have to treat and attempt to turn back the clock.”

Dr. González cites a study published in 2015 on the long-term effects of onabotulinumtoxinA on facial lines in identical twins. “… twins were followed for a period of 19 years. One received treatment with botulinum toxin regularly every 4 to 6 months to the forehead, glabella and crow’s feet, the other twin only received 4 treatments over the 19-year period,” Dr. González says. “Photographic documentation showed no glabellar lines at rest for the treated twin, whereas the sporadically treated twin demonstrated static glabellar lines at rest. Similar findings were seen on the crow’s feet area, demonstrating the preventive effects of Botox.”

Dr. González says she practices what she preaches, having started “prejuvenation” in her mid-20s. “There’s no right age to start, but I am definitely an advocate of starting treatments early on if you have a need for it. I talk to [patients] about my experience,” Dr. González says. “I think we are starting to see younger patients become more aware of their skincare needs, and now with social media, they are also more aware of the range of treatment options out there. So, it’s very important to know which treatments are appropriate and cost-effective for them, and not necessarily turn these patients away.”

Joshua Zeichner, M.D., director of Cosmetic and Clinical Research in Dermatology at Mount Sinai Hospital, says that cosmetic dermatology, like other specialties in medicine, is moving from treatment to prevention. Dr. Zeichner’s fastest growing group of cosmetic patients are women coming in to treat their “11” lines for their 30th birthdays, he says.

“Rather than address lines that are already etched into the skin, it is much easier and more effective to address these issues early and prevent them from progressing,” Dr. Zeichner says. “I typically recommend considering a neurotoxin treatment to adult patients when lines start to set in at rest. This may occur at 21 years old in one patient or 41 years old in another. If a line is not there, I do not presume that it will develop any time soon, so I do not recommend treatments to those patients.”

The American Academy of Facial Plastic and Reconstructive Surgery (AAFPRS) President Phillip R. Langsdon, M.D., agrees that providers should not treat unless there is a condition to be treated. “My opinion is there is not enough evidence of the efficiency of any kind of supposed prevention or of the safety in treating people that don’t yet have defects to improve. That is why I err on the side of caution,” Dr. Langsdon says. “My feeling regarding Botox [Allergan] is that people should be treated only if they have a condition in which we can see a clinical improvement after treatment. Fillers, we use when a person has a defect or they’re showing the signs of aging. I don’t treat patients thinking I’m going to prevent aging; I treat them to try and reverse the signs of aging with fillers.”

But Dr. Langsdon says there are ways to prevent skin aging using sun protection. He says he’ll treat early signs of aging with medical-grade daily skin exfoliation and superficial chemical peels to rejuvenate skin and stave off skin aging. “If there’s any use in the term ‘prejuvenation’ it would be in skin protection from the elements and sun exposure,” Dr. Langsdon says.

**Skin tightening success requires setting realistic expectations**

ing: monopolar capacitive-coupled radiofrequency and micro-focused ultrasound with visualization, according to authors of a paper published January 2019 in *Dermatologic Surgery.*

Those authors conducted a randomized, split-face, evaluator-blind clinical trial comparing the devices for lifting and tightening skin on the face and upper neck. They found both led to significant improvements in face and neck laxity and there were no statistical differences between the two device types in standardized investigator measures of face and neck laxity, patient satisfaction and adverse events. Dr. Fabi notes the limitation of this study was that the standard protocol was used on the micro-focused ultrasound with visualization treated side and no customization based on tissue depth was utilized.

A QUESTION OF PAIN

While Steven L. Davis, D.O., a plastic surgeon in Cherry Hill, N.J., agrees that results are similar between radiofrequency and micro-focused ultrasound options, he prefers radiofrequency because, he says, in his hands it’s more tolerable for patients. “We started off using Ultherapy…and tried it for a little while to treat the neck. The problem was that it was so intense for the patient. I had to inject local anesthetic into the neck. By the time that was infiltrated and the neck was already completely numb, I could literally make a small incision in the submental area and use a radiofrequency probe that goes under the skin and allows me to emulsify the fat and liposuction the fat away.” As a result, he transitioned to radiofrequency technologies FaceTite and NeckTite (BodyTite, InMode). According to the company, these work by gently removing fat while simultaneously tightening and contouring the treatment area.

**Disclosures**

Dr. Fabi is an investigator and consultant for Merz, Allergan, Goldfarma, Valeant, Revance, Elan, and other companies.

Dr. Davis is a speaker and trainer for Allergan and Goldfarma.

**References**


“Ultrasound visualization allows users to target tissue by visualizing where they’re applying the micro-focused ultrasound energy.”
NANO-PULSE STIMULATION ("NPS", Pulse Biosciences) represents novel technology for delivering cellular specific therapy that is being investigated for its potential to treat both benign and malignant dermatologic lesions.

NPS involves the delivery of low energy, high voltage, ultra-short (nanosecond) electrical pulses to the targeted lesion. It has been shown to result in regulated cell death and likely activation of an adaptive host immune response. Studies completed so far show promising results using NPS technology as treatment for sebaceous hyperplasia (SH) and seborrheic keratosis (SK) lesions. Ongoing clinical trials are investigating its use for treating verruca vulgaris and basal cell carcinoma (BCC).

"NPS is a non-thermal, versatile technology that has shown positive results as a treatment for seborrheic keratosis and sebaceous hyperplasia. Ongoing trials are investigating its use for treating verruca vulgaris and basal cell carcinoma.

Lesions, including lesions at distant sites," said Gilly S. Munavalli, MD, MHS, Assistant Clinical Professor of Dermatology, Wake Forest University School of Medicine, Winston-Salem, NC, and founder and Medical Director, Dermatology, Laser and Vein Specialists of the Carolinas, Charlotte, NC. "NPS does not affect non-cellular targets, such as the dermal connective tissue, hair follicles, or blood vessels, and so unlike current treatment options for lesion destruction, it holds promise for minimally disrupting normal skin appearance. We look forward to findings from studies designed to support its further development."

NPS is performed using a proprietary device (CellFX System, Pulse Biosciences). A pulse generator delivers electrical pulses to a handpiece that is fitted with a sterile treatment tip containing micro-needles. Application of the electrical pulses through the micro-needles to the targeted lesion...
causes poration of the cellular plasma membrane and of the membranes of intracellular organelles (mitochondria and endoplasmic reticulum). Ions influx through the openings in the membranes and activate cell signaling pathways that lead to regulated cell death, as confirmed by evidence of caspase-3 immunoreactivity within 2 to 4 hours post-treatment.

“Histological evaluations also showed sparing of the non-cellular dermal structures and a minimal inflammatory response with re-epithelialization by day 60 post-treatment,” said Dr. Munavalli.

Corresponding with the destruction of lesion cells, internal and surface cell antigens are released that may trigger an adaptive immune response and the potential for eradication of malignant growths and distant lesions via the action of cytotoxic T-cells.

“Findings from preclinical studies in a murine model of malignant lesions showed that NPS induced immunogenic cell death with subsequent exposure of unique cancer cell antigens to the immune system and mounting of an adaptive immune response targeted against the cancer cells,” Dr. Munavalli said.

### CLINICAL TRIALS

The first clinical trial evaluating a dermatologic application of NPS investigated its use to clear or remove off-facial SK lesions. The study enrolled 58 patients and found that after a single treatment, 82% of 174 lesions were judged to be “clear” or “mostly clear” by the investigator at follow-up 106 days post-treatment. Consistent with the investigator assessments, patients indicated being “satisfied” or “mostly satisfied” with the outcome for 78% of lesions.

“The treatment was performed under local anesthesia and was well-tolerated. During the treatment, patients noticed a slight twitching sensation and 93% of the treatments were rated as causing no more than moderate pain,” Dr. Munavalli said, adding that future studies may evaluate NPS treatment under topical anesthesia.

“The most common post-treatment adverse events were erythema and hyperpigmentation, both of which were generally mild and transient.”

A second completed clinical trial evaluated NPS to treat facial SH lesions. Patients received one or two NPS treatments per lesion, and at 60 days post-treatment, 99.5% of 222 treated lesions were rated as “clear” or “mostly clear” by the investigator.

“SH is a relatively common condition for which there is no specific laser therapy. In the NPS study, post-treatment histology showed that the NPS energy destroyed the target lesion without causing adverse changes in surrounding normal skin,” Dr. Munavalli told Dermatology Times.

An ongoing multicenter study of NPS technology for BCC is designed primarily to investigate the treatment’s potential to generate an adaptive immune response. The study is enrolling patients with biopsy-confirmed BCC who will be treated with NPS and then undergo BCC resection. The excised tissue will be evaluated for elimination of BCC cells, and both the tissue samples and blood specimens will be analyzed for biomarkers of an immune response. The study is also including a control group of patients whose tumors will be treated with cryotherapy.

The study of NPS for treatment of verruca vulgaris is designed as a feasibility trial. It is enrolling patients with non-genital common cutaneous and plantar warts and has investigator and subject rated resolution of the lesion as its endpoint.

In February, 2019, Pulse Biosciences submitted the 510(k) Premarket Notification for its CellFX system to the US FDA seeking clearance for commercial use to remove general benign dermatologic lesions, including SH and SK.

Dr. Munavalli is on the medical advisory board and an investigator for Pulse Biosciences.

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**A.** Untreated control shows healthy epidermal cells with dark nuclei.

**B.** One day post-treatment, showing cells in the treated epidermis as nonviable (ghost cells). And, the cell membranes and surrounding acellular tissue are intact.

**C.** Seven days post-treatment, showing healthy epidermis is emerging, and the treated epidermal layer is peeling away.

*Photos: Pulse Biosciences*
Artificial intelligence is a large group of image-based data that guides computer-made decisions. People might use machine learning, artificial intelligence and augmented intelligence interchangeably, but each is different and important for the future of patient care.

Artificial intelligence brings the different components of artificial intelligence together to enhance the way dermatologists and other clinicians practice.

“However, it is up to us as dermatologists to transform this technological shift into an opportunity to ‘augment’ our practice with dermatologists at the helm of this paradigm,” says Dr. Lewandrowski.

“With the expected AI revolution in front of us, it is of para-
digm importance for dermatologists to familiarize themselves
with the ABCDs of machine learning to help guide further development and implementation,” she says.

People might use machine learning, artificial intelligence and augmented intelligence interchangeably, but each is different and important for the future of patient care.

Artificial intelligence is a large group of image-based data to guide a computer or network to make decisions, according to Pooja Sodha, M.D., assistant professor of dermatology at Duke University Medical Center, and medical advisor and vice president of research and development for FaceMD+, which uses artificial intelligence and machine learning for management of benign skin conditions.

“Machine learning is a subset within artificial intelligence in which large computational networks try to learn through trial and error,” Dr. Sodha says. “In dermatology, the data is image-based. You basically train that algorithm to recognize certain features of the data set images so it can deduce how to go from an image to an actual diagnosis. The ability of the algorithm is dic-
tated by how much data there is. The more data and the more training you offer it, the better it is able to pick up nuances between images, which may vary in quality and resolution.

“If it incorrectly recognizes an image, the great thing about
machine learning is that it has the ability to take feedback and correct itself. So, you can train these networks and machine learning programs to identify nuances and be able to overlook the variability between images but pick up on the true identifying diagnostic features. That’s what makes it a powerful tool for diagnosis of nevi, melanoma, skin cancers and more.”

Augmented intelligence brings the different components of artificial intelligence together to enhance the way dermatologists and other clinicians practice. It complements dermatologists’ decision making, Dr. Lewandrowski says.

Studies suggest artificial intelligence and machine learning have the potential to be at least as accurate as dermatologists for diagnosing melanoma, says Art Papier, M.D., associate professor of der-
atology and medical informatics at the University of Rochester.

Using large image datasets to train software algorithms to pick up on features of skin lesions through pattern recognition isn’t entirely new to the specialty, but it’s a rapidly evolving field in der-
atology and other visual specialties, says Dr. Papier, who is CEO of VisualDx, a healthcare informatics company that develops dig-
ital health products to enhance diagnostic accuracy.

The technologies will need more than proven efficacy to penetrate dermatology and other specialties, he says.

“I don’t know if dermatologists and the medical-legal system are ready for software to help diagnose melanoma, for example. If you have software that’s aiding the diagnosis of melanoma, and the software makes a mistake, who is responsible? It’s not really clear. There isn’t a comfort level yet, though the technol-
gies are getting better and better,” Dr. Papier says.

“I believe looking out five or 10 years into the future you could easily imagine arrays of cameras taking pictures of patients, tracking their changes in their nevi and detecting melanoma much more accurately than people. That’s how fast technology is evolving, but the healthcare system—the legal system—both on the reimbursement side and the medical-legal side need to catch up with these technologies once they’re really proven.”

However, new generation 2D and 3D total body scanning technologies are currently changing the ways in which derma-
tologists monitor melanoma, according to a handout presented by Josep Malvehy, M.D., from the Melanoma Unit at the Hospi-
tal Clinic Barcelona, Spain, during the “Melanoma: The Future is Now” panel at this year’s AAD annual meeting.

“In monitoring melanocytic lesions, dermatologists have tra-
ditionally [worked] on naked eye examination and dermoscopy assessment, clinical memory recall and, when available, a 2D digital camera,” Dr. Malvehy says.

One example of how scanners have evolved: Vectra (Canfi eld) is a 3D whole body photomaging technology. The device cap-
tures images via 92 cameras with white or cross-polarized lighting.

“The cameras capture the images simultaneously and then construct a digital 3D avatar of the patient. The image capture happens in just a matter of seconds—the 3D representation facil-
itates a 360-degree rotation to view all body angles, including curved surfaces. We can use florescence and regular photogra-
phy to track lesions, giving us the ability to see every single lesion on the body,” says Miami, Fla., dermatologist Jill Waihel, M.D., who is on staff at the Miami Cancer Institute. “The Vectra also gives you the ability to analyze all nevi on a patient’s body from darkest to lightest, and the most irregular shape. It gives derma-
tologists one more analytical tool. The Vectra also has dermoscopy capabilities, which enables us to track individual lesions every three months.”

THERAPEUTIC TECHNOLOGY OFFERS ALTERNATIVE TO SURGERY

EVOLVING TECHNOLOGIES are not only help-
ing dermatologists to detect and monitor skin cancer, but also treat it. Superficial radiation therapy (SRT) is an old approach that has evolved and resurged in recent years because of the rapidly aging population, according to Mark S. Nestor, M.D., Ph.D., a dermatologist and researcher in Aventura, Fla.

Dr. Nestor who uses the SRT-100 (Sensus Healthcare) says patients are looking for alternatives to surgery for non-melanoma skin cancer and insurance general-
lly covers SRT.

“The cure rates using SRT for the treatment of basal cell and squamous cell carcinomas are around 95%. You don’t have to have sur-
gery, so a lot of the complications with sur-
gery—such as infections—are much lower. Because the science has advanced so much, some of the concerns with side effects from radiation treatments, are much less common with superficial radiation therapy,” Dr. Nestor says. “One of the best aspects of SRT is it’s per-
formed in the office by Dermatologists. We assess the patients and follow them.”

Dr. Nestor, lead author on the recently published Consensus Guidelines on the Use of Superficial Radiation Therapy for Treating Non-
melanoma Skin Cancers and Keloid1, says dermatologists should use SRT primarily on elderly. Exceptions include younger patients with nonmelanoma skin cancers where they might not want surgery—on the central face, scalp and lower extremities.

Patients with multiple lesions might also be better candidates for SRT than for surgery. But patients with a small skin cancer that can be easily managed with either excision or destruction tend not to be SRT candidates, Dr. Nestor says. ◆


Disclosure: Dr. Nestor is a consultant for Sensus Healthcare and advisor for Castle and Nevisense.
Dr. Suelyn C. Chen, M.D., M.S., professor and chair of dermatology at Emory University and director of teledermatology for the Veterans Integrated Service Network 7.

Dermatologists and their patients are among those tapping into a growing market for apps that claim to help diagnose, treat and prevent skin cancers, including melanoma.

“Apps, telemedicine and wearables can provide both convenient and quick access to dermatologic care,” Dr. Chen says.

So, it’s important for dermatologists who might recommend these devices and options to patients or use them in practice to understand their strengths and limitations.

Key points for dermatologists regarding skin cancer apps, according to Dr. Chen, are that today’s apps are good for helping patients remember when to perform skin checks as a means of early detection of all skin cancers, including melanoma.

“The apps also enable patients to save photos of their moles to secure clouds, so that they can use them as a comparison when checking their skin,” she says.

However, current apps cannot reliably make diagnoses, Dr. Chen says.

That could change with time and these apps might become increasingly useful for diagnosing melanoma and non-melanoma skin cancers, thanks to ongoing artificial intelligence, she says.

Using teledermatology apps for direct-to-patient communication is feasible, but that, too, has challenges, according to Dr. Chen. Teledermatology apps allow patients to transmit photos of lesions to providers to evaluate in a secure fashion. The technology goes beyond textographs for secure image transmission, according to Dr. Chen.

“There is not a specific app that is better currently,” she says. “The shortcoming on teledermatology now is the lack of adequate reimbursement for providers in store-and-forward telemedicine.”

The Centers for Medicare and Medicaid Services (CMS) released its final rule on payment for store-and-forward teledermicine. The Centers for Medicare and Medicaid Services (CMS) released its final rule on payment for store-and-forward telemedicine, in which data and images are collected from patients and sent to a dermatologist or other specialist to be viewed at a later time. The final rule is disappointing and limiting, according to Dr. Chen. For example, dermatologists are reimbursed $12.61 for a remote evaluation of images submitted by an established patient.

Wearable technologies seem to be the rage among consumers and, while their use is limited in skin cancer diagnosis and treatment, wearables can be useful in skin cancer prevention.

“The wearables are mostly reminders for sunscreen usage,” she says. “If consumers find them more reliable than a timer for reapplication of sunscreen, then dermatologists can recommend these wearables.”

The factors that Dr. Chen believes will have the biggest influences on how these technologies impact dermatologists and their patients in the future will be increased access to artificial intelligence for adjunct diagnostics and changing legislation for reimbursement of store-and-forward telemedicine.

Disclosure: Dr. Chen receives royalties from Menlo, is an investigator with Incyte, and is a scientific advisory committee member for LEO Pharma.
More data necessary to back SLNB for melanoma

ILYA PETROU, M.D. | Staff Correspondent

Sentinel lymph node biopsy (SLNB) has classically been performed for regional disease control and to hopefully prevent disease metastasis; however, according to one expert, there has not been any good evidence to support this practice. As such, it is important for clinicians to focus on the evidence when planning the treatment and management of their advanced melanoma patients.

“The premise is off, because if you’re performing SLNB on a lot of people and the complication rate is low but the number of patients who are getting the procedure is high, the long-term complication rate in a group of people who you manage with SLNB actually have more complications than the smaller group of patients who have a complete node dissection from palpable disease,” Dr. Zitelli said.

Controversy revolving around the role of SLNB and its true usefulness in melanoma therapy and management continues today. The current contemporary wisdom is that SLNB should be performed because the results could help determine which patients would be more amenable to adjuvant therapy. According to Dr. Zitelli, there still isn’t any good evidence supporting the use of adjuvant therapies in patients with stage IIIA disease. However, there is some emerging evidence indicating the usefulness of SLNB in patients with an ulcerated primary melanoma tumor where those patients with a positive SLNB would possibly benefit from targeted adjuvant therapy.

“The changing role of SLNB has been going on for about ten years now and the procedure is still trying to find its perfect niche in the quickly evolving and dynamic field of melanoma therapy and management.”

John Zitelli, M.D., University of Pittsburgh Medical Center, Pittsburgh, Penn.

Disclosures
Dr. Zitelli reports no relevant disclosures.

References
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Photos provided by Dr. Michael H. Gold, M.D. FAAD

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MKT-SRT-03B-B
Although prescribers who provide in-office dispensing must satisfy applicable state and other requirements, a recent ruling against Allergan’s attempt to shut down Prescriber’s Choice appears to pave the way for expansion of these services, according to Wm. Philip Werschler, M.D.

Since the onset of healthcare reform, in-office dispensing of prescription medications has exploded, says Dr. Werschler, a Spokane, Wash.-based dermatologist in private practice and a clinical teaching professor at the University of Washington. Currently, Dr. Werschler says, a sizeable number of the approximately 14,000 dermatologists practicing in the United States utilize Prescriber’s Choice dispensing services, as he does. Such services grew out of the Federal Food, Drug and Cosmetic Act Section 503B, which was issued after the New England Compounding Center (NECC) tragedy. As a result of contaminated NECC compounding, more than 800 patients contracted meningitis infections starting in 2012, resulting in 76 deaths.

In revisiting compounding regulations, says Dr. Werschler, who presented on this topic at Fall 2018 Cosmetic Bootcamp, the new section of the law known as the Drug Quality and Security Act created new opportunities for physicians. Chief among the changes is the ability to order from an FDA-registered 503B outsourcing facility. This new entity type is required to follow Current Good Manufacturing Practices (CGMP). “Ultimately,” he says, “Congress and the FDA recognized the need for compounded medications but insisted that they be made in a quality environment.”

The new law allows physicians to keep compounded inventory on hand, rather than having to write individualized prescriptions that each patient provides to a compounding pharmacy. “The FDA essentially allowed physician offices to maintain office stock.” Although FDA guidance does not specify how much, he adds, dermatologists generally interpret this guidance as a 90-day supply. “That was a significant fundamental change in how a dermatology office operates.”

**IN-OFFICE DISPENSING VS PHARMA**

The new legal landscape underlies both the explosion in physician dispensing, Dr. Werschler says, and the pharmaceutical industry’s associated concerns. In 2017, Allergan sued Prescriber’s Choice and its affiliated FDA-registered 503B outs-
When he started practicing 28 years ago, few off-dermatology to its roots, adds Dr. Werschler.

RESURRECTING COMPOUNDING

“...and frequently less expensively, at the point of service. It’s disruptive in exactly the same way that Uber and Airbnb have been disruptive. Patients love it.”

Wm. Philip Werschler, M.D., Spokane, Wash.

Using an outsourcing facility also ensures that patients get exactly what their dermatologists prescribe, Dr. Werschler says. According to Prescriber’s Choice, more than 70% of patients who prescriber’s Choice and Sincerus. I would also expect to see more outsourcing facilities become registered with the FDA, and that is going to be a third pathway, filling the gap between a traditional pharmacy and a pharmaceutical manufacturer.”

Using an outsourcing facility also ensures that patients get exactly what their dermatologists prescribe, Dr. Werschler says. According to Prescriber’s Choice, more than 70% of patients who encounter prior authorization (PA) get substitute medications.

“We want our patients to get the medicines that we want them to have, expeditiously and affordably. And we want to prescribe what, in our belief as the dermatologist, is going to be the best medicine for them as an individual,” he says.

Outsourcing facilities do not tell physicians what to use their products for, says Dr. Werschler. “A compounded medication doesn’t have a label with an indication. That is up to the prescribing doctor.”

RESURRECTING COMPOUNDING

The growth in use of outsourcing facilities returns dermatology to its roots, adds Dr. Werschler. When he started practicing 28 years ago, few off-the-shelf dermatology medications existed, he says. “Dermatologists were all master compounders; it was part of our training. We’d write a compounded formula on a prescription sheet.” Such recipes gave rise to dermatology staples ranging from Kligman’s formula to metronidazole capsules dissolved into a vehicle, says Dr. Werschler.

Compounding largely disappeared through the 90s and early 2000s as pharmacists gravitated toward dispensing ready-made products. But under Section 503B, Dr. Werschler says, highly educated Pharm.D.’s began teaming with dermatologists to resurrect largely forgotten compounding formulations.

“Prescriber’s Choice worked with dermatologists and said, ‘we have the ability to assist you in developing customized formulas. We will enable the doctor to provide these at the time of the visit at a price point the patient can afford.”

Many commercially available dermatologic drugs may have undesirable side effects; however, compounding can be used to mitigate these issues, Dr. Werschler says. For example, a patient may be allergic to benzoyl peroxide in a topical product, but they may be able to tolerate it compounded without preservatives.

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Wm. Philip Werschler, M.D., Spokane, Wash.

Outsourcing facility, Sincerus, both based in Pompano Beach, Fla., claiming that these companies were selling unapproved drugs under the guise of compounding.

In January, a California federal judge ruled against Allergan, saying that Sincerus is permitted to operate as an outsourcing facility provided it complies with FDA regulations and guidance, according to published accounts. “That’s the big lawsuit that other pharmaceutical companies were watching. And I don’t see any other impediments,” says Dr. Werschler. Had Allergan prevailed, he says, drug manufacturers most likely would have filed similar lawsuits against outsourcing facilities.

“Now that we have clarity from a legal perspective, I believe you’ll see a lot more of my colleagues begin to utilize the services of Prescriber’s Choice and Sincerus. I would also expect to see more outsourcing facilities become registered with the FDA, and that is going to be a third pathway, filling the gap between a traditional pharmacy and a pharmaceutical manufacturer.”

Using an outsourcing facility also ensures that patients get exactly what their dermatologists prescribe, Dr. Werschler says. According to Prescriber’s Choice, more than 70% of patients who encounter prior authorization (PA) get substitute medications.

“We want our patients to get the medicines that we want them to have, expeditiously and affordably. And we want to prescribe what, in our belief as the dermatologist, is going to be the best medicine for them as an individual,” he says.

Outsourcing facilities do not tell physicians what to use their products for, says Dr. Werschler. “A compounded medication doesn’t have a label with an indication. That is up to the prescribing doctor.”

Physicians can legally order compounded medicines from FDA-registered 503B outsourcing facilities, maintain office stock (generally interpreted as a 90-day supply), and provide patients with on-the-spot medicines and instructions.

Dr. Werschler’s staff loves Prescriber’s Choice, he added. “Every week, it gets worse with denials, chart note requests, step edits (even for generics), pre-authorizations and excessive co-pays. This isn’t just for biologics — this can even be for acne and rosacea creams. We now have a full-time medical assistant who works the ‘denial desk.”’

Since starting with in-office dispensing, however, Dr. Werschler estimates his practice has reduced the PA time and cost burden on topical products between 50% and 75%.

Disclosures
Dr. Werschler dispenses Prescriber’s Choice but has no ownership interest in the company. He did not receive compensation for the lecture or this article, which also includes comments from a January 23 phone interview with Dr. Werschler.

References
Derm drug company launches Rx program

LISETTE HILTON | Staff Correspondent

Quick Takes
A new program offers fixed-price Rx products.
Program eliminates the need for prior authorizations and sticker shock.
Branded options are closely priced to generic.

It’s no secret that dermatologists and patients are up in arms about the hoops they have to jump through to get many of the drugs they need for treatment. Prior authorization is among the hurdles. Then, it’s often a mystery what drugs might cost when the patient finally gets to the pharmacy counter.

Ortho Dermatologics, a prescription dermatology company with a portfolio of medications including those that treat psoriasis, actinic keratoses, acne and atopic dermatitis, has launched a new program provides doctors and patients with predictable, affordable access to a range of treatment options for certain disease states. There’s no prior authorization or step therapy and the prescriptions don’t go the traditional route through government or private insurance. Rather, dermatologists e-prescribe one of the eight available Ortho Dermatologics branded medications, each with a fixed price ranging from $50 to $115. Patients pay the full price (no copays) and receive the medication in 48 hours by mail or, in some cases, can go to their local pharmacies.

Doctors want predictability, according to Mark D. Kaufmann, M.D., chief medical officer of The Dermatology Group and associate clinical professor of dermatology at the Icahn School of Medicine at Mount Sinai.

Dr. Kaufmann has used the Ortho Dermatologics program when prescribing Altreno (tretinoin 0.05%) Lotion. On the Ortho Dermatologics cash-pay program, Altreno, which was FDA approved in August 2018 for acne, costs $115. He explains to patients that they can go through their insurance and possibly get a generic or pay cash for Altreno and receive a 45-gram tube that will last them anywhere from three to six months.

“I have had that conversation with patients and to my surprise people are loving it. Patients know they’re not going to get on a carousel that’s endless, kind of like musical chairs, not knowing where they’ll end up when the music stops, asking how much is this going to be?” Dr. Kaufmann says.

Dr. Kaufmann also uses the cash-pay option when prescribing Efudex (fluorouracil) Topical Cream, 5%, which costs a fixed $85.

“Getting a couple of treatment cycles out of a tube of Efudex for $85 for your actinic keratoses, is easier than going to fight with the pharmacist or call the doctor’s office 12 times. It’s a done deal,” Dr. Kaufmann says.

Doris Day, M.D., clinical associate professor of dermatology at NYU Langone Health, prescribes Altreno through the cash-pay program because she says she likes the product, it eliminates the need to spend time dealing with denials and prior authorizations or warning patients about the vast range of pricing they may experience, and she can instead focus on actual skin care and patient issues.

“I like that transparency and I think it’s set at a reasonable price point. Too often I don’t know how much medications will cost a patient when they get to the pharmacy. It’s frustrating when I get a call back from a patient or pharmacy saying that a prescription is not going to be covered or it’s going to insanely expensive or, if I have to waste staff time on prior authorizations. It not only gets costly for the office to have to do that, it delays my patients from getting their medication in a timely manner,” Dr. Day says. “Now patients won’t get sticker shock at the pharmacy from exorbitant prices that I had no idea about, instead they go in knowing exactly what the cost will be and about how long the prescription should last, and we can then move on with appropriate doctor patient relationship and reason for their visit rather than focusing on the administrative aspects of getting the prescription filled.”

Bill Humphries, president, Ortho Dermatologics, says this is the first-of-its-kind cash-pay prescription program in dermatology.

“We’ve made this program very straightforward. It was designed to provide patients direct access to trusted high-quality dermatology treatments in a simple and affordable manner and really to focus on lessening the administrative burden for patients and healthcare professionals,” he says.

Ortho Dermatologics prices the medications to ensure the branded options are close in price to or sometimes less than generic alternatives.

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As more physicians become employed, learning how to successfully negotiate an employment contract becomes a crucial skill to learn.

A common issue is that many physicians simply don’t negotiate, and just sign what’s put in front of them, says Michael S. Sinha, M.D., J.D., a Regulatory Science Fellow at the Harvard-MIT Center for Regulatory Science.

Dr. Sinha, who presented a session on negotiation basics at the American College of Physicians annual conference in Philadelphia, discussed key aspects of negotiation vital for physicians to learn.

Q: What is a common mistake physicians make when negotiating contracts?

Dr. Sinha: Often, physicians will eagerly sign a binding letter of intent or agree to terms of a contract with little or no negotiation—in some cases, they aren’t even aware of what can be negotiated!

The key is to consult a healthcare lawyer early in the process. Find someone who specializes in physician employment contracts in that state. They will have a lot more insight as to what can, and should, be negotiated.

Ultimately, if you don’t negotiate, you’re only cheating yourself.

Q: What areas in an employment contract are most important to focus on?

Dr. Sinha: The first thing to do, before any financial compensation is discussed, is to clearly define the duties and responsibilities in the contract. Get any promises that are important to you in writing. Only when those details have been hammered out can you get an estimate of your true market value.

It will also affect the salary structure that works best for you. Perhaps you have a lot of administrative responsibilities that would cut into meeting pre-defined relative value unit (RVU) thresholds—this may mean you’ll miss out on bonuses under an incentive-based contract, and a fixed salary would make more sense.

Flexibility and vacation time may also be up for negotiation, but at the expense of your base pay. Here, an incentive-based contract may mean that, as long as you’ve hit appropriate metrics, you’ll have more time off with no salary repercussions.

That said, be sure that you have access to the performance reviews or quality metrics that are being used to determine bonuses. Get it in writing!

Q: What can/should physicians negotiate for that they tend to overlook?

Dr. Sinha: I would start with student loan repayment. Some newly-minted physicians are coming out of residency with $200,000 to $300,000 in student loan debt. There are usually ways to get the hospital to pay some of it off. They may be reluctant to pay a lump sum directly to you, but may be happy to write a check straight to the lender. They’re also less likely to pay any of it up front, but may agree to annual installments, payable after each year of service.
Dr. Brian Biesman and Dr. Michael Gold invite you to the 2019 Music City SCALE Meeting. The meeting is for physicians and clinicians interested in enhancing their practice and learning more about the latest procedures in aesthetic medicine. In addition to the educational sessions, there are live patient workshops and an exhibit hall with the leading members of the industry.

2019 TOPICS

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PART 1: May 9, 2019 8:30AM – 12:30PM at the Hilton Hotel
PART 2: May 10, 2019 2:00PM – 4:00PM at the Hilton Hotel
This program will cover the basics to advanced applications. There will be discussions on lasers, IPL, Radio Frequency, microwave, magnets, LLLT, light/drug therapy, and much more.
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Cub membership bestows privileges on both patients and medical aesthetic practices, ranging from reduced patient pricing to a more steady flow of patients.

“You want to reward your patients for their loyalty, which seems really basic,” says Sara Meyer, creative director and CEO of MOD Marketing, an aesthetic marketing and consulting firm in Philadelphia. “The reality, though, is that there are a ton of competitors in the field for these types of treatments, whether it is Botox or skincare. Patients have many options to choose from, so if they choose you, you do want to reward them in some way.”

According to HubSpot, 82% of people are loyal to a specific brand, plus rewards program members spend up to 18% more than non-loyal customers.

Moreover, according to Harvard Business Review, it can cost up to 25 times more to acquire a new customer versus retaining an existing one.

“Securing loyal customers is a surefire way to boost revenue, if you know what you are doing,” Meyer tells Dermatology Times.

Through club membership, practices have the opportunity to upsell and cross-sell within all profit centers. “For example, if a patient comes in for a mole removal or concerns about skin cancer, once that patient becomes part of a loyalty club, she can start to learn what other services you offer, such as Botox, fillers or laser, and make that patient part of the aesthetic side of your practice.”

Conversely, patients initially visiting a practice for aesthetic reasons can be exposed to the medical side with skin checks, for instance.

A club membership can also reduce the number of hosted monthly events or specials you offer because members are already receiving special pricing. “Every time you have an event or are running campaigns, it is more work for the staff,” Meyer notes.

In addition, club membership ensures a steady flow of business all month long, in contrast to events and specials that cause a spike in sales during the event and then a sharp dip directly after. “Membership makes it easier on the staff and provides some stability,” Meyer says.

Membership can also modify patient purchasing behavior. “Non-members will typically come in when they know you are having an event or special, and that is it, even though the patient needs Botox or fillers,” Meyer says. “But if a patient is part of the club and given special pricing, regardless of when they come in, she will likely abide by the protocol, such as once every 90 days for Botox.”

Furthermore, membership targets patients who value quality and the practice’s expertise, not simply the lowest price. “People who are Grouponers would never join a loyalty club because they bounce around from practice to practice and doctor to doctor,” says Meyer, who is scheduled to speak on club membership in February at the annual meeting of the Association of Dermatology Administrators and Managers (ADAM).

Members entitled to product discounts are more likely to purchase from the practice than from online. “You can guarantee authenticity, too,” Meyer says. “When you purchase a product from Amazon, you do not always know if you are getting the real product.”

Increased rebooking rates are also likely with a membership club. “It is important to rebook the patient before they leave,” Meyer says. “By not rebooking, the patient loses some of the benefits of membership.”

To increase interest in patients joining a loyalty program, Meyer suggests that the practice create literature like a brochure to describe the club and tout the benefits. “It is also important for providers to talk about the club to patients, whether it is the aestheticians in the room or the receptionist when patients are checking out,” she says. “Staff members should be comfortable delivering an elevator pitch that touches on all of the major selling points. Also, send patients home with literature.”

Promoting membership on the practice’s website and in
social media are also effective marketing resources. Paid social ads on Facebook and Instagram can target both current and new followers.

“Everyone should come up with a club name that is different from your practice name,” Meyer says. One of her clients decided on the name Skin365.

Meyer recommends that practices charge roughly $100 for a monthly membership fee in return for discounts. For instance, instead of the normal price of $150 for a session of microdermabrasion, club members might be charged $99 instead. Similarly, by upgrading to a chemical peel that usually costs $200, the patient is charged only $149.

In addition, members could receive 10% to 15% savings on products and 10% off all injectables. “Also, if you normally charge for consultations, you can make that complimentary to members,” Meyer says. “You want members to benefit in every which way that makes sense to them.” Meyer has observed an uptick in membership clubs among medical aesthetic practices. However, practices are so used to hosting Botox events and monthly specials that even after they roll out a club they continue those events and specials, which discourages club membership. “Why join a club if you can receive the benefits without joining?” says Meyer, who had one client who offered financial incentives through monthly specials that were better than what members paid.

Program offers fixed-price Rx products FROM PAGE 42

flexible spending or health saving account, according to Humphries.

The pharma company partnered with the online pharmacy MedVantx. Dermatologists can e-prescribe using just about any electronic medical record. Ortho Dermatologics has also partnered with some pharmacies, including Walgreens, which have agreed to honor the pricing.

Humphries says the cash-pay program also addresses the problems patients face when insurers deny a drug.

“We’ve actually taken a new product, Altreno, a tretinoin lotion 0.05%, that we took through all the FDA requirements to get approved and priced it at $115, fully recognizing that in many cases adult female acne patients stand no chance of having this product covered by insurance if it was prescribed. That’s because certain payers or managed healthcare programs block adult females from getting a retinoid due to concerns of offlabel use,” Humphries says.

Dr. Kaufmann said he likes the idea of knowing the drugs he prescribes actually end up in patients’ possession.

“We prescribe hundreds of medicines a day but have no idea what percent are being filled as written,” Dr. Kaufmann says. “Here’s an opportunity to say that whatever I’m prescribing is actually ending up in my patients’ hands.”

Ortho Dermatologics plans to add five more medications from its portfolio this year and another five or 10 next year. The goal is to have 20 products in the cash-pay program by end of 2020, according to Humphries.

The pharma company also plans to keep prices predictable, transparent and affordable, says Humphries.

“Predictable pricing is one of the cornerstones of our program, so when the dermatologist tells a patient that it’s $85 for Efudex, if it’s $86 that’s the wrong answer. If it’s $80 that’s the wrong answer, too, because what we want to do is rebuild or keep the trust between the physician and their patient,” he says.

Keeping medications in the program affordable and a good value is important, according to Dr. Day.

“It’s a price where when I look at what the product is, the quality of it and the formulation, and the fact that this is almost never covered for the majority of patients for whom I write it, that’s a good value for the patient,” Dr. Day says.

Dermatologists can learn more by going to Dermatology.com. Ortho Dermatologics’ salespeople will be educating doctors’ offices about the program starting in mid-May, according to Humphries, who has 30 years’ experience with companies specializing in dermatology pharmaceuticals, including Allergan, Dermik, Stiefel and Merz.

Disclosures
Dr. Kaufmann is a consultant and an advisor to Ortho Dermatologics. Dr. Day is a speaker for Ortho Dermatologics.

Innovation: Understand intellectual property agreements FROM PAGE 7

back to the university. As an inventor, I share a proportion of the potential future windfall. However, university resources, which vary institution to institution, is not infinite. Hard decisions have to be made about whether a specific invention is worth the cost of patenting — this cost can start easily in the tens of thousands of dollars and reach hundreds of thousands of dollars as the patent moves through the process and international coverage is desired. This is part of the discussion that must occur between you as the inventor and the university. There may be instances where the university finds your invention worthwhile, but not developed fully requiring more research and work. I would not be discouraged. There are also instances where you and your university’s technology transfer office disagree. If you see commercial value in the invention and you’re willing to put up the upfront cost, you can try to negotiate a transfer of assignment to you as the inventor. More often than not, the university will elect to maintain their ownership rights and enter a licensing negotiation with you as the inventor absent of other potential commercial parties. We will go through the basics of licensing negotiations in next month’s column.
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WEARABLE SENSOR MEASURES PERSONAL PH LEVELS

L’Oréal recently showcased MY SKIN TRACK PH, a thin and flexible sensor with an accompanying app that measures skin pH levels to provide personalized product recommendations for its wearer. The product uses a network of microchips to detect pH levels from trace amounts of sweat. According to the company, the sensor can produce an accurate assessment of the wearer’s skin pH within 15 minutes.

To use the product, the wearer must first place it on the inner arm for five to 15 minutes or until the two center dots become colorized. Then, the wearer must take a picture of the sensor using the accompanying mobile app. The app’s algorithm assesses the pH measurement and the wearer’s local sweat loss to determine skin health. It then creates recommendations of La Roche-Posay products to improve the skin health of the wearer.

The sensor will be available to select La Roche-Posay dermatologists with the goal of eventually launching a consumer product once more research is conducted.

FOR MORE INFORMATION: lorealusa.com

DEFENAGE® RESURFACING MASK WINS AWARD

DEFENAGE 2-MINUTE REVEAL MASQUE was recently named “Best Brightening Mask” by NewBeauty. The environmentally friendly cream mask contains ultra-fine Sugar Crystals and plant-based Triple Enzyme technology that resurfaces the skin without irritation. The formula does not contain microbeads or fragrance.

“DefenAge’s team is very proud that this unique formula that delivers high-performance while being a gentle treatment, caught the attention of NewBeauty’s editors,” said Progenitor Biologics’ CEO, Nikolay Turovets, Ph.D.

FOR MORE INFORMATION: defenage.com

DELUXE CRÈME FIGHTS SIGNS OF AGING

IS CLINICAL recently released a deluxe version of their YOUTH INTENSIVE CRÈME, which is now available in twice the size of the original release. According to the company, the antiaging crème smooths fine lines and wrinkles, promoting more visibly plump and radiant skin.

The formula includes copper tripeptide growth factor, which fights premature signs of aging and reduces wrinkles; superoxide dismutase (SOD), which is a natural enzyme that nurtures skin health and protects against photo-damage; hyaluronic acid, which hydrates the skin; and tetrahexyldecyl ascorbate, which is a stabilized form of vitamin C that calms the skin and fights signs of photo-damage.

FOR MORE INFORMATION: isclinic.com

QOSMEDIX INTRODUCES NEW COLLECTION OF BOTTLES

Qosmedix announced the launch of its new line of printed cylinder bottles for storing liquid or spray cosmetics and cosmeceuticals. The line features 250 ml black bottles with white labels, and includes spray top caps, lotion pump tops, and disc-top caps. Bottles can be customized for minimum orders of 10,000 pieces, and orders can be placed via the company website.

FOR MORE INFORMATION: inductiontherapies.com
Caregiver assessment tools

Because a patient’s atopic dermatitis may also have a profound effect on parental caregivers, clinicians should seek to make an assessment of parental emotional and psychosocial well-being, and offer patient educational materials to help bring awareness to the issue. Caregivers may be chronically sleep-deprived, exhausted or depressed and, therefore, less equipped to implement time-consuming treatment regimens, regulate their child’s behavior, and help the child cope with his or her illness. Experts suggest several tools clinicians can use to screen caregivers for sleep disturbance, fatigue and emotional health.

The Pittsburgh Sleep Quality Index1

A VALIDATED tool to measure adult quality and patterns of sleep, the 9-question self-rate tool helps a clinician assess a patient who is sleeping poorly. On a 0-3 scale, where 3 reflects a negative extreme, patients respond to questions about their sleep patterns in seven domains: A total sum of 5 or more on the tailored responses would indicate a poor sleeper.

1. How long (in minutes) has it taken you to fall asleep each night?
2. How many hours of actual sleep do you get at night? (This may be different than the number of hours you spend in bed.)
3. During the past month, how often have you had trouble sleeping because you...
   a. Cannot get to sleep within 30 minutes
   b. Have to get up to use the bathroom
   c. Other reason(s), please describe, including how often you have had trouble sleeping because of this reason(s)
4. During the past month, how would you rate your sleep quality overall?

The Patient Health Questionnaire-9 (PHQ-9)2,3

A SELF-ADMINISTERED diagnostic assessment for common mental disorders, the PHQ-9 is the 9-item depression module taken from the full PHQ. A diagnosis of depression is made if 5 or more of the 9 depressive symptom criteria have been present “more than half the days” in the past 2 weeks...

Over the last 2 weeks have you been bothered by any of the following problems?

a. Feeling down, depressed or hopeless
b. Trouble falling asleep, staying asleep or sleeping too much
c. Feeling bad about yourself — or that you are a failure or have let yourself or your family down

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home or get along with other people?

Generalized Anxiety Disorder 7-item scale4

GENERAL anxiety disorder is commonly seen in medical practice and is one of the most common anxiety disorders in the general population. This 7-item scale is used to identify probable cases of anxiety disorder and severity.

Over the last 2 weeks have you been bothered by any of the following problems?

a. Feeling nervous, anxious or on edge
b. Not being able to stop or control worrying
c. Feeling afraid as if something awful might happen

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home or get along with other people?

Sources:
INDICATIONS AND USAGE

Initial U.S. Approval: 1990

BRIEF SUMMARY OF PRESCRIBING INFORMATION

Hypothalamic-Pituitary-Adrenal (HPA) Axis Suppression

BRYHALI has been shown to suppress the hypothalamic-pituitary-adrenal (HPA) axis. Systemic effects of topical corticosteroids may include reversible HPA axis suppression with the potential for glucocorticosteroid insufficiency. This may occur during treatment or upon withdrawal of treatment with the topical corticosteroidal.

The potential for hypothalamic-pituitary-adrenal (HPA) axis suppression with BRYHALI was evaluated in a study of 19 adult subjects with moderate to severe plaque psoriasis involving ≥20% of their body surface area (BSA). HPA axis suppression was reported for 1 (5.6%) subject at Week 4 and for 3 (15.8%) subjects at Week 8. All 3 subjects had normal HPA axis function in full suppression test with discontinuation of treatment (see Clinical Pharmacology in full Prescribing Information).

Because of the potential for systemic absorption, use of topical corticosteroids, including BRYHALI, may require that patients be evaluated periodically for evidence of HPA axis suppression. Factors that predispose a patient using a topical corticosteroid to HPA axis suppression include the use of more potent corticosteroids, use over large surface areas, occlusive use, use on an altered skin barrier, concomitant use of multiple corticosteroid-containing products, liver failure, and young age. An adrenocorticotropic hormone (ACTH) stimulation test may be helpful in evaluating patients for HPA axis suppression.

If HPA axis suppression is documented, attempt to gradually withdraw the drug, reduce the frequency of application, or 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.

Systemic effects of topical corticosteroids may also include Cushing’s syndrome, hyperglycemia, and glucosuria. Use of more than one corticosteroid-containing product at the same time may increase the total systemic exposure to corticosteroids. Pediatric patients may be more susceptible than adults to systemic toxicity from the use of topical corticosteroids due to their larger surface-to-body mass ratios (see Use in Specific Populations).

ADVERSE REACTIONS

Local Adverse Reactions

Local adverse reactions from topical corticosteroids may include atrophy, striae, telangiectasias, burning, itching, irritation, dryness, folliculitis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, and miliaria. These may be more likely with occlusive use, prolonged use, or use of higher potency corticosteroids, including BRYHALI. Some local adverse reactions may be irreversible.

Concomitant Skin Infections

Use an appropriate antimicrobial agent if a skin infection is present or develops. If a favorable response does not occur promptly, discontinue use of BRYHALI until the infection has been adequately treated.

Allergic Contact Dermatitis

Allergic contact dermatitis with corticosteroids is usually diagnosed by observing failure to heal rather than noting a clinical exacerbation. Consider confirmation of a clinical diagnosis of allergic contact dermatitis by appropriate patch testing. Discontinue BRYHALI if allergic contact dermatitis occurs.

ADVERSE REACTIONS

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 clinical practice. In randomized, double-blind, multicenter, vehicle-controlled clinical trials, 426 adults with plaque psoriasis were treated with BRYHALI and had post-baseline safety data. Subjects applied BRYHALI once daily for up to eight weeks. Table 1 presents adverse reactions that occurred in at least 1% of subjects treated with BRYHALI and more frequently than in vehicle-treated patients.

Table 1: Adverse Reactions Occurring in ≥1% of the Subjects Treated with BRYHALI through Week 8

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>BRYHALI (N=284)</th>
<th>Vehicle (N=142)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper Respiratory Tract Infection</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Application Site Dermatitis</td>
<td>1%</td>
<td>0%</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>1%</td>
<td>0%</td>
</tr>
</tbody>
</table>

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

There are no available data on BRYHALI use in pregnant women to inform a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes.

In animal reproduction studies, increased malformations, including cleft palate and omphalocele, were observed after oral administration of halobetasol propionate during organogenesis to pregnant rats and rabbits. The available data do not support relevant comparisons of systemic halobetasol propionate exposures achieved in the animal studies to exposures observed in humans after topical use of BRYHALI.

The background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Data

Animal Data

Halobetasol propionate has been shown to cause malformations in rats and rabbits when given orally during organogenesis at doses of 0.04 to 0.1 mg/kg/day in rats and 0.1 mg/kg/day in rabbits. Halobetasol propionate was embryotoxic in rabbits but not in rats. Cleft palate was observed in both rats and rabbits. Omphalocele was seen in rats but not in rabbits.

Lactation

Risk Summary

There are no data on the presence of halobetasol propionate or its metabolites in human milk, the effects on the breastfed infant, or the effects on milk production after treatment with BRYHALI.

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 human milk.

The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for BRYHALI and any potential adverse effects on the breastfed child from BRYHALI.

Clinical Considerations

Advise breastfeeding women not to apply BRYHALI directly to the nipple and areola to avoid direct infant exposure.

Pediatric Use

Safety and effectiveness of BRYHALI in pediatric patients under the age of 18 years have not been evaluated.

Because of higher skin surface area to body mass ratios, 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 also at greater risk of adrenal insufficiency during or after withdrawal of treatment. Adverse reactions including striae have been reported with use of topical corticosteroids in infants and children (see Warnings and Precautions).

HPA axis suppression, Cushing’s syndrome, linear growth retardation, delayed weight gain, and intraocular hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include low plasma cortisol levels and an absence of response to ACTH stimulation. Manifestations of intraocular hypertension include bulging fontanelles, headaches, and bilateral papilledema (see Warnings and Precautions).

Geriatric Use

Of 284 subjects exposed to BRYHALI in clinical trials, 61 subjects were 65 years or older. Clinical trials of BRYHALI did not include sufficient numbers of subjects age 65 years and older to determine whether they respond differently from younger subjects.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies have not been performed to evaluate the carcinogenic potential of halobetasol propionate.

Halobetasol propionate was not genotoxic in the Ames assay, in the sister chromatid exchange test in Chinese hamster somatic cells, in chromosome aberration studies of germinal and somatic cells of rodents, or in a mammalian spot test. Positive mutagenicity effects were observed in a mouse lymphoma gene mutation assay in vitro and in a Chinese hamster micronucleus test.

Studies in rats following oral administration of halobetasol propionate at dose levels up to 0.05 mg/kg/day indicated no impairment of fertility or general reproductive performance.

PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Manufactured for:

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U.S. Patent Numbers: 6,517,847 and 8,809,307

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Based on 9652102 November 2018 BRY.0032.USA.18
BRYHALI™ (halobetasol propionate) Lotion, 0.01%

FOR ADULTS WITH PLAQUE PSORIASIS

CHART A COURSE TO SYMPTOMATIC RELIEF

The efficacy of Class 1 halobetasol with safety proven for up to 8 weeks of dosing

A NEW POTENCY CLASS OF STEROID LOTION

2 PIVOTAL PHASE 3 TRIALS

POTENT TO SUPERPOTENT CLEARANCE:

Continued results 4 weeks post treatment

Significant symptomatic relief as early as week

No increased epidermal atrophy observed through 8 weeks of treatment

Local adverse reactions from topical corticosteroids may include atrophy, striae, telangiectasias, hypopigmentation and allergic contact dermatitis. Some local adverse reactions may be irreversible.

STUDY RESULTS: 36.5% of patients in trial 1 and 36.4% in trial 2 achieved treatment success* at week 8 (primary endpoint) vs 8.3% and 12.2% of patients with vehicle, respectively (P<0.001 in both trials).

STUDY DESIGN: The safety and efficacy of BRYHALI Lotion were assessed in 2 prospective, multicenter, randomized, double-blind, phase 3 clinical trials in 430 adult patients with moderate-to-severe plaque psoriasis. Patients were treated with BRYHALI Lotion or vehicle lotion, applied once daily. Primary efficacy endpoint was treatment success evaluated at week 8. Secondary efficacy endpoint was treatment success evaluated at weeks 2, 4, 6, and 12 (4 weeks post treatment). Tertiary efficacy endpoint was a 2-grade improvement from baseline at each time point for the individual signs of psoriasis erythema, plaque elevation, and scaling.

Indication
BRYHALI™ (halobetasol propionate) Lotion, 0.01% is a corticosteroid indicated for the topical treatment of plaque psoriasis in adults.

Important Safety Information

Warnings and Precautions

• BRYHALI Lotion has been shown to suppress the hypothalamic-pituitary-adrenal (HPA) axis during treatment or upon cessation of treatment; periodic evaluation may be required.

• Systemic effects of topical corticosteroids may also include Cushing’s syndrome, hyperglycemia, and glucosuria.

• Children may be more susceptible to systemic toxicity when treated with topical corticosteroids.

• Local adverse reactions may include atrophy, striae, telangiectasias, hypopigmentation, and allergic contact dermatitis. Some local adverse reactions may be irreversible.

• Use of topical corticosteroids may increase the risk of posterior subcapsular cataracts and glaucoma. If visual symptoms occur, consider referral to an ophthalmologist.

• Use an appropriate antimicrobial agent if a skin infection is present or occurs, and if prompt response is not seen, discontinue use until infection has been adequately treated.

• Discontinue BRYHALI Lotion if allergic contact dermatitis occurs.

Adverse Reactions

• The most common adverse reactions (≥1%) were upper respiratory tract infection, application site dermatitis, and hyperglycemia.

To report SUSPECTED ADVERSE REACTIONS, contact Customer Service at 1-800-321-4576 or FDA at 1-800-FDA-1088.

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

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