New and forthcoming options bring opportunity for optimizing patient care.

CHERYL GUTTMAN KRADER, BS PHARM | Staff Correspondent

One-third of pediatric patients with atopic dermatitis (AD) have moderate to severe disease, and the affected proportion increases with age. Although systemic medications should be considered for these patients when optimal therapy using basic management strategies and topical agents fails, safety concerns with systemic medications have limited their appropriate use.

PEDIATRIC AD CONTINUES ON PAGE 13

Read Aesthetic Authority’s Smart Skin Care section, starting on page 21, to dive into the latest on novel facial hair transplants, top surgery protocol, regenerative topical skin care, and more.

AESTHETIC TREATMENTS BENEFIT GENDER-DIVERSE PATIENTS

JOHN JESITUS | Staff Correspondent

Providing aesthetic procedures such as injectables and hair removal for lesbian, gay, bisexual, transgender, and queer (LGBTQ+) as well as sexual and gender minority (SGM) patients requires more than medical and aesthetic expertise, according to a panel of experts who spoke at the American Academy of Dermatology 2021 Virtual Meeting Experience (AAD VMX) in April. Serving such patients also demands an understanding of consent and medical insurance issues unique to these populations, they said.1

GENDER-DIVERSE PATIENTS CONTINUES ON PAGE 48
FOR ADULT PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS (PsA)

HELPS
RELIEVE
PROTECT
CLEAR

3 REASONS TO TREAT WITH

HUMIRA®
adalimumab®

In a clinical trial of adult patients with active PsA who had an inadequate response to NSAIDs that were treated with HUMIRA 40 mg every other week (EOW) or placebo1,2:

Helps relieve PsA symptoms
• 58% of HUMIRA-treated patients (n=151) achieved ACR20 vs 14% treated with placebo (n=162) at Week 12; *P<0.001 [co-primary endpoint]1,2†

Helps protect against further joint damage
• Mean change in mTSS from baseline for HUMIRA-treated patients (n=133) at Week 48 vs placebo (n=141) at Week 24: −0.2 vs 0.9; *P<0.001 [co-primary endpoint]1,3‡ §

Helps clear skin
• For patients who had at least 3% body surface area psoriatic skin involvement at baseline: 42% of HUMIRA treated-patients (n=69) achieved PASI 90 vs 0% on placebo (n=69) at Week 24; *P<0.0011,2II

*Analysis of the ITT population, using NRI methodology. Patients who withdrew, had missing data, or received rescue therapy were considered nonresponders.
†ACR20 indicates an improvement of at least 20% in tender joint count, swollen joint count, and at least 3 of the other ACR parameters, including CRP levels, Health Assessment Questionnaire–Disability Index (HAQ-DI), pain, physician global assessment, and patient global assessment.
‡Extrapolated analysis. For HUMIRA-treated patients who did not have an mTSS at Week 48, mTSS was imputed by linear extrapolation using the baseline and Week 24 scores. The mTSS was used by the reader blinded to treatment group to assess the radiographs.
§mTSS measures narrowing, as well as radiographic changes specific to patients, including DIP joints, with a maximum score of 570.
II P=0.0044

Indication1
Psoriatic Arthritis: HUMIRA is indicated, alone or in combination with non-biologic DMARDs, for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active psoriatic arthritis.

Safety Considerations1
Serious Infections
Patients treated with HUMIRA are at increased risk for developing serious infections that may lead to hospitalization or death. These infections include active tuberculosis (TB), reactivation of latent TB, invasive fungal infections, and bacterial, viral, and other infections due to opportunistic pathogens. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.

Malignancies
Lymphoma, including a rare type of T-cell lymphoma, and other malignancies, some fatal, have been reported in patients treated with TNF blockers, including HUMIRA.

Other Serious Adverse Reactions
Patients treated with HUMIRA also may be at risk for other serious adverse reactions, including anaphylaxis, hepatitis B virus reactivation, demyelinating disease, cytopenias, pancytopenia, heart failure, and a lupus-like syndrome.

Please see additional Important Safety Information, including BOXED WARNING on Serious Infections and Malignancy, on the following page of this advertisement.

Please see Brief Summary of Full Prescribing Information on the following pages.
IMPORTANT SAFETY INFORMATION for HUMIRA® (adalimumab)

SERIOUS INFECTIONS

Patients treated with HUMIRA are at an increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.

Discontinue HUMIRA if a patient develops a serious infection or sepsis.

Reported infections include:
- Active tuberculosis (TB), including reactivation of latent TB. Patients with TB have frequently presented with disseminated or extrapulmonary disease. Test patients for latent TB before HUMIRA use and during therapy. Initiate treatment for latent TB prior to HUMIRA use.
- Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized, disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Consider empiric anti-fungal therapy in patients at risk for invasive fungal infections who develop severe systemic illness.
- Bacterial, viral, and other infections due to opportunistic pathogens, including Legionella and Listeria.

Carefully consider the risks and benefits of treatment with HUMIRA prior to initiating therapy in patients:
- 1. with chronic or recurrent infection, 2. who have been exposed to TB, 3. with a history of opportunistic infection, 4. who resided in or traveled in regions where mycoses are endemic, 5. with underlying conditions that may predispose them to infection. Monitor patients closely for the development of signs and symptoms of infection during and after treatment with HUMIRA, including the possible development of TB in patients who tested negative for latent TB infection prior to initiating therapy.
- Do not initiate HUMIRA during an active infection, including localized infections.
- Patients older than 65 years, patients with co-morbid conditions, and/or patients taking concomitant immunosuppressants may be at greater risk of infection.
- If an infection develops, monitor carefully and initiate appropriate therapy.
- Drug interactions with biologic products: A higher rate of serious infections has been observed in RA patients treated with rituximab who received subsequent treatment with a TNF blocker. An increased risk of serious infections has been seen with the combination of TNF blockers with anakinra or abatacept, with no demonstrated added benefit in patients with RA. Concomitant administration of HUMIRA with other biologic DMARDs (e.g., anakinra or abatacept) or other TNF blockers is not recommended.

HEMATOLOGIC REACTIONS

- There is a known association between intermediate uveitis and central demyelinating disorders.
- Exercise caution when considering HUMIRA for patients with these disorders; discontinuation of HUMIRA should be considered if any of these disorders develop.

CONGESTIVE HEART FAILURE

- TNF blockers, including HUMIRA, have been associated with rare cases of new onset or exacerbation of central nervous system and peripheral demyelinating diseases, including multiple sclerosis, optic neuritis, and Guillain-Barré syndrome.
- Exercise caution when considering HUMIRA for patients with these disorders; discontinuation of HUMIRA should be considered if any of these disorders develop.

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INFECTIONS

- Patients on HUMIRA should not receive live vaccines.
- Pediatric patients, if possible, should be brought up to date with all immunizations before initiating HUMIRA therapy.
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PREVENTION OF INFECTION

- Evaluate patients at risk for HBV infection for prior evidence of HBV infection before initiating TNF blockers.
- Use of TNF blockers, including HUMIRA, may increase the risk of reactivation of hepatitis B virus (HBV) in patients who are chronic carriers. Some cases have been fatal. Evaluate patients at risk for HBV infection for prior evidence of HBV infection before initiating TNF blocker therapy.
- Exercise caution in patients who are carriers of HBV and monitor them during and after HUMIRA treatment.
- Discontinue HUMIRA and begin antiviral therapy in patients who develop HBV reactivation. Exercise caution when resuming HUMIRA after HBV treatment.

HYPERSENSITIVITY

- Anaphylaxis and angioedema have been reported following HUMIRA administration. If a serious allergic reaction occurs, stop HUMIRA and institute appropriate therapy.
- Hepatitis B Virus Reactivation
- Use of TNF blockers, including HUMIRA, may increase the risk of reactivation of hepatitis B virus (HBV) in patients who are chronic carriers. Some cases have been fatal. Evaluate patients at risk for HBV infection for prior evidence of HBV infection before initiating TNF blocker therapy.
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- Discontinue HUMIRA and begin antiviral therapy in patients who develop HBV reactivation. Exercise caution when resuming HUMIRA after HBV treatment.

NEUROLOGIC REACTIONS

- Rare reports of pancytopenia, including aplastic anemia, have been reported with TNF blockers. Medically significant cytopenia has been infrequently reported with HUMIRA.
- Consider stopping HUMIRA if a significant hematologic abnormality occurs.

CONGESTIVE HEART FAILURE

- Worsening or new onset congestive heart failure (CHF) has been reported with TNF blockers. Cases of worsening CHF have been observed with HUMIRA; exercise caution and monitor carefully.

AUTOIMMUNITY

- Treatment with HUMIRA may result in the formation of autoantibodies and, rarely, in development of a lupus-like syndrome. Discontinue treatment if symptoms of a lupus-like syndrome develop.

IMMUNIZATIONS

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REFERENCES


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If patients develop a serious systemic illness and they reside or travel in regions where mycoses are endemic, infection prior to initiating therapy. Tests for latent tuberculosis infection may also be falsely negative while on with HUMIRA, including the development of tuberculosis in patients who tested negative for latent tuberculosis

WARNINGS AND PRECAUTIONS

Infections

HUMIRA is indicated for the treatment of moderately active Crohn's disease in adults and pediatric patients aged 16 and older. Infections and Infection Reactions

Increased Risk of Infection when Used with Anakinra

Increased Risk of Infection when Used with Abatacept

Increased Risk of Infection with Use of TNF-Blocking Therapy in Patients with HIV

MALIGNANCY

Increased Risk of Malignancies in Inflamed Tissues

Carcinogenesis

Clinical Trials Experience

Table 1. Adverse Reactions Reported by ≥5% of Patients Treated with HUMIRA During Placebo-Controlled Clinical Trials

ADVERSE REACTIONS

The following summary of adverse reactions is provided in alphabetical order by body system and by decreasing frequency of incidence:

Skin Disorders

Anaphylaxis

Lymphoma and Leukemia

In the controlled clinical trials of all the TNF-blockers in adults, more cases of lymphoma have been reported in patients treated with TNF blockers compared to placebo-treated patients. The majority of reported cases of lymphoma have occurred in patients with aggressive disease course and have been fatal. The majority of reported TNF blocker cases have occurred in patients with Crohn's disease or ulcerative colitis and the majority were in adolescent and young adult patients. The risk of lymphoma may be increased when TNF blockers are used in combination with conventional therapies, such as alkylating agents or antimetabolites. The risk of lymphoma is not increased when TNF blockers are used in combination with corticosteroids or nonbiologic disease-modifying antirheumatic drugs (NBDMARDs).

Increased Risk of Infection when Used with Abatacept

Patients should be monitored for the development of (or worsening of) infection, including mycobacterial, fungal, bacterial, viral, and protozoal infections.

If patients develop a serious systemic illness and they reside or travel in regions where mycoses are endemic, infection prior to initiating therapy. Tests for latent tuberculosis infection may also be falsely negative while on with HUMIRA, including the development of tuberculosis in patients who tested negative for latent tuberculosis

Liver and Biliary Disorders

Increased Risk of Infection when Used with Abatacept

Increased Risk of Infection when Used with Anakinra

Lymphoma and Leukemia

The proportion of patients who discontinued treatment due to adverse reactions during the double-blind, placebo-controlled trials was 20% in patients treated with HUMIRA and 15% in patients treated with placebo. The most common adverse reaction in patients treated with HUMIRA that was reported to be at least 3% greater than placebo was injection site reactions (erythema and/or itching, hemorrhage, pain). These reactions were usually mild and generally did not necessitate drug discontinuation.

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Table 2: Anti-Adalimumab Antibody Development Determined by ELISA and ECL Assay in Patients with HUMIRA

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Duration</th>
<th>Adalimumab Dose</th>
<th>Anti-Adalimumab Antibody Development (n/N)</th>
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</thead>
<tbody>
<tr>
<td></td>
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<td>ELISA</td>
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<td></td>
<td></td>
<td>Positive</td>
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<tr>
<td>Study I</td>
<td>2 years</td>
<td>40 mg/week</td>
<td>1/100</td>
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<tr>
<td>Study II</td>
<td>2 years</td>
<td>40 mg/week</td>
<td>1/100</td>
</tr>
<tr>
<td>Study III</td>
<td>1 year</td>
<td>40 mg/week</td>
<td>1/100</td>
</tr>
</tbody>
</table>

**Note:** Anti-Adalimumab antibodies were determined by ELISA and ECL assay in patients treated with HUMIRA for up to 3 years. The incidence of anti-Adalimumab antibodies was assessed in patients receiving 40 mg/week of adalimumab for up to 3 years. The results were as follows:

- **Study I:** 2 years, 40 mg/week - 1/100 (1.0%)
- **Study II:** 2 years, 40 mg/week - 1/100 (1.0%)
- **Study III:** 1 year, 40 mg/week - 1/100 (1.0%)

**Incidence by ECL Assay:**

- **Incidence at 1 year:** 1/100 (1.0%)
- **Incidence at 2 years:** 1/100 (1.0%)
- **Incidence at 3 years:** 1/100 (1.0%)

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QUESTIONS LINGER AROUND COVID-19’S ORIGIN

by MIKE HENNESSY SR

WAS IT NATURAL ZOONOTIC SPILLOVER that catapulted SARS-Cov-2 from an emerging virus into a pandemic pathogen or was it something much more sinister? Is it at all possible that a lab leak in Wuhan, China, was the spark that lit the fuse?

Debate about the origin of the virus that causes COVID-19 has been at the forefront of the global consciousness since the first cases were reported in December 2019.

Early on, whispers of a potentially engineered virus quickly grew to a roar and fueled speculation that China was behind the pandemic. This narrative was so pervasive that, in February 2020, a group of 27 public health scientists published a letter in The Lancet disputing the lab leak theory and announcing their support of their counterparts in China: the scientists, public health officials, and medical professionals combating the pandemic.

“The rapid, open, and transparent sharing of data on this outbreak is now being threatened by rumors and misinformation around its origins,” wrote the authors, who all declared no competing interests in their disclosures as recommended by the International Committee of Medical Journal Editors. “We stand together to strongly condemn conspiracy theories suggesting that COVID-19 does not have a natural origin.”

And although it’s true that analyses of the genomic sequence of the virus subsequently pointed to natural origins, the questions regarding China’s role persisted, led by pesky discrepancies and conflicting reports.

Fast forward to June 2021 and new evidence that has breathed new life into those origin questions. In an update to the February 2020 letter, The Lancet has published an addendum with revised disclosure statements from virologist Peter Daszak, one of the 27 authors. In the revised document, Daszak noted that his remuneration is paid solely in the form of a salary from EcoHealth Alliance, a New York-based nonprofit research foundation of which he is president. The company has reportedly worked directly with Wuhan laboratories and funded gain-of-function research at China’s Wuhan Institute of Virology.

Consider, too, other odd associations. Recent reports have uncovered financial ties between genetic and EcoHealth Alliance. This comes after accusations that the tech giant was censoring lab leak “conspiracy theory” stories in its search results. Google’s health lead, David Feinberg, has dismissed those reports, insisting that the company is simply taking steps to protect users from unfounded information.

Are these coincidences or “where there’s smoke, there’s fire” situations? It’s unclear. But they add to the book of troublesome questions standing in the way of the truth about COVID-19.

The questions extend beyond origin theory, though. With the FDA’s green-lighting of vaccines for adolescents and young adults comes hesitation over long-term effects: What is the effect on fertility? Do the vaccines cause heart inflammation? Robert Malone, MD, the inventor of the mRNA technology, appeared on television recently, expressing strong concern over the risk-benefit analysis of vaccination for young adults and the Centers for Disease Control and Prevention’s Advisory Committee on Immunization Practices recently met to discuss instances of myocarditis and pericarditis in people 30 years and younger who have received an mRNA COVID-19 vaccine. Of course, the answer to our ultimate question is that we may never know.

We may never know where this virus came from. We may never know what triggered the global pandemic that has claimed more than 3.8 million lives. And we won’t know the long-term effects until enough time has elapsed. What we do know for certain is that the incredible strength and collaboration of the scientific community have allowed us to regain our footing.

Our mission is to 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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Aesthetic Authority™
Patient engagement is a cornerstone of health care quality, driving active collaboration and shared decision-making among patients, families, and providers. Now more than ever, patients are becoming informed consumers of health care services, leveraging increased access to their digital health records and extensive condition-specific information available online.

This dynamic presents an important opportunity for health care providers to build more effective patient partnership models throughout the customer’s life cycle. Today’s patients want—and need—access to trusted health care content and digital health technology that empowers them to make educated care decisions.

Provider organizations are best positioned to fill this need by providing consistent, authentic, and personalized connections by adopting advanced digital platforms and other technologies that not only address patients’ immediate needs but also support their overall health and well-being goals.

Many patient engagement approaches attempt to convey information that changes customer behavior, drives informed decision-making, and helps people achieve their highest potential for good health.

In the past, engagement efforts focused primarily on education at the point of care. Patients are accustomed to receiving printed materials at the end of their encounter in the form of discharge instructions or leaflets. Some go further, conducting follow-up calls to see if the patient has questions about their care.

Working toward an authentic patient partnership that lasts throughout the customer life cycle helps health care providers progress beyond these steps, leading to comprehensive programs that set measurable goals and objectives that encourage alignment between patients and their care teams.

New technologies are revolutionizing patient engagement, allowing for ongoing communication across the care continuum. It’s important for providers and provider organizations to build trust at every patient touchpoint to achieve sustained behavior change through informed decision-making.

It’s important, too, that the communication emulate the nurturing experience of a clinical professional who listens with empathy and responds without judgment.

Here are the steps providers can take to help patients make the right care choice at the right time, ultimately improving clinical, financial, and quality outcomes:

1. Patient education is the basic requirement for patient engagement across the enterprise. Providing educational materials such as patient summaries, discharge instructions, or written materials on new medications helps patients better understand their condition(s) and available treatment options.

2. Effective engagement deepens understanding of overall health and wellness. But it also requires that providers shift from a one-size-fits-all way of informing patients to using multiple communication and education mediums as well as tailoring solutions to specific service lines and care encounters. This includes addressing concerns around socioeconomic status, culture, race, gender, or sexual orientation that, if left unaddressed, could marginalize patients or create unnecessary barriers to care.

Better informed and better engaged patients are more likely to participate in preventive care and wellness activities. At this stage, patients and providers shift from reactive care within a health episode to proactive health and wellness care.

Coaching helps facilitate the transition from transactional to longitudinal care. It helps patients adhere to their treatment and wellness plans, and addresses barriers to adherence. Better adherence leads to fewer hospitalizations and readmissions, contributing to improved outcomes and quality, while reducing the cost of care.

Remote monitoring capabilities support coaching and care management to ensure patients receive timely advice from a trusted source.

Partnership is the final, aspirational step of the patient-provider relationship. Patients become valued partners of the care team who are incentivized to improve health outcomes. Partnership supports whole-person care through real-time, personalized interaction throughout the customer lifecycle.

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Chat Room Referral Could Redefine the Physician-Patient Relationship

by DAVID J. GOLDBERG, MD, JD

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 Mount Sinai; and adjunct professor of law at Fordham University School of Law, New York, New York.

Dr D had an active dermatology practice before the COVID-19 pandemic. Faced with the negative impacts of lockdowns and business downturns, he sought ways to increase revenue in his office. After considering a variety of practice enhancement options, he hired a webmaster, who designed his new, highly interactive website.

Leveraging this new site, Dr D now performs telemedicine visits, has a strong social media presence, and enjoys all the new patients he is seeing both virtually and in the office. In fact, he spends hours answering email questions. He had been advised, and has been very careful, not to “practice medicine” on all these virtual sites.

One month into the pandemic, he was sent an email by a woman who lived 5 hours from his practice. According to the e-mail, the patient had been seeing her local dermatologist for 3 years for a diagnosis of multiple skin cancers. She had been treated with a variety of methods, and 1 particular area on her cheek was not responding. She stated in her email that she was unable to travel to Dr D’s office and desperately needed his help.

Dr D corresponded with the patient 6 times over the next 2 months. He was very careful not to discuss the actual diagnosis of her condition with her. However, he did give her extensive advice about the pros and cons of the treatments she had previously received.

Dr D never suggested any changes in her treatment and, much to his dismay, he never received any payments from her for his time. In his last email to the patient, he advised her to join a web-based “chat group.” She thanked him for this advice and joined such a group. Because of the homeopathic and naturopathic suggestions she received from the chat group, she did not seek further dermatologic care for the next 4 months.

During that time, the same area of her cheek began to bleed. She went to see a new dermatologist. A biopsy of the suspicious area revealed amelanotic melanoma. After initial surgery she became infected, was hospitalized, and, ultimately, had a large scar across her cheek. Further evaluation revealed metastatic disease, and she died 6 weeks later.

Her estate sued a variety of individuals, including Dr D. The basis of the claim against Dr D was that she delayed treatment because he advised her to join a skin cancer chat group. Dr D knows that he cannot lose the lawsuit unless his email advice established a physician-patient relationship. The answer involves an understanding of the physician-patient relationship in our information-based world. The lawsuit hinges on whether the referral to a chat group constitutes the practice of medicine. If the referral is not determined to be a form of medical practice, then such activity cannot form the basis for creating a physician-patient relationship.

To determine if a given activity is medical practice, one must look at the laws of each jurisdiction. The laws may vary from state to state. For example, in Virginia there is a generic statute that defines the practice of medicine as “the prevention, diagnosis and treatment of human physical or mental ailments, conditions, diseases, pain or infirmities by any means or method.” Maryland law goes further and articulates a list of elements to characterize the practice of medicine, stating that the practice of medicine includes “diagnosing, healing, treating, preventing and prescribing.”

There are very few states that apply this concept to telemedicine, the practice of medicine via the web. In Arizona, a telemedicine law defines this area as “the practice of health care delivery, diagnosis, consultation, treatment, transfer of medical data and education through interactive audio, video or data communications.” In those states where either statutory or boards of medicine examiner regulations exist, the question that must always be asked is whether the electronic activity in question relates to treatment or diagnosis.

Dr D referred his patient to a chat group. Undoubtedly, recommendations from members of the chat group are outside the bounds of organized medicine. Whether the referral would be outside the practice of medicine would depend on the intent behind Dr D’s referral. This will be determined by a court of law.

“"To determine if [an] activity is medical practice, look at laws of each jurisdiction.”
Examining Eyebrows

by ZOE DIANA DRAELOS, MD

Draelos is a consulting professor of dermatology at Duke University School of Medicine in Durham, North Carolina, and chief medical editor of Dermatology Times®.

Q: **Is microblading of the eyebrows safe?**

Microblading has become very popular for women with thinning eyebrows and men who also desire increased eyebrow thickness. Microblading is basically a superficial eyebrow area tattoo. The tattoo ink color is selected and blended to match hair color, then small cuts are made in the eyebrow area to mimic hairs. The pigment is pushed into the cuts to create a semipermanent tattoo. Microblading is designed to last 1 to 3 years, but most women require a yearly touch-up. Some of the tattoo ink is removed with scabbing that follows the procedure, which may necessitate a touch-up shortly after the initial procedure. With time, additional tattoo ink will become phagocytized by white blood cells and transported to lymph nodes, accounting for pigment fading.

It is critical that no water contact the freshly microbladed area for 1 week. This is because washing and water can remove the pigment that was superficially deposited in the skin until healing occurs. Once the skin has healed, the pigment is trapped in the skin. Avoiding water contact includes not only washing but also sweating and swimming.

Microblading has largely replaced eyebrow tattooing because the small cuts resemble hairs better than a solid tattooed line. Microblading is also not permanent, allowing for changes in the eyebrow architecture with aging. Loss of subcutaneous fat on the forehead results in lowering of the eyebrow area.

Q: **How should eyebrows be shaped?**

There are many different opinions on the optimal female eyebrow. Basically, eyebrows should be shaped by the female patient to frame the eye in the most attractive manner possible. I generally give patients who desire eyebrow assistance, for either too much or too little growth, the following 3 points. (I tell them to get a pen to use as a straight line for identification of facial landmarks.)

1. The eyebrow should start at a point defined by a line drawn from the corner of the nose to the inner canthus.
2. The eyebrow should arch at a point defined by a line drawn from the corner of the nose to the midpupil.
3. The eyebrow should end at a point defined by a line drawn from the corner of the nose to the lateral canthus.

Eyebrows that follow these ideal proportions, laid out originally by the ancient Greeks, are appropriate for all sizes and ethnicities of female faces. In contrast, the male face is characterized by a flattened eyebrow without the female arch.

Q: **What is the safest way to groom unruly eyebrows?**

One of the reasons mature women undergo microblading is because eyebrow growth no longer occurs due to overplucking. If a woman heavily plucks her eyebrows to achieve the Greta Garbo look, eventually traumatic plucking will result in failure of the eyebrow hairs to grow. Most eyebrow hair removal methods involve some type of potential trauma to the hair follicle. Threading, waxing, and tweezing all yank the hair from the follicle. Gentle removal of unwanted eyebrow hairs is very important. Using a good pair of tweezers and exerting firm, steady pressure until the hair is epilated is important. Do not yank or aggressively pull the hair. It is hard for young female patients to imagine a day when their eyebrows will not grow; however, this day will come even for those with bushy eyebrows. Moderation in plucking is important. Tell female patients to pluck only those hairs that they would never want to regrow at any time in their life.

Q: **What is microblading?**

Microblading has largely replaced eyebrow tattooing because the small cuts resemble hairs better than a solid tattooed line. Microblading can re-create the lateral eyebrow in an artistic manner in the hands of an excellent technician.

The biggest challenge to microblading is finding a skilled technician who has the same vision of the patient’s eyebrows as the patient. I recommend patients take a younger picture of themselves to the salon to show the technician how to re-create the desired eyebrow. It is best to re-create the youthful eyebrow of the patient rather than try to create eyebrows randomly selected by the patient from a magazine picture. Asking about friends’ experiences and getting recommendations from others who have undergone the procedure is the best way to ensure an attractive result. Microblading costs between $500 and $1200, depending on the location and reputation of the salon.

Q: **Is microblading of the eyebrows safe?**

Microblading has become very popular for women with thinning eyebrows and men who also desire increased eyebrow thickness. Microblading is basically a superficial eyebrow area tattoo. The tattoo ink color is selected and blended to match hair color, then small cuts are made in the eyebrow area to mimic hairs. The pigment is trapped in the skin. Avoiding water contact includes not only washing but also sweating and swimming.

Microblading has largely replaced eyebrow tattooing because the small cuts resemble hairs better than a solid tattooed line. Microblading is also not permanent, allowing for changes in the eyebrow architecture with aging. Loss of subcutaneous fat on the forehead results in lowering of the eyebrow area. Loss of subcutaneous fat on the forehead results in lowering of the eyebrow area with aging. Loss of subcutaneous fat on the forehead results in lowering of the eyebrow area with aging. Loss of subcutaneous fat on the forehead results in lowering of the eyebrow area with aging. Loss of subcutaneous fat on the forehead results in lowering of the eyebrow area with aging. Loss of subcutaneous fat on the forehead results in lowering of the eyebrow area with aging. Loss of subcutaneous fat on the forehead results in lowering of the eyebrow area with aging. Loss of subcutaneous fat on the forehead results in lowering of the eyebrow area with aging. 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Loss of subcutaneous fat on the forehead results in lowering of the eyebrow area with aging.
**F**indings of a retrospective review of pediatric patients add to existing evidence suggesting a role for dupilumab (Dupixent; Sanofi/Regeneron Pharmaceuticals, Inc) as a systemic treatment for severe and refractory alopecia areata (AA).

In a letter published in the *Journal of the American Academy of Dermatology*, Leslie Castelo-Soccio, MD, PhD, reported on 16 children with coexisting atopic dermatitis (AD) and AA who were receiving subcutaneous dupilumab 300 mg every 2 weeks. Four children also had concurrent asthma.

Dupilumab was well tolerated and appeared safe in this small series of patients. The only adverse events were mild injection-site reactions.

Responses of patients with AA after starting dupilumab varied. Improvement occurred in 4 of 6 patients with flaring/active AA, and hair regrowth was seen in 1 additional patient. Six patients maintained hair regrowth. Among patients who experienced benefit, the Severity of Alopecia Tool (SALT) score improved by an average of 33.3 after 12 months.

“A single center trial [NCT03359356] at the Icahn School of Medicine at Mount Sinai led by Emma Guttman-Yassky, MD, PhD, investigating dupilumab for treating AA in adults with and without concomitant AD has been completed, and the results should be available soon,” Castelo-Soccio explained.

“Dupilumab was being used more broadly at our center for treating children with severe AD, and anecdotally, I had noticed hair regrowth and reduction in flares among patients who also had AA,” Castelo-Soccio noted. “I undertook this retrospective review to get a clearer idea of how AA was responding.”

**TREATMENT RATIONALE**

Interest in dupilumab as a treatment for AA and an explanation for its possible benefit is supported by genome-wide association studies investigating susceptibility loci for AA that showed an IL-13 signature in some patients.

“Dupilumab could control the inflammatory response in AA and help with AA flares because it blocks the IL-13 signaling pathway by binding to the IL-4Rα subunit shared by the IL-4 and IL-13 receptor complexes,” Castelo-Soccio explained.

“Dupilumab was being used more broadly at our center for treating children with severe AD, and anecdotally, I had noticed hair regrowth and reduction in flares among patients who also had AA,” Castelo-Soccio noted. “I undertook this retrospective review to get a clearer idea of how AA was responding.”

**DATA DETAILS**

Among the 16 patients included in the review, the duration of AA prior to starting dupilumab ranged from less than 1 year to 11 years. Median number of prior therapies for AA was 4, and 8 children were on 1 or more additional therapies while being treated with dupilumab.

Types of AA among the 16 children included universalis (n = 7), ophiasis (n = 5), and patchy (n = 4). The AA was active in 6 patients. SALT scores at dupilumab initiation ranged from 0 to 100. The 2 patients with active disease who did not respond to dupilumab had SALT scores of 100 when starting dupilumab.

In 4 patients, AA worsened during the first 1 to 2 months after starting dupilumab, but it improved with time in the 2 patients who had further follow-up—and both patients had a SALT score of 0 at 12 months after starting dupilumab. Two patients with SALT scores of 0 when starting dupilumab were already receiving tofacitinib and able to undergo dose reduction of the Janus kinase inhibitor without increased hair loss.

Exploring potential characteristics associated with a better response, Castelo-Soccio observed that all the patients who improved had moderate to severe AD when starting dupilumab. Compared with the nonresponders, the responders had a lower median age at AD diagnosis (6 years vs 13 years) and a longer median duration of AD (6 years vs 1 year).

“A previous report also found that patients whose AA responded to dupilumab had more severe and long-standing histories of AD,” Castelo-Soccio said.

**more ONLINE**

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Patients with adult female acne (AFA) often have their quality of life (QOL) negatively affected by the condition. To overcome this, AFA requires aggressive treatment, according to a recent review. Specifically, the review’s authors recommend adopting a holistic approach that addresses lifestyle-related factors and use of antiandrogenic treatments whenever possible.1

By improving their understanding of AFA, dermatologists have the power to reduce its substantial impact on QOL, said study coauthor Marco Alexandre Dias da Rocha, MD, PhD, a volunteer professor of dermatology at the Universidade Federal De São Paulo in Brazil. “These patients experience a huge negative impact on quality of life, even with mild disease,” Dias da Rocha told Dermatology Times.2 “It’s not about the number of lesions, the grade, or the pustules and nodules.”

Teensagers with acne typically know many peers with pimples. However, according to Dias da Rocha, adult women with acne often feel alone in their struggles and wonder why they have acne later in life. Because AFA presents on the face, often along the bottom third, it can cause problems when applying makeup, as well as ongoing psychological challenges relating to self-esteem. Women with AFA may experience difficulties in romantic relationships, professional situations, and socializing with friends, he added. They commonly experience depression and anxiety.

Most women with acne do not have hormonal problems such as polycystic ovary syndrome (PCOS) or adrenal disease. According to Dias da Rocha, the problem resides within the sebaceous glands, which can produce testosterone from cholesterol and dehydroepiandrosterone.

WOMEN WITH ACNE CONTINUES ON PAGE 12
Adolescent acne typically stops when the innate immune system restores balance within the sebaceous glands. But in some of the adult female population, the immune system is overactivated. It never stops.”

Marco Alexandre Dias da Rocha, MD, PhD, São Paulo, Brazil.

Women With Acne

Peripheral androgen production fuels the lengthy duration of AFA, he added. “Adolescent acne typically stops when the innate immune system restores balance within the sebaceous glands,” Dias da Rocha said. “But in some of the adult female population, the immune system is overactivated. It never stops.”

He recommended that dermatologists talk to women with adult acne about the need for patience in dealing with the chronic, often relapsing nature of AFA. Study authors added that lesion-reduction and maintenance phases of treatment are equally important in this population.

“I don’t believe antibiotics are a great way to treat these patients because we know we have to use these drugs for a long time and we have bacterial resistance problems with the microbe,” Dias da Rocha said. Regarding topical antibiotics, the authors wrote that it remains unclear whether sarecycline (Sensara; Paratek and Almirall) provides better efficacy and safety than older tetracycline antibiotics. However, its narrow spectrum of action may reduce resistance potential. As with older tetracyclines, it is contraindicated in women who are pregnant, breastfeeding, or attempting conception, they pointed out.

Hormonal treatments block or reduce sebaceous gland function, interrupting the production of sebum. The authors recommended considering androgen blockers such as spironolactone. “We hope to use the new topical androgen blocker clascoterone, combined with different topical drugs, to better treat these patients,” Dias da Rocha said. Combining clascoterone (Winlevi; Cassiopea) with spironolactone may allow for lower spironolactone dosing, he noted. Switching to a topical androgen blocker such as clascoterone in the morning and retinoids in evening also may improve outcomes, Dias da Rocha added. “There are many possibilities with this new type of drug to block androgen receptors in sebaceous glands.”

Combined oral contraceptives (COCs) have been shown to block the androgenic system, thereby reducing inflammatory and noninflammatory lesion counts. In 1 meta-analysis, COCs proved as effective as oral antibiotics during 6 months of treatment. Among COC formulations, combining ethinyl estradiol with progesterin works best in AFA. Nonsteroidal androgen receptor (AR) blockers include flutamide, enzalutamide, and bicalutamide. With a better safety profile than flutamide, bicalutamide has been used off label to treat acne and other manifestations of PCOS successfully, even at low doses, the authors wrote.

“It’s important to understand that these drugs can be used 1 or 2 times weekly because they have a long half-life in the plasma compared with spironolactone,” Dias da Rocha said. “Maybe we can use bicalutamide [Casodex; AstraZeneca] twice weekly to reduce adult female acne because it is such a powerful androgen blocker.” Bicalutamide does not cause menstrual dysfunction, which can be associated with spironolactone use, he added.

Understanding AFA also requires appreciating the influence of environmental and socioeconomic factors. Pollution, stress, loss of sleep, sedentary lifestyle, poor eating habits, and misuse of cosmetics and skin care products can all trigger or aggravate AFA, he said.

Conversely, the authors wrote, nonprescription interventions such as sun protection, gentle skin care, and appropriately selected makeup should be considered part of the therapeutic regimen for AFA.

“Skin care in acne is important [in general],” Dias da Rocha said. “But in the adult female population, it’s one of the most important factors.”

Because ceramide levels in the skin decrease with age, women with AFA may have very sensitive skin. “When you have low ceramides, the skin cannot hold water,” Dias da Rocha pointed out. Without adjunctive skin care, treating adult female acne patients with topical agents such as retinoids, azelaic acid, and dapson can result in irritation, eczema, and/or dermatitis. “[Patients] need to use gentle cleansers, oil-free moisturizers, and oil-free sun protection to prevent post-inflammatory hyperpigmentation,” Dias da Rocha advised.

Additionally, Dias da Rocha believes diet can exert powerful therapeutic effects. In this regard, consensus favors a low glycemic index diet combined with oral probiotics, the latter of which help modulate the immune system.

Dias da Rocha said additional research is needed in many areas, including comparisons of drugs for AFA in different populations, such as women with and without PCOS and comparisons of spironolactone against spironolactone plus topical drugs. “We have a lot of work to understand more about this population. We are just starting to gain the knowledge to better treat adult female acne,” he noted.

Disclosures

Dias da Rocha reported no relevant or financial disclosures.

References


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Pediatric AD from page 1

The current and future availability of more targeted therapy for AD, however, promises to lower the threshold for starting systemic therapy and improving quality of life for pediatric patients with moderate to severe disease, said Amy S. Paller, MD, Walter J. Hamlin Professor and chair of the Department of Dermatology and professor of pediatrics at Northwestern University Feinberg School of Medicine in Chicago, Illinois (Table).

“With its safety and lack of need for laboratory monitoring, dupilumab has revolutionized systemic treatment for moderate to severe AD in pediatric patients aged 6 years and older, and we can expect more advances in the future. Dupilumab is now being studied in children as young as 6 months of age, and pediatric trials are ongoing evaluating other biologics as well as oral Janus kinase [JAK] inhibitors,” Paller said.

She added: “In the future, identification of biomarkers, including those that can be obtained noninvasively by tape stripping, may help predict the course of AD and its response to systemic medications and improve our therapeutic decision-making capabilities. In addition, pediatric-specific guidelines on AD reflecting new data are being developed to provide evidence-based recommendations. I expect these guidelines will be available within the next year.”

The algorithm for treatment of moderate to severe AD follows a step-wise approach that begins with topical anti-inflammatory medications and basic management strategies. If the AD is not responding, consideration should be given to nonadherence, misdiagnosis, the need to treat a secondary infection, or presence of a contact allergy or another allergic trigger, as well as intensity of topical treatment.

“We always want to ensure that topical therapy is optimized before considering commitment to a biologic,” Paller told Dermatology Times®. “I have seen children with moderate to severe AD who dramatically improved with appropriate topical therapy. But there are risks associated with using potent topical steroids chronically, especially if being applied in more sensitive areas. If appropriate, use topical steroids coupled with nonsteroidal topical alternatives, and if it does not turn the situation around, dupilumab may be considered to offer a safer option than chronic application of large amounts of a more potent topical steroid, especially with only partial improvement.”

When systemic therapy becomes indicated for AD in pediatric patients, the traditional options have been cyclosporine A, methotrexate, mycophenolate mofetil, and azathioprine.

“Outside the realm of pediatric dermatologists, treatment with systemic steroids remains the most commonly used approach, especially by primary care physicians. However, systemic steroids are too toxic for continued use in pediatric patients, and AD often rebounds once steroids are discontinued, so that use of systemic steroids in children with AD should be extremely restricted,” Paller said.

Cyclosporine has been the favored immunosuppressant systemic treatment for AD among pediatric dermatologists because of its rapid onset, and it remains the first option for children who cannot be on dupilumab (Dupixent; Sanofi Genzyme/Regeneron Pharmaceuticals) for any reason. However, cyclosporine is generally used for just 3 to 4 months to achieve control, and then patients are transitioned to a less toxic agent, such as methotrexate, using an overlap period.

Offering advice for starting dupilumab, Paller suggested giving any required live immunizations at least 1 month before starting the biologic.

“Is it not known that receiving a live immunization while on the biologic is unsafe, and theoretically it is not, because dupilumab only blocks the Th2 signaling pathway. Nevertheless, the safety of live immunization while taking dupilumab has not been formally tested,” Paller said.

She called attention to the recommended age- and weight-based dosing schemes for dupilumab and cautioned against abruptly stopping any existing systemic treatment. With regard to the latter, Paller shared her practice of continuing any existing systemic agent (unless there is an adverse event) for 1 month and then reducing the dose by half for 1 month before discontinuation.

Topical steroids should be continued during the transition and until no longer needed to augment the effects of dupilumab. More potent topical steroids can be added for a short course as well to manage flares that may occur while the patient is on dupilumab, she said.

Not all patients respond to dupilumab, and although evidence of improvement is usually seen by 2 months in those who are likely to benefit from the biologic, dupilumab should be continued for at least 4 months before it is deemed ineffective. “We can see improvement in some chil-

### TABLE

**WHAT’S IN THE PIPELINE**

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AD, atopic dermatitis

Source: Compiled by Dermatology Times®.
Pregnancy outcomes in patients exposed to dupilumab while pregnant are being monitored. To date there is no evidence of risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes, but topical treatment is largely preferred during pregnancy, Paller said.

Two IL-13 inhibitors are being developed as treatment for AD in children and/or adolescents. Tralokinumab (LEO Pharma) has completed studies enrolling adolescent patients and is being investigated in a trial of children 6 years and older. Lebrikizumab (LY3650150; Eli Lilly and Company/Dermira, Inc) is being evaluated in ongoing trials including children 12 years and older. Studies to date suggest the same safety profile as dupilumab.

Nemolizumab (CD14152; Galderma), a monoclonal antibody targeting the receptor of IL-31, is now being studied in pediatric patients 12 years and older.

“IL-31 is an itch-specific cytokine, and in studies of adults, nemolizumab had an early and dramatic effect on itch. It appears, however, that nemolizumab should be coupled with a topical corticosteroid to achieve the best effect on skin inflammation,” Paller said.

Three oral JAK inhibitors are also being investigated as treatment for AD in pediatric patients: abrocitinib (PF-04965842; Pfizer), which has completed a trial in patients 12 years and older; upadacitinib (Rinvoq; AbbVie Inc), which has completed a trial in the same age group and is now being studied in patients 6 months and older; and baricitinib (Olumiant; Eli Lilly and Incyte), which is in a study of adolescents 12 years and older.

Paller said available data from studies of the JAK inhibitors suggest high efficacy and a rapid potent effect on itch. The JAK inhibitors are also attractive for their administration schedule and route—once daily by mouth—and because they are rapidly cleared from the body, AEs may be the limiting factor for their use. The most common AEs in clinical trials have been nausea, headache, and acne.

“The opportunity to easily start and stop the JAK inhibitors suggests they may have a role for controlling AD flares or seasonal involvement,” Paller said.

“It remains to be seen if there are differences in [adverse] effect profiles among the JAK inhibitors that will favor using any one of these agents in the pediatric population. The good news is that there are no signals for malignancy, thromboembolism, or high-risk infections with their administration in the AD trials, although it remains to be seen what risks might emerge post approval with expanded and longer-term use,” Paller said.

Disclosures
Paller said she is an investigator and/or consultant for companies that market and/or are developing systemic treatments for AD.
At Incyte, we’re committed to improving patients’ lives through meaningful science. That’s why we’re researching and developing innovative solutions for a number of dermatologic conditions, including atopic dermatitis and vitiligo.

Learn more at Incyte.com/derm.
FDA Approves Secukinumab for Pediatric Patients

Novartis’ Cosentyx can be used for children and adolescents with moderate to severe plaque psoriasis.

LINDA STOCUM | Assistant Editor

The FDA has approved secukinumab (Cosentyx; Novartis) for the treatment of moderate to severe plaque psoriasis in patients 6 years or older who are also candidates for systemic therapy or phototherapy.

Secukinumab was approved as a treatment for adults in 2015. There are 5 years of data showing the long-term efficacy and a consistent safety profile for treatment of moderate to severe plaque psoriasis, psoriatic arthritis, and ankylosing spondylitis among adult patients.

“Treating moderate to severe plaque psoriasis in children can be complicated; we need to balance the ability of a treatment to provide symptom relief while considering the safety profile as the top priority,” said John Browning, MD, MBA, FAAD, FAAP, clinical trial investigator and an adjunct associate professor of pediatrics and dermatology at the University of Texas Health, in San Antonio and associate professor at Baylor College of Medicine in Houston, Texas.

“In the pediatric pivotal study, the majority of patients treated with Cosentyx were able to achieve clear or almost clear skin with a safety profile consistent with previous clinical trials in adults,” he said. “Due to the systemic nature of the disease, Cosentyx is a welcome addition as a treatment option for families dealing with this challenging condition.”

The approved dosing for secukinumab is 75 mg or 150 mg depending on patient weight. It is administered by skin injection every 4 weeks after initial dose. Once trained by the physician and given proper counseling, an adult caregiver can administer dosage.

“The impact of psoriasis on children is much deeper than skin and can potentially lead to life course impairment. [The] FDA approval further demonstrates our commitment to reimagine medicine for patients with pediatric plaque psoriasis,” said Angelika Jahreis, MD, PhD, global head of Novartis’ Immunology, Hepatology & Dermatology Development Unit in Cambridge, Massachusetts. “With more than 400,000 patients treated in more than 100 countries worldwide,
People often think of psoriasis as being an adult-only skin disease but, it’s really a pediatric disease as well. Often there can be facial involvement, scalp involvement, or inverse involvement, and it can be misdiagnosed as atopic dermatitis or contact dermatitis.”

John Browning, MD, MBA, PAAD, FAAP, Houston, Texas

we continue to build on the established safety and efficacy profile of Cosentyx, with plans to expand to 10 indications over the next 10 years.”

The approval is based on 2 phase 3 studies that demonstrated that both low and high doses of secukinumab were effective and safe.

In the first study (NCT02474069), which was a 52-week randomized, double-blind, placebo- and active-controlled trial, data showed secukinumab reduced psoriasis severity at week 12 compared with placebo. Dosing was determined by patient weight, with patients less than 50 kg receiving a 75-mg dose and those weighing more than 50 kg receiving a 150-mg dose. Psoriasis Area Severity Index (PASI) 75 response was 55% of patients dosed at 75 mg vs 10% placebo and 86% of patients dosed at 150 mg vs 19% placebo. Overall, 70% of secukinumab patients achieved PASI 75, compared with 15% of placebo patients. The Investigator’s Global Assessment (IGA) modified 2011 skin response showed that 32% of the 75-mg treatment arm and 81% of the 150-mg treatment arm achieved IGA 0/1.1

For the second phase 3 study (NCT02471144)—a randomized open-label, 208-week trial—safety was the primary end point. The study consisted of 84 participants 6 years or older with moderate to severe plaque psoriasis. The main adverse events from the studies were injection site or hypersensitivity.

There was no difference between patient reaction to treatment in age, gender, affected body surface area (BSA), race, or presence of comorbidities.

“People often think of psoriasis as being an adult-only skin disease, but it’s really a pediatric disease as well,” Browning told Dermatology Times 3. “Often there can be facial involvement, scalp involvement, or inverse involvement, and it can be misdiagnosed as atopic dermatitis or contact dermatitis.”

This gap in the understanding spurred investigators to further look into ways to help pediatric patients with psoriasis.

A phase 3 trial (NCT03668613) is collecting data up to 252 weeks to study the long-term safety and efficacy of secukinumab, according to Browning. Of the 156 patients from the first study (NCT02474069), 151 went on to participate in the long-term trial. The safety profile for pediatric patients is consistent with that of adult patients. Results from the trial will not be available for approximately 4 to 5 years.

There are treatments for pediatric psoriasis, such as topical creams and ointments, that are impractical for patients with an affected BSA of more than 10%. When this situation arises, systemic therapies and phototherapy are other options, Browning said.

“Phototherapy is very safe, but it involves coming to the office 3 times a week for months,” Browning said. “A lot of kids simply can’t do that [because] they have to go to school,” said Mark Lebwohl, MD, dean for clinical therapeutics at the Kimberly and Eric J. Waldman Department of Dermatology, Icahn School of Medicine at Mount Sinai, in New York, New York, and chairman emeritus of the medical board of the National Psoriasis Foundation, headquartered in Portland, Oregon.

Clinicians often have to decide between oral treatments and injectables. According to Lebwohl, it is a misconception that injections are more dangerous than pills.

Other injectable treatments for pediatric patients with psoriasis include etanercept (Enbrel; Amgen), ustekinumab (Stelara; Janssen Biotech), and ixekizumab (Taltz; Eli Lilly and Company).

“The other objection to injection treatment is the possible pain for the patient. According to Lebwohl, secukinumab injection does not cause pain because is administered with a pen. This treatment does not need to be used in combination with another and has category B status with the FDA.

“Living with psoriasis is challenging and can be highly stressful for children and adolescents,” said Randy Beranek, president and CEO of the National Psoriasis Foundation. “Having expanded treatment options for this patient population is a step in the right direction to help reduce the burden of plaque psoriasis.”

There was significant improvement in the quality-of-life index in patients who were treated with secukinumab. Psoriasis can prevent pediatric patients from participating in sports, social interaction, and school activities. It’s important for dermatologists to recognize the signs of psoriasis such as cracked fingertips, chronic scaly scalps, and pain in folds of the skin, according to Browning.

“I still remember when I was in school, [there was] a kid probably [with] retrospective ichthyosis, and [I was] thinking that the kid was contagious and knowing that other kids thought so, too. That’s what happens to [individuals with] psoriasis. They’re not treated well,” Lebwohl said.

There is potential for more investigation into length of remission or relapse for patients, as this has not yet been studied.

Disclosures Browning is consultant and investigator for Novartis.


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What you need to know about teledermatology

Used strategically, teledermatology can put new life into your practice

By Dhaval Bhanusali, MD, Shirley Chi, MD, Jeffrey Fromowitz, MD, Mark Kaufmann, MD, Ted Lain, MD, Angelo Landriscina, MD, Rebecca Smith, MD, and Christine Stanko, MD

**CLINICAL PEARLS**
- Fueled by technologic advances, teledermatology has seen steady growth and patient acceptance
- Teledermatology offers an added income stream, flexibility, convenience, and a vehicle for education
- Teledermatology consultations can occur in real time or (more commonly) asynchronously
- Top indications for teledermatology include acne, atopic dermatitis, rosacea, psoriasis, and hair loss
- User-friendly teledermatology platforms and networks have simplified the logistics of this modality

Teledermatology—dermatologic services provided at a distance from the patient—has evolved considerably over the past decade and has taken a further leap forward during the COVID-19 pandemic. As one of the most visually dependent medical specialties, dermatology lends itself especially well to this style of service delivery.

Technologic innovations have enabled clinicians to care for patients requiring skin expertise efficiently and cost-effectively. Patient receptivity has evolved with the technology, and today’s patients place a high value on connectivity. Employers have likewise embraced the sea change: in a 2017 survey conducted by the National Business Group on Health, 96% of large employers stated they expected to reimburse telehealth services within 2 years.

These factors, combined with the rising rates of common skin conditions such as atopic dermatitis and psoriasis, are driving a steady growth in the teledermatology market. Valued at $USD 4.8 billion in 2019, the market is expected to climb to $USD 44 billion in 2027. Teledermatology now boasts its own guidelines and is even being incorporated into dermatology residency programs.

The adoption rate among derms triples, online consultations reached 15% total

### Teledermatology in the US: facts & figures
- Between 2016 and 2020, the proportion of US dermatologists providing telehealth consultations tripled (from 15 to 45%)
- In 2020, the proportion of dermatology consultations that occurred via teledermatology more than doubled compared to the previous year (12-15% vs 5-6%)
- The top indications treated via teledermatology are acne (35-40%), atopic dermatitis (20-23%), rosacea (16-18%), psoriasis (11-13%), and hair loss (8-10%)
- In 2019-20, the average price of a teledermatology consultation was $USD 65
How teledermatology fits into clinical practice

Teledermatology offers a new and diversified income stream to today’s practicing dermatologist. Benefits also include flexibility, convenience, ability to serve remote patients, and limiting unnecessary contact in the post-pandemic world. The average waiting time for a traditional dermatology consultation has climbed up to over 30 days, and teledermatology substantially reduces the time to dermatology consultations and referrals. Clinicians can use teledermatology as a tool for triaging patients, allowing them to make the most productive use of their office time. As Villanova, Pennsylvania dermatologist Christine Stanko reports, “after we identify acne patients and isotretinoin refills as ideal indications for virtual visits, it frees up more time to see patients who actually need to be in the office.”

Teledermatology has limitations, of course. It is difficult to conduct full body scans or visualize hair-bearing areas via videoconference. The quality of the image may limit the ability to accurately visualize and diagnose textured or pigmented lesions (although teledermatology has been successfully used to screen lesions for skin cancer1). Most clinicians agree that teledermatology comes into its own in the diagnosis and management of common, chronic skin conditions such as acne, rosacea, atopic dermatitis, psoriasis, and keratosis pilaris—conditions that account the bulk of many dermatologic consults. According to clinicians who use the teledermatology platform SkyMD, as many as 2 out of 3 patients can be fully managed via teledermatology.2

South Florida dermatologist Mark Kaufmann expects more and more patients with chronic skin disorders to embrace teledermatology. “The pandemic has forced us all to interact remotely, and we’ve discovered that in some situations it works a lot better than expected,” he says. Realizing how convenient and effective it is, “patients won’t want to go back to the old way.”

Teaching tool

Beyond its usefulness as a consulting modality, teledermatology can also facilitate education. For example, patients connected to a teledermatology platform can receive educational messages about their condition (such as a video on common eczema triggers and ev-3

The proliferation of direct-to-consumer services has forced us all to interact remotely, and we’ve discovered that in some situations it works a lot better than expected,” he says. Realizing how convenient and effective it is, “patients won’t want to go back to the old way.”

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Quick Takes

Dermoscopy alone can help identify specific findings for papulopustular rosacea but cannot diagnose Demodex folliculorum proliferation without a secondary method.

The tool can be used in identifying early-stage papulopustular rosacea.

Specific dermoscopic findings of mild papulopustular rosacea include tiny papules and pustules; polygonal vessels, or vascular polygons; yellow dots, or dilated follicular infundibula filled with keratotic material and/or sebum; and follicular scales.

Dermoscopy Plays Role in Demodex Diagnosis

Results need confirmation by other diagnostic methods.

LISETTE HILTON | Staff Correspondent

Dermoscopy, by itself, is not a strong enough tool for diagnosing Demodex folliculorum mite proliferation in papulopustular rosacea, according to the results of a study recently published in Clinical and Experimental Dermatology.1

Rosacea is estimated to affect more than 16 million Americans, according to the National Rosacea Society.2 And mask wearing during the COVID-19 pandemic appears to have worsened rosacea in untreated patients, according to findings from a study published in Dermatologic Therapy.3

“Although the diagnosis of rosacea is mainly clinical, dermoscopy may contribute to the diagnostic process,” study author Ilaria Trave, MD, a dermatologist at the University of Genoa, Ospedale Policlínico San Martino in Italy, told Dermatology Times.4 “Moreover, dermoscopic indicators of Demodex mite proliferation, such as Demodex tails—gelatinous, whitish creamy threads, 1 to 3 mm in length—and Demodex follicular openings—dilated follicular openings containing round, amorphic, grayish light-brown plugs surrounded by an erythematous halo—are usually evaluated in primary demodicosis, such as pityriasis folliculorum, and are less studied in papulopustular rosacea.”

Trave and colleagues prospectively studied dermoscopy images and skin surface biopsies in 60 Caucasian male and female patients with papulopustular rosacea with almost clear, mild, and moderate disease.

The investigators report that Demodex folliculorum mites were found in 20 of the 60 patients with standardized skin surface biopsy. But patients with the mites were no more likely to have more Demodex tails or follicular openings than the patients without. Compared with standardized skin surface biopsy, dermoscopy showed 50% sensitivity and 77.5% specificity for Demodex mitre infestation diagnoses.

“This study shows that papulopustular rosacea presents specific dermoscopic findings and that some of them, such as Demodex follicular openings, follicular scales, follicular pustules, and honeycomb pigment pattern, are more frequent in moderate than almost clear rosacea,” Trave noted.

“Regarding demodicosis in papulopustular rosacea, we show that dermoscopy alone is not a strong enough method for diagnosis and that it needs to be confirmed by means of a standardized skin surface biopsy or reflectance confocal microscopy.”

Standardized skin surface biopsy is a sampling method in which 1 cm² of the superficial layer of the stratum corneum and its follicular content is obtained for analysis. These samples were examined with an optical microscope (10 and 40 magnifications). Samples with 5 Demodex/cm² or more are considered Demodex positive, according to Trave.

“Dermoscopy might be a valuable tool for dermatologists in case of doubtful diagnoses of facial dermatitis,” the authors wrote.

The absence of a control group and exclusion of severe papulopustular rosacea cases are potential study limitations.

Disclosure
Trave reports no conflicts of interest.

References
Smart Skin Care

Top Surgery Protocol

- DAXI AND HA FILLER STUDY DATA
- TREATING POSTPARTUM SKIN LAXITY
- MYELLEVATE FACIAL TIGHTENING
- REGENERATIVE SKIN CARE REALITIES
- BUILDING A SUCCESSFUL SKIN CARE BRAND
- FACIAL HAIR TRANSPLANTS
All signs and data point to the fact that we are finally turning the corner on this horrible pandemic. Our practices have not only weathered the storm but most ultimately thrived. Stimulus money, vacation time, Zoom dysphoria, and other factors have certainly played a role. However, is this sustainable long term? Will there be new challenges ahead?

Most of our practices are small businesses, and the small business environment in our country is challenging for many reasons, such as COVID-19 compliance; difficulty in keeping and finding employees, given enhanced unemployment benefits; rising health care costs; rising material and supply costs; and the threat of an escalating tax burden.

Now it is time to be wise and prudent and consider many dilemmas:
1. How do we ramp up staffing without a significant effect on our bottom line?
2. How can we be wise and prudent in future buying decisions without exceeding our cash flow?
3. How do we change our message regarding team safety?
4. Are there new services we should consider?
5. Should we be focusing on our younger patients, people of color, or people of diverse gender?
6. Will we be working more and taking home less?

Just as many of our colleagues in other fields were acquired by hospital groups, we are finding that many of our own practices are being courted by private equity. Some practitioners are coming to the conclusion that the advantages of independence are not as clear as they once were.

How will that affect our industry, our societies, our conferences, and the way we practice in this new decade?

In the end, however, the strong will survive. Those that work the hardest and spend the most time will be rewarded. We have come to understand that the number of providers will continue to escalate, but we must also believe that the cream rises to the top. Those who offer patients the best care and the most consistent result will succeed. In today’s world, this is measured empirically rather than by clever marketing. Reviews are now perhaps the No. 1 reason many patients choose to come to us.

Practice management and effective marketing have risen to a new level of importance. The premier meetings spend as much time on teaching these topics as on making clinical presentations. It is crucial that we include our staff members in this new awakening.

We must also be mindful of the increasing threat of cybersecurity breaches and related issues. I hear of more and more practitioners who have been affected by these criminals, and some have even been forced to pay large ransoms to secure their data and photos. To combat this, we must learn from experts and help one another. We must inform and train our respective staff members. Global Aesthetics Conference will make this an area of focus in November.

We must insist that our societies be proactive rather than reactive. Societies must expand their role and provide tangible member benefits or they, too, will continue to lose momentum and strength.

Running a Small Business

FROM OUR MEDICAL ADVISER

Randy Waldman
a facial plastic surgeon in Lexington, Kentucky
Study Shows Longer-lasting Benefits of DAXI, HA Filler

Revance presents 4 AAD VMX posters examining phase 3 study data for DAXI and the impact of HA filler manufacturing technologies on HA chain degradation.

Joel Schlessinger, MD
Omaha, Nebraska

KATIE HOBBINS
Revance Therapeutics, an aesthetic biotechnology company, recently presented 4 abstracts highlighting the long-lasting effects of daxibotulinumtoxinA (DAXI) 3 months post treatment. The company presented the study data at the American Academy of Dermatology Virtual Meeting Experience (AAD VMX) 2021 in April. Three abstracts highlighted data from the phase 3 SAKURA-1 and SAKURA-2 trials (NCT03014622 and NCT03014635) of Revance’s investigational DAXI neurotoxin for injection to treat glabellar lines (GL).3 The findings included the elimination of GL with DAXI through a novel graphical representation of the entire distribution of GL severity ratings and changing scores used to depict patterns of efficacy over time.3

Pooled data revealed that 80% of participants treated with DAXI were rated as “none” at week 4, and 35% at week 12. Among patients rated “severe” at baseline, 68% and 24% were also rated as “none” at weeks 4 and 12, respectively. This represents a 3-point improvement from baseline with 90% of all patients achieving a 2-point or greater improvement from baseline to week 4.1

“The concept of a longer-lasting form of neurotoxin has always been one that is the holy grail,” says Joel Schlessinger, MD, a dermatologist and cosmetic surgeon in Omaha, Nebraska, who was involved in the studies of both DAXI and RHA filler (TEOSYAL RHA 2; Teoxane Laboratories). “With these data, it does seem that therapeutic benefit lasts well into the third month and remains active in a significant amount of the population at week 12.”

The second poster included data from a subgroup analysis of the efficacy, duration, and safety of DAXI injections among adult women across multiple SAKURA age cohorts.2 The proportion of patients who achieved none or mild GL per investigator assessment at week 4 were 97.2% (18-45 years), 96.3% (> 45-55), 96.9% (> 55), and 96.7% (≥ 65).2

The third poster showcased results from an evaluation of how repeated DAXI use could affect the progression of static or resting GL.3 “DAXI-treated [participants] showed substantial and progressive improvement in static GL with repeated treatment,” wrote the study authors.3 “The extended duration of therapeutic benefit observed with DAXI in dynamic GL provides a longer window of muscle hypoactivity, permitting an extended period for dermal remodeling to occur. This can potentially account for the progressive improvement in static GL observed over repeated DAXI treatments.”

“There are many trials now that are aimed at optimizing neurotoxins to conceivably maximize the ability to approach 24 weeks, but DAXI was the first to even consider it,” Schlessinger notes. “They have laid down the gauntlet in this arena, and it remains to be seen if they will come to market with a different package insert than other neurotoxins, but that would be a valuable marketing tool.”

Revance also presented a poster on the impact of hyaluronic acid (HA) filler manufacturing technologies on HA chain degradation.
The authors examined soluble HA (sHA) fraction chain length, along with the distribution in commercial filler products.

“The concept of sHA is one that bears investigation,” Schlessinger says. “This area is... particularly of note given the concerns about reactions from COVID-19 and the vaccinations for COVID-19. Patients are looking for a longer-lasting product, so these types of studies further elaborate on the options available, while adding to the science behind fillers.”

Investigators used 13 US-marketed fillers from 5 manufacturing technologies and size exclusion chromatography (SEC) to examine the mean molecular weight of sHA released from the final formulation per syringe, and fragment sizes (< 30 kDa, < 100 kDa, and < 250 kDa).

Investigators concluded that most products using high molecular weight HA undergo significant HA chain degradation during the manufacturing process.

“These data continue to underscore the innovation that drives Revance’s aesthetics portfolio, including our investigational neuromodulator product, daxibotulinumtoxinA for injection, and the RHA Collection, which was launched in September 2020,” noted Roman Rubio, senior vice president of clinical development at Revance, in a press release announcing the posters.

REFERENCES
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Postpartum Abdominal Laxity Combination Therapy

Combining microwave and microablative CO$_2$ laser treatment is both safe and effective for treating postpartum abdominal laxity.

Microwave and microablative CO$_2$ laser treatment is effective for postpartum abdominal laxity, according to findings of a 2020 study published in the *Journal of Cosmetic Dermatology*. Laxity can occur post pregnancy due to loss of muscle tone and abdominal elasticity, wrote study coauthors Paolo Bonan, MD, and Alice Verdelli, MD, of the Laser Cutaneous Cosmetic & Plastic Surgery Unit at Villa Donatello Clinic in Florence, Italy. The study's goal was to assess the efficacy of combined microwave and fractional microablative CO$_2$ laser treatment to improve these postpartum effects.

The investigators examined 15 women who were 18 years or older (median age, 38) and at least 12 months post delivery. The patients received microwave treatments (ONDA Coolwaves; Deka) to the abdomen once a month for 3 months followed by fractional microablative CO$_2$ laser (SmartXide2; Deka) 1 month later, for a total of 4 months of treatment.

Coolwaves, a patented microwave technology, reduces localized adiposities in the abdomen and other areas, according to Deka. It dissolves fat, tightens and contours the skin, and firms tissue. The technology is to be used in place of radiofrequency for tightening and skin toning, according to the company.

SmartXide2 uses a CO$_2$ fractional microablative system to cause a rapid tightening of the skin; it reduces blemishes and softens irregularities and scarring. The laser stimulates collagen production, making the skin look younger and plumper. This collagen production in turn helps prolong the treatment effects and gives more even results.

Patients were instructed to maintain the same eating and exercise habits prior to the treatments throughout the study. The investigators also did a follow-up of patients' eating habits and weight. They used

“Convenient and time-saving options for women in the postpartum phase are important, and with the variety of complex physiological changes in the skin during pregnancy, [we need] to have solutions.”

Jessica A. Shepherd, MD, MBA, Dallas, Texas
a patient satisfaction index, abdominal laxity score and measurements, and digital and 3D photography to assess the treatment’s effectiveness.

The investigators reported the overall mean circumference as 3.6 cm plus/minus 1.2 cm. Both physicians and patients reported great improvement in tightening and skin laxity, and striae distensae were also reduced. The investigators noted umbilicus repositioning following the treatment and reported that the procedure was well tolerated, with no adverse effects.

“This initial study confirms that the combined ONDA Coolwaves and SmartXide2 (microablative CO2 laser) treatment are safe and effective for the treatment of postpartum skin laxity and striae distensae,” the study authors wrote. “Thus, combined treatment could be a promising option for those patients who refuse surgical procedures in the rapidly growing demand for non-invasive aesthetic treatment.”

Jessica A. Shepherd, MD, MBA, an aesthetic gynecologist and CEO and founder of Sanctum Med + Wellness in Dallas, Texas, spoke with Aesthetic Authority™ as an independent commentator on the study. She says postpartum abdominal skin laxity is caused by a combination of genetics, hormonal changes, and weight gain. She adds that an increase in relaxin decreases adhesiveness between collagen fibers and that formation of ground substance creates striae in areas causing stretch marks and loose skin. Shepherd notes that even with weight loss through diet and exercise, factors such as genetics and number of pregnancies also affect abdominal skin laxity.

“Alternative therapies for skin tightening that do not require significant downtime or surgical intervention are important options to present to women,” Shepherd says.

Regarding the study, she notes that using this particular type of laser treatment not only tightened the skin but also improved the appearance of its texture. “The upgraded technology of the Coolwaves brings the energy to 3 times the efficiency and selectively targets subdermal fat,” she explains.

Shepherd emphasizes that although the study had a small population, the findings highlight the sustainable changes in the reduction of circumference and appearance of skin, which is appealing for women seeking marked changes in this area.

“Convenient and time-saving options for women in the postpartum phase are important, and with the variety of complex physiological changes in the skin during pregnancy, we need to have solutions,” she says. “This combined technology...seems promising and may create another innovative option that is safe and decreases the need for surgical intervention.”

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Female to Male Top Surgery Protocols

Mark Mandell-Brown, MD, details his treatment protocol for addressing female to male breast reduction surgically and through minimally invasive procedures.

Chest masculinization, also known as top surgery, is the most common operation performed for gender affirmation, according to the findings of a 2020 study published in Plastic and Reconstructive Surgery.1 Gender-affirming surgery can help transgender patients with gender dysphoria feel more comfortable in their bodies. In addition, results from a 2021 survey show that the surgery has been associated with decreased rates of mental health disorders and improved psychosocial function.2,3

Patient demand for female to male breast reduction is increasing, says cosmetic surgeon Mark Mandell-Brown, MD, who recently talked with Aesthetic Authority™ about treatment options, surgical protocols, and his experience with the procedure.4

“Realistically, we are reducing the breasts, and there are different ways of doing that,” says Mandell-Brown, president of the American Academy of Cosmetic Surgery and a triple-board-certified cosmetic surgeon at Mandell-Brown Plastic Surgery Center in Cincinnati, Ohio. “As a surgeon, you have to approach it in a stepwise fashion.”

Mandell-Brown often recommends liposuction as a stand-alone treatment for patients with small breasts—an A or B cup, potentially a small C—with no breast ptosis, or sagging.

“If the patient has a larger areola, we remove some of the areola in a circular fashion. We make 2 incisions, an outer circle and an inner circle, and remove the excess areola or breast skin. Then we close the outer and inner circle,” he says.

There are 3 categories of breast ptosis. The first category includes nipples that are on the breast fold level—when one puts a finger under the breast on the crease—with minimal sagging. The second category includes nipples that fall below that line. Nipples that point downward toward the ground are considered to be category 3 ptosis.

To address sagging, Mandell-Brown often uses Renuvion (Apyx Medical), which delivers helium plasma and radiofrequency energy to provide controlled coagulation and contraction of soft tissue. The small entry points and reduced pain result in shorter recovery times.
“We use Renuvion in combination with liposuction,” he says. “Often that will shrink the breast down, making it more compatible with a male breast.”

Whether using liposuction as monotherapy or combination therapy, Mandell-Brown says his goal is to use minimally invasive options when possible. These, for example, limit incisions to 2-mm openings on each breast.

When reducing larger breasts, he often uses a 2-step approach. The first step involves the previously discussed procedures for smaller breasts.

“We see how much the tissues contract,” Mandell-Brown says. “I would say 80% of patients are happy with [the initial stage].”

If patients are not yet satisfied, he fine-tunes results with either more liposuction or additional reduction around the areola in a circular fashion. Patients with very large breasts—a D cup or larger and class 3 ptosis—might be candidates for a “double incision” technique.

“A double incision technique is where we make an incision along that breast fold and then have the patient flex,” he explains. “The upper [flexed] portion shows you where the border of the pectoralis muscle is. You make a separate incision there and remove that tissue between the 2 horizontal lines.”

On men, the nipple/areola sits off to the outer third of the chest and is smaller compared to that of a cisgender woman.

“For the male, if you divide the collarbone into thirds, it should be between the middle and the outer third and should be just at the border of the pectoralis muscle,” Mandell-Brown says. “The nipple and areola should be about 2 cm wide as opposed to [that of] most females, which is about 4 cm wide.”

Mandell-Brown advises his breast surgery patients to avoid aspirin and acetaminophen, fish oil, and vitamin E, all of which promote bleeding. Nipple and areola numbness can occur temporarily but is rarely permanent when using a keyhole or periareolar technique. 

performing a free areola or nipple graft causes permanent numbness to the area, which Mandell-Brown prefers to avoid. “With the free areola or nipple graft, you are actually taking off the areola, setting it aside, reducing the breast, and then sewing it back on with what we call bolster dressing, which holds it in place,” he says. “With that technique, you do have 100% loss of sensation.”

Scarring is another major factor. Mandell-Brown notes that he makes every attempt to minimize scarring because breast reduction surgery scars can be aesthetically disabling.

In general, patients transitioning have a high satisfaction rate and tend to be grateful, he says. Most of those who come to Mandell-Brown’s Cincinnati practice for female to male top surgery are from 26 to 38 years old.

Performing chest masculinization has been a satisfying part of practice for Mandell-Brown, but he recommends that surgeons first check with patients’ endocrinologists and/or psychologists to make sure patients are ready both emotionally and physically for the change.

REFERENCES
MyEllevate Rejuvenation

Expert physicians highlight the rise in minimally invasive procedures using the MyEllevate light-guided suture technology for facial rejuvenation.

Now that the days of safe in-person services are returning, and thanks to consumers with pent-up buying impetus and a year’s worth of savings, the dermatology and cosmetic surgery sectors are experiencing a notable trend: The popularity of minimal to noninvasive cosmetic procedures is surging. Chief among those procedures is the patented MyEllevate light-guided suture technology for facial rejuvenation. As clients experience these innovative techniques and their significant results with negligible recovery time, they are referring their friends and coming back for more. MyEllevate has become the poster child for minimally invasive procedures. Cynosure’s recent acquisition of MyEllevate confirms the method’s arrival as the leader of this new and improved generation of technology.1

But what is MyEllevate? And how did this paradigm shift occur in a steadfast industry like cosmetic surgery?

Gregory Mueller, MD, FACS, a plastic surgeon in Beverly Hills, California, developed MyEllevate and the ICLED light-guided suture system. The highly effective facial rejuvenation technique has minimal downtime and long-lasting results. In addition to having a speedy recovery time, MyEllevate effectively treats a broad range of aging-related concerns, from excess fat to bulging glands and prominent platysma bands.2

MyEllevate was designed very simply as a percutaneous approach to placing a suspension suture. Vincent C. Giampapa, MD, FACS, and Barry DiBernardo, MD, published an article in 2000 on placing a neck suspension suture during an open facelift.3 Mueller took this concept and over a 15-year period developed the MyEllevate procedure. Initial variations had issues with the depth of suture placement, which led to the light-guided approach of the procedure. He experimented with many types of absorbable and permanent sutures, finally deciding on a 4-0 braided permanent suture.

The surgeon performs the procedure in an operating or procedure room under local anesthesia or intravenous sedation of general anesthesia, according to the patient’s wishes. The approach is simplified and broken down into easy-to-learn steps.

**Step 1**
The patient is prepped and the platysma bands, if present, are marked and injected with local anesthetic.
A puncture wound is made adjacent to the bands with a specialized puncture tool, and then the attachments are cleared with a “clearing” tool that is part of the ICLED kit. The rod and Suturod suture, also included in the kit, are placed deep and superficial to the band. The band is then cut by sawing the suture back and forth until the suture pulls through.

**Step 2**

The neck is tumesced with 300 to 400 cc of standard tumescent solution. If desired, the physician can use an energy-based device internally; however, this step may be omitted. Commonly used devices include Precision Tx SmartLipo (Cynosure), FaceFite (InMode), Renuvion (Apyx Medical), and the Vaser ultrasonic system (Solta Medical). Liposuction is then performed and damaged fat is removed, and the area is additionally undermined by the liposuction cannula.

**Step 3**

Additional puncture wounds are created [Illustration]. The light is activated and placed on the rod, and then the light-guided suture is placed through standardized puncture sites. The suture is tied through the first puncture site and cut. The rod is then used to help bury the knot. Finally, a dressing is applied.

The procedure is routinely performed in under 1 hour and patient recovery is swift. Patients are asked to wear a soft collar for 10 days after surgery, and many resume normal activities within 48 hours.

The MyEllevate team vets all physicians before they are trained in the procedure to help maintain quality control. Physicians are asked to go to Myellevate.com to register and then watch a recorded procedure. Live training is available at 4 US sites, and a trainer is sent to observe the physician’s first 2 cases.

**Impact of the Zoom Boom**

The procedure has been rapidly implemented by physicians and has generated much interest from patients in recent times. An article in Elle Magazine brought national exposure to MyEllevate in its December 2020/January 2021 print issue, dubbing the procedure the Zoom Lift.

The procedure’s popularity started with the struggle shared by many people during the early days of COVID-19, which in turn abruptly introduced the work-from-home culture. Dermatologists and plastic surgeons were suddenly inundated with requests and complaints about previously unobserved “trouble areas,” and their appointment books began to fill quickly. On a global scale, working professionals went from looking at their faces for perhaps 30 minutes each day—from a glimpse in the mirror to a quick FaceTime call and the occasional selfie—to staring at them for 8-plus hours daily on Zoom as they worked remotely. This increased, targeted focus on facial features led to many plastic surgeons’ clients scrutinizing their imperfections on an intensified level that substantially raised the demand for cosmetic procedures, including MyEllevate.

**DISCLOSURES**

Mueller is the creator of MyEllevate. Pozner and DiBernardo are both stockholders and trainers for MyEllevate.

**REFERENCES**


Regenerative Skincare Realities

Lisa Hilton

Skin care companies are marketing regenerative topicals featuring stem cells, exosomes, and platelet-rich plasma (PRP).

But do they work? And is it safe to use stem cells, exosomes, and PRP in skin care?

Dermatology Times® and its sister publication, Aesthetic Authority®, asked experts in the regenerative skin care space for answers.

"There are no products that contain stem cells in over-the-counter skin care," says Amy Forman Taub, MD, FAAD, founder and medical director of Advanced Dermatology in Lincolnshire, Illinois. "There are companies that have cultured media [extracted growth factors] from these cells, but these products have not been proven to be more effective than what we currently have from cultured media; ie, growth factor products from prenatal or perinatal tissue."

The use of stem cells in skin care has taken a decade to evolve after early issues with stem cell sources, such as embryonic vs adult stem cells, and the requisite clinical studies to demonstrate consistent efficacy, according to Lawrence A. Rheins, PhD, chief scientific officer at Aesthetics Biomedical in Phoenix, Arizona, creator of SoME Skincare. "A few years ago, there was interest in using botanical stem cells for skin care products. Frankly, I do not understand how that would work," Rheins says. "Those stem cells are not going to get into the skin. [Plus], how physiologically relevant are botanical stem cells to human skin? Adipose adult stem cells are finding a significant growing role in aesthetic medicine, including facial rejuvenation."

According to Taub, exosomes are noncellular and may be able to lyophilize, but research is in the early phases.

In other research, Mayo Clinic investigators reported in Science Daily that purified exosomal product, known as PEP, an off-the-shelf, room-temperature-stable exosome, can heal wounds that do not have adequate blood supply in single exosome application.1

Safety concerns are a hurdle for stem cells and exosomes in skin care. The FDA regulates products containing stem cells and exosomes.2 Although exosome-containing products are available in the marketplace, some companies that make them have received FDA warning letters, according to Rheins.

These FDA safety concerns could limit the commercial potential of exosome-containing skin care topicals for the near term, he says.

PRP Opens the Regenerative Door

The use of a patient’s own PRP growth factors in personalized skin care has gained rapid momentum in recent years as clinical science has shown its safety and efficacy, according to Rheins.

SoME, which features patients’ autologous PRP in a serum mixture for topical application, has proved to be stable and able to keep growth factors alive. Autologous PRP is safe, according to Taub.

"SoME is stable for 3 months, if refrigerated," Taub says. "PRP is great for healing, so this could afford some correction of damage, but this does require drawing your patient’s blood and spinning it down to extract the PRP."

According to Rheins, SoME took a different approach in product development.

"We are not taking stem cells. We are not taking synthetic exosomes. We are using the body’s own autologous physiological growth factors," he says. "Consumers want personalized and more individualized skin care products. There is nothing more individualized or personalized than your own growth factors."

Aesthetics Biomedical has patented a way of preserving platelet function for more than 90 days in SoME products, Rheins says.

After centrifuging a patient’s blood, the physician drops 3 mL of the patient’s PRP into the prepared SoME serum bottles. The patient takes the 3 bottles home in a supplied mini refrigerator and uses the product twice daily for the next 90 days.

“It’s the unique physiological electrolyte base formula of 23 ingredients that provides us with the opportunity to keep the platelets stable,” Rheins says. “The change in temperature, going from the small refrigerator to air temperature to skin temperature, causes platelet activation, and the granules inside the platelets begin to degranulate to release hundreds of the growth factors including exosomes… which are small enough to get into the skin. The patient puts the bottle back in the fridge and the platelets basically go back into a senescent state.”

Scientific journals published 2 studies on SoME in recent years. Investigators of the first study, published in 2019 in Journal of Cosmetic Dermatology, studied 20 female and male participants aged 30 to 60 years in a single-site, investigator-blinded, vehicle-controlled, split-face study to look at the effect of serum containing PRP vs the serum alone on facial photaging. Study results showed the serum contained stable PRP for 90 days, and PRP-treated facial skin biopsies showed improvement in skin architecture and upregulation for collagen...
type I, with concomitant upregulation of mRNA for collagen after 8 weeks of topical use. In the second study, which was published in 2020 in Journal of Drugs in Dermatology, investigators reported that platelets remained viable for up to 120 days in a refrigerated cosmetic base serum vehicle. The product demonstrated clinical, histological, light, and scanning electron microscopy end points to demonstrate a mechanism of action leading to PRP facial benefits. PRP kits of 20-mL and 60-mL volumes for topical PRP were shown to be equally efficacious.

Aesthetic providers typically use SoME alone for facia rejuvenation to improve the appearance of fine lines, sun damage, hyperpigmentation, and sallowness. However, professional aesthetic practices are increasingly using SoME for posttreatment care following radiofrequency microneedling or other invasive devices, including various lasers, to assist in the healing process, according to Rheins.

“SoME has been on the market for 2 years, and no one has complained of any irritant or allergic reactions,” he says. “The physiological electrolytes of SoME provide additional product safety.”

Vivian Bucay, MD, FAAD, founder and president of Bucay Center for Dermatology and Aesthetics in San Antonio, Texas, discusses the evolution of topical growth factors using SoME Skincare. According to Bucay, dermatologists and other aesthetic physicians are using PRP for several indications, so integrating the PRP process into skin care is seamless for many. Whereas some patients come in specifically to get their blood drawn and spun for SoME Skincare, others may come in for PRP injections for hair growth or to be used for postlaser resurfacing, she says.

“The real innovation [in the case of SoME] is this serum actually keeps the platelets stable for 90 days,” Bucay says. “I use it. I still believe in using topical antioxidants. I still use a retinol in the evenings. I use a sunscreen. This is adding something else to [skin rejuvenation], and it is super well tolerated.”

SoME, according to Bucay, represents the trend toward personalized skin care, which has become increasingly more accessible over the years. However, it is not yet mainstream, according to Taub, who coauthored the 2018 review “Stem Cells in Dermatology and Anti-aging Care of the Skin.”

“It seems cumbersome to utilize the tissues of our own bodies for skin care products because the extraction process is difficult. There is the need to extract fat, bone marrow, or blood,” Taub says. “Until those processes become easier, it’s unlikely for those to be mainstream skin care products.”

Taub says she believes the future revolves around understanding regenerative processes in the skin. Currently the most advanced products that use a messenger to stimulate dormant stem cells to action in patients’ skin is DefenAge [Progenitor Biologics], which utilizes proprietary defensins.

“In the future I do think we will be able to synthesize specific growth factors in the correct amount and mixture that will do more than mimic healing. Exosomes are promising, as these are small packets of cellular signaling proteins and could be developed for antiaging. And, yes, we need to make sure that these products do not also stimulate carcinoiogenic cells.” Taub says.

REFERENCES

Three patients before and after using SoME Skincare for 90 days.
Paul Nassif, MD: Building a Successful Skin Care Brand

Beverly Hills facial plastic surgeon Paul Nassif, MD, FACS, of NassifMD Plastic Surgery in California, knows how to create a successful brand. His image alone creates awareness with anyone who has tuned into E! Entertainment’s Dr. 90210 or Botched.

Among his many claims to fame, Nassif developed and markets NassifMD Dermaceuticals. He shared strategies for building a successful skin care line with colleagues during the April 17 International Society of Aesthetic Plastic Surgery (ISAPS) Business School.

Launching a skin care line is not easy, according to Nassif.

“This is more of a long-term investment, and really, if you are going to do this, you need dedication and, of course, a lot of money,” he says.

Aesthetic physicians and surgeons have different reasons for creating proprietary skin care lines.

“You have to think about ‘What is my endgame? Am I doing this because it is a passion project of mine? Am I doing this as a source of passive income?’” he says. “I did this for my patients because when you do surgery, what happens to the quality of the skin? Nothing. If you have surgery plus great skin care...it makes your surgery look better.”

Regardless of the reason, says Nassif, the goal of creating a skin care line should be to develop great products because repeat business is the key to long-term success.

“You can always get someone to buy the product, but the question is, are they going to keep using it? That is why the product has to be fantastic,” he says.
PRODUCT TESTING AND CLINICAL STUDIES
Science and testing should be the foundation of any physician-developed skin care brand. That includes developing thoughtful formulations as well as formal and informal testing and feedback.

“I chose to individually formulate each product to ensure control of ingredients, potency, and efficacy and to tailor each [product] to my patients’ needs and input,” he says.

Proper product testing is a time-consuming endeavor, but it’s necessary. For his line, Nassif worked with chemists to achieve efficacy and potency for each product, whether it was designed for the face, neck, under eyes, nose, or other areas.

“There are probably 7 to 8 different tests that you have to do with your chemist,” Nassif explains.

Nassif’s skin care products went through laboratory testing, consumer perception studies, before and after studies, hydration studies, skin pathology testing, and Visia (Skin Analysis System; Canfield Scientific) studies. He also funded clinical trials that incorporated side-by-side visual comparisons. Additionally, he received qualitative and quantitative feedback from friends, colleagues, patients, and staff.

During the ISAPS Business School presentation, Nassif shared images from a Visia study that had 30 participants. In the study, patients wearing fluorescent makeup cleansed their faces using soap and water on one side of the face and his NassifMD Detox Pads on the other to remove dirt, makeup, and residue.

“My [detox pads were] 104% more effective than soap and water,” he says.

Although companies do the actual testing for providers such as Nassif, it’s the providers who foot the bill, he says. He also commissioned a perception study in which 32 participants wrote down what they thought about products.

“Providers should highlight before and after images for each product, he says, noting that consumers look to these transformations when deciding what to buy. In his presentation, Nassif showed before and after images of his Deco-Lift and Peri-Orbital Complex products.

“What I focus on here is the luminosity and glow. I look at the color and the crow’s-feet and also…at the lifting ability,” he says. “This is from a key ingredient called Vin-upLift that gives immediate temporary hydration and lifting.”

Formulating products with key ingredients that may not be widely available but are backed up by science to suggest they work is important for product differentiation. Nassif describes the Vin-upLift ingredient as “a unique tightening ingredient that is derived from Swiss ice wine” on his website NassifMDskincare.com.

“Your ingredients have to be excellent,” he says. “You have to have the science behind the different products.”

MARKETING AND SALES
Nassif uses many avenues to reach his target audience for skin care products, including TV shopping and e-commerce. His product line is featured on HSN in the United States and international shopping channels such as TVSN in Australia, QVC UK, and TSC in Canada.

As for e-commerce, Nassif markets the brand on NassifMDskincare.com and also sells the line on additional websites. The brand has its own consumer page on Amazon.

The skin care line has a large social media presence, with advertisements on popular platforms and lifestyle websites, such as PopSugar. Social media marketing is a conduit to reach specific demographics, he says, adding that it is also important to use online influencers and their high-profile engagement.

Brick-and-mortar is a separate conversation, according to Nassif. On-air skin care sales, coupled with a robust online and social media presence, help educate buyers, develop brand awareness, fuel sales, and build an international viewership, he says.

Of course, Nassif’s practice also generates product sales. His practice integrates skin care into surgical treatments, and the skin care line also supplements his medical spa and aesthetic treatments.

“This is more of a long-term investment, and really, if you are going to do this, you need dedication and, of course, a lot of money.”

Paul Nassif, MD, FACS

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Paul Nassif, MD, FACS

Women’s use of facial skin care products rose in 2020, according to an NPD Group, a market research company.

22% of US women reported changing their skin care routine because of the pandemic.

“Most are washing or moisturizing their face more often than pre-pandemic, one-third have expanded their routine to include more products, and the majority of those using more products intend to stick with their new routine when things normalize,” according to an NPD press release.

Cleansers and moisturizers as well as treatments such as exfoliators/scrubs and masks, saw the biggest boosts in use since 2019.

Women are more likely to research skin care products online before purchasing, according to NPD.

Released in 2019, the NPD Women’s Facial Skincare Consumer Report noted that nearly half of women surveyed prefer to research products online prior to buying them in store, citing online reviews and ratings, as well as social media influencers, as their sources of information.

Engaged consumers are looking at ingredients and want transparency, according to the NPD Group.

46% of facial skin care users report purchasing products free of sulfates, phthalates and/or gluten.

“This represents a 6-point uptick over the past 2 years. In addition, more than half of women look for skin care products made from organic ingredients. The report also found that brands making a public commitment to ingredient transparency have become top of mind for consumers, with several of the more well-known transparent brands ranking among the top 25 in highest awareness-to-purchase conversions,” according to an NPD press release.

REFERENCES

60% of women say they are using skin care products today, reports the npd group/npd group
No Good Deed Goes Unpunished

MOST PRACTITIONERS ARE INDEBTED to their community for the success of their practices. I truly believe that most fulfilled and successful doctors are eager to give back to their communities. I, like many readers of this article, have provided pro bono services, participated in volunteer efforts, become involved with numerous charitable organizations, and simply tried to make my community a better place. I performed many charitable reconstructive surgeries on children in the earlier part of my career. I have 2 special needs children with severe disabilities but was active in helping children years before my sons were born. Having said that, much of my current charitable work centers around children and adults with disabilities.

Like many, my practice is called on frequently for charitable donations. Just when we thought we had everything under control, a member of my staff noticed that a person who had requested auction items for various “charity golf tournaments” had not only picked up the certificate from our office but also personally redeemed it. At first this did not set off red flags. I have seen auction chairs purchase an item for themselves, one that the bidder possibly requested from a practice because they either wanted the service or product themselves or wanted to drive up the value for the organization.

However, the reality was that the person collecting these golf tournament certificates would pick them up and redeem them when different staff members were in my office. We had no rules and assumed it would be an easy situation.

In years past, some people would come to the practice holding tattered auction certificates issued 3 years prior, and others would show up with a certificate they personally did not bid on.

We quickly learned there had to be some rules, so we reined our certificates. We began putting a chronological number on the certificate as well as issuing an expiration date and declaring that the certificates are nontransferable. This immediately solved some of our problems but not all. After updating the rules, I would ask certificate recipients what price they had paid in the auction. Frequently, and especially for nationally known charities, the bidder had paid far more than what the actual auction item was worth in the fun of a charitable bidding war.

Other times, people would show up with a certificate for treatments that had a retail worth of $1000 and they had spent only $20 for the winning bid. After this, we started informing charities that if the item did not sell for a reasonable portion of its value, it should not be auctioned, and we would reevaluate the price next year.

To protect and safeguard ourselves, we now investigate any organization that requests a charitable gift. This situation made us review our entire process and add safeguards. First and foremost, we issued a compliance list for receiving, auctioning, and redeeming a charitable certificate, with the following requirements:

1. The certificate cannot be redeemed by the person requesting it or collecting it from the office.
2. The person picking up the certificate in office must provide a photo ID, which is copied and kept.
3. Charities must provide detailed information about the certificate winner in a form that we supply and must also include the amount of the winning bid. The certificate cannot be honored without this information.

Needless to say—and shame on us for not doing more research—we now investigate any organization that requests a charitable gift. Like anything else in life, fundraising presents situations where people take advantage of one’s generosity. After learning this the hard way, I would like to pass along some caveats:

1. Investigate all requesting organizations for legitimacy and look into the requesting individual.
2. Invest time into a certificate that includes:
   a. A serial number, expiration date of service or product redemption, and statement of non-transferability; and
   b. An accompanying form that must be filled out and followed exactly for redemption.
3. Clearly state the necessity of this form on the actual certificate.
4. Request personal pickup, don’t mail anything.
5. Inform that fraud will be reported to authorities.

I still believe that the more you give, the more you get. Just give wisely.
On behalf of Aesthetics Biomedical® Inc. we are honored to invite you to our unique boutique style symposium, Perspectives: The Evolution of Aesthetics. Designed to be an interactive exchange of personal perspectives and conversations that will focus on hot topics, the latest aesthetic trends, combination therapies, disruptive technologies, marketing strategies with local social media influencers and best practices. This exclusive conference will be held in a private, safe, and socially distant environment bringing together leading aesthetic key opinion leaders for a full-day of educational curated content.

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Cosmetic Dermatologist
Shino Bay Aguilera, MD
Board Certified Dermatologist
Vivian Bucay, MD, FAAD
Dermatologist
E. Victor Ross, MD
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The Growing Rate of Facial Hair Transplants

Facial hair grafting is becoming an increasingly popular procedure, with methods such as follicular unit extraction and follicular unit transplantation to improve the appearance of beards and eyebrows.

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though scalp hair transplants are common in aesthetics, using hair transplant technology to improve facial hair outcomes is gaining in popularity for patients who wish to improve beard and eyebrow fullness. In an interview with Aesthetic Authority™, Gary Linkov, MD, a board-certified facial plastic and hair surgeon and founder and medical director of City Facial Plastics in New York, New York, gives an overview of beard and eyebrow grafting to improve patient facial hair appearance.1,2

First, when patients are preparing for grafting, he says, they are directed to stop all oral supplements along with over-the-counter medications that can cause blood thinning.

“Vitamin C and vitamin K a week before the facial hair transplant procedure can help improve healing and minimize bleeding,” he notes.

Patients shower the night before or the morning of the procedure to prevent infection and are also prescribed an antibiotic, an anti-inflammatory pill, a sedative, and an anxiolytic on the morning of the procedure, he explains. Following patient consent, the beard or eyebrow area is marked carefully to incorporate the patient’s wishes.

Patients then undergo follicular unit extraction (FUE), in which hair strands with the follicles attached are taken from one body site and transplanted to the desired area. Another method of transplanting hair is follicular unit transplantation (FUT), which excises a strip of skin with hair follicles to be used.

“Once the grafts are removed, recipient site creation and then placement of the grafts takes place,” Linkov says. “The overall process may take a few hours for smaller cases and up to a full day for larger cases, and occasionally may require an extra day. A lunch break is provided for longer cases.”

Explaining the procedure downtime, bleeding, swelling, and bruising are all possible after a facial hair transplant. “The most important precaution in the recovery phase of a beard transplant is to not get the transplanted hairs wet for the first 5 days. This allows them to set in the proper orientation and to eventually grow,” he emphasizes. Post procedure, patients also receive both an oral and a topical antibiotic for the donor area.

For beard transplants, patients are able to shave after 10 days. Linkov explains that after about 3 weeks, the shafts of the transplanted hairs will usually fall out. Hair regrowth then starts at 4 to 6 months, with patients having final results assessed at 1 year.

The procedure carries some risks, one of which is poor angulation. “Despite every best effort to use an acute angle to the skin surface when making recipient sites and placing grafts, occasionally grafts may still grow at a more perpendicular angle and may need to be removed,” he notes.
There is also the chance of bump formation. “The main area at risk of small bump formation is the goatee area under the lower lip,” Linkov says. “These can be difficult to correct.”

The risk of poor regrowth, although possible, is rare, according to Linkov. “The face has very good blood supply, and [the procedure] typically results in excellent hair regrowth. A touch-up procedure is sometimes needed after 10 months if certain areas show poor growth.”

Finally, inclusion cysts can occur but are very rare in the transplant-ed beard area. They may need to be incised and drained or removed, he says.

Linkov explains that scar formation is another consideration. Small circular scars are left after using the FUE method, “but they are barely noticeable even with a shaved head,” he notes. The FUT method, however, leaves a linear scar across the back of the head, which makes it more difficult to wear shorter hairstyles.

“The recipient area where the new beard hairs grow should not display any scars,” he explains.

Medical conditions that are incompatible with local anesthesia containing epinephrine include contraindications to FUE and FUT facial hair transplantation. “Contraindications to facial hair transplants are scarring alopecia or the autoimmune [disease] alopecia areata, in which the body will continue to try to destroy the hair follicles,” Linkov says, adding that having minimal hair supply for transplantation to the facial area is also a contraindication.

REFERENCES


The most important precaution in the recovery phase of a beard transplant is to not get the transplanted hairs wet for the first 5 days.”

Gary Linkov, MD, New York, New York
**INDICATIONS AND USAGE**

ZILXI (minocycline) topical foam, 15% is a tetracycline-class drug indicated for the treatment of inflammatory lesions of rosacea in adults.

**Limitations 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, ZILXI should be used only as indicated.

**IMPORTANT SAFETY INFORMATION**

**Contraindications**

Persons who have shown hypersensitivity to any of the tetracyclines or any other ingredient in ZILXI.

**Warnings and Precautions**

**Flammability:** The propellant in ZILXI is flammable. Instruct the patient to avoid fire, flame, and smoking during and immediately following application.

ZILXI is a topical foam. While systemic absorption of ZILXI is low, and serious adverse reactions were not seen in clinical studies, the following adverse reactions associated with oral minocycline should be considered:

**IMPORTANT SAFETY INFORMATION, CONTINUED**

- **Teratogenic effects, inhibition of bone growth & permanent tooth discoloration:** Use 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.
- **Clostridioides difficile associated diarrhea (CDAD):** If CDAD occurs, discontinue ZILXI.
- **Hepatotoxicity & metabolic effects:** If renal impairment exists or if liver injury suspected, discontinue ZILXI.
- **Central nervous system effects:** Patients experiencing light-headedness, dizziness or vertigo should be cautioned about driving vehicles or operating heavy machinery.
- **Intracranial hypertension:** Clinical manifestations include headache, blurred vision, diplopia, and vision loss. Discontinue ZILXI immediately if symptoms occur.
- **Autoimmune syndromes:** Symptoms may be manifested by fever, rash, arthralgia, and malaise. Discontinue ZILXI immediately if symptoms occur.

**REFERENCES:**

1. Zilxi 1.5% topical foam contains the following inactive ingredients: propellants (butane + isobutane + propane).1

**Visit ZilxiHCP.com to learn more.**

**It’s Time Minocycline Got On Top of Rosacea**

Take on inflammatory lesions of rosacea from the top down.
The first time minocycline has been approved for rosacea

**Zilxi is the first and only topical minocycline proven effective in adult patients with inflammatory lesions of rosacea**

- Evaluated in 2 large, 12-week phase 3 trials (N=1522)
- Significantly reduced inflammatory lesion count by Week 12
- Demonstrated improvement in IGA treatment success by Week 12

**Proven safe and well-tolerated on already-sensitive skin**

- The most commonly reported adverse reaction was diarrhea (1%)
- Zilxi was well-tolerated throughout the treatment period

**Delivered in a gentle, proprietary foam vehicle**

- Leverages Molecule Stabilizing Technology (MST)™ for stable topical delivery
- Contains naturally moisturizing ingredients, is surfactant-free, and does not contain drying agents, such as ethyl alcohol

**IMPORTANT SAFETY INFORMATION, CONTINUED**

- **Photosensitivity:** Patients should minimize or avoid exposure to natural or artificial sunlight while using ZILXI. Advise patients to discontinue treatment with ZILXI at the first evidence of sunburn.
- **Hypersensitivity reactions:** Discontinue ZILXI immediately if symptoms of anaphylaxis, serious skin reactions, erythema multiforme, and drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome occur.
- **Tissue hyperpigmentation:** Discoloration of organs, including nails, bone, skin, eyes, thyroid, visceral tissue, oral cavity (teeth, mucosa, alveolar bone), sclerae and heart valves.
- **Superinfection:** Overgrowth of non-susceptible organisms, including fungi if superinfection occurs, discontinue ZILXI and institute appropriate therapy.

**Adverse Reactions**

The most common adverse reaction reported during clinical trials of ZILXI was diarrhea.

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<td><strong>Zilxi</strong></td>
<td>is a trademark of an affiliate of VYNE Therapeutics Inc. © 2020 VYNE Therapeutics Inc. All rights reserved. COM-ZIL-US-200041 09/2020</td>
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ZILXI™ (minocycline) topical foam, 1.5%
BRIEF SUMMARY OF FULL PRESCRIBING INFORMATION. PLEASE SEE FULL PRESCRIBING INFORMATION.

INDICATION
ZILXI is indicated for the treatment of inflammatory lesions of rosacea in adults. Limitations 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, ZILXI should be used only as indicated.

CONTRAINDICATIONS
This drug is contraindicated in persons who have shown hypersensitivity to any of the tetracyclines or any other ingredients within ZILXI.

WARNINGS AND PRECAUTIONS
• Flammability: The propellant in ZILXI is flammable. Instruct the patient to avoid fire, flame, and smoking during and immediately following application. Do not puncture and/or incinerate the containers. Do not expose containers to heat/temperature above 120°F(49°C).
• Teratogenic Effects: Minocycline, like other tetracycline-class drugs, may inhibit bone growth when administered orally during pregnancy. Based on animal data, when administered orally, tetracyclines cross the placenta, are found in fetal tissues, and can cause skeletal malformation and retardation of developmental on the developing fetus.
• Tooth Discoloration: The use of tetracycline class drugs orally during tooth development (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). This adverse reaction is more common during long-term oral use of the tetracycline but has been observed following repeated short-term courses. Enamel hypoplasia has also been reported with oral tetracycline drugs. Use of tetracycline drugs is not recommended during tooth development.
• Inhibition of Bone Growth: All tetracyclines form a stable calcium complex in any bone-forming tissue. A decrease in fibula growth rate has been observed in premature human infants given oral tetracycline in doses of 25 mg/kg every 6 hours. This reaction was shown to be reversible when the drug was discontinued. Results of animal studies indicate that oral tetracyclines cross the placenta, are found in fetal tissues, and can cause retardation of skeletal development on the developing fetus. Evidence of embryotoxicity has been noted in animals treated orally early in pregnancy.
• Clostridioides difficile Associated Diarrhea: Clostridioides difficile associated diarrhea (CDAD) has been reported with nearly all antibacterial agents, including oral minocycline, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C. difficile. C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents. If CDAD is suspected or confirmed, antibiotic use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated.
• Hepatotoxicity: Post-marketing cases of serious liver injury, including irreversible drug-induced hepatitis and fulminant hepatic failure (sometimes fatal) have been reported with oral minocycline use.
• Metabolic Effects: The anti-anabolic action of the tetracyclines may cause an increase in blood urea nitrogen (BUN). In patients with significantly impaired function, higher serum levels of tetracycline-class drugs may lead to azotemia, hyperphosphatemia, and acidosis. If renal impairment exists, recommended oral or parenteral doses may lead to excessive systemic accumulations of the drug and possible liver toxicity. Under such conditions, adjust the dose downward, and if therapy is prolonged, serum level determinations of the drug may be advisable.
• Central Nervous System Effects: Central nervous system side effects including light-headedness, dizziness or vertigo have been reported with oral minocycline therapy. Patients who experience these symptoms should be cautioned about driving vehicles or using hazardous machinery while on minocycline therapy. These symptoms may disappear during therapy and may disappear when the drug is discontinued.
• Intracranial Hypertension: Intracranial hypertension has been associated with the use of tetracycline-class drugs. Clinical manifestations of intracranial hypertension include headache, blurred vision, diplopia and vision loss; papilledema can be found on fundoscopy. Women of childbearing age who are overweight or have a history of IH are at a greater risk for developing intracranial hypertension. Patients should be questioned for visual disturbances prior to initiation of treatment with tetracyclines. Concomitant use of isoretinoin and tetracycline should be avoided because isoretinoin, a systemic retinoid, is also known to cause intracranial hypertension. Although intracranial hypertension typically resolves after discontinuation of treatment, the possibility for permanent visual loss exists. If visual disturbance occurs during treatment, prompt ophthalmologic evaluation is warranted. Because intracranial pressure can remain elevated for weeks after drug cessation, patients should be monitored until they stabilize.
• Autoimmune Syndromes: Tetracyclines have been associated with the development of autoimmune syndromes. The long-term use of oral minocycline has been associated with drug-induced lupus-like syndrome, autoimmune hepatitis and vasculitides. Sporadic cases of serum sickness have presented shortly after oral minocycline use. Symptoms may be manifested by fever, rash, arthralgia, and malaise. In symptomatic patients, immediately discontinue the use of all tetracycline-class drugs, including ZILXI.
• Photosensitivity: Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking oral tetracyclines; this reaction has been reported less frequently with minocycline. Although ZILXI did not induce phototoxicity or photoallergic responses in human dermal safety studies, patients should minimize or avoid exposure to natural or artificial sunlight (tanning beds or UVAB treatment) while using minocycline. If patients need to be outdoors while using ZILXI, they should wear loose-fitting clothes that protect skin from sun exposure and discuss other sun protection measures with their physician. Advise patients to discontinue treatment with ZILXI at the first evidence of sunburn.
• Serious Skin/Hypersensitivity Reaction: Cases of anaphylaxis, serious skin reactions (e.g. Stevens Johnson syndrome, erythema multiforme, and drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome have been reported postmarketing with oral minocycline use. DRESS syndrome consists of cutaneous reaction (such as rash or exfoliative dermatitis), eosinophilia, and one or more of the following visceral complications such as: hepatitis, pneumonitis, nephritis, myocarditis, and pericarditis. Fever and lymphadenopathy may be present. In some cases, death has been reported with oral minocycline use. If this syndrome is recognized, discontinue ZILXI immediately.
• Tissue Hyperpigmentation: Oral tetracyclines are known to cause hyperpigmentation. Tetracycline therapy may induce hyperpigmentation in many organs, including nails, bone, skin, eyes, thyroid, visceral tissue, oral cavity (teeth, mucosa, alveolar bone), sclerae and heart valves. Skin and oral pigmentation has been reported to occur independently of time or amount of drug administration, whereas other tissue pigmentation has been reported to occur upon prolonged administration. Skin pigmentation includes diffuse pigmentation as well as pigmentation over sites of scars or injury.
• Development of Drug-Resistant Bacteria: ZILXI has not been evaluated in the treatment of infections. Bacterial resistance to the tetracyclines may develop in patients using ZILXI, therefore, the susceptibility of bacteria associated with infection should be considered in selecting antimicrobial therapy. Because of the potential for drug-resistant bacteria to develop during the use of ZILXI, it should be used only as indicated.
• Superinfection/Potential for Microbial Overgrowth: Use of ZILXI may result in overgrowth of non-susceptible organisms, including fungi. If superinfection occurs, discontinue ZILXI and institute appropriate therapy.

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 practice. In three (two Phase 3 and one Phase 2) multicenter, randomized, double-blind, vehicle-controlled trials, adult subjects applied ZILXI or vehicle once daily for 12 weeks. A total of 1,087 subjects were treated with ZILXI and 591 with vehicle. The majority of subjects were White (97%) and female (70%). Approximately 67% were non-Hispanic/Latino. The mean age was 50.0 years and ages ranged from 18 to 86 years.
• The most common adverse reaction reported by ≥1% of subjects treated with ZILXI and more frequently than in subjects treated with vehicle was diarrhea (1% vs. 0%), respectively.
• During the two Phase 3 trials, local tolerability evaluations were conducted at each study visit by assessment of erythema, telangiectasia, burning/stinging, flushing/blushing, dryness, itching, peeling and hyperpigmentation. Subjects treated with ZILXI had improved local tolerability signs and symptoms at Week 12 when compared with corresponding baseline values. These occurred at a similar frequency and severity as subjects treated with the vehicle component of ZILXI. The local tolerance assessments in ZILXI patients (N = 1,008, of which 897 had local tolerability assessments at week 12) by incidence rate (%) and severity grade were as follows (mild, moderate, severe): erythema (36.2%, 18.3%, 0.7%), Telangiectasia (61.0%, 18.8%, 0%), burning/stinging (13.3%, 2.8%, 0%), flushing/blushing (39.0%, 9.6%, 0.9%), dryness (23.9%, 4.0%, 0.1%), itching (30.0%, 3.3%, 0%), skin peeling (16.1%, 1.9%, 0.1%), and hyperpigmentation (22.5%, 2.8%, 0%). Hyperpigmentation was most frequently assessed as characteristic of inflammatory and post-inflammatory changes associated with inflammatory lesions of rosacea. In a 40-week open-label extension safety study (for a total of up to 52 weeks of treatment) [NCT03276936], frequency and severity of local tolerability signs and symptoms at Week 52 were comparable to those reported at Week 12.

DRUG INTERACTIONS
• Anticoagulants: Because tetracyclines have been shown to depress plasma prothrombin activity, patients who are on anticoagulant therapy may require downward adjustment of their anticoagulant dosage.
• Penicillin: Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, it is advisable to avoid giving tetracycline-class drugs in conjunction with penicillin.
• Drug/Laboratory Test Interactions: False elevations of urinary catecholamine levels may occur due to interference with the fluorescence test.

USE IN SPECIFIC POPULATIONS
• Pregnancy: Risk Summary: Available data with ZILXI use in pregnant women are insufficient to evaluate for a drug-associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes. Systemic absorption of ZILXI in humans is low following once daily topical administration of ZILXI under maximal clinical use conditions. Because of low systemic exposure, it is not expected that maternal use of ZILXI will result in significant fetal exposure to the drug. Tetracycline-class drugs may cause permanent discoloration of teeth and reversible inhibition of bone growth when administered orally during pregnancy. Animal reproduction studies were not conducted with ZILXI. In animal reproduction studies, oral administration of minocycline administered to pregnant rats and rabbits during organogenesis induced skeletal malformations in fetuses at systemic exposures of 2,000 and 1,300 times, respectively, the maximum recommended human dose (MRHD based on AUC comparison) of ZILXI (see Data). The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.
• Data: Animal Data: Results of animal studies indicate that tetracyclines cross the placenta, are found in fetal tissues, and can cause retardation of skeletal development of the developing fetus. Minocycline induced skeletal malformations (bent limb bones) in fetuses when orally administered to pregnant rats and rabbits during the period of organogenesis at doses of 30 mg/kg/day and 100 mg/kg/day, respectively, (2,000 and 1,300 times, respectively, the systemic exposure at the MRHD based on AUC comparison). Reduced mean fetal body weight was observed when minocycline was orally administered to pregnant rats during the period of organogenesis at a dose of 10 mg/kg/day (680 times the systemic exposure at the MRHD based on AUC comparison).
• Minocycline was assessed for effects on peri- and post-natal development of rats in a study that involved oral administration to pregnant rats during the period of organogenesis through lactation, at doses of 5, 10, or 50 mg/kg/day. In this study, body weight gain was significantly reduced in pregnant females that received 50 mg/kg/day (1,700 times the systemic exposure at the MRHD based on AUC comparison). No effects of treatment on the duration of the gestation period or the number of live pups born per litter were observed. Gross external anomalies observed in F1 pups (offspring of animals that received oral minocycline) included reduced body size, improperly rotated forelimbs, and reduced size of extremities. No effects were observed on the physical development, behavior, learning ability, or reproduction of F1 pups, and there was no effect on gross appearance of F2 pups (offspring of F1 animals).

• Lactation: Risk Summary: Tetracycline-class drugs, including minocycline, are present in breast milk following oral administration. It is not known whether minocycline is present in human milk after topical administration to the nursing mother. There are no data on the effects of minocycline on milk production. Because of the potential for serious adverse reactions, advise patients that breastfeeding is not recommended during treatment with ZILXI.
• Pediatric Use: The safety and effectiveness of ZILXI for the treatment of inflammatory lesions of rosacea have not been evaluated in pediatric patients.
• Geriatric Use: There were 278 subjects aged 65 or older in the clinical trials of ZILXI (16.6% of 1,678 subjects). No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

NONCLINICAL TOXICOLOGY
• Carcinogenesis, Mutagenesis, Impairment of Fertility: In a carcinogenicity study in which minocycline hydrochloride was orally administered to male and female rats once daily for up to 104 weeks at dosages up to 200 mg/kg/day, minocycline hydrochloride was associated in both sexes with follicular cell tumors of the thyroid gland, including increased incidences of adenomas, carcinomas and the combined incidence of adenomas and carcinomas in males, and adenomas and the combined incidence of adenomas and carcinomas in females. In a carcinogenicity study in which minocycline hydrochloride was orally administered to male and female mice once daily for up to 104 weeks at dosages up to 150 mg/kg/day, exposure to minocycline hydrochloride did not result in a significantly increased incidence of neoplasms in either males or females. Minocycline was not mutagenic in vitro in a bacterial reverse mutation assay (Ames test) or CHO/HGPRT mammalian cell assay in the presence or absence of metabolic activation. Minocycline was not clastogenic in vitro using human peripheral blood lymphocytes or in vivo in a mouse micronucleus test.
• Male and female reproductive performance in rats was unaffected by oral doses of minocycline of up to 300 mg/kg/day (27,500 times the systemic exposure at the MRHD based on AUC comparison). However, oral administration of 100 or 300 mg/kg/day of minocycline to male rats (10,000 or 27,500 times, respectively, the systemic exposure at the MRHD based on AUC comparison), adversely affected spermatogenesis. Effects observed at 300 mg/kg/day of oral minocycline included a reduced number of sperm cells per gram of epididymis, an apparent reduction in the percentage of sperm that were motile, and (at 100 and 300 mg/kg/day) increased numbers of morphologically abnormal sperm cells. Morphological abnormalities observed in sperm samples included absent heads, misshapen heads, and abnormal flagella.

HANDLING: Allow the can to warm to room temperature before first use. Shake well before use.

WARNING: Flammable. Avoid fire, flame, or smoking during and immediately following application. Contents under pressure. Do not puncture or incinerate. Do not expose to heat or temperatures above 49°C (120°F).

For more information, including the FDA-approved Prescribing Information, go to www.ZILXI.com or call 1-844-375-3673.

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AAD Work Group Issues Guidelines for Managing Actinic Keratosis

LINDA STOCUM | Assistant Editor

In April, a multidisciplinary work group published new guidelines in the Journal of the American Academy of Dermatology for the management of actinic keratosis (AK).

The group’s goal was to analyze the current reports of management of AK and provide recommendations for treating patients with the condition.

The investigators worked to address 5 questions:
1. What are the efficacy, effectiveness, and adverse effects (AEs) of surgical and chemical peel treatments for AK?
2. What are the efficacy, effectiveness, and AEs of topically applied agents for AK?
3. What are the efficacy, effectiveness, and AEs of energy devices and other miscellaneous treatments for AK?
4. What are the efficacy, effectiveness, and AEs of combination therapy for the treatment of AK?
5. What are the special considerations to be taken when treating AK in immunocompromised individuals?

The work group used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach to assess the quality of the evidence to formulate and grade clinical recommendations. The population of the randomized controlled trials (RCTs) included in the decision-making were adults 18 years or older with a clinical or histopathologic diagnosis of AK treated with standard approved treatments that are regularly used in the United States.

Current treatment options for AK include topical creams, gels, and solutions; cryosurgery; and photodynamic therapy (PDT). The RCTs demonstrated sunscreen use to prevent UV exposure results in a small reduction in AK incidence and development.

The work group recommended that individuals use UV protection, such as broad-spectrum sunscreen; avoid the sun and wear sun-protective clothing.

Using topical creams, gels, and solutions for the management of AK is common practice. Based on current literature, there was support for a strong treatment recommendation with either 5-fluorouracil (5-FU) or imiquimod. The decision for the 5-FU was based on multiple trials, including a field treatment of 5% 5-FU twice a day for 4 weeks compared with placebo. After 6 months, skin clearance was 38% for 5-FU and 17% for placebo. In 4 other placebo-controlled studies, a dose of .05% of 5-FU was evaluated for safety and efficacy. These studies suggested the lower dose may be more effective than placebo for treatment. These 2 studies provided skin irritation data on treatment with 0.5% 5-FU/hyaluronic acid (a combination topical).

For imiquimod, 12 randomized, placebo-controlled studies on the efficacy and safety of the treatment were reviewed. Multiple concentrations of imiquimod were examined, including 5%, 3.75%, and 2.5%, with the efficacy of each in question.

For the 5% dose, 8 trials were considered with a clearance rate average of 29.3% with the topical being applied 2 or 3 times a week for 1 or 2 treatment courses. The 3.75% dose applied daily between 2 periods of 3 weeks with a break of 3 weeks between treatments reported complete clearance rates of 34% for imiquimod treated patients and 5.5% for placebo. Another study with imiquimod applied daily for 2 weeks followed by a 2-week break and 2 weeks on again saw clearance rates of 35.6%.

Efficacy and safety of the 2.5% concentration were studied in 3 trials. When applied daily for 2-week periods with a 2 week break inbetween, this concentration had complete clearance rates of 30.6% and 33.3% at 14 weeks and 12 months, respectively. The longer treatment studies, in which imiquimod was applied daily for 2 periods of 3 weeks with a break of 3 weeks between, reported complete clearance rates of 25% and 43.2% at 17 weeks and 12 months.

The main adverse event (AE) was severe local skin reactions occurring in 41.5% of patients receiving 42 doses of 2.5% imiquimod. Influenza-like illness was reported in 3.7% of these patients.

Use of 5-FU in combination therapy with calcipotriene needs greater study data before the work group can determine guidance. Conditionally, they recommended the use of diclofenac because
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Managing Actinic Keratosis FROM PAGE 44

it has a lower quality of evidence. There is no recommendation for the use of ingenol mebutate as treatment for AK. Tirbanibulin (Klisyri) was approved as treatment for AK on the face and scalp by the FDA after the analysis was complete.

Cryosurgery is also strongly recommended as a treatment for AK. It has been reported to clear between 57% and 98% of AK after follow-up between 3 months to 8 and a half years. The rates of clearance changed based on the freeze times. A duration of 5 seconds had a rate of 39%, 5 to 20 seconds had a 69% rate, and more than 20 seconds achieved an 83% rate. The AEs during and after treatment were discomfort and dyschromia.

PDT with 5-aminolevulinic acid (ALA)–red light data was considered over 4 studies. In the studies, investigators used the 10% ALA gel and found it was more effective than placebo for lesion reduction, complete AK clearance, and prevention of carcinoma development. The overall quality of evidence was low. The work group also conditionally recommended treatment with ALA–red light PDT over 35% trichloroacetic acid peel for AK management.

ALA–blue light PDT achieved better benefits than placebo in complete clearance, partial clearance, lesion reduction, and prevention of carcinoma development, results showed. “At week 8, pooled data suggest that 82.2% of AKs treated with 1 course of ALA–blue light PDT cleared from baseline compared with 28.8% treated with placebo-blue light PDT,” the authors wrote. “An additional study reports that 8 weeks after 1 treatment, a greater proportion of participants receiving ALA–blue light PDT achieved complete clearance and partial clearance compared with participants receiving placebo-blue light PDT.”

AEs included erythema, edema, stinging, and burning at the treatment site. With this in mind, the work group conditionally recommended ALA–blue light PDT as a treatment for AK and against pretreatment with alpha hydroxy acid solution before. This was based on low-quality evidence.

The authors compared liquid nitrogen with red light PDT to 8-mg ALA patches for managing mild to moderate AK. At 12 weeks after treatment, there were fewer case of AK cleared, and clearance rates were lower from cryosurgery vs ALA–patch PDT from baseline. Based on this, the work group conditionally recommended ALA–patch PDT over cryosurgery for managing AK.

For combination therapy, there were 5 recommendations. Two studies investigated the use of 5-FU and cryosurgery together. One of the studies looked at a 1-week pretreatment of 0.5% of 5-FU cream before cryosurgery. This saw a small improvement in treatment and the extent of benefit from repeated cycles of the therapies dissipated compared with cryosurgery alone. There were nonsignificant differences in AEs after the first combination treatment cycle.

The work group recommended the combine 5-FU cream and cryosurgery conditionally over cryosurgery alone. Studies compared the use of imiquimod in 3.75% or 5% concentrations after cryosurgery to cryosurgery with placebo, and all study outcomes supported combined treatment over cryosurgery alone. Rates of complete clearance were 22.6% in patients treated with a combination of 5% imiquimod and cryosurgery compared with approximately 9% in patients treated with placebo cream and cryosurgery, 22 weeks after treatment. Patients in the 3.75% imiquimod treatment arm in combination with cryosurgery had a rate of complete clearance at 26 weeks after treatment of 30.2% compared
with 3.3% for placebo. These patients had increased rates of AEs compared with placebo.

2 The group conditionally recommended imiquimod and cryotherapy combination therapy over cryotherapy alone.

There was a multicenter, open-label study that investigated the efficacy and safety of topical diclofenac sodium (DFS) after cryosurgery to maximize the complete clearance of AK. A study investigated patients 90 days after cryosurgery treatment. They were randomized to receive either 3% DFS topical or cryosurgery by itself. The DFS treatment arm had a higher complete clearance rate (45.9%) vs cryosurgery alone (29.9%). The discontinuation rate was much higher in combination therapy at 8.4% compared with the cryosurgery alone at 1.2%.

3 The group conditionally recommended against combination of diclofenac and cryosurgery.

Another therapy combination examined was the use of adapalene gel and cryosurgery. A randomized, comparative study investigated the effectiveness of the daily application of 0.1% adapalene gel for 90 days starting 10 days after cryosurgery for AK lesion reduction.

The work group considered the addition of a 90-day topical diclofenac treatment to represent a burden likely to diminish treatment value for patients, given the modest increase in clearance reported with the combined use of diclofenac and cryosurgery.

“The mean baseline number of AKs in the cryosurgery plus adapalene gel group was 7.54 ± 3.66, compared with 7.20 ± 3.60 for the cryosurgery plus placebo group,” the work group wrote. “The mean number of lesions was reduced to 3.44 ± 2.71 (percent change from baseline -54.79 ± 3.8%) in the adapalene group and 3.68 ± 2.97 (percent change from baseline -48.60 ± 4.5%) in the placebo group.”

4 The group conditionally recommended against the use of adapalene gel in addition to cryosurgery for the treatment of AK.

The combined treatment of 5% imiquimod cream after ALA–blue light PDT was studied. Following 2 months of 2 cycles of ALA blue light PDT treatment, imiquimod was used as twice-weekly therapy for 16 weeks and was studied in a split-face fashion, with half of the face randomized to placebo cream and the other side to 5% imiquimod. There was a small significant increase in lesion reduction in the imiquimod-treated side.

The reduction in lesions at 12 months was 89.9% on the imiquimod-treated side and 74.5% on the placebo side, but there was no difference in rates of complete clearance between sides or AEs.

5 The work group conditionally recommended against the use of imiquimod topically after ALA–blue light PDT because treatment would add cost and patient burden.

Further research is needed in immune-compromised patients and for keratinocyte carcinoma prevention.

“These guidelines will be considered current for a period of 5 years from the date of publication unless reaffirmed, updated, or retired before that time,” the authors concluded.

Visit the Boehringer Ingelheim exhibit booth #1011 at the AAD Summer Meeting to hear more.
INJECTABLE IMPETUS

Even modest changes in a transgender, or gender transitioning, patient’s self-perception can deliver major quality-of-life (QOL) improvements, said Lauren Meshkov Bonati, MD, a dermatologist in private practice at Mountain Dermatology with offices in Edwards and Frisco, Colorado.2

“It’s important for us to recognize that gender dysphoria is a classified diagnosis in the Diagnostic and Statistical Manual of Mental Disorders [DSM-5].”3 Meshkov Bonati said.

Gender dysphoria is categorized as a feeling of distress that may occur in those whose gender identity differs from their sex assigned at birth or sex-related physical characteristics, according to Mayo Clinic.3

Additionally, 1.4 million Americans self-identify as transgender, she added.

As with any patient community, caring for LGBTQ+/SGM patients requires an understanding of that population’s holistic needs. Dermatologists should be cognizant of the fact that suicide rates among transgender individuals greatly outpace those in the general population—41% vs 4.6%, respectively—and that QOL improves for transgender people who have undergone transition, Meshkov Bonati said.4

“What does that mean for a dermatologist who’s not performing these types of surgeries?” she asked. “We know that there are approaches we can use to help the patient achieve a more masculine or feminine appearance. We see cosmetic dermatologists can employ an injectable strategy that will enhance masculine or feminine features for the purpose of helping relieve the gender incongruity that transgender patients feel.”

To explore the QOL impact of injectable treatments in transgender individuals, Meshkov Bonati and colleagues undertook a pilot trial involving 9 patients who had not previously undergone injectable treatments. The trial used a metric called the Gender Continuum Self-Percception Scale, which enabled patients to pinpoint their gender self-perception before and after treatment compared to societal male and female ideals.5

“Subjects overall desired to look from 65% to 100% more masculine or feminine than they did at the moment,” she said. “However, 8 of 9 patients said they would be happy looking equally or even less gendered than what they considered society’s ideal.”

These patients were realistic in her view, she continued. “They didn’t have wild expectations of having a brand-new forehead or jawline,” said Meshkov Bonati. “They understood that injectables can’t accomplish the dramatic results that can be achieved with surgery. So we shouldn’t be afraid to treat these patients.”

Post treatment, patients achieved an average 44% shift toward gender ideals. Three patients flipped their gender perception completely from male to female or vice versa. Global Aesthetic Improvement Scale and Dermatology Life Quality Index results mirrored these findings. “Most patients reported reduced self-consciousness and embarrassment,” Meshkov Bonati said.

Even more telling were the patients’ comments, she added. For example, one subject reported that friends noticed they were posting more frequently on social media. Other patients reported feeling more comfortable in gender-specific clothing and hairstyles. “One patient said, ‘I’m not sure if it’s the treatment itself or just knowing that I’m doing something that makes a difference.’ That’s what this is all about: empowering transgender individuals so that they feel more in control of their gender and how they’re feeling, improving quality of life, and reducing suicidality.”

Because World Professional Association for Transgender Health (WPATH) standards of care fail to address noninvasive or reversible gender-affirming procedures, a recent paper by Waldman et al recommends establishing such standards, particularly for transgender teens.6 “It’s an open field out there,” Meshkov Bonati said. And dermatologists have the opportunity to set such standards, which may include allowing mature teens to consent to reversible procedures, she adds.

Untreated gender dysphoria may lead to anxiety and depression that persist throughout adulthood, Meshkov Bonati noted: “That’s a huge burden of disease that could potentially be prevented.”

Accordingly, she said, injectable interventions for transgender patients should not be

Gender-Diverse Patients FROM PAGE 1

 Injectable can provide a noninvasive first step toward feminizing or masculinizing the features. Most patients have realistic expectations, with 44% achieving gender ideals with injectables. Insurance coverage varies widely for transgender transitioning procedures.

BY THE NUMBERS

4.6%

PROPORTION of insurance companies that covered permanent hair removal without restrictions;

26%

PROPORTION of insurance companies that covered only preoperative hair removal for genital surgery;

28.7%

PROPORTION of insurers that had no policies regarding transgender hair removal.

This [injectable intervention] isn’t the 65-year-old woman who comes in complaining of marionette lines or brown spots on her face. These are individuals who very deeply know that they are in the wrong body.”

Lauren Meshkov Bonati, MD, Colorado

CONTINUES ON PAGE 50

“
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viewed as cosmetic. “This isn’t the 65-year-old woman who comes in complaining of marionette lines or brown spots on her face. These are individuals who very deeply know that they are in the wrong body,” Meshkov Bonati said.

With this in mind, she said, injectable treatments are crucial to patient dignity. “It’s medically necessary, ethical care that will help adolescents affirm who they are,” Meshkov Bonati added. If dermatologists do not provide safe, ethical, accessible care, she cautioned that transgender patients will seek treatment elsewhere, sometimes with disastrous results.

One day, minimally invasive aesthetic treatments might be considered part of the pretreatment regimen required before gender-reassignment surgery, she said, adding, “Perhaps injectables are something we can use as a way to help the patient dip their toe in and see how it feels to start transitioning physically.”

As insurers’ willingness to cover hair removal for transgender patients grows, so will dermatologists’ role in securing coverage, said Erica D. Dommasch, MD, MPH, a dermatologist at Beth Israel Deaconess Medical Center and an assistant professor of dermatology at Harvard Medical School, both in Boston, Massachusetts.

In a study coauthored by Dommasch, 4.6% of 174 policies analyzed covered permanent hair removal without restrictions. According to the authors, the remaining 160 policies (95.4%) broadly excluded or did not mention gender-affirming care, prohibited coverage of hair removal or did not mention it, or only permitted coverage of hair removal preoperatively for genital surgery. Dommasch reported that 26% covered only preoperative hair removal for genital surgery, and 28.7% had no policies regarding transgender hair removal. 4

The Affordable Care Act (ACA) marketplace policies in states without transgender care protections were less likely to cover hair removal without restrictions than ACA policies in states with protections—2 of 85 policies (2.4%) in states without transgender care protections vs 5 of 38 policies (13.2%) in states with transgender care protections, and Medicaid policies were less likely to cover preoperative or nonsurgical hair removal compared with ACA policies—6 of 51 Medicaid policies (11.8%) vs 47 of 123 ACA policies (38.2%).

“Anecdotally, insurance coverage seems to be getting a little better over time,” she said. “Many insurance plans will cover permanent hair removal preoperatively, especially if they are covering the gender-affirming surgery.” Some insurers may occasionally cover hair removal in aesthetic areas such as the face, added Dommasch, who also works part time at Fenway Health, a Boston-based community health center that specifically serves the LGBTQ+ community.

Laser hair removal (LHR) is FDA approved for permanent hair reduction. Additionally, electrolysis is approved for hair removal because it reduces the number of hair follicles. The FDA’s distinction between permanent hair reduction and removal does not mean that electrolysis is more effective than laser hair removal, said Dommasch: “In fact, probably the contrary is true.”

Many insurance plans will cover permanent hair removal preoperatively, especially if they are covering the gender-affirming surgery.

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“Many insurance plans will cover permanent hair removal preoperatively, especially if they are covering the gender-affirming surgery.”

Many transgender patients require presurgical hair removal to prevent complications such as urinary retention and infections after gender-affirming surgery (GAS). Phalloplasty, the most common type of GAS used in transmasculine patients, involves creating a neovagina using skin flaps from the medial forearm or anterolateral thigh, both of which may need presurgical hair removal. 9

Creating a neovagina for transfeminine patients typically involves skin from the penile shaft or scrotum, the latter of which typically requires hair removal. “Areas of the scrotum that may be treated include either the midline, if using a pedicled scrotal flap, or entire scrotum, for free scrotal skin full-thickness grafts,” Dommasch said.

Because patients typically require 6 to 12 months of hair removal before undergoing GAS, she advised that it is crucial for dermatologists to confirm with patients and surgeons which genital areas and donor sites require treatment long before surgery.

“This can be done via photos or permanent ink markings of the sites. Keep in mind that the surgeon may want more than 1 site treated—they may want both forearms or legs treated,” she said. 10

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“In a recent study, 56% of patients undergoing phalloplasty consuls had forearm tattoos.” 10 If patients choose skin flaps from tattooed areas, that means the neophallus is going to have a tattoo, Dommasch explained. Additionally, tattoos can interfere with LHR: “If patients choose to use the forearm site, and they have a tattoo, these patients may need electrolysis for these areas.”

Dermatologists serving transgender patients must know that securing prior authorizations for hair removal will be time-consuming and may require dedicated staff, she said. “Keep trying,” she said. “These policies are continually changing. Insurers are very confused about what they should and should not cover in the context of gender-affirmation surgeries.”

Accordingly, Dommasch recommended becoming familiar with policies of the most common private insurers in the practice’s area—especially Medicaid—and creating templated prior authorization letters tailored to each insurer. Where possible, these letters should mirror language used in specific policies. She added that before covering presurgical hair removal, many insurers require documenting that patients have met all applicable WPATH criteria, 7 which are extensive.

Regarding billing, she suggested having a price list available for all potential hair removal sites. “Many insurers will pay a standard percentage of the asking price,” Dommasch said, while also recommending tracking reimbursement rates so that one can set prices commensurately. “Remember, if you increase your price for these patients, you may be increasing the price for patients who pay out of pocket,” she said. Dermatologists may bill permanent hair removal with CPT code 17999, unlisted skin procedure, which has no standard negotiated price.

“Looking forward, dermatologists are going to be very important in ensuring affordable, safe access to hair removal,” Dommasch said. “We need to work closely with policy makers, insurance companies, and other stakeholders. Hopefully, down the road we will get designated CPT codes for these gender-affirming procedures, and hair removal as well, which will make everyone’s life easier.”

Disclosures

Meshkov Bonati’s study was funded by Allergan. Dommasch reported no relevant conflicts of interest.

More Online

Scan for full reference list.
Incyte announced positive results from 2 phase 3 studies investigating the efficacy and safety of ruxolitinib cream (Jakafi; Incyte) for treatment of vitiligo in patients 12 years or older, according to a news release. Ruxolitinib is a Janus kinase (JAK) 1/2 inhibitor that is being evaluated for vitiligo and atopic dermatitis.

In the 2 phase 3 studies, TRuE-V1 (NCT04052425) and TRuE-V2 (NCT04057573), ruxolitinib cream met its primary end point of a proportion of patients achieving a greater than 75% improvement from baseline in the facial vitiligo area scoring index (F-VASI). Results demonstrated that significantly more patients treated with ruxolitinib cream 1.5% twice daily achieved F-VASI 75 than patients treated with vehicle at week 24. Both studies also met their secondary end points.

Additionally, the safety profiles for TRuE-V1 and TRuE-V2 were consistent with previously reported outcomes in phase 2 data, with no new safety signals being observed. The company plans to continue the long-term safety and efficacy portions of the studies, according to the news release.

Data from the studies will be submitted for publication and presented at an upcoming scientific meeting during the second half of 2021, according to Incyte.

“These positive results—the first phase 3 data to demonstrate significant improvements in facial and total body repigmentation—confirm the potential of ruxolitinib cream to be a meaningful treatment option for individuals living with and seeking treatment for their vitiligo,” said Jim Lee, MD, group vice president of inflammation and autoimmunity at Incyte in Wilmington, Delaware. “We look forward to working with regulators to bring this much-needed treatment option to patients. If approved, this would be the first and only treatment for repigmentation in vitiligo.”

Incyte reported it plans to submit marketing applications for ruxolitinib cream for patients 12 years or older to the FDA and European Medicines Agency in the second half of 2021. Currently, the FDA is reviewing the new drug application for ruxolitinib cream for the treatment of atopic dermatitis in patients 12 years and older.

“Vitiligo is a chronic immune-mediated skin condition that can significantly impact quality of life for those living with and [experiencing] this disease,” said David Rosmarin, MD, vice chair of research and education in the Department of Dermatology at Tufts Medical Center in Boston, Massachusetts. “As a clinician, I am extremely encouraged by the initial findings from the TRuE-V program and the potential to have ruxolitinib cream as a future topical treatment option for patients with vitiligo, who currently have limited therapies available that effectively and safely address repigmentation.”

Reference

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FOR MORE INFO: laroche-posay.us

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IMPORTANT SAFETY INFORMATION (cont.)

WARNINGS AND PRECAUTIONS

Infections

COSENTYX may increase the risk of infections. In clinical trials, a higher rate of infections was observed in COSENTYX treated subjects compared to placebo-treated subjects. In placebo-controlled clinical trials in subjects with moderate to severe plaque psoriasis, higher rates of common infections, such as nasopharyngitis (11.4% versus 8.6%), upper respiratory tract infection (2.5% versus 0.7%) and mucocutaneous infections with candida (1.2% versus 0.3%) were observed with COSENTYX compared with placebo. A similar increase in risk of infection was seen in placebo-controlled trials in subjects with psoriatic arthritis and ankylosing spondylitis. The incidence of some types of infections appeared to be dose-dependent in clinical studies. In the postmarketing setting, serious and some fatal infections have been reported in patients receiving COSENTYX. Exercise caution when considering the use of COSENTYX in patients with a chronic infection or a history of recurrent infection.

Instruct patients to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops a serious infection, monitor the patient closely and discontinue COSENTYX until the infection resolves.

Pre-treatment Evaluation for Tuberculosis

Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with COSENTYX. Avoid administration of COSENTYX to patients with active TB infection. Initiate treatment of latent TB prior to administering COSENTYX. Consider anti-TB therapy prior to initiation of COSENTYX in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Monitor patients closely for signs and symptoms of active TB during and after treatment.

Inflammatory Bowel Disease

Caution should be used when prescribing COSENTYX to patients with inflammatory bowel disease. Exacerbations, in some cases serious, occurred in COSENTYX treated subjects during clinical trials in plaque psoriasis, psoriatic arthritis, and ankylosing spondylitis. In addition, new onset inflammatory bowel disease cases occurred in clinical trials with COSENTYX. In an exploratory trial in 59 subjects with active Crohn’s disease, there were trends toward greater disease activity and increased adverse events in the secukinumab group as compared to the placebo group. Patients who are treated with COSENTYX should be monitored for signs and symptoms of inflammatory bowel disease.

Hypersensitivity Reactions

Anaphylaxis and cases of urticaria occurred in COSENTYX treated subjects in clinical trials. If an anaphylactic or other serious allergic reaction occurs, administration of COSENTYX should be discontinued immediately and appropriate therapy initiated.

The removable caps of the COSENTYX Sensoready® pen and the COSENTYX 1.0 mL and 0.5 mL prefilled syringes contain natural rubber latex, which may cause an allergic reaction in latex-sensitive individuals. The safe use of the COSENTYX Sensoready pen or prefilled syringe in latex-sensitive individuals has not been studied.

Immunizations

Prior to initiating therapy with COSENTYX, consider completion of all age appropriate immunizations according to current immunization guidelines. COSENTYX may alter a patient’s immune response to live vaccines. Avoid use of live vaccines in patients treated with COSENTYX.

MOST COMMON AdVERSE REACTIONS

Most common adverse reactions (>1%) are nasopharyngitis, diarrhea, and upper respiratory tract infection.

Please see additional Important Safety Information and Indications on the following page. Please see Brief Summary of full Prescribing Information on the previous pages.

STUDY DESIGNS:

The ERASURE and FIXTURE pivotal studies were Phase III, multicenter, randomized, double-blind, placebo-controlled trials. ERASURE evaluated 738 adults who received COSENTYX 300 mg (n=245), COSENTYX 150 mg (n=245), or placebo (n=248). FIXTURE evaluated 1306 adults who received COSENTYX 300 mg (n=327), COSENTYX 150 mg (n=327), placebo (n=326), or bialcitabine (n=326) subcutaneously at weeks 0, 1, 2, 3, and 4, followed by the same dose every 4 weeks. All patients were adults with moderate to severe plaque psoriasis who had a BSA ≥10%, PASI score ≥12, and IGA mod 2011 score ≥3, and were candidates for systemic therapy or phototherapy. Co-primary endpoint was the proportion of subjects who achieved a reduction in PASI score of ≥75% (PASI 75) from baseline to week 12 and clear or almost clear on the IGA mod 2011 at week 12 evaluated using NRI analysis. Other evaluated outcomes included improvements in itching, pain, and scaling at week 12 based on the Psoriasis Symptom Diary©.

FUTURE 2 was a Phase III, multicenter, randomized, double-blind, placebo-controlled trial that evaluated 397 adult patients with active PsA (≥3 swollen joints and ≥3 tender joints) despite use of NSAIDs, corticosteroids, or DMARDs. Patients had a diagnosis for ≥5 years and were randomized in a 1:1:1 ratio to receive COSENTYX 150 mg (n=132), COSENTYX 300 mg (n=132), or placebo (n=133) subcutaneously at weeks 0, 1, 2, 3, and 4, followed by the same dose every 4 weeks. Patients who received placebo were rerandomized (1:1) to COSENTYX 150 mg or COSENTYX 300 mg every 4 weeks, at week 16 or week 24, based on responder status. The primary endpoint was the percentage of patients with ACR20 response at week 24. Study population was mixed: ≥3/5 of patients were anti-TNFα-naive and ≥1/3 were anti-TNFα-experienced (patients could have been exposed to up to 3 different TNFα inhibitors). At baseline, 44% of patients treated with COSENTYX were treated with concomitant MTX.

TRANSFIGURE was a double-blind, randomized, placebo-controlled study examining the safety and efficacy of COSENTYX in patients with moderate to severe nail psoriasis. All patients were adults with chronic moderate to severe plaque psoriasis (PASI score ≥12 and BSA ≥10%) and significant nail involvement (fingernail NAPSI score ≥18 and ≥4 fingernails involved), who were candidates for systemic therapy. Patients were randomized to 1 of 3 arms: COSENTYX 300 mg (n=68), COSENTYX 150 mg (n=67), or placebo (n=65). Initial dosing: once weekly for 5 weeks; maintenance dosing: once every 4 weeks. At week 16, patients initially receiving placebo were rerandomized (1:1) to COSENTYX 150 mg or COSENTYX 300 mg; initial dosing once weekly for 5 weeks followed by once every 4 weeks. Primary end point NAPSI assessment at week 18.

MTX=methotrexate; NAPSI= Nail Psoriasis Severity Index; TNFα= tumor necrosis factor.

COSENTYX® (secukinumab) injection, for subcutaneous use

COSENTYX® (secukinumab) for injection, for subcutaneous use

Initial U.S. Approval: 2015

1 INDICATIONS AND USAGE

1.1 Plaque Psoriasis

COSENTYX® is indicated for the treatment of moderate to severe plaque psoriasis in patients 6 years and older who are candidates for systemic or phototherapy.

1.2 Psoriatic Arthritis

COSENTYX® is indicated for the treatment of adult patients with active psoriatic arthritis.

1.3 Ankylosing Spondylitis

COSENTYX® is indicated for the treatment of adult patients with active ankylosing spondylitis.

1.4 Non-Radiographic Axial Spondyloarthritis

COSENTYX® is indicated for the treatment of adult patients with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation.

2 CONTRAINDICATIONS

COSENTYX® contains a previous serious hypersensitivity reaction to secukinumab or to any of the excipients in COSENTYX. Cases of anaphylaxis have been reported during treatment with COSENTYX (see Warnings and Precautions (5.4)).

5 WARNINGS AND PRECAUTIONS

5.1 Infections

COSENTYX® may increase the risk of infections. In clinical trials, a higher rate of infections was observed in COSENTYX treated subjects compared to placebo-treated subjects. In placebo-controlled clinical trials in subjects with moderate to severe plaque psoriasis, higher rates of common infections, such as nasopharyngitis (11.4% versus 8.6%), upper respiratory tract infection (2.3% versus 0.7%) and mucocutaneous infections with candida (2.2% versus 0.3%) were observed with COSENTYX compared with placebo. A similar increase in risk of infection was seen in placebo-controlled trials in subjects with psoriatic arthritis, ankylosing spondylitis and non-radiographic axial spondyloarthritis. The incidence of some types of infections appeared to be dose-dependent in clinical studies (see Adverse Reactions (6.1)). In the postmarketing setting, serious and some local infections have been reported in patients receiving COSENTYX.

Exercise caution when considering the use of COSENTYX in patients with a chronic infection or a history of recurrent infection.

Instruct patients to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops a serious infection, monitor the patient closely and discontinue COSENTYX until the infection resolves.

5.2 Pre-Treatment Evaluation for Tuberculosis

Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with COSENTYX. Avoid administration of COSENTYX to patients with active TB infection. Indicate treatment of latent TB prior to administering COSENTYX. Consider anti-TB therapy prior to initiation of COSENTYX in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Monitor patients closely for signs and symptoms of active TB during and after treatment.

5.3 Inflammatory Bowel Disease

Caution should be used when prescribing COSENTYX to patients with inflammatory bowel disease.

Exacerbations, in some cases serious, occurred in COSENTYX treated subjects during clinical trials in plaque psoriasis, psoriatic arthritis, ankylosing spondylitis and non-radiographic axial spondyloarthritis. In addition, new onset inflammatory bowel disease cases occurred in clinical trials with COSENTYX. In an exploratory trial in 53 subjects with active Crohn’s disease, there were trends toward greater disease activity and increased adverse events in the secukinumab group compared to the placebo group. Patients who are treated with COSENTYX should be monitored for signs and symptoms of inflammatory bowel disease [see Adverse Reactions (6.1)].

5.4 Hypersensitivity Reactions

Anaphylaxis and cases of urticaria occurred in COSENTYX treated subjects in clinical trials. If an anaphylactic or other serious allergic reaction occurs, administration of COSENTYX should be discontinued immediately and appropriate therapy initiated [see Contraindications (4), Adverse Reactions (6.1)].

5.5 Risk of Hypersensitivity in Latent-Sensitive Individuals

The restoration of the skin of the COSENTYX 1 mL and 0.5 mL prefilled syringes contain natural rubber latex, which may cause an allergic reaction in latent-sensitive individuals. The safe use of COSENTYX Sensoray pen or prefilled syringe in latex-sensitive individuals has not been studied.

5.6 Immunizations

Prior to initiating therapy with COSENTYX, consider completion of all age appropriate immunizations according to current immunization guidelines. COSENTYX may alter a patient’s immune response to live vaccines. Avoid use of live vaccines in patients treated with COSENTYX.

6 ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail elsewhere in the labeling: • Infections [see Warnings and Precautions (5.1)] • Inflammatory Bowel Disease [see Warnings and Precautions (5.3)] • Hypersensitivity Reactions [see Warnings and Precautions (5.4)]

6.1 Clinical Trials Experience

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

Adult Plaque Psoriasis

A total of 3430 plaque psoriasis subjects were treated with COSENTYX in controlled and uncontrolled clinical trials. Of these, 1641 subjects were exposed for at least 1 year.

Four placebo-controlled Phase 3 trials in plaque psoriasis subjects were pooled to evaluate the safety of COSENTYX in comparison to placebo up to 12 weeks after treatment initiation, in Trials PsO1, PsO2, PsO3, and PsO4. In total, 2077 subjects were evaluated (691 to COSENTYX 300 mg group, 692 to COSENTYX 150 mg group, and 694 to placebo group). Subjects randomized to COSENTYX received 300 mg or 150 mg doses subcutaneously at Weeks 0, 1, 2, 3, and 4 followed by the same dose every 4 weeks [see Clinical Studies (14) in the full prescribing information).

Table 2 summarizes the adverse reactions that occurred at a rate of at least 1% and at a higher rate in the COSENTYX groups than the placebo group during the 12-week placebo-controlled period of the placebo-controlled trials.
to CONSENTYX with the incidences of antibodies to other products may be misleading. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may develop antidrug antibodies, approximately one-half had antibodies that were classified as neutralizing. Therefore, the incidence of antibody development might not have been reliably determined. Of the subjects who this assay has limitations in detecting anti-secukinumab antibodies in the presence of secukinumab; there-

As with all therapeutic proteins, there is the potential for immunogenicity. The immunogenicity of CONSENTYX was studied in one randomized, double-blind, placebo-controlled non-radiographic axial spondyloarthritis trial with 555 patients (165 patients on with load CONSENTYX, 184 patients on without load CONSENTYX and 186 patients on placebo). The safety profile for patients with nr-axSpA treated with CONSENTYX was overall similar to the safety profile seen in patients with AS and other previous experience with CONSENTYX. Patients in nr-axSpA study who received the loading dosing regimen compared to those without the loading regimen, had higher incidence of infections and infestations (92 per 100 patient-years vs 72 per 100 patient-years), including nasopharyngitis, upper respiratory tract infection and urinary tract infection, and gastrointestinal disorders (27 per 100 patient-years vs 22 per 100 patient-years), including gastritis, lower abdominal pain, colitis, diarrhea, and hematochezia.

6.2 Immunogenicity

As with all therapeutic proteins, there is the potential for immunogenicity. The immunogenicity of CONSENTYX was evaluated using an electrochemiluminescence-based bridging immunoassay. Less than 1% of subjects treated with CONSENTYX developed antibodies to secukinumab in up to 52 weeks of treatment. However, this assay has limitations in detecting anti-secukinumab antibodies in the presence of secukinumab; therefore, the incidence of antibody development might not have been reliably determined. Of the subjects who developed antidrug antibodies, approximately one-half had antibodies that were classified as neutralizing. Neutralizing antibodies were not associated with loss of efficacy. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors, including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of incidence of antibodies to CONSENTYX with the incidences of antibodies to other products may be misleading.

7 DRUG INTERACTIONS

CYP450 Substrates

The formation of CYP450 enzymes can be altered by increased levels of certain cytokines (e.g., IL-1, IL-6, IL-10, TNFα, IFN) during chronic inflammation. Upon initiation or discontinuation of CONSENTYX in patients who are receiving concomitant CYP450 substrates, particularly those with a narrow therapeutic index, consider monitoring for therapeutic effect or drug concentration and consider dosage adjustment of the CYP450 substrate as needed [see Clinical Pharmacology (12.3) in the full prescribing information].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Limited available human data with CONSENTYX use in pregnant women are insufficient to inform a drug-associated risk of adverse developmental outcomes. In an embryo-fetal development study, no adverse developmental effects were observed in fetuses born to pregnant monkeys after subcutaneous administration of secukinumab during organogenesis at doses up to 30 times the maximum recommended human dose (MRHD) (see Data). The background risk of major birth defects and miscarriage for the indicated population is unknown; however, the background risk in the U.S. general population of major birth defects is 2% to 4% and of miscarriage is 15% to 20% of clinically recognized pregnancies.

Data

Animal Data

An embryo-fetal development study was performed in cynomolgus monkeys with secukinumab. No malformations or embryo-fetal toxicity were observed in fetuses from pregnant monkeys that were administered secukinumab weekly by the subcutaneous route during the period of organogenesis at doses up to 30 times the MRHD (on a mg/kg basis at a maternal dose of 150 mg/kg). A pre- and post-natal development toxicity study was performed in mice with a murine analog of secukinumab. No treatment-related effects on functional, morphological or immunological development were observed in fetuses from pregnant mice that were administered the murine analog of secukinumab on gestation days 6, 11, and 17 and on postpartum days 4, 10, and 16 at doses up to 150 mg/kg/dose.

8.2 Lactation

Risk Summary

It is not known whether secukinumab is excreted in human milk or absorbed systemically after ingestion. There are no data on the effects of CONSENTYX on the breastfed child or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for CONSENTYX and any potential adverse effects on the breastfed child from CONSENTYX or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of CONSENTYX have been established in pediatric subjects aged 6 years and older with moderate to severe plaque psoriasis [see Adverse Reactions (6.1), Clinical Studies (14.2) in the full prescribing information]. Safety and effectiveness of CONSENTYX in pediatric patients with plaque psoriasis below the age of 6 years have not been established. The safety and effectiveness of CONSENTYX in pediatric patients in other indications have not been established.

8.5 Geriatric Use

Of the 3430 plaque psoriasis subjects exposed to CONSENTYX in clinical trials, a total of 230 were 65 years or older, and 32 subjects were 75 years or older. Although no differences in safety or efficacy were observed between older and younger subjects, the number of subjects aged 65 years and older was not sufficient to determine whether they responded differently from younger subjects.

10 OVERDOSAGE

Doses up to 30 mg/kg intravenously have been administered in clinical trials without dose-limiting toxicity. In the event of overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment be instituted immediately.

Manufactured by:
Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936
US License Number 1244
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T2021-66
Help your patients shine past their plaque psoriasis

The Complete Cosentyx Approach

Give your patients a chance to

Look Better®
Move Better®
Feel Better®

Make COSENTYX your 1st-choice systemic treatment for your appropriate patients

>195,000 patients prescribed in the US2†
>2,000,000 prescriptions written in the US2†

Jordan has been an actual COSENTYX patient since 2016. She has found relief from her plaque psoriasis, nail psoriasis, and psoriatic arthritis.*

*Individual results may vary. Jordan has been compensated for her time.

‡Across plaque psoriasis, psoriatic arthritis, and ankylosing spondylitis indications.

Please see ERASURE, FIXTURE, FUTURE 2, and TRANSFIGURE study designs on previous page.

ACR=American College of Rheumatology; IGA=Investigator’s Global Assessment modified 2011; PASI=Psoriasis Area and Severity Index; PsO=plaque psoriasis.

INDICATIONS

COSENTYX® (secukinumab) is indicated for the treatment of moderate to severe plaque psoriasis in patients 6 years and older who are candidates for systemic therapy or phototherapy.

COSENTYX is indicated for the treatment of adult patients with active psoriatic arthritis.

COSENTYX is indicated for the treatment of adult patients with active ankylosing spondylitis.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

COSENTYX is contraindicated in patients with a previous serious hypersensitivity reaction to secukinumab or to any of the excipients in COSENTYX. Cases of anaphylaxis have been reported during treatment with COSENTYX.

Please see additional Important Safety Information on the previous page.

Please see Brief Summary of full Prescribing Information on previous pages.