Although most skin conditions are not life-threatening, they can negatively affect quality of life. It is important for children and adolescents to fit in with their peers and not feel that they are different. Dermatologists need to think a bit differently when dealing with patients with vitiligo, a loss of skin color that occurs when pigment-producing cells in the body die or stop functioning. A productive patient-clinician relationship for this disorder starts with the first encounter.

Continue reading on page 32

Keith Loria, Staff Correspondent

Talking About Vitiligo

Opening a dialogue about an adolescent’s skin disorder
News just for you, 24/7

You might notice a small logo on the cover of this issue—it represents our Medical World News’ channel. If you are not familiar with this 24/7 platform, I invite you to visit it whenever you have the chance: https://www.medicalworldnews.com/

Easy to navigate and now in its seventh season, this website dedicated to medical news offers viewers 6 shows:

Medical Minutes™ is a nightly news show that recaps the news of the day from all of the medical brands at MJH Life Sciences®.

Inside the Practice™ highlights a unique, nonclinical aspect of a specialty—for example, a hospital’s celebration to mark a patient’s discharge.

Deep Dive™ offers an in-depth exploration of a high-impact topic, such as the latest news on COVID-19 vaccines and children.

Wellbeing Checkups™ shares health care providers’ tips for staying mentally and physically healthy, including suggestions regarding regular exercise, proper nutrition, and meditation practice.

After Hours™ reveals what clinicians do when they’re not working: They’re scuba diving, playing piano, traveling, etc.

Second Opinion™ gives 2 medical experts a platform to discuss a compelling and timely health topic.

Behind the Science™ poses the same question to multiple physicians, garnering a variety of perspectives on some of the most important issues in the health care space.

In each issue of Dermatology Times®, we feature a page dedicated to the latest news on COVID-19 vaccines and children.

Behind the Science™ highlights a unique, nonclinical aspect of a specialty—for example, a hospital’s celebration to mark a patient’s discharge.

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In each issue of Dermatology Times®, we feature a page dedicated to the latest news segments (page 45). We hope you will take some time out of your hectic schedule to enjoy these shows.

Mike Hennessy Jr. is the President and CEO of MJH Life Sciences®.
In adults with moderate to severe PsO who are candidates for systemic therapy or phototherapy and for adults with active PsA

Treat the Big Picture

Consider the seen, unseen, and unforeseen in your adult patients

**Seen**

2/3 of adults with psoriasis may have more than 1 manifestation, often including scalp and nail

**Unseen**

Up to 41% of adults with psoriasis may also have PsA

**Unforeseen**

PsA inflammation can be tied to irreversible joint damage

*Involvement in the nails, scalp, palms, or soles, or concomitant PsA.
†According to real-world data from the Corrona Registry among 2042 patients with PsO. All Corrona psoriasis patients aged 18 years or older enrolled by May 10, 2018, on a biologic therapy were included. Patients were diagnosed by a dermatologist and indicated starting a qualifying biologic psoriasis treatment at the enrollment visit or within the 12 months prior to the enrollment visit. The primary objective of this report was to compare patient demographics, clinical characteristics, PROs, and treatment characteristics in psoriasis patients with hard-to-treat areas (scalp, nail, and palmoplantar) compared to those without scalp, nail, or palmoplantar psoriasis in patients enrolled in the Corrona PsO Registry. Because the data source was a US registry, the results might not be generalizable to all patients with moderate to severe psoriasis. Participation in the Corrona Psoriasis Registry by patients and their dermatologists was voluntary.

PRO, patient-reported outcome; PsA, psoriatic arthritis; 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 active psoriatic arthritis in patients 2 years of age and older.
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 next page. Please see Brief Summary of full Prescribing Information on the following pages.
IMPORTANT SAFETY INFORMATION

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 8.8%), 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. 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 and psoriatic arthritis. 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 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 on the previous page. Please see Brief Summary of full Prescribing Information on the following pages.

Clinical and radiological study of early psoriatic arthritis: an early synovitis clinic experience.

Immunization guidelines. COSENTYX may alter a patient’s immune response to live vaccines. Avoid use of live vaccines in prefilled syringe in latex-sensitive individuals has not been studied.

The removable caps of the COSENTYX Sensoready® pen and the COSENTYX 1 mL and 0.5 mL prefilled syringes contain natural inflammatory bowel disease. Compared to the placebo group. Patients who are treated with COSENTYX should be monitored for signs and symptoms of inflammatory bowel disease.

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 [see Adverse Reactions (6.1)].

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 [see Warnings and Precautions (5.4)].

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 PsA, AS and ps-aXSpA. 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 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.

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In 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.

The safety of COSENTYX was assessed in two Phase 3 trials in pediatric subjects with plaque psoriasis. The first was a randomized, double-blind, placebo and active-controlled, 236-week trial (Trial PsO6) that enrolled 162 pediatric subjects aged 4 years and older, with severe plaque psoriasis (defined by PASI score ≥ 20, a IGA modified 2011 score of ≥ 4, and involving ≥ 10% of the body surface area) who were candidates for systemic therapy. The 162 subjects were randomized to receive placebo, a biologic active comparator, or COSENTYX. In the COSENTYX groups, subjects with body weight ≥ 30 kg who had body weight ≥ 50 kg received either 300 mg or 150 mg of secukinumab every 3 weeks [see the safety profile reported in these trials was consistent with the safety profile reported in adult plaque psoriasis trials. Infections

In the adult plaque-controlled period of the trials in patients with PsA, the overall proportion of patients with adverse events was similar in the secukinumab and placebo treatment groups (59% and 58%, respectively). The adverse events that occurred at a proportion of at least 2% and at a higher proportion in the COSENTYX treatment groups than the placebo group during the 12-week placebo-controlled period of the placebo-controlled trials.

Table 2: Adverse Reactions Reported by Greater Than 1% of Subjects With Plaque Psoriasis Through Week 12 in Trials PsO1, PsO2, PsO3, and PsO4

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>COSENTYX 300 mg n (%)</th>
<th>COSENTYX 150 mg n (%)</th>
<th>Placebo n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasopharyngitis</td>
<td>79 (11.4)</td>
<td>85 (12.3)</td>
<td>60 (8.6)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>28 (4.1)</td>
<td>18 (2.6)</td>
<td>10 (1.4)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>17 (2.5)</td>
<td>22 (3.2)</td>
<td>5 (0.7)</td>
</tr>
<tr>
<td>Mucocutaneous infections</td>
<td>10 (1.4)</td>
<td>10 (1.4)</td>
<td>5 (0.7)</td>
</tr>
<tr>
<td>Oral herpes</td>
<td>5 (0.7)</td>
<td>5 (0.7)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>8 (1.2)</td>
<td>7 (1.0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Urticaria</td>
<td>4 (0.6)</td>
<td>8 (1.2)</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>8 (1.2)</td>
<td>2 (0.3)</td>
<td>1 (0.1)</td>
</tr>
</tbody>
</table>
| Adverse reactions that occurred at rates less than 1% in the placebo-controlled period of Trials PsO1, PsO2, PsO3, and PsO4 through Week 12 included: sinusitis, tinea pedis, conjunctivitis, tonsillitis, oral candidiasis, inguinal, oropharyngeal, otitis media, otitis externa, inflammatory bowel disease, increased liver transaminases, and neutropenia.

Infections

In the placebo-controlled period of the clinical trials in plaque psoriasis (a total of 1382 subjects treated with COSENTYX and 694 subjects treated with placebo up to 12 weeks), infections were reported in 28.7% of subjects treated with COSENTYX compared with 18.9% of subjects treated with placebo. Serious infections occurred in 0.14% of subjects treated with COSENTYX and in 0.9% of subjects treated with placebo.

Over the entire treatment period (a total of 3430 plaque psoriasis subjects treated with COSENTYX for up to 12 weeks for the majority of subjects), infections were reported in 47.5% of subjects treated with COSENTYX (0.9 per patient-year of follow-up). Serious infections were reported in 1.2% of subjects treated with COSENTYX (0.015 per patient-year of follow-up).

Phase 3 data showed an increasing trend for some types of infection with increasing serum concentration of secukinumab. (see Warnings and Precautions (5.4)).

Cases of serious infections were associated with neutropenia; however the causal relationship was not established.

In the open-label extension of Trials PsO1 and PsO2, neutropenia (ANC < 1 x 10^9/L) was reported in 1% of COSENTYX treated subjects (0.3 per 100 patient-years). Some cases of serious infections were associated with neutropenia; however the causal relationship was not established.

Influenza

Influenza is a common viral infection that can cause serious illness, hospitalization, and death in susceptible patients, especially in the elderly.

The safety of COSENTYX was assessed in two Phase 3 trials in pediatric subjects with plaque psoriasis. The first was a randomized, double-blind, placebo and active-controlled, 236-week trial (Trial PsO6) that enrolled 162 pediatric subjects aged 4 years and older, with severe plaque psoriasis (defined by PASI score ≥ 20, a IGA modified 2011 score of ≥ 4, and involving ≥ 10% of the body surface area) who were candidates for systemic therapy. The 162 subjects were randomized to receive placebo, a biologic active comparator, or COSENTYX. In the COSENTYX groups, subjects with body weight ≥ 30 kg who had body weight ≥ 50 kg received either 300 mg or 150 mg of secukinumab every 3 weeks.
Similar to the clinical trials in patients with psoriasis, there was an increased proportion of patients with infections in the COSENTYX groups (29%) compared to placebo group (26%).

There were cases of Crohn’s disease and ulcerative colitis that include patients who experienced either exacerbations or the development of new disease. There were three cases of inflammatory bowel disease, of which two patients received secukinumab and one received placebo.

**Ankylosing Spondylitis**

COSENTYX was studied in a two-placebo-controlled AS trials with 590 patients (394 patients on COSENTYX and 196 patients on placebo). Of the 394 patients who received COSENTYX, 145 patients received a subcutaneous load of COSENTYX (study AS1), and 249 received an intravenous loading dose of secukinumab (study AS2) followed by COSENTYX administered by subcutaneous injection every four weeks. During the 16-week placebo-controlled period of the trials in patients with AS, the overall proportion of patients with adverse events was higher in the secukinumab groups than the placebo-treatment groups (66% and 59%, respectively). The adverse events that occurred at a proportion of at least 2% and at a higher proportion in the COSENTYX groups than the placebo groups during the 16-week placebo-controlled period were nasopharyngitis, nausea, and upper respiratory tract infection. The safety profile observed in patients with ankylosing spondylitis treated with COSENTYX is consistent with the safety profile in psoriasis. In a third controlled study of AS (study AS3), the safety profile of the 300 mg dose of COSENTYX was consistent with the safety profile of the 150 mg dose of COSENTYX. Similar to clinical trials in patients with psoriasis, there was an increased proportion of patients with infections in the COSENTYX groups (31%) compared to the placebo group (18%).

In the original AS program, with 571 patients exposed to COSENTYX there were 8 cases of inflammatory bowel disease during the entire treatment period (5 Crohn’s (0.7 per 100 patient-years) and 3 ulcerative colitis (0.4 per 100 patient-years)). During the placebo-controlled 16-week period, there were 2 Crohn’s disease exacerbations and 1 new onset ulcerative colitis case that was a serious adverse event in patients treated with COSENTYX compared to none of the patients treated with placebo. During the remainder of the study when all patients received COSENTYX, 1 patient developed Crohn’s disease, 2 patients had Crohn’s exacerbations, 1 patient developed ulcerative colitis, and 1 patient had an ulcerative colitis exacerbation.

**Non-Radiographic Axial Spondyloarthritis**

COSENTYX was studied in one randomized, double-blind, placebo-controlled nr-axSpA trial with 535 patients (185 patients on with load COSENTYX, 184 patients on without load COSENTYX and 166 patients on placebo). The safety profile for patients with nr-axSpA treated with COSENTYX was overall similar to the safety profile seen in patients with AS and other previous experience with COSENTYX. Patients in nr-axSpA study who received the loading dosing regimen compared to those without the loading regimen, had higher incidence of infections and infections (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 hematocrit. Juvenile Psoriatic Arthritis and Enthesitis-Related Arthritis

COSENTYX was studied in one double-blind, placebo-controlled, event-driven, randomized trial in 86 pediatric patients aged 2 to 18 years old with Juvenile Psoriatic Arthritis (JPsA) and ERA. The safety profile reported in this study was consistent with the safety profile of secukinumab.

**Immunogenicity**

As with all therapeutic proteins, there is the potential for immunogenicity. The immunogenicity of COSENTYX was evaluated using an electrochemiluminescence-based bridging immunosay. Less than 1%, of subjects treated with COSENTYX 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 COSENTYX with the incidences of antibodies to other products may be misleading.

**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, IFNγ) during chronic inflammation.

Upon initiation or discontinuation of COSENTYX 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).

**Use in Specific Populations**

**Pregnancy**

**Risk Summary**

Limited available human data with COSENTYX 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 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 postnatal 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.

**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 COSENTYX 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 COSENTYX and any potential adverse effects on the breastfed child from COSENTYX or from the underlying maternal condition.

**Pediatric Use**

The safety and effectiveness of COSENTYX have been established in patients weighing 15 kg or more with body surface area ≥1.5 m² with ankylosing spondylitis treated with COSENTYX is consistent with the safety profile in psoriasis. In a third controlled study of AS (study AS3), the safety profile of the 300 mg dose of COSENTYX was consistent with the safety profile of the 150 mg dose of COSENTYX.

**Pediatric Use**

The safety and effectiveness of COSENTYX have been established in pediatric patients 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 COSENTYX in pediatric patients with plaque psoriasis before the age of 6 years have not been established.

The safety and effectiveness of COSENTYX have been established in patients weighing 15 kg or more with JPsA (2 years and older) and ERA (4 years and older) (see Adverse Reactions (6.1), Clinical Studies (14.6) in the full prescribing information).

The safety and effectiveness of COSENTYX in pediatric patients below the age of 2 years and with body weight less than 15 kg have not been established.

**Geriatric Use**

Of the 3430 plaque psoriasis subjects exposed to COSENTYX 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.

**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 © Novartis T2921-182
Dermatologist Tells a Patient That He Performs Plastic Surgery. Is This Fraud?

LEGAL EAGLE with David J. Goldberg, MD, JD

DR SURGERY IS KNOWN in the dermatologic community as an aggressive, highly competent dermatologic surgeon. He has been doing blepharoplasty and facelift procedures for years. In fact, he even has privileges to do these procedures in the surgery department of the local hospital. Recently Dr Surgery expanded his horizons and began performing abdominoplasties. Unfortunately, the third time he did an abdominoplasty, the patient became septic. She survived but had permanent lung and kidney damage secondary to the sepsis. The patient has sued Dr Surgery, contending that he fraudulently misrepresented himself as a plastic surgeon. He contends that he tells his patients that he does plastic surgery, but he does not state that he is a plastic surgeon. Does his patient, the suing plaintiff, have a claim based on fraud?

It is well established that physicians are required to disclose all material information to their patients to help them make informed decisions. But is the physician's experience part of the relevant information that is crucial for a patient to make informed decisions? Most courts have determined that it is. But the question to be asked is whether the lack of such disclosure raises an issue of fraud.

In Howard v. UMDNJ, a New Jersey court case decided in 2002, the plaintiff patient went to see the defendant physician for a consultation concerning back problems that he had as a result of 2 car accidents. The physician contended that during a consultation, when corrective surgery was recommended, he had informed the plaintiff of all the alternatives and risks. After hearing the information, the plaintiff elected to undergo surgery. The plaintiff claimed that he was not made aware of all of the risks during the consultation. Specifically, the plaintiff contended that when the physician was asked if he was board certified in neurosurgery, he said that he was, even though he was not. Plaintiff also contended that it was only after the doctor misrepresented the number of times he had performed this procedure that the plaintiff agreed to undergo the procedure. There were subsequent complications from the procedure, and the plaintiff became quadriplegic. The plaintiff tried to bring a claim for fraudulent misrepresentation as well as lack of informed consent. The court said that the case raised the issue of whether a patient’s consent to surgery obtained through alleged misrepresentations about the physician’s professional experience and credentials is properly addressed in a claim of lack of informed consent, or battery, or if it should constitute a separate and distinct claim based on fraud. The court was not convinced that misrepresentation of experience and credentials was enough to be considered as an independent fraud claim. This issue, the court stated, could be evaluated simply as an issue of informed consent. The court stated that although personal credentials and experience may not be a required part of an informed consent disclosure under the current standard of care required of doctors, the question raised in this case is whether significant misrepresentations concerning physician’s qualifications can affect the validity of consent obtained. The answer obviously is they can.

In the end, Dr Surgery’s actions are more likely to be evaluated based on the actual surgery performed or on the appropriateness of informed consent, rather than on whether he was a plastic surgeon or was a doctor performing plastic surgery. It is not likely that a fraud claim will hold up in court.

Phase 1/2 Study of Topical Biologic Shows Positive Results for the Management of Basal Cell Carcinoma

Kaitlyn Bader, Associate Editor

MEDIWOUND, A BIOPHARMA-CUTICAL COMPANY that develops and produces biotherapeutic solutions for tissue repair and regeneration, announced positive initial data from a US phase 1/2 study of topical biologic MW005 for the management of low-risk basal cell carcinoma (BCC). Eleven of the 16 participants in the continuous open-label study achieved complete histological clearance of their target lesions following the use of MW005. Participants had either superficial or nodular BCC and received 7 topical applications of MW005 once a day, every other day. At the end of the treatment course, participants were monitored for 8 weeks to assess the healing status of their lesions and any adverse effects. At the end of 8 weeks post treatment, all participants had their targeted lesions excised and specimens were collected for an independent histological examination. The resulting data suggest that MW005 was safe and well-tolerated by the participants. A self-administered topical therapy for basal cell carcinoma would be a tremendous asset to dermatology, especially for basal cell carcinomas located in difficult-to-treat facial locations. Topical nonsurgical basal cell carcinoma therapy would provide effective treatment without facial deformity,” said Zoe Diana Draelos, MD, adjunct assistant professor in the Department of dermatology at the Duke University School of Medicine in Durham, North Carolina.

MW005 is a topical biologic drug with a concentration of proteolytic enzymes enriched in bromelain. The development of MW005 is supported by data found in several toxicological and other preclinical studies. In 2021 a clinical case series published in a peer review paper, MW005 was used to destroy basal cell carcinoma and provided preliminary clinical proof of concept that its use could be safe and effective.

With the positive results from the phase 1/2 study of MW005, there is hope that a topical biologic for patients with basal cell carcinoma will be available. Rather than always relying on surgical excisions, patients may be able to find relief through a self-applied topical treatment. MediWound expects to announce the study’s final data by the end of 2022.

References
**Microbiome Musings**

_COSMETIC CONUNDRUMS_ with Zoe Diana Drae coal, MD

**Q** What does “microbiome friendly” mean on skin care product labels?

The microbiome is a hot research and product development topic. As dermatologists, we are really microbiome physicians managing many skin diseases representing dysbiosis, such as impetigo, atopic dermatitis, seborrheic dermatitis, and acne. It is compelling to think that by changing the microbiome with a skin care product you could manage these common diseases. This has captivated the imagination of cosmetic chemists. Unfortunately, creating products that change the microbiome has proved very difficult, and assessing the change requires large numbers of participants in extensive, expensive consumer testing.

This has led to the adoption of the term microbiome friendly. It means the product basically does not change the microbiome. Is this important? Yes, because the microbiome is necessary for skin health and is determined by the immune system. Skin devoid of a microbiome is susceptible to the overgrowth of pathogenic organisms. Is it possible to permanently destroy the microbiome? No. The microbiome can be altered temporarily by cleansing, for example, but is restored back to the organism mix unique to the individual as nonpathogenic organisms quickly reproduce. Thus, most skin care products are microbiome friendly. This claim can be supported by swabbing and culturing the microbiome before and after product application and noting minimal change in the organism amount and species mix. Although microbiome friendly is an important claim, it can be easily achieved with most cosmetic skin care products.

**Q** How do products work with the microbiome to sustain skin health?

Working with your microbiome is another commonly used phrase on the labels of skin care products. It really means the same thing as microbiome friendly. Both claims indicate the microbiome does not change with product use. However, the microbiome can change temporarily, which could cause problems with skin health. For example, if you shake hands with a person infected with methicillin-resistant _Staphylococcus aureus_ (MRSA), which was a transient organism on your skin. If you do not wash your hands and then put your finger inside your nose, the organism could become part of your nasal mucosa microbiome, reproduce, and create an infection. The purpose of hand washing for hygiene purposes is to remove transient pathogenic organisms from the skin surface. You might say that all cleansers, no matter what type, work with your microbiome to sustain skin health simply by removing transient pathogenic organisms.

You could also say that all moisturizers work with your microbiome to sustain skin health by improving the skin barrier. An intact barrier without microflora due to dehydration is better at preventing the entry of bacteria into the skin. Moisturizers also create an environment for barrier repair by decreasing transepidermal water loss. This also improves skin health and prevents the entry into the viable epidermis of pathogenic organisms.

**Q** Can skin care products really change the skin microbiome?

Cleansers can transiently change the microbiome, but what about moisturizers? There are several categories of moisturizer formulations designed to modify the microbiome. One category contains ingredients designed to improve the growth of good bacteria. The most commonly used ingredient for this purpose is inulin, a dietary fiber composed of polysaccharides, that functions as a prebiotic. The other category contains live bacteria designed to repopulate the skin with good bacteria and is known as a probiotic. Under excellent conditions, the skin only retains approximately 16% of the bacteria in a probiotic, and even these bacteria disappear over time. True probiotic preparations with live bacteria must be refrigerated. They cannot contain preservatives, which function in room temperature formulations to kill bacteria. Most currently marketed room temperature probiotic formulations contain dead lyophilized bacteria incapable of colonizing the skin. Thus, I would say that skin care products may temporarily change the skin microbiome, but the change is likely not durable.

Can skin care products really change the skin microbiome? In a 2019 review, she and her coauthors wrote that “large, double-blind, placebo-controlled trials are required to determine the effect of microminutrient supplementation on hair growth in those patients with both micronutrient deficiency and nonscarring alopecia to establish any association between hair loss and micronutrient deficiency.” Tosti believes research conducted since the publication of the review has not clarified the picture, especially as it pertains to the role of iron, folate, vitamin B₁₂, and zinc in managing AA, AGA, or TE. However, Tosti noted, which is not to say that supplements don’t offer some benefits. “Supplements may prevent AA and possibly prevent or halt AGA, but neither of those conclusions is evidence-based. They can halt TE, but only in case of deficiencies,” she said.

She also cited misinformation as a major issue with supplementation. “I often see patients taking supplements that contain ingredients that are not useful and can even worsen hair loss, such as vitamin A. Patients often take biotin and are not informed that it can affect blood test results. Supplements can cause [adverse] effects, and people often don’t know,” she noted.

Tosti remains a supplement skeptic. “This is a misconception, confusing supplements and effective treatments,” she told Dermatology Times.

**Disclosures**

Tosti listed the following relevant disclosures: DL Laboratories, Eli Lilly and Company, Monat Global, Pfizer, Springer Science + Business Media, Taylor & Francis, and Thirty Madison.

**References**

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THE MOST VALUABLE ASSET: For nearly every dermatologist is their ability to practice their profession, as the future income stream from this asset is significant and quantifiable. To protect this asset for themselves and for others dependent on them, dermatologists rely on disability and life insurance as fundamental "asset protectors." Young dermatologists should secure these tools early on in their careers, and established physicians should regularly review existing insurance policies to ensure they are maintaining necessary levels of protection.

We covered disability insurance in Part 1 of this 2-part article (see the August issue of Dermatology Times®), and now we will focus on the basics physicians need to know about life insurance in Part 2.

Term Life Insurance
A term life insurance policy pays a specific lump sum to your designated beneficiary upon your death. As such, it plays an important role in providing temporary income protection for your family (or practice/partners as part of a buy-sell arrangement).

Given its affordability, term is the most common type of life insurance policy. The premium on a term policy is low compared with other types of life insurance policies because the term policy carries no cash value and provides protection for a limited period of time (referred to as a term; usually 5, 10, 15, or 20 years). Term policies work simply— you pay a premium each year, typically, and the policy pays out if you die within the term period. If not, there is no payment or accumulated value. The vast majority of term policies never pay out because the insured lives past the end of the term.

Permanent Life Insurance
The category of permanent life insurance comprises products that, unlike those of term policies, carry cash values along with death benefits and can last for the entirety of the insured’s life—to age 100, 115, or beyond. (Of course, these products are “permanent” only as long as the required premiums are paid on time.) Because there are several different products in the general category of permanent insurance, and they are more complex than term policies, we will cover them in more depth.

One significant advantage of all permanent policies is that they enjoy tax-free growth of cash value and, if properly managed, tax-free access to the cash value. These tax benefits, along with asset protection in many states, is what attracts many dermatologists to permanent insurance.

Although there are more than 5 major categories of permanent life insurance, we only have room here to describe 2. For more depth on this topic, see the “special offers” at the end of this article to request or download our free book.

1 Whole Life Insurance
Whole life (WL) insurance pays a death benefit to the beneficiary you name and offers you a cash value account with tax-deferred cash accumulation.

Pros: WL insurance has a savings element (cash value) that is tax deferred. The cash value grows based on the life insurance company paying a dividend. This dividend is determined by the life insurance company, is not guaranteed, and is likely to change annually. Because of the low interest-rate environment over the last 15 years, dividend rates on WL policies have been decreasing.

You can borrow from this account free of income tax, or, if it is properly structured, you can cash in the policy during your lifetime. It has a fixed premium that can’t increase during your lifetime (as long as you pay the planned amount), and your premium is invested for you long term. Because it has the cash accumulation component, WL insurance can offer benefits such as tax reduction, wealth accumulation, asset protection, estate planning, and tax diversification of asset classes.

Cons: WL insurance does not allow you to invest in separate accounts (eg, money market, stock, and bond funds). Thus, your policy’s returns will be tied to the life insurance company’s dividend credit based on that company’s underlying investments. It also does not allow you to split your money among different accounts or move your money between accounts, and it does not allow premium flexibility or face amount (the death benefit amount) flexibility.

2 Equity-Indexed Universal Life Insurance
Equity-indexed universal life (EIUL) insurance is a universal life policy (which has more premium and policy flexibility than a WL product) that allows you to select from a list of stock market indices to grow your cash value. If the investments fail, there is a guaranteed minimum death benefit paid to your beneficiary upon your death.

EIUL insurance gives you more upside than a traditional universal life policy because the insurance company contractually agrees to credit the policy’s cash value with the same return as the stock market index the policy holder chooses (typically, the S&P 500 Index, but it can be the Dow, NASDAQ, or others) realized over the same period of time, subject to a cap and a floor. Thus, the policy owner has the upside of the indices (up to the cap) but the risk of the same indices (but only to the floor). Typical floors for an annual return begin at near 0% (no loss of principal), with caps around 10%.

Pros: EIUL insurance enables you to get potentially more upside in the cash value accounts than WL but also gives you downside protection.

Cons: Products are relatively complex, with many choices of indices, participation rates, floors, and caps, and they vary significantly from insurance carrier to insurance carrier. Working with a professional who can help you make good decisions about policy placement and annual management is essential.

Is Permanent Life Insurance a “Good” Investment?
When thinking about permanent life insurance, many dermatologists want to understand whether it is a “good” or “bad” investment. But how can permanent life insurance be a “good” or “bad” investment when the choices within permanent products are so broad and deep? In other words, the structure of a permanent life insurance policy allows for an almost limitless number of underlying investments within the structure, and those investments will provide the policy’s returns.

As we explained, WL insurance offers a bond-based, dividends-type return. Is this good or bad? It depends on what the rest of the market does, doesn’t it? In 2008-09, an asset with such a return would likely have been the best-performing asset class on a physician’s balance sheet. For EIUL insurance,
Conclusion: Protecting Your Most Valuable Asset Throughout Your Career

All physicians, including dermatologists, should review their disability and life insurance policies regularly throughout their careers to ensure they are maintaining adequate coverage for the most cost-effective premiums.

An experienced insurance advisor can assist you in evaluating your options and selecting policies that fit your needs and long-term financial goals. The authors welcome your questions.

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Infusion Center

Add an Outpatient Infusion Center to Your Dermatology Practice

Fazila Rajab, Staff Correspondent

DURING HER PRESENTATION at the National Infusion Center Association Annual Conference in June 2022, Barbara McElroy, MSN, CRNI, VA-BC, discussed best practices for creating an infusion center, such as vascular access for outpatient infusion, the standard of care after leaving an infusion center, and ways to prevent various complications and improve the patient experience. Through the advent of FDA-approved biologic medications in dermatological practice proved to be a revolution in the treatment of inflammatory skin conditions, the real challenge lies in making these biologics accessible to patients, McElroy noted. Initially, hospital outpatient centers were the only lifeline for patients needing biologic treatments for their medical conditions. However, patients now find these facilities can be inconvenient and less cost- and time-effective.

Not all hospitals have an outpatient infusion center, and for those that do, most don’t have specialized staff, which leads to complications for patients, including placement-related injuries, infections, and phlebitis. Moreover, hospital infusion centers charge 3 to 5 times as much for their treatment as the same treatment offered at in-office infusion centers. Having an in-office infusion center provides patients with a hassle-free, intimate care setting under the care of their usual dermatologist, McElroy said.

According to the American Academy of Dermatology Association, psoriasis affects some 7.5 million individuals in the United States, but not every patient with psoriasis requires infusion therapy. To start an infusion center, you need enough patients to cover the basic payroll of your infusion team, McElroy said.

Moreover, a dedicated space, adequate equipment, and well-trained staff are required to operate a successful infusion center workflow. Setting up an in-office infusion center has challenges, including paying high startup and maintenance costs, resources to train the staff, creating a comfortable environment to provide an excellent patient experience, managing inventory, and dealing with denial of insurance claims and prior authorization requests, McElroy noted.

Finally, McElroy stressed that in-office infusion centers give clinicians the ability to deliver medical services in a supportive environment and allows more time with each patient to fully understand their concerns, thus improving the patient-physician relationship.

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What’s the diagnosis?

Shin Guard Dermatitis

A new allergen, acetophenone azine with generalized autoeczematization, is the cause of “shin guard dermatitis.”

Nuthan Bhat and Bernard A. Cohen MD

A HEALTHY 14-YEAR OLD BOY was evaluated for an intensely pruritic shin rash (Figure) that developed 2 weeks prior and had been treated with oral antibiotics for 10 days. On examination, the rash appeared more severe, with discrete, confluent, crusted, red papules and plaques on the shins, with relative sparing of the knees and ankles, progressing to the trunk and parts of the face and ears. He was upset because the rash interfered with his ability to play soccer.

The Case

Additional history taken from the patient’s father revealed that the boy was an avid soccer player and a goalkeeper on his school team. The father also explained that the inner lining of the boy’s protective shin guards was frayed. Owing to the initial location of the eruptions and the lack of improvement on antibiotics, a diagnosis of allergic contact dermatitis due to a component of the shin guards was suspected. The dissemination of the rash was undoubtedly caused by autoeczematization. Patch testing to standard allergens and various components of the patient’s soccer shin guards was planned.

Details of the Diagnosis

Contact dermatitis is a common inflammatory skin condition characterized by erythematous, scaly, crusted, pruritic, and/or painful skin lesions after contact with a foreign substance. The condition can be irritant or allergic. Irritant contact dermatitis, the most common type, is caused by nonimmunemodulated chemical damage to the skin. Allergic contact dermatitis is a delayed hypersensitivity reaction (type 4) to contact antigens, and skin changes occur with reexposure.

Autoeczematization, or id reaction, is a disseminated eczematous reaction that occurs when the antigen is released after exposure to a stimulus at a primary site, with the reaction spreading to distant sites.

Differential Diagnosis

When determining the diagnosis, irritant contact dermatitis due to friction and sweat generally comes to mind first. However, the id reaction is typical of allergic contact dermatitis, and this patient’s history favors the contact allergen acetophenone azine, a relatively new allergen, from his shin guards. The differential also includes atopic dermatitis, fungal infection, and psoriasis. The differences in the presentation of irritant and allergic contact dermatitis are summarized in the Table.

When must one suspect acetophenone azine contact dermatitis? The distribution of the primary rash and history of fraying shin guards should make this a high priority. In this setting, patch testing with a piece of the shin guard and the specific allergen, if available, should be considered. Patch testing is recommended when avoiding the suspected allergen fails to bring improvement.

Management

Avoidance of the allergen is the mainstay of prevention of recurrent allergic contact dermatitis. In this case, using shin guards and shoes made of other materials and/or placing barriers between the skin and the shin guards can help treat the patient and confirm the diagnosis. Unfortunately, acetophenone azine is presently unavailable as a commercial patch-test preparation.

Cool compresses and calamine lotion can soothe the acute symptoms. Localized lesions are often successfully treated with mid- or high-potency topical steroids, such as triamcinolone 0.1% or clobetasol 0.05% applied twice a day for 2 to 3 weeks.

If allergic contact dermatitis involves an extensive area of skin, the symptoms are extremely severe, or there is autoeczematization, systemic steroid therapy is often required and generally offers relief within 12 to 24 hours. It is important to recognize that if the allergen is removed and no effective therapy is instituted, it can take 2 to 3 weeks for the reaction to resolve. Therefore, an initial course of at least 5 to 7 days of prednisone, 0.5 to 1 mg/kg daily, is recommended. If the patient is comfortable after this initial therapy, the dose may be tapered over the next 7 to 10 days.

In patients with severe dermatitis and/or autoeczematous dermatitis, the most common type, is caused by nonimmunemodulated chemical damage to the skin. Allergic contact dermatitis is a delayed hypersensitivity reaction (type 4) to contact antigens, and skin changes occur with reexposure.

Table. Different presentations of irritant and allergic contact dermatitis

<table>
<thead>
<tr>
<th>Features</th>
<th>Irritant contact dermatitis</th>
<th>Allergic contact dermatitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td>Usually the hands but may involve any site</td>
<td>Usually exposed areas, often the hands</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Burning, pruritis, pain</td>
<td>Mainly pruritis</td>
</tr>
<tr>
<td>Surface appearance</td>
<td>Dry, fissured skin; prolonged exposure may cause blistering, ulceration</td>
<td>Scaling, crusting, vesicles and bullae</td>
</tr>
<tr>
<td>Lesion borders</td>
<td>Discrete, distinct borders</td>
<td>Distinct angles, borders, and lines that become edematous and spread</td>
</tr>
</tbody>
</table>

September 2022 | dermatologytimes.com
reaction, oral prednisone should be tapered over 2 to 3 weeks in combination with emollients and cool compresses with high-potency topical steroids applied to the worst areas.4

Emollients, moisturizers, or barrier creams may be instituted as secondary prevention strategies to help avoid continued exposure.4

What is Known About Acetophenone Azine

A case report published in 2016 recognized the occurrence of severe, dramatic shin contact dermatitis in a young football player that progressed to generalized dermatitis.3 On further investigation and patch testing, acetophenone azine was found to be the culprit. High-performance liquid chromatography (HPLC) identified the chemical substance at concentrations of approximately 20 μg/g of shin pad samples. Patch tests gave strongly positive reactions to pieces of shin pads and to acetophenone azine down to dilutions of 0.001% in acetone.3

Several articles later recognized the potent new allergen to cause rash even on exposure to footwear containing ethylene vinyl acetate (EVA).6,7 Acetophenone azine is not a component that is directly added to EVA during the manufacture of shin guards, shoe insoles, flip-flops, and other athletic gear and footwear. Though the exact chemical reactions that lead to its formation are unknown, it is presumed that it is due to cross-reactions with other materials added during EVA synthesis.8 A hypothesis states that acetophenone azine arises from the degradation of dicumyl peroxide and hydrazine in the foaming agent azodicarbonamide.4

On patch testing with materials including rubber, plastic, and shavings from the inner foam lining the shin guards, the only positive reaction was to the foam shavings that contained EVA. This material was sent to a well-equipped laboratory, where HPLC revealed the allergen to be acetophenone azine.

The American Contact Dermatitis Society chose acetophenone azine as its 2021 Allergen of the Year.9

Treatment and Recovery

The antibiotic was continued for another 4 days, and a course of oral prednisone at 1 mg/kg/day was added to the patient’s treatment regimen. He improved dramatically over the next 48 to 72 hours, at which point the antibiotics were discontinued, and the prednisone was tapered over the next 10 days.6

References

Managing Atopic Dermatitis in Skin of Color

Ilya Petrou, MD, Staff Correspondent

Despite the recent significant advances in both topical and oral dermatologic therapy, atopic dermatitis (AD) remains a difficult-to-treat skin disease and can be particularly challenging in patients with skin of color. Three experts recently convened to discuss the nuances and recent developments in the quickly evolving treatment and management of this very common and potentially debilitating skin disease.

"Atopic dermatitis is certainly on the rise, and we're not sure [whether] that's because it's increasing—which we think it is—or [because] it's being diagnosed more often. This is something that will carry on into our conversations, because oftentimes, AD is misdiagnosed in patients who have darker skin," said Angela J. Lamb, MD, director of the Westside Mount Sinai Dermatology Faculty Practice, associate professor of dermatology, system vice chair of Clinical Operations and Strategy, medical director of the Mount Sinai Doctors Patient Access Center, and chief technology officer, Department of Dermatology, Mount Sinai Hospital, New York New York.

There are distinct differences in AD among patients with White, Brown, and Black skin. African American patients with AD do not exhibit filaggrin mutations and have distinct attenuations of Th17 and Th1 axes activation, whereas Asian patients have a stronger Th17 and Th22 activation than both African American patients and White patients with AD. Future precision medicine therapies could enable more targeted treatments for patients with AD, according to the individual patient’s phenotype, Lamb explained.

In darker Fitzpatrick skin types, several different factors must be considered that can impact the severity of AD and disease exacerbation, including the different endotypes, immune mechanisms, barrier features, types of foods and allergens, water hardness, and bathing frequency.

"When talking to patients, we know a lot of cultural practices can come into play, if we’re scrubbing the skin too much, if we’re exfoliating—sometimes if we’re just using a washcloth or a loofah—that might contribute to exacerbating someone’s AD or skin condition," said Omar Noor, MD, FAAD, medical director and co-owner at Rao Dermatology in New York and New Jersey.

There may be nuances to the way patients treat their skin that may be making it more difficult for physicians to help them improve their symptoms. Having good communication with patients, especially in dermatology but in all of medicine, is critical to providing the best care possible, according to Noor.

"Even more so, it is directing patients to the resources we want them to follow so they don’t get the wrong information, whether it be from social media, Dr Google, or the neighbor next door who knows more than we do. We always say, ‘Your Google search is not as good as my medical degree.’ So it’s probably worth having that same conversation," said Neal Bhata, MD, director of clinical dermatology at Therapeutics Clinical Research in San Diego, California.

Fortunately, therapeutic options in AD have expanded from corticosteroids, emollients, and antihistamines to also include novel biologics such as dupilumab (Dupixent) and tralokinumab-Idrm (Adbrx), as well as oral and topical Janus kinase (JAK) inhibitors, including upadacitinib (Rinvoq) and abrocitinib (Cibinno), and ruxolitinib (Opleurora), respectively.

"What I see so often with darker skin tones is that it’s not just the AD, it’s also the hyperpigmentation. [Patients] are really concerned about being scarred, so my threshold is a little lower. I want to talk to them about these new treatment options a little sooner sometimes, because they can have that lasting postinflammatory hyperpigmentation that can be so disfiguring. Ideally, if we can stop the cycle of the damage to the skin, the skin will repair itself," Lamb said.

Along with the novel treatments that have recently become available, it is paramount that dermatologists maintain a high standard of care for their patients. This requires an in-depth consultation and discussion with patients about the Investigator Global Assessment (IGA) score, Eczema Area and Severity Index (EASI), and body surface area (BSA). Erythema is more difficult to assess in darker skin types and is a major component when evaluating patients for clinical trials. When it comes to skin of color, educating physicians begins with clinical trials.

The current mechanisms or tools used for evaluating erythema in clinical trials are flawed, Noor said. And because of those flaws in evaluating patients at baseline, the clinical trial percentages and results show physicians have grown accustomed to systemic and topical medications, do not fully encompass what type of benefit patients with darker skin types are getting, and may not fully capture the severity of some patients with darker skin types.

"All dermatologists should strive to incorporate EASI, BSA, IGA, Patient-Oriented Eczema Measures, and Dermatology Life Quality Index [scores] in their clinical assessments, because what we do in research can easily translate to clinical practice. It will help bring objective measures to how things are going [and] help get some of these systemic drugs covered. Unfortunately, I think a lot of dermatologists have given up the fight on trying to get the FDA-approved drugs covered, whether it’s biologics, JAK inhibitors, [or] others," Bhata said.

Because many of these new medications come in the form of a pill or injection, adher-
ence] remains an issue in patients with AD, which can be particularly true in the pediatric population. As such, Noor stressed the importance for physicians to effectively communicate the ins and outs of a patient’s AD condition and the different treatment options available to them, which can prove to be life-changing therapies.

“We are lucky now, in 2022, that we have more advanced therapeutic options for patients, and everything comes together as far as communication goes. After discussing all the options and adverse effects, adverse events, and efficacy, the physician and patient can move forward together on the appropriate therapeutic path to take,” Noor said. “What I want my patients to know when I choose a medication for them is my comfort level with that medication in the patients I’ve used it on, what I’ve grown to like in it, as much as possible. What skin types, and what they should expect to see. When they understand that in a very communicative way, we are able to have open discussions and be factual.”

followed through Week 52 was similar to the safety profile observed at Week 16 in AD-1025. The long-term safety profile of DUPIXENT ± TCS in subjects with atopic dermatitis (CHRONOS) was similar to the safety profile from trials in adults and pediatric subjects 12 to 17 years of age with atopic dermatitis. The antibody titers detected in both DUPIXENT and placebo subjects were mostly low in subjects who received DUPIXENT, development of high titers of antibodies to dupilumab was associated with lower serum dupilumab concentrations [see Clinical Pharmacology (12.3) in the full prescribing information].

Two adult subjects who experienced high titer antibody responses developed serum sickness or serum sickness-like reactions during DUPIXENT therapy [see Warnings and Precautions (5.1)].

8.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to DUPIXENT during pregnancy. To contact: 1-877-311-8972 or go to https://mothersandbabies.ongoing-study/dupixent/ to enroll in or to obtain information about the registry.

Risk Summary

Available data from case reports and case series with DUPIXENT use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Human IgG antibodies are known to cross the placental barrier; therefore, DUPIXENT may be transmitted from the mother to the developing fetus. In an enhanced safety and postnatal development study, no adverse development effects were observed in offspring born to pregnant monkeys after subcutaneous administration of a homologous antibody against interleukin-4 receptor alpha (IL-4Ra) during organogenesis through parturition at doses up to 10 times the maximum recommended human dose (MRHD) [see Data]. The background risk of major birth defects and miscarriage for the indicated populations are 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% to 4% and 15% to 20%, respectively.

Data

Animal Data

In an enhanced pre- and postnatal development toxicity study, pregnant cynomolgus monkeys were administered weekly subcutaneous doses of homologous antibody against IL-4Ra up to 10 times the MRHD (a mg/ kg basis of 100 mg/kg/week) from the beginning of organogenesis to parturition. No treatment-related adverse effects on embryofetal development, or malformations, or on morphological, functional, or immunological development were observed in the infants from birth through 6 months of age.
way, they can appreciate what I think is going to happen, then we go from there. It [goes] back to better communication, which plays a large role."

Setting the appropriate expectations for patients is also crucial. In patients with darker skin types, there’s some distrust with medicine, Noor said. There can be many reasons for this, starting with the clinical trials and some of the advertisements. It is the responsibility of the physician to effectively communicate this with patients in an educated way, according to Noor.

"Try to get ahead of and anticipate [the patient’s] concerns—that’s the art of good doctors. If we’re able to get ahead of what [patients] are going to ask about and give them confidence, that goes a long way and gives the doctor credibility that they know what they’re talking about," Lamb said.

8.2 Lactation

Risk Summary

There are no data on the presence of dupilumab in human milk, the effects on the breastfed infant, or the effects on milk production. Maternal IgG is known to be present in human milk. The effects of local gastrointestinal and limited systemic exposure to dupilumab on the breastfed infant are unknown. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for DUPIXENT and any potential adverse effects on the breastfed child from DUPIXENT or from the underlying maternal condition.

8.4 Pediatric Use

Atopic Dermatitis

The safety and effectiveness of DUPIXENT have been established in pediatric patients 6 months of age and older with moderate-to-severe atopic dermatitis [see Clinical Studies (14.1) in the full prescribing information]. Use of DUPIXENT in this age group is supported by data from the following clinical trials:

- AD-1536 which included 251 pediatric subjects 12 to 17 years of age with moderate-to-severe atopic dermatitis treated with DUPIXENT
- AD-1852 which included 367 pediatric subjects 6 to 11 years of age with severe atopic dermatitis treated with DUPIXENT + TCS
- AD-1539 which included 161 pediatric subjects 6 months to 5 years of age with moderate-to-severe atopic dermatitis treated with DUPIXENT + TCS
- AD-1434, an open-label extension study that enrolled 275 pediatric subjects 6 to 17 years of age with severe atopic dermatitis treated with DUPIXENT + TCS, and 180 pediatric subjects 6 months to 5 years of age treated with DUPIXENT + TCS

The safety and effectiveness were generally consistent between pediatric and adult patients [see Adverse Reactions (6.1) and Clinical Studies (14.1) in the full prescribing information]. In addition, hand-foot-and-mouth disease was reported in 2 (2%) pediatric subjects and skin papilloma was reported in 4 (2%) pediatric subjects 6 months to 5 years of age treated with DUPIXENT + TCS. These cases did not lead to study drug discontinuation [see Adverse Reactions (6.1)].

Safety and effectiveness in pediatric patients younger than 6 months of age with atopic dermatitis have not been established.

8.5 Geriatric Use

Clinical studies of DUPIXENT in atopic dermatitis did not include sufficient numbers of subjects aged 65 years and over to determine whether they respond differently from younger subjects [see Clinical Pharmacology (12.3) in the full prescribing information].

10 OVERDOSAGE

There is no specific treatment for DUPIXENT overdose. In the event of overdose, contact Poison Control (1-800-222-1222) for the latest recommendations and monitor the patient for any signs or symptoms of adverse reactions and institute appropriate symptomatic treatment immediately.

17 PATIENT COUNSELING INFORMATION

Advisers and/or caregivers to read the FDA-approved patient labeling (Patient Information and Instructions for Use). Precautions (5.8)

Advisers to inform their healthcare provider if they have any symptoms of systemic hypersensitivity reactions [see Warnings and Precautions (5.1)].

Hypersensitivity

Advisers to discontinue DUPIXENT and seek immediate medical attention if they experience any symptoms of systemic hypersensitivity reactions [see Warnings and Precautions (5.1)].

Concurrent Use of Other Medications

Advisers to inform their healthcare provider if they are taking DUPIXENT and any other medications or are planning to start any new medications.

Pregnancy

Advisers to inform their healthcare provider if they are pregnant or plan to become pregnant.

Breastfeeding

Advisers to inform their healthcare provider if they are breastfeeding.

References:


Manufactured by: Regeneron Pharmaceuticals, Inc., Tarrytown, NY 10591 U.S. License # 1760; Marketed by sanofi-aventis U.S. LLC, Bridgewater, NJ 08807 and Regeneron Pharmaceuticals, Inc., Tarrytown, NY 10591. DUPIXENT™ is a registered trademark of Sanofi Biotechnology/© 2022 Regeneron Pharmaceuticals, Inc./sanofi-aventis U.S. LLC. All rights reserved. Issue Date: June 2022. DUP.22.06.0028.
Teens, Acne, and Mental Health

Rachael Zimlich, Staff Correspondent

Acne may be seen as a rite of passage in the adolescent years, affecting more than 80% of all teenagers at some point.1 However, newer reports suggest that the psychological effects of this inflammatory skin disorder may be underestimated and deserve more attention in treatment plans.

Multiple studies over the past several years have highlighted the impact of acne on adolescent mental health—especially since adolescence is already a time of intense transition. Self-esteem, social relationships, anxiety, and depression can all factor into the effects of chronic acne in the teenage years, according to researchers.2,3

Mohammad Jaff erany, MD, a clinical professor of psychodermatology and psychiatry at Central Michigan University in Saginaw and a board-certified psychiatrist who coauthored a 2020 report on the psychodermatology of acne, said a lot of factors are at play when it comes to the psychological impact of acne.

Acne is the most common inflammatory condition of the skin, he said, adding that hormones and stress in the adolescent years can increase prevalence. The fact that acne usually appears primarily on the face doesn’t help because it can be difficult to conceal or camouflage severe papules and comedones. “[Adolescents] end up feeling very stigmatized,” Jaff erany noted. “Their self-esteem is very poor, and psychological conditions often develop around the same time [as acne appears].”

On top of stressing about their appearance and how acne may affect their social relationships, teenagers can also get easily frustrated by mixed messages about acne treatment, Jaff erany explained.

Acne treatment should be holistic and multidisciplinary, he said, with diet, hormonal consideration, and psychological impact all considered in the overall clinical plan. Many teenagers turn to friends or social media for help in managing early acne and then get frustrated when certain treatments fail to produce results. Without proper treatment early in the process, acne—and its psychological impact—usually get worse, Jaff erany said. Adolescents with severe acne often stop going out with friends and interacting with others, and Jaff erany said that studies have shown suicides rates are often higher in teenagers with acne than those with clear skin.

The American Academy of Dermatology clinical guidelines for acne treatment briefly mention the mental impact of acne on teenagers and the risk of increased depression or suicidal ideation with certain treatment regimens.4 However, the guidelines do note that “acne can take a toll on one’s emotional health” and that people with acne can develop anxiety, depression, low self-esteem, poor self-image, decreased quality of life, and a feeling of being alone.5

The guidelines recommend oral isotretinoin for the treatment of severe nodular acne in adolescents. Several studies in recent years have investigated the link between this popular medication and suicidality, but Jaff erany says the strength of the association between isotretinoin use and suicide risk remains questionable. One 2020 report suggests that there doesn’t appear to be a definitive risk and that isotretinoin shouldn’t be completely avoided in teenagers with depression,6 but the American Academy of Pediatrics suggests that the medication be used “cautiously” in adolescent patients with depression and that they be monitored during therapy by both a dermatologist and a psychiatrist.7

Jaff erany agreed with this recommendation, noting that it’s not unusual for clinicians to send teenagers for a psychiatric screening prior to prescribing isotretinoin.

Other treatment options are available besides isotretinoin.

References


TREATMENT OPTIONS

Topical treatments*5,7
- Benzoyl peroxide alone or with other topical treatments for mild acne
- Benzoyl peroxide plus topical retinoids or systemic antibiotics for moderate to severe acne
- Retinoids alone for primarily comedonal acne
- Retinoids plus oral or topical antimicrobials for mixed/pri-
marily inflammatory acne
- Topical dapsone 5% gel for inflammatory acne
- Azelaic acid for postinflam-
matory pigmentation problems

Complementary and alternative treatments*5,7
- Tea tree oil
- Topical and oral ayurvedic compounds
- Oral barberry extract
- Gluconolactone solution
- Diet and nutrition counseling

Physical treatment methods and therapies*5,7
- Comedo removal
- Pulsed dye laser
- Potassium-titanyl-phosphate laser
- Fractionated and nonfractionated infrared lasers
- Fractionated carbon dioxide laser
- Photodynamic therapy
- Glycolic acid peels
- Salicylic acid peels
- Intraleisional corticosteroid injections for larger individual acne nodules

The American Academy of Dermatology guidelines for acne vulgaris can be found at jaad.org/article/S0190-9622(15)02614-6/fulltext
The Role of Nonprescription Products in the Management of Acne

Kaitlyn Bader, Associate Editor

Joshua Zeichner, MD, an associate professor of dermatology and director of cosmetic and clinical research in the Department of Dermatology at Mount Sinai Hospital in New York, New York; and Mona Gohara, MD, a dermatologist at Dermatology Physicians of Connecticut in Hamden, Connecticut, and president of the Women’s Dermatologic Society discussed their experiences and preferences in treating acne with nonprescription drugs.

To determine adherence issues related to acne drugs and their adverse effects, Zeichner and Gohara first discussed a 2019 study1 that analyzed adherence issues of topical treatments for acne vulgaris. Patients from the study used retinoids, antibacterial treatments, benzoyl peroxide, retinoid antibacterial treatments, and formulas containing resorcinol salicylic acid. Nearly half of the patients discontinued topical therapy before their scheduled time, citing unresponsiveness and adverse effects as primary reasons. Gohara began the discussion by saying she is not surprised by the number of patients who discontinue topical therapies, noting that many of her patients have told her their topical therapies did not work.

Gohara stressed that retinoids and benzoyl peroxide are the gold standards for acne treatment in dermatology, but only when used correctly. Other topical treatments include formulas containing resorcinol salicylic acid. While these OTC drugs are not prescription strength, they can still be irritating to the skin when used in large quantities or mixed with other irritating agents. Other adverse effects include irritation, erythema, scaling, itching, and stinging. Gohara explained that she gives her patients a handout that shows how to use the product, as well as realistic expectations.

Zeichner echoed these experiences, saying he gives his patients specific guidance on how much product to use, how often, and what other OTC products to combine with topical therapies for the best results. He noted that a pea-sized amount of product is typically all you need; a cherry tomato-sized amount is too much. Overall, Zeichner sees that many patients want results too quickly; most patients will not see results until approximately week 12. Another way Zeichner tries to understand his patients’ expectations is by asking them to walk him through their skin care regimen. This helps Zeichner know what they already use and what kind of results they desire.

“I always say to patients when they come back, ‘First of all, how do you feel about your skin?’ I like to hear what they have to say before I make a comment and I’ll say to them, ‘Take me through your regimen.’ I always ask open-ended questions. We have to be nonjudgmental, educate our patients, and set realistic expectations,” said Zeichner.

Most importantly, both experts stressed that it’s crucial not to be judgmental. Asking patients questions will benefit both the dermatologist and the patient to come up with an agreed-upon acne treatment plan. Gohara also mentioned a few tricks, such as mixing a light moisturizing cream with a retinoid or benzoyl peroxide to cut the irritation and not using retinoids as a spot treatment.

Zeichner and Gohara discussed nonprescription cleansers and moisturizers for acne-prone skin. In a 2020 study2, 4 name-brand, lipid-free cleansers were studied and compared. Gohara began by pointing out the beneficial ingredients of each product. She stressed that hydrating ingredients are always beneficial, no matter the type of skin. Lipid-free cleansers are the most appropriate type of cleanser for acne-prone skin due to their low-risk skin irritation and a near physiological stratum corneum pH.

Both Zeichner and Gohara mentioned the importance of a healthy skin barrier. A strong skin barrier is not always the first thought in acne management, but it’s the skin’s line of defense. The best way to keep the skin barrier from breaking down is with hydrating cleansers and moisturizers. Skin barrier dysfunctions related to blockages in the pores that contribute to acne.

“Lipid-free cleansers are primarily composed of water and glycerin; those are the 2 primary ingredients, which are very highly rated,” said Gohara. “We can see that primarily, these cleansers will have very low rates of irritation on the skin and can help the skin barrier, which is what we were talking about before. Lipid-free cleansers can mitigate the irritation that patients may be getting from retinoids and benzoyl peroxides.”

The main goal of moisturizers is to repair significant defects in the skin barrier and assist with acne treatment. Gohara said dermatologists and patients must be deliberate when selecting a moisturizer. Additionally, moisturizers can have other ingredients such as sunscreen that are also beneficial to the skin.

Both Zeichner and Gohara praised 3 top ingredients for hydrating skin in moisturizers:

• occlusives: create a blanket to prevent transepidermal water loss (TEWL)
• humectants: suck water up from the dermis and epidermis
• emollients: a layer between epidermal cells to stop TEWL

Moisturizers ideal for acne-prone skin should also include oil-absorbing and anti-inflammatory and/or barrier replenishing properties. They should have more ingredients than just a humectant, as humectants are great at grabbing water, not trapping it.

Zeichner and Gohara concluded that OTC skin care products such as cleansers and moisturizers should never compromise the integrity of the skin barrier. Products should include ingredients that will protect, soften, and hydrate the skin, not irritate it. Clinicians and patients should work together to discuss the best cleansers and moisturizers for acne-prone skin based on hydrating ingredients that will protect and replenish the skin barrier. Clinicians should also advise their patients on how to pick a cleanser or moisturizer that will work well with their retinoid or benzoyl peroxide to avoid irritation and achieve maximum skin protection. Discussing OTC products and individualized treatment plans with acne-prone patients will result in better adherence rates as well as achievable expectations.

Reference:
In a study of patients with acne, almost 40% of treatment non-adherence was due to side effects.

Strategic use of OTC skincare, including gentle cleansers and moisturizers, can promote adherence by improving tolerability.


Use products only as directed.

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Study Suggests Ideal Method for Classifying, Treating Acne

Near 80% of adolescents have acne vulgaris at some point, with clinical features ranging from mild acne to fulminant acne with systemic symptoms. The main manifestations are comedones, papules, pustules, nodules, cysts, and scarring. Not only teens are challenged by this condition: 12% of women and 3% of men continue to be affected well into middle age. Because acne changes the appearance of adolescents and irregular treatments may cause serious, irreversible harm to patients physically and mentally, accurate evaluation is needed for effective, standardized management of acne.

A recent study by researchers at Ningbo Medical Center Li Huili Hospital in Ningbo, Zhejiang, China, and Zhejiang University School of Medicine, Hangzhou, Zhejiang, China, sought to assess acne vulgaris quantitatively using high-frequency ultrasonography (HF-USG) and power Doppler (PD). The study, “High-frequency ultrasonography evaluation of acne by thickness and power Doppler analysis,” was recently published in the Journal of Ultrasound in Medicine, and showed the feasibility and application value of HF-USG and PD in acne vulgaris.

Investigators enrolled 105 patients given diagnoses of acne vulgaris by a dermatologist, with information collected between November 1, 2020, and January 31, 2021. Working independently, 2 attending dermatologists using 3 degrees with 4 category levels clinically classified all patients, evaluating only the severest lesions. Mean age of the patients was 23 years; there were 75 females and 30 males.

Using grayscale ultrasound, investigators assessed thickness of the lesions and then calculated the thickness ratio. They used PD equipped with Qpack, semiquantitative analysis software to assess blood signals of the lesion prior to calculating Qpack ratio and peak. Of the cohort, according to Chinese guidelines for the management of acne vulgaris, 23 cases were comedones, 33 were papules, 26 were pustules, and 23 were nodules/cysts. The study revealed significant differences in thickness ratio (P < .001), Qpack ratio (P < .001), and Qpack peak (P < .001) among the 4 groupings.

Investigators concluded that HF-USG and PD equipped with semiquantitative analysis software could best assess acne vulgaris quantitatively, providing a good basis for the classification and treatment of acne. “By using those technologies, acne lesions can be observed quantitatively under noninvasive conditions, which provides a good basis for the classification and the treatment of acne,” investigators said. “Their features include thickness ratio, Qpack ratio, and Qpack peak, with the latter 2 being the sensitive features for the early efficacy evaluation.”

The authors noted several limitations to the study due to the sample size being relatively small in grouping, especially after treatment. Therefore, investigators plan to expand the sample size for future research.

Christopher G. Bunick, MD, PhD, associate professor of dermatology at Yale School of Medicine in New Haven, Connecticut, noted that the study most likely will not have any impact on dermatology practices but could foster more clinical advancements. The strength of the study, Bunick said, is that there are volumetric differences that can be measured in acne lesions and they are quantifiable, which may help to stratify patients in clinical trials more accurately.

“There is a potential application here for clinical trials, where if you’re trying to more accurately grade the severity of patients, this could be a way of standardizing how you quantify or bend patients into your mild/moderate/severe categories,” he said. “In the clinic, doctors will look at the patients and base the therapy they need based on the severity they’re at, and measure the volume of the lesion without advanced ultrasound needed.”

References

Subscribe for practical tips and valuable resources.
Precision Medicine With Transcriptomics May Revolutionize Psoriasis Management

Fazila Rajah, Staff Correspondent

Transcriptome profiling techniques, such as microarrays and RNA sequencing, can be helpful in determining the regulatory networks underlying the disease of psoriasis. Analyzing RNA alternative isoforms is essential to design personalized treatment strategies and improve clinical outcomes, according to a recent review published in May in *The International Journal of Molecular Science* that evaluated several studies.1

Psoriasis is an autoimmune inflammatory skin condition with visible signs of inflammation, including cutaneous erythema and scaly skin. It accelerates the process of skin cell production, leading to painful and itchy scaly plaques. The global prevalence rate of the condition varies and ranges from 0.09% to 11.4%. The disease affects more than 7.5 million adults in the United States, more than 3% of the US adult population.2 Approximately 90% of individuals with psoriasis contract its most common form, psoriasis vulgaris.

Keratinocytes normally grow and shed in a month, maintaining epidermal homeostasis. This balance is impaired in inflammatory diseases such as psoriasis, and the keratinocytes, instead of shedding, off, pile up on the skin surface, making it scaly and increasing the burning sensation.

Although psoriasis is not contagious, the inflammation may spread from 1 body part to another. Individuals with psoriasis have an increased risk of developing at least 1 autoimmune condition in their lifetime, study results show.1 Though the pathogenesis of these comorbid conditions remains unclear, shared inflammatory pathways, genetic susceptibility, and cellular mediators are contributing factors.

Furthermore, the exact etiology of psoriasis remains unknown, although it is widely recognized as a multifactorial disease caused by an interaction between environmental triggers and inherited genes. Having a family history increases the likelihood of contracting the disease.

The current review focused on the findings of large cohort transcriptomic analyses. The investigators looked at the benefits of such studies in identifying underlying molecular pathways of the disease and determining therapeutic targets and biomarkers for managing psoriasis. Their findings showed several differentially expressed genes, which are potential targets for further research and treatment strategies. Evidence suggests that genes are differentially expressed in psoriatic versus healthy skin.

Several genome-wide association studies have helped investigators identify underlying immunological dysfunction driven by immune cells and proinflammatory cytokines, showing a strong association between disease severity and cytokine levels. The pathway is now targeted by modern biologics that show commendable results. To date, 63 psoriasis susceptibility loci have been identified, highlighting the role of NFκB and interferon pathways and helping with understanding the pathogenesis of the disease.

The epidermal differentiation complex (EDC) encodes genes associated with epidermal differentiation. Because impairment in epidermal differentiation is the main psoriatic feature, EDC genes are among the important psoriatic markers.

“In addition to allowing for identification of specific triggers of psoriasis, the transcriptome allows us to pick therapies that are safe for specific patients and have a low risk of triggering complications [such as] associated gastrointestinal and rheumatological disorders. This also allows us to minimize the risk of immunosuppression as a complication of therapy,” noted Bernard A. Cohen, MD, director of Pediatric Dermatology at the Johns Hopkins University School of Medicine in Baltimore, Maryland.

The investigators also focused on alternative splicing of mRNAs, which has previously received little attention in the field. Evidence suggests that nearly 95% of genes undergo alternative splicing. It is a fundamental regulatory mechanism of gene expression, which can generate different isoforms from pre-mRNA by arranging exons at different combinations. The isoforms from a single gene can lead to the production of different protein variants, affecting gene function through various mechanisms.

Results of a study by Li et al found 18 exon-skipping events and several factors that regulate splicing in psoriasis,3 which are potential candidates for further research aimed at designing personalized therapies and biomarkers for managing psoriasis.

“[mRNA alternative splicing] allows us to identify specific inflammatory mediators and to target them with specific therapies,” Cohen said. “By targeting specific inflammatory mediators, we can reduce the risk of immunosuppression triggered by many treatments.”

There is an association between S100A7 and inflammatory skin diseases, such as psoriasis and atopic dermatitis, according to results of another study.4 Among 21 low molecular weight S100 proteins, 14 S100 protein genes are located in EDC on chromosome 1q21, and 11 are expressed in the epidermis. The S100A7/A15 (koebnerisin) protein, with 2 alternative spliced isoforms, is overexpressed in psoriasis and is among the important markers in psoriasis.

Another example is CARD4, an activator of NFκB within the epidermis. The splicing variants of CARD4 produce protein variants, affecting NFκB activation differently. Hence RNA isoform-based analysis helps identify multiple transcripts for a gene and is important for designing new management strategies for psoriasis.

Recent studies investigated transcriptomic changes in the blood and found neutrophils to be the potential hallmark in the pathogenesis of the disease. Previously a generalized approach was used to manage the condition depending on clinical assessments. However, a more precise strategy is needed, considering patients’ genes, environmental factors, and lifestyle, to improve clinical outcomes for individual patients.

The huge amount of transcriptomic data available for psoriasis may prove helpful in managing the condition through a precision medicine approach. The data may also help predict the effects of drugs, thereby reducing the trial-and-error approach to the available biologics and increasing the efficacy of patients’ treatments.

References

Opzelura™ (ruxolitinib) cream 1.5%

INDICATION
OPZELURA is indicated for the topical treatment of nonsegmental vitiligo in adult and pediatric patients 12 years of age and older.

Limitations of Use: Use of OPZELURA in combination with therapeutic biologics, other JAK inhibitors, or potent immunosuppressants such as azathioprine or cyclosporine is not recommended.

The facial vitiligo area scoring index (F-VASI) is a composite measurement of the overall area of facial vitiligo patches and degree of depigmentation within patches. As assessed, the face did not include surface area of the lips, scalp, or ears.5

P-values from exact logistic regression: [response at Week 24 = treatment + stratification factors (Fitzpatrick skin type I and II vs. Fitzpatrick skin type III, IV, V, and VI, Region North America/Europe)].3

52-week data were reported as observed. Therefore, no conclusions of safety or efficacy should be made based on these results.‡

OPZELURA was studied in 2 double-blind, randomized, vehicle-controlled trials of identical design that enrolled 674 adult and adolescent patients with nonsegmental vitiligo ≥12 years of age. Patients had depigmented areas affecting ≥0.5% facial body surface area (F-BSA), ≥3% nonfacial BSA, and total body vitiligo area (facial and nonfacial) of up to 10% BSA. Patients with complete leukotrichia within any facial lesion were excluded. Phototherapy was not permitted during the trials. In both trials, patients were randomized 2:1 to treatment with OPZELURA or vehicle cream twice daily (BID) for 24 weeks followed by a 28-week open-label extension, wherein patients originally assigned to vehicle could switch to OPZELURA.1,4

Limitations of an open-label extension: In an open-label extension, there is a potential for enrichment of the long-term data in the remaining patient populations since patients who are unable to tolerate or do not respond to the drug often drop out.

Nearly 1 in 3 patients achieved at least 75% improvement in the facial vitiligo area scoring index* (F-VASI75) at 24 weeks (primary endpoint; 29.9% vs. 7.5% (P < 0.0001) and 29.9% vs. 12.9% (P < 0.01))†

Data from an open-label extension at Week 52

About half the patients remaining in the study who applied OPZELURA from Day 1 achieved F-VASI75 at 52 weeks: ≈51% for OPZELURA and ≈28% for vehicle-to-OPZELURA (Week 24 to Week 52). Data were reported as observed.
Now you can prescribe OPZELURA, the **FIRST + ONLY FDA-APPROVED**
treatment for nonsegmental vitiligo repigmentation. Proven results
with a topical.¹

**F-VASI 75 AT 24 WEEKS**

Nearly 1 in 3 patients achieved at least **75% improvement** in the facial vitiligo
area scoring index* (F-VASI75) at 24 weeks (primary endpoint; 29.9% vs. 7.5%
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²P-values from exact logistic regression: [response at Week 24 = treatment + stratification factors (Fitzpatrick skin type I and II vs. Fitzpatrick
skin type III, IV, V, and VI, Region North America/Europe)].³

³52-week data were reported as observed. Therefore, no conclusions of safety or efficacy should be made based on these results.

**IMPORTANT SAFETY INFORMATION**

**SERIOUS INFECTIONS**

Patients treated with oral Janus kinase inhibitors for inflammatory conditions are at risk for
developing serious infections that may lead to hospitalization or death. Reported infections include:

- Active tuberculosis, which may present with pulmonary or extrapulmonary disease.
- Invasive fungal infections, including cryptococcosis and pneumocystosis.
- Bacterial, viral, including herpes zoster, and other infections due to opportunistic pathogens.

Avoid use of OPZELURA in patients with an active, serious infection, including localized infections. If a serious infection develops, interrupt OPZELURA until the infection is controlled. Carefully consider the
benefits and risks of treatment prior to initiating OPZELURA in patients with chronic or recurrent infection.

Closely monitor patients for the development of signs and symptoms of infection during and after
treatment with OPZELURA.

Serious lower respiratory tract infections were reported in the clinical development program with
topical ruxolitinib.

No cases of active tuberculosis (TB) were reported in clinical trials with OPZELURA. Cases of active TB were
reported in clinical trials of oral Janus kinase inhibitors used to treat inflammatory conditions. Consider
evaluating patients for latent and active TB infection prior to administration of OPZELURA. During OPZELURA use,
monitor patients for the development of signs and symptoms of TB.

Viral reactivation, including cases of herpes virus reactivation (e.g., herpes zoster), were reported in clinical
trials with Janus kinase inhibitors used to treat inflammatory conditions including OPZELURA. If a patient
develops herpes zoster, consider interrupting OPZELURA treatment until the episode resolves.

Hepatitis B viral load (HBV-DNA titer) increases, with or without associated elevations in alanine
aminotransferase and aspartate aminotransferase, have been reported in patients with chronic HBV
infections taking oral ruxolitinib. OPZELURA initiation is not recommended in patients with active hepatitis B
or hepatitis C. (cont. on next page)

Please see the Brief Summary of the Full Prescribing Information,
including Boxed Warning, on following pages.
IMPORTANT SAFETY INFORMATION FOR OPZELURA™ (RUXOLITINIB) CREAM 1.5% (CONTINUED)

MORTALITY
In a large, randomized, postmarketing safety study in rheumatoid arthritis (RA) patients 50 years of age and older with at least one cardiovascular risk factor comparing an oral JAK inhibitor to tumor necrosis factor (TNF) blocker treatment, a higher rate of all-cause mortality, including sudden cardiovascular death, was observed with the JAK inhibitor. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OPZELURA.

MALIGNANCIES
Malignancies were reported in patients treated with OPZELURA. Lymphoma and other malignancies have been observed in patients receiving JAK inhibitors used to treat inflammatory conditions. In RA patients treated with an oral JAK inhibitor, a higher rate of malignancies (excluding non-melanoma skin cancers) was observed when compared with TNF blockers. Patients who are current or past smokers are at additional increased risk. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OPZELURA, particularly in patients with a known malignancy (other than successfully treated non-melanoma skin cancers), patients who develop a malignancy when on treatment, and patients who are current or past smokers.

Non-melanoma skin cancers, including basal cell and squamous cell carcinoma, have occurred in patients treated with OPZELURA. Perform periodic skin examinations during OPZELURA treatment and following treatment as appropriate. Exposure to sunlight and UV light should be limited by wearing protective clothing and using broad-spectrum sunscreen.

MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE)
In RA patients 50 years of age and older with at least one cardiovascular risk factor treated with an oral JAK inhibitor, a higher rate of major adverse cardiovascular events (MACE) (defined as cardiovascular death, myocardial infarction, and stroke) was observed when compared with TNF blockers. Patients who are current or past smokers are at additional increased risk. Discontinue OPZELURA in patients who have experienced a myocardial infarction or stroke. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OPZELURA, particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. Patients should be informed about the symptoms of serious cardiovascular events and the steps to take if they occur. Discontinue OPZELURA in patients that have experienced a myocardial infarction or stroke.

THROMBOSIS
Thromboembolic events were observed in trials with OPZELURA. Thrombosis, including pulmonary embolism (PE), deep venous thrombosis (DVT), and arterial thrombosis have been reported in patients receiving JAK inhibitors used to treat inflammatory conditions. Many of these adverse reactions were serious and some resulted in death. In RA patients 50 years of age and older with at least one cardiovascular risk factor treated with an oral JAK inhibitor, a higher rate of thrombosis was observed when compared with TNF blockers. Avoid OPZELURA in patients at risk. If symptoms of thrombosis occur, discontinue OPZELURA and treat appropriately.

Thrombocytopenia, Anemia, and Neutropenia
Thrombocytopenia, anemia, and neutropenia were reported in the clinical trials with OPZELURA. Consider the benefits and risks for individual patients who have a known history of these events prior to initiating therapy with OPZELURA. Perform CBC monitoring as clinically indicated. If signs and/or symptoms of clinically significant thrombocytopenia, anemia, and neutropenia occur, patients should discontinue OPZELURA.

Lipid Elevations
Treatment with oral ruxolitinib has been associated with increases in lipid parameters including total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides.

Adverse Reactions
In nonsegmental vitiligo, the most common adverse reactions (incidence ≥ 1%) are application site acne (6%), application site pruritus (5%), nasopharyngitis (4%), headache (4%), urinary tract infection (2%), application site erythema (2%), and pyrexia (1%).

Pregnancy
There is a pregnancy registry that monitors pregnancy outcomes in pregnant persons exposed to OPZELURA during pregnancy. Pregnant persons exposed to OPZELURA and healthcare providers should report OPZELURA exposure by calling 1-855-463-3463.

Lactation
Advise women not to breastfeed during treatment with OPZELURA and for approximately four weeks after the last dose (approximately 5–6 elimination half-lives).

Please see the Brief Summary of the Full Prescribing Information, including boxed Warning, on following pages.
Opzelura™ (ruxolitinib) cream 1.5%

OPZELURA™ (ruxolitinib) cream, for topical use

Brief Summary of FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE: OPZELURA is indicated for the topical treatment of nonsegmental vitiligo in adult and pediatric patients 12 years of age and older.

Limitations of Use: Use of OPZELURA in combination with therapeutic biologics, other JAK inhibitors, or potent immunosuppressants such as azathioprine or cyclosporine is not recommended.

WARNING: SERIOUS INFECTIONS, MORTALITY, MALIGNANCY, MAJOR ADVERSE CARDIOVASCULAR EVENTS, AND THROMBOSIS

SERIOUS INFECTIONS
Patients treated with oral Janus kinase inhibitors for inflammatory conditions are at risk for developing serious infections that may lead to hospitalization or death [see Warnings and Precautions and Adverse Reactions].

Reported infections include:
- Active tuberculosis, which may present with pulmonary or extrapulmonary disease.
- Invasive fungal infections, including cryptococcosis, and pneumocystis.
- Bacterial, viral, including herpes zoster, and other infections due to opportunistic pathogens.

Avoid use of OPZELURA in patients with an active, serious infection, including localized infections. If a serious infection develops, interrupt OPZELURA until the infection is controlled.

The risks and benefits of treatment with OPZELURA should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection.

Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with OPZELURA [see Warnings and Precautions].

MORTALITY
In a large, randomized, postmarketing safety study in rheumatoid arthritis (RA) patients 50 years of age and older with at least one cardiovascular risk factor comparing an oral JAK inhibitor to tumor necrosis factor (TNF) blocker treatment, a higher rate of all-cause mortality, including sudden cardiovascular death, was observed with patients treated with the JAK inhibitor compared with TNF blockers. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OPZELURA.

MALIGNANCIES
Malignancies were reported in patients treated with OPZELURA. Lymphoma and other malignancies have been observed in patients receiving JAK inhibitors used to treat inflammatory conditions. In RA patients treated with an oral JAK inhibitor, a higher rate of malignancies (excluding non-melanoma skin cancer) (NMSC) was observed when compared with TNF blockers.

Discontinue OPZELURA in patients who are current or past smokers at additional increased risk. Consider evaluating patients for latent malignancy (other than skin cancer) before initiating therapy with OPZELURA.

MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE)
In RA patients 50 years of age and older with at least one cardiovascular risk factor treated with an oral JAK inhibitor, a higher rate of major adverse cardiovascular events (MACE) (defined as cardiovascular death, myocardial infarction, and stroke), was observed when compared with TNF blockers.

Discontinue OPZELURA in patients who are current or past smokers at additional increased risk. If symptoms of thrombosis occur, discontinue OPZELURA and treat appropriately [see Warnings and Precautions].

THROMBOSIS
Thromboembolic events were observed in clinical trials with OPZELURA. Thrombosis, including pulmonary embolism (PE), deep venous thrombosis (DVT), and arterial thrombosis have been reported in patients receiving JAK inhibitors used to treat inflammatory conditions. Many of these adverse reactions were serious and some resulted in death. In RA patients 50 years of age and older with at least one cardiovascular risk factor treated with an oral JAK inhibitor, a higher rate of thrombosis was observed when compared with TNF blockers. Avoid OPZELURA in patients at risk.

Warnings and Precautions

Serious Infections: Serious and sometimes fatal infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens have been reported in patients receiving oral Janus kinase inhibitors. Serious lower respiratory tract infections were reported in the clinical development program with topical ruxolitinib. Avoid use of OPZELURA in patients with an active, serious infection, including localized infections. Consider the risks and benefits of treatment prior to initiating OPZELURA in patients with chronic or recurrent infection; with a history of a serious or an opportunistic infection; who have been exposed to tuberculosis; who have resided or traveled in areas of endemic tuberculosis or endemic mycoses; or with underlying conditions that may predispose them to infection. Close monitoring for the development of signs and symptoms of infection during and after treatment with OPZELURA. Interrupt OPZELURA if a patient develops a serious infection, an opportunistic infection, or sepsis. Do not resume OPZELURA until the infection is controlled.

Tuberculosis: No cases of active tuberculosis (TB) were reported in clinical trials with OPZELURA. Cases of active TB were reported in clinical trials of oral Janus kinase inhibitors used to treat inflammatory conditions. Consider evaluating patients for latent TB infection prior to administration of OPZELURA. During OPZELURA use, monitor patients for the development of signs and symptoms of TB.

Viral Reactivation: Viral reactivation, including cases of herpes virus reactivation (e.g., herpes zoster), were reported in clinical trials with Janus kinase inhibitors used to treat inflammatory conditions including OPZELURA. If a patient develops herpes zoster, consider interrupting OPZELURA treatment until the episode resolves.

Hepatitis B and C: The impact of Janus kinase inhibitors used to treat inflammatory conditions including OPZELURA on chronic viral hepatitis reactivation is unknown. Patients with a history of hepatitis B or C infection were excluded from clinical trials.

Hepatitis B viral load (HBV-DNA) increases, with or without associated elevations in alanine aminotransferase and aspartate aminotransferase, have been reported in patients with chronic HBV infections taking oral ruxolitinib. OPZELURA initiation is not recommended in patients with active hepatitis B or hepatitis C.

Mortality: In a large, randomized, postmarketing safety study of an oral JAK inhibitor in rheumatoid arthritis (RA) patients 50 years of age and older with at least one cardiovascular risk factor, a higher rate of all-cause mortality, including sudden cardiovascular death, was observed in patients treated with the JAK inhibitor compared with TNF blockers. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OPZELURA.

Malignancy and Lymphoproliferative Disorders: Malignancies, including lymphomas, were observed in clinical trials of oral JAK inhibitors used to treat inflammatory conditions. Patients who are current or past smokers are at increased risk. Malignancies, including lymphomas, have occurred in patients receiving JAK inhibitors used to treat inflammatory conditions. In a large, randomized, postmarketing safety study of an oral JAK inhibitor in RA patients, a higher rate of malignancies (excluding non-melanoma skin cancer) was observed in patients treated with the JAK inhibitor compared to those treated with TNF blockers. A higher rate of lymphomas was observed in patients treated with the JAK inhibitor compared to those treated with TNF blockers. A higher rate of lung cancer was observed in current or past smokers treated with the JAK inhibitor compared to those treated with TNF blockers. In this study, current or past smokers had an additional increased risk of overall malignancies. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OPZELURA, particularly in patients with a known malignancy (other than successfully treated non-melanoma skin cancers), patients who develop a malignancy when on treatment, and patients who are current or past smokers.

Non-melanoma Skin Cancers: Non-melanoma skin cancers including basal cell and squamous cell carcinoma have occurred in patients treated with OPZELURA. Perform periodic skin examinations during OPZELURA treatment and follow-up treatment as appropriate. Exposure to sunlight and UV light should be limited by wearing protective clothing and using broad-spectrum sunscreen.

Major Adverse Cardiovascular Events (MACE): In a large, randomized, postmarketing safety study of an oral JAK inhibitor in RA patients 50 years of age and older with at least one cardiovascular risk factor, a higher rate of major adverse cardiovascular events (MACE) defined as cardiovascular death, non-fatal myocardial infarction (MI), and non-fatal stroke was observed with the JAK inhibitor compared to those treated with TNF blockers. Patients who are current or past smokers are at additional increased risk. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OPZELURA, particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. Patients should be informed about the symptoms of serious cardiovascular events and the steps to take if they occur. Discontinue OPZELURA in patients that have experienced a myocardial infarction or stroke.

Thrombosis: Thromboembolic events were observed in clinical trials with OPZELURA. Thrombosis, including deep vein thrombosis (DVT), pulmonary embolism (PE), and arterial thrombosis have been reported in patients receiving JAK inhibitors used to treat inflammatory conditions. Many of these adverse reactions were serious and some resulted in death. In RA patients 50 years of age and older with at least one cardiovascular risk factor treated with an oral JAK inhibitor, a higher rate of thrombosis was observed when compared with TNF blockers. Avoid OPZELURA in patients at risk. If symptoms of thrombosis occur, discontinue OPZELURA and treat appropriately [see Warnings and Precautions].
Thrombocytopenia, Anemia, and Neutropenia: Thrombocytopenia, anemia, and neutropenia were reported in the clinical trials with OPZELURA. Consider the benefits and risks for individual patients who have a known history of these events prior to initiating therapy with OPZELURA. Perform CBC monitoring as clinically indicated. If signs and/or symptoms of clinically significant thrombocytopenia, anemia, and neutropenia occur, patients should discontinue OPZELURA.

Lipid Elevations: Treatment with oral ruxolitinib has been associated with increases in lipid parameters including total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides.

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 two double-blind, vehicle-controlled clinical trials (TRUE-V1 and TRUE-V2), 449 adult and pediatric subjects 12 years of age and older with nonsenesthetic vitiligo were treated with OPZELURA twice daily for 24 weeks. In the OPZELURA group, 55% of subjects were females, and 81% of subjects were White, 5% were Black, and 4% were Asian. The adverse reactions reported by OPZELURA treated subjects with an incidence of ≥ 1% and at least 1% greater incidence than in the vehicle arm in the 24-week double-blind period are as follows for OPZELURA (N=449) vs Vehicle (N=224), respectively: Subjects with any treatment emergent adverse event (TEAE) 214 (48%) vs 79 (35%), Application site acne 26 (6%) vs 2 (1%), Application site pruritus 23 (5%) vs 6 (3%), Nasopharyngitis 19 (4%) vs 5 (2%), Headache 17 (4%) vs 6 (3%), Urinary tract infection 7 (2%) vs 1 (1%), Application site erythema 7 (2%) vs 1 (1%), and Pyrexia 6 (1%) vs 0 (0%).

Adverse reactions that occurred in TRUE-V1 and TRUE-V2 in ≥ 0.5% to < 1% of subjects in the OPZELURA group and none in the vehicle group were: application site dermatitis, hypertension, anxiety, application site discoloration, application site folliculitis, contusion, dermatitis, diarrhea, fever, gastritis, gastrinoma, hereditary hemochromatosis, histoplasmosis, influenza-like illness, insomnia, nasopharyngitis, and vomiting.

DRUG INTERACTIONS

Drug interaction studies with OPZELURA have not been conducted. Ruxolitinib is known to be a substrate for cytochrome P450 3A4 (CYP3A4). Inhibitors of CYP3A4 may increase ruxolitinib systemic concentrations whereas inducers of CYP3A4 may decrease ruxolitinib systemic concentrations.

Chronic inhibitors of CYP3A4: Avoid concomitant use of OPZELURA with strong inhibitors of CYP3A4 as there is a potential to increase the systemic exposure of ruxolitinib and could increase the risk of OPZELURA adverse reactions.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Exposure Registry: There is a pregnancy registry that monitors pregnancy outcomes in pregnant persons exposed to OPZELURA during pregnancy. Pregnant persons exposed to OPZELURA and healthcare providers should report OPZELURA exposure by calling 1-855-463-3463.

Risk Summary: Available data from pregnancies reported in clinical trials with OPZELURA are not sufficient to evaluate a drug-associated risk for major birth defects, miscarriage, or other adverse maternal or fetal outcomes. In animal reproduction studies, oral administration of ruxolitinib to pregnant rats and rabbits during the period of organogenesis resulted in adverse developmental outcomes at doses associated with maternal toxicity. The background risks of major birth defects and miscarriage for the indicated populations are unknown. All pregnancies carry some risk of birth defects, loss, or other adverse outcomes. The background risk in the U.S. general population of major birth defects and miscarriage is 2-4% and 15-20%, respectively.

Data

Animal Data: Ruxolitinib was administered orally to pregnant rats or rabbits during the period of organogenesis, at doses of 15, 30, or 60 mg/kg/day in rats and 10, 30, or 60 mg/kg/day in rabbits. There were no treatment-related malformations at any dose. A decrease in fetal weight of approximately 9% was noted in rats at the highest and maternally toxic dose of 60 mg/kg/day. This dose resulted in systemic exposure approximately 22 times the clinical systemic exposure at the maximum recommended human dose (MRHD); the clinical systemic exposure from ruxolitinib cream, 1.5% applied twice daily to 25-40% atopic dermatitis-affected body surface area is used for calculation of multiples of human exposure. In rabbits, lower fetal weights of approximately 6% and increased late resorptions were noted at the highest and maternally toxic dose of 60 mg/kg/day. This dose resulted in systemic exposure approximately 70% the MRHD clinical systemic exposure. In a pre- and postnatal development study in rats, pregnant animals were dosed with ruxolitinib from implantation through lactation at doses up to 30 mg/kg/day. There were no drug-related adverse effects on embryofetal survival, postnatal growth, development parameters or offspring reproductive function at the highest dose evaluated (3.1 times the MRHD clinical systemic exposure).

Lactation

Risk Summary: There are no data on the presence of ruxolitinib in human milk, the effects on the breastfed child, or the effects on milk production. Ruxolitinib is present in the milk of lactating rats. When a drug is present in animal milk, it is likely that the drug will be present in human milk. Because of the serious adverse findings in adults, including risks of serious infections, thrombocytopenia, anemia, and neutropenia, advise women not to breastfeed during treatment with OPZELURA and for approximately four weeks after the last dose (approximately 5-6 elimination half-lives).

Data: Lactating rats were administered a single dose of [14C]-labeled ruxolitinib (30 mg/kg) on postnatal Day 10, after which plasma and milk samples were collected for up to 24 hours. The AUC for total radioactivity in milk was approximately 13 times the maternal plasma AUC. Additional analysis showed the presence of ruxolitinib and its metabolites in milk, all at levels higher than those in maternal plasma.

Pediciatric Use: Nonsenesthetic Vitiligo: The safety and effectiveness of OPZELURA for the topical treatment of nonsenesthetic vitiligo have been established in pediatric patients 12 to 17 years of age. Use of OPZELURA in this age group is supported by evidence from TRUE-V1 and TRUE-V2, which included 55 pediatric subjects aged 12 to 17 years with nonsenesthetic vitiligo. No clinically meaningful differences in safety or effectiveness were observed between adult and pediatric subjects. The safety and effectiveness of OPZELURA in pediatric patients younger than 12 years of age with nonsenesthetic vitiligo have not been established.

Juvenile Animal Toxicity Data: Oral administration of ruxolitinib to juvenile rats resulted in effects on growth and bone mineralization. When administered starting at postnatal day 7 (the equivalent of a human newborn) at doses of 1.5 to 75 mg/kg/day, evidence of fractures occurred at doses ≥ 30 mg/kg/day, and effects on body weight and other bone measures [e.g., bone mineral content, peripheral quantitative computed tomography, and x-ray analysis] occurred at doses ≥ 5 mg/kg/day. When administered starting at postnatal day 21 (the equivalent of a human 2-3 years of age) at doses of 5 to 60 mg/kg/day, effects on body weight and bone occurred at doses ≥ 15 mg/kg/day, which were considered adverse at 60 mg/kg/day. Males were more severely affected than females in all age groups, and effects were generally more severe when administration was initiated earlier in the postnatal period. These findings were observed at systemic exposures that are at least 40% the MRHD clinical systemic exposure.

Geriatric Use: Of the 831 total subjects enrolled with nonsenesthetic vitiligo in clinical trials with OPZELURA, 65 (8%) were 65 years of age and older. Clinical trials of OPZELURA in subjects with nonsenesthetic vitiligo did not include sufficient numbers of subjects 65 years of age and older to determine whether they respond differently from younger adult subjects.

PATIENT COUNSELING INFORMATION

Advise the patient or caregivers to read the FDA-approved patient labeling (Medication Guide).

Infections: Inform patients that they may be at increased risk for developing infections, including serious infections, when taking Janus kinase inhibitors. Instruct patients to tell their healthcare provider if they develop any signs or symptoms of an infection. Advise patients that Janus kinase inhibitors increase the risk of herpes zoster, and some cases can be serious [see Warnings and Precautions].

Malignancies and Lymphoproliferative Disorders: Inform patients that Janus kinase inhibitors may increase the risk for developing lymphomas and other malignancies including skin cancer. Instruct patients to inform their health care provider if they have ever had any type of cancer. Inform patients that periodic skin examinations should be performed while using OPZELURA. Advise patients that exposure to sunlight, and UV light should be limited by wearing protective clothing and using a broad-spectrum sunscreen [see Warnings and Precautions].

Major Adverse Cardiovascular Events: Advise patients that events of major adverse cardiovascular events (MACE) including non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death, have been reported in clinical studies with Janus kinase inhibitors used to treat inflammatory conditions. Instruct all patients, especially current or past smokers or patients with other cardiovascular risk factors, to be alert for the development of signs and symptoms of cardiovascular events [see Warnings and Precautions].

Thrombosis: Advise patients that events of DVT and PE have been reported in clinical studies with Janus kinase inhibitors used to treat inflammatory conditions. Instruct patients to tell their healthcare provider if they develop any signs or symptoms of a DVT or PE [see Warnings and Precautions].

Thrombocytopenia, Anemia, and Neutropenia: Advise patients of the risk of thrombocytopenia, anemia, and neutropenia with OPZELURA. Instruct patients to tell their healthcare provider if they develop any signs or symptoms of thrombocytopenia, anemia, or neutropenia [see Warnings and Precautions].

Administration Instructions: Advise patients or caregivers that OPZELURA is for topical use only [see Dosage and Administration].

Patients should limit treatment to one 60 gram tube per week or one 100 gram tube per 2 weeks [see Dosage and Administration].

Provide the patient with instructions to report their pregnancy to Incyte Corporation at 1-855-463-3463 [see Use in Specific Populations].

Lactation: Advise a patient not to breastfeed during treatment with OPZELURA and for about four weeks after the last dose [see Use in Specific Populations].

Manufactured for: Incyte Corporation 1801 Augustine Cut-off Wilmington, DE 19803

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Talking to Children and Adolescents About Vitiligo

Frank discussions about managing the disorder can boost patients’ self-esteem and quality of life

Keith Loria, Staff Correspondent

The First Visit
When greating a child or adolescent for the first time in your dermatology practice, Angela S. Casey, MD, of the Center for Surgical Dermatology & Dermatology Associates in Westerville, Ohio, always looks them in the eye, introduces herself, and extends her hand for them to shake.

“Tell them, ‘I am so glad that you’re here today, and I look forward to talking with you and seeing how I can help,’” she said. She follows that up with questions about themselves, such as “What grade are you in?” and asks them about their interests and hobbies.

“I also tell them, ‘We’re just going to talk today’ to reassure them that there are no needles or procedures involved at this visit. It never ceases to amaze me how much anxiety young people can have about going to the doctor because they don’t know what to expect,” Casey said.

“I find that the approach of getting to know them and being clear about what will happen at the visit alleviates much of their stress. It also empowers them with the courage to be honest and communicates that our team is interested in them as an individual and not just focused on the problem at hand.”

Aaron M. Secrest, MD, PhD, MBA, vice chair of business strategy and assistant professor in the Departments of Dermatology and Population Health Sciences at the University of Utah in Salt Lake City noted how essential it is to talk to both the patient and the parents.

He begins each visit by introducing himself, using his first name to better connect. He then asks a few questions about their life to establish a report. “My patient is the child or teen, so I spend as much of the visit talking to them,” he said. “The parents can listen and hear the same thing, but talking to the patient helps me ensure I’m not talking over their heads.”

Cory Gaskins, MD, resident medical expert at BestBotox.ca, a resource for patients looking for physicians who specialize in Botox, noted when meeting with a child or adolescent who has vitiligo, it is important to let them warm up to you. “A comfortable environment is key for communication,” he said. “Make sure to communicate on their level, using terms they understand. It is also important to be respectful and understanding of their feelings.”

Key Questions
An important question at the beginning is, “What brings you in today?” For a child or adolescent with vitiligo, follow-up questions should typically focus on when they first noticed the condition; what treatments, if any, have been tried; and the results of such treatment.

After this, Casey will delve into the rest of their medical history, including other medical conditions, medications, and family history. “I also ask if they have seen anything online or on social media about vitiligo,” she said. “This gives them an opportunity to open up and gives me a glimpse into how they might be feeling about their condition. It is also a chance to dispel some of the myths that might be floating around.”

It’s also important to understand patients’ level of adherence and any potential barriers to treatment—such as cost, support for consistency with prescribed treatment, and ability to get to appointments. “Taking a step back and looking at the entirety of the situation sets us up for success in executing their treatment plan,” Casey said.

At Secrest’s clinic, he gives every patient the SkinIndex-16 assessment, 16 quick questions answered online and used as validated measures of the effects of skin disease on quality of life. “This covers questions about their symptoms, their physical functioning, and how their skin issue affects their mood. It shows Secrest the emotional effects the skin issue has on the patient so that he can directly say something like that, ‘It appears this is really bothering you.’”

“I find that it helps to focus the visit, and my teen patients are much more straightforward answering questions on an iPad or on their phone than in person to me face-to-face,” he said.

Other Skin Conditions
For patients with acne and atopic dermatitis, things can be a little bit different. “If the patient is picking their acne or scratching their eczema, I don’t ask if they are bothered by their condition,” he said. “I know the answer; they know the answer.”

“I just make statements of fact. ‘It looks like you pick at this’ or ‘This looks very itchy; I see the scratches.’ If they are embarrassed, I show them my cuticles and let them know that picking at things is very common and people do it when they’re stressed subconsciously.”

Many of the same quality-of-life questions apply to acne and atopic dermatitis, though because they are more common, many children and adolescents are more familiar with them and don’t often have as much anxiety as patients with vitiligo.

“I might ask if they have siblings or friends who have had similar conditions to get a read on their understanding and how they perceive it,” Casey said. “The questions about online and social media are equally important as there are all sorts of acne and eczema treatment ‘hacks’ out there; their appointment is an opportunity to address these.”

Psychosocial Concerns
Asking the patient about how they’re feeling about their condition and if it’s bothering them is important in getting a read on how they are adjusting to their issue. “Just a simple statement like that is validating and usually gets the patient to open up,” Casey said. “I know that kids and teens go through so much, but you can’t get insight if you don’t ask.”

Casey will try to get feedback about peer relationships and how these have influenced their feelings about their condition. “I find that the best approach is a direct and honest conversation to build trust and encourage open communication,” she said. “I direct them to support groups or communities online, such as The Vitiligo Society, which can be very helpful in reassuring them that they are not alone in their feelings and concerns.”

Fortunately, there are many positive role models today, such as Winnie Harlow, a Canadian fashion model with vitiligo, who serve as a good example that skin does not define a person. Casey noted that individuals such as Harlow are revered for their beauty and share the message that “we are all unique individuals, and sometimes those characteristics that make us different are exactly what make us exceptional.”

Building a Solid Relationship
Establishing trust in the first visit will help keep a relationship strong throughout the course of the treatment. Casey assures her patients that she is there to help and will do everything that she can to improve the condition. She makes patients a promise that her team will take
the very best care of them and be there to support them on their journey, and though there may be some bumps along the way, they are in this together.

One of Casey’s patients was a 12-year-old girl who had generalized vitiligo. The condition started with affected areas on her hands, but she didn’t come in for treatment until the vitiligo had spread to her face. “Her mother shared with me the difficulty that she experienced because the boys at school were starting to tease her, and one of the girls in her class had started a rumor that other students could ‘catch’ this skin disease if they came in contact with her,” Casey said. “Middle school is difficult enough without having this additional stress added into the mix.”

When Casey first met with her, the patient couldn’t make eye contact with her, and despite encouragement from her mom, the girl had a hard time expressing how she felt because she was shy and embarrassed. “I calmly talked with her about her diagnosis, some of the treatment options, timeline, and expectations,” Casey said. “We started her on topical treatment, but it was many months before we started to see any improvement. And even with the improvement, we still didn’t clear all of her vitiligo. However, the most impactful parts of her treatment were the conversations that we had along the way, about how she was feeling about her condition, any frustrations or fears she had about whether the treatment will work, and ways that we could help her feel better and boost her confidence.”

Casey also took the opportunity to educate the girl’s classmates about vitiligo through several school emails and informational messages that went out to parents and students in her class, which created a better environment for the patient. “Being open about the fact that sometimes treatments don’t work is important so that we can set realistic expectations,” she said. “Additionally, being as clear as we can on timelines is key: letting a patient know that a particular treatment will likely take months before we see an improvement helps manage their expectations and creates a sense of security.”

Reference
Skin of Color Society Summit: An Overview

Hiring investigators of color, educating and building trust with potential participants, and addressing funding can make clinical trials more diverse.

Nicole A. Nghenebor, MD, Staff Correspondent

In June 2022, the Skin of Color Society (SOCS) hosted its first Meeting the Challenge Summit: Diversity in Dermatology Clinical Trials. This groundbreaking meeting brought together stakeholders from multiple disciplines and sectors to Washington, DC, to discuss the underrepresentation of individuals of color in dermatologic studies. During the conference, physicians, investigators, industry members, experts from academia, members from the National Institutes of Health (NIH) and the FDA, journal editors, and patients discussed barriers, challenges, and ways to increase diversity in dermatology clinical trials.

Provider Barriers

“Clinical trials are difficult now,” Amy McMichael, MD, FAAD, professor and chair of the Dermatology Department and director of cosmetic dermatology at Wake Forest University in Winston-Salem, North Carolina, said during her presentation.1 McMichael noted that she has conducted thousands of trials over the past 28 years and recently decided to take a step back because the barriers for clinical trials have become so high, such as the fact that investigators of color may have inadequate knowledge of clinical research and trial methodology. More training courses are needed to help both physicians and research staff become familiar with how to run a clinical trial and report unexpected and severe adverse events, McMichael said. For successful trial completion and initiation, investigators also need more assistance to help train their staff, she said.

McMichael also noted that a lack of research funding heavily burdens physicians. The shrinking budgets for research may not be able to cover the salaries for staff, which may lead to inappropriately asking medical trainees and research staff for underpaid or unpaid work. She proposed that companies provide startup funds for the initial work as it takes a considerable amount of time to write up contracts and research proposals for institutional review boards. She ended her presentation by pointing out that there are also inadequate infrastructures for clinical trials, which may be more pronounced for physicians of color, and a dire need for robust mentorship to help meet providers where they are in the clinical trial process.

In an interview with Dermatology Times®, McMichael said, “I don’t think anyone can really predict how quickly things will change regarding increasing diversity in dermatology clinical trials. What is exciting is that we are working toward both increased diversity of participants in the trial as well as diversity in those conducting the trials. This first step is very promising since the meeting of all the stakeholders had never occurred before the [the summit]. Now it is up to all of us to keep the momentum going for more change. In the meantime, we can continue to treat our patients with new drugs, but we have to pay close attention to outcomes, [adverse] effects, and complications that may arise and, if warranted, report this information to drug companies and/or publish these findings. As we move forward, it will become clearer that diversity is needed at the start of trials rather than after the fact.”

Patient Barriers

Multiple speakers at the conference also examined the patient barriers for clinical trials. Jonathan S. Weiss, MD, FAAD, adjunct clinical professor of dermatology at Emory University School of Medicine and president of Georgia Dermatology Partners in Atlanta, outlined that access for patients may be limited by time, distance, or trust with the medical field.2 In an interview with Dermatology Times®, he said, “The lack of diversity causes significant gaps in our ability to treat patients of all skin tones and skin types optimally. Different skin types respond differently to the same disease states in terms of appearance and sequelae (for example, postinflammatory pigmentation), and without diversity in studies, we have no way of knowing how these different skin types will respond to treatment. Further, what we consider to be medically excellent results may not be considered acceptable to patients of different skin types.”

Some patients may not have the transportation to consistently travel to a clinical site. Jocelyn Ashford, head of cardioirural global patient advocacy at BridgeBio, focused on the psychological, logistical, and health care-related restrictions that lead to decreased trial recruitment and retention of diverse patients.3 She spoke about the strict inclusion and exclusion criteria (eg, high blood pressure and body mass index) that often exclude diverse populations from participating in trials. Consent forms that are too long and a lack of providing forms in multiple languages are major patient barriers brought up by Neelam Vashi, MD, FAAD, associate professor of dermatology at Boston University School of Medicine and founder and director of Center for Ethnic Skin in Massachusetts.4

History of Inclusivity in Dermatology Clinical Trials

“We need dermatology to be all-inclusive,” Adam Friedman, MD, FAAD, professor, chair, and associate program director of dermatology and director of translational research at George Washington University in Washington, DC, said during his presentation.1 The field of dermatology has struggled with diversity in its workforce as well as diversity in clinical trials. Friedman stated that Black dermatologists comprise 3% of dermatologists but are Black individuals are 12.8% of the US population. This means that we are not seeing a robust pipeline to increase diversity of residents and workforce. Friedman detailed the history of racism in clinical trials and the subsequent barriers that have continued to affect participant recruitment and retention. He noted the history of racism with the Tuskegee Syphilis Study, and he discussed Albert Kligman, MD, who conducted medical experiments on prisoners at Holmesburg Prison in Philadelphia, Pennsylvania, from 1951-1974.4

Multiple speakers touched on the desire for patients wanting to trust their providers. Therefore, they noted, providers interested in increasing diversity in trials should work to gain patient’s trust. Friedman set the stage by describing the current landscape of clinical trials and how the terms race, ethnicity, and skin color are used often incorrectly to categorize patients. He detailed how race is not a scientific term and was originally used to separate groups based on slavery. He went on to say that the Fitzpatrick scale has been incorrectly used as a marker of skin color in dermatology clinical trials; it was originally created to assess skin cancer risk. For clinical trials, he proposed investigators let patients self-identify their ethnicity and skin color to improve the accuracy of reporting and categorization of patients. He also noted need for more inclusive scales to measure disease in different skin tones in research trials. Friedman cited results of a study that showed more than 50% of clinical trials in dermatology do not report race or ethnicity data. Furthermore, for the

>> continues on 36
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Gastroenteritis: Gastroenteritis includes gastroenteritis and viral gastroenteritis. See Warnings and Precautions.

Herpes Simplex Infections: Herpes simplex infections include herpetic whitlow, herpetic whitlow with vesicles or ulcers, herpetic whitlow with vesicles or ulcers; all cases were mild to moderate in severity and did not lead to discontinuation of TREMFYA. See Warnings and Precautions.

Elevated Liver Enzymes: Elevated liver enzymes were reported more frequently in the TREMFYA group compared to the placebo group. See Warnings and Precautions.

Guselkumab and Herpes Infections: Herpes infections include herpes simplex infections, and herpes zoster infections. See Warnings and Precautions.

Rash: Rash includes all cutaneous reactions. See Warnings and Precautions.

Infections: Infections include respiratory tract infections, gastroenteritis, tinea infections, and herpes infections. See Warnings and Precautions.

Elevated Liver Enzymes: Elevated liver enzymes were reported more frequently in the TREMFYA group compared to the placebo group. See Warnings and Precautions.

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Rash: Rash includes all cutaneous reactions. See Warnings and Precautions.
Creating Diverse Teams Takes Work, But Is Worth the Effort

Jeff Bendix, Senior Editor Medical Economics

INCORPORATING DIVERSITY, EQUITY, AND INCLUSION (DEI) into work teams and organizations requires strong leadership and a great deal of effort. But the result—improved performance and emotional well-being among employees—makes the undertaking worthwhile.

That message was at the heart of “Diversity, Equity and Inclusion as the Secret to Successful Teams,” a panel discussion at the American College of Physician’s 2022 Internal Medicine Meeting.

“You’re not doing this work because it’s a box you’ve got to check,” said Susan Hingle, MD, MACP, associate dean for human and organizational potential at the Southern Illinois University (SIU) School of Medicine. “It will allow members of your team or your organization to reach their full potential. And in order to do that, people need to feel like they belong.”

“Leaders are role models,” she added. “They are the ones who really establish the culture. And culture is the piece that links DEI and emotional well-being.”

One of the most important things leaders can do to create successful diverse and inclusive teams is to build relationships with team members. “Leaders who do this [DEI] well focus on getting to know team members, and making them feel valued for what they can bring to the table,” she said.

John M. Flack, MD, MACP, professor and chair of the internal medicine department/hypertension at SIU School of Medicine, emphasized the importance of communication in building widespread support for DEI efforts.

“We need to understand why it’s important to have an inclusive team. There’s data showing that companies in the top quartile of diversity have higher profits than those who aren’t.”

“One of the hardest things in messaging [about DEI] is getting people to understand that it’s not a zero-sum game, where somebody loses if somebody else wins,” he added. He cited the example of a gender-based survey measuring equity in salary and promotions at the school. “We found that [bias] cuts both ways, it wasn’t just the usual thing you say where women get the short end of the stick,” he said. “So men shouldn’t be bummed out by a focus on gender equity because at the end of the day it makes things better for everyone.”

Tiffany Leung, MD, FACP, assistant professor of health, medicine and life sciences at Maastricht University in the Netherlands, and the panel’s moderator, noted that organizations seeking to build DEI sometimes fail to distinguish between “surface level” and “deeper level” diversity.

“Diversity on the basis of individual surface characteristics is important, but to unleash a team’s full potential you need that deeper level of diverse values and experiences as well,” she said.

Another pitfall in building DEI, according to Hingle, is over-reliance on the concept of “hiring for fit.”

“Certainly it’s important that someone fits because if they feel like they don’t fit they’re unlikely to succeed,” she said. “But using ‘hiring for fit’ in evaluation tools allows implicit bias to enter into the decision.” And while everyone has biases to a certain extent, it’s important to be aware of them so they don’t influence the decision of whether someone is a good fit for your organization.

“The emphasis should always be on trying to build environments where people feel they can be their authentic selves, where their lived experiences can inform everything they do,” Hingle added.

In another session, Fabian Sandoval, MD, CEO and research director of the Emerson Clinical Research Institute in Washington, DC, discussed cultivating trust by engaging community members, educating them about diseases, and providing resources.

“In a follow-up interview with Dermatology Times,” Friedman said, “An immediate threat to our practice and to our patients if clinical trial [participant] populations do not mirror the composite of the general population is that we cannot reliably anticipate how a diagnostic or drug will behave in everyone.”

When asked what the dangers to effective medical care would be if this problem remains unaddressed, he noted, “There are sadly many [dangers], but the most obvious ones are direct immediate harm to patients who are either misdiagnosed/mismanaged due to a lack of comfort or experience with all skin tones. Indirect harm through microaggression-type statements [such as] ‘I need to refer you to someone else’ or ‘I don’t know how to take care of your skin’ can also result, furthering the trust divide [between patients and providers in clinical research trials].”

Establishing Community Trust

“Our grandma has done so much,” David Lacks Jr and Veronica Robinson said during the summit. Lacks and Robinson, descendants of Henrietta Lacks, detailed the scientific use of the cells from Lacks without the consent of her or her family for more than 20 years. In the 1950s, Lacks, who was diagnosed with cervical cancer, had her cells retrieved and, because of how unusual they were in nature, were taken to labs around the United States to be studied, without the consent of Lacks or any member of her family.

The family now has a say in how and when the cells of Henrietta Lacks are being used. The family’s partnerships with the NIH and World Health Organization symbolize the relationship with patients and medical research.

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Johnson noted that it is important to educate community members outside of clinical trials by partnering with churches and schools, hosting community panels, and making sure that community leaders understand the mission. She has found success in creating pipeline programs in schools. These programs help to encourage marginalized students see themselves as able to change disease disparities. Sandoval echoed this sentiment and the need for creating training programs at the undergraduate level and beyond.

James H. Powell, MD, president of Strategic Medical Associates and co-founder and chief medical officer of knowRx, focuses on making diversity a priority in recruitment of patients. He is the principal investigator for the National Medical Association’s program Project IMPACT (Increase Minority Participation and Awareness of Clinical Trials). This program includes engaging minority patients in the discussion of clinical trials, developing cultural competence, and addressing the business of being a clinical investigator for physicians of color. He stressed that to create a better future for diversity in dermatology trials, there must be an establishment of mentors for the inclusion of novice investigators and that trusted physicians need to share information with patients about trials beyond their institution. He stated that it costs more for companies at the end of their trial to backtrack and try to identify diverse participants if they did not originally have diversity in their studies. It is more beneficial and cost-effective to begin a trial with the intention of recruiting diverse participants, he said.

An expert in medical and cosmetic clinical trials, Cheryl Burgess, MD, FAAD, president and medical director of Center for Dermatology and Dermatologic Surgery in Washington, DC, offered several actionable items for clinical investigators to increase diversity in trials. Using the SWOT (strengths, weaknesses, opportunities, and threats) analysis framework, she suggested that the research community educate underrepresented communities about trials in general, provide race concordant patient-physician relationships, and hire diverse and bilingual staff. She emphasized the importance of focusing outreach to minority communities about specific trials.

David Chu, MD, PhD, FAAD, executive director of Arcutis Biotherapeutics, stated his company seeks to include investigators of color and has created a program initiative to establish new investigators of color. They have increased geographic diversity in site selection to include having a more representative patient cohort in their studies.

Representatives from companies such as AbbVie, Sanofi, L’Oréal, Galderma, Revision Skincare, Bristol Myers Squibb, Janssen, and Eli Lilly discussed their upcoming programs and similar plans for improving diversity in dermatology.

“We have a bright future ahead,” said Angel Byrd, MD, PhD, an assistant professor at Howard University College of Medicine in Washington, DC. Her words were a reminder that when we collectively remain passionate about increasing diversity in dermatology clinical trials, we can decrease the disparities in health outcomes.

Valerie Harvey, MD, president of SOCS, said in an interview, “As president of the Skin of Color Society, I was honored to host this historic meeting, which convened numerous stakeholders across the research ecosystem. My hope is that this meeting represents the beginning of critical discussions, collaborations, and initiatives. Together we can change the existing landscape to bring about more equitable participant and investigator representation in dermatology clinical trials.”

For full list of references, visit dermatologytimes.com
Best Practices for Treating Stretch Marks in Pregnancy

Fazila Rajab, Staff Correspondent

Stretch marks, also known as stretch marks, affect up to 90% of pregnant women. They develop when the skin stretches or shrinks rapidly, rupturing the collagen and elastin.

Research suggests that women who get pregnant at a young age or those who gain weight quickly tend to have stretch marks more frequently than their counterparts. Results of several studies also revealed the role of cortisone, a hormone released by the adrenal gland, in stretch mark development. In addition, individuals who take corticosteroids or have conditions such as Cushing syndrome get stretch marks more frequently. The most affected body areas include the buttocks, hips, breasts, abdomen, and thighs.

Initially, stretch marks may appear as red, purple, or pink slightly raised itchy scars. During this phase, they are called striae rubrae and are easier to manage. Over time they change into streaks of white lines, during which they are called striae albae and are more difficult to manage. Stretch marks mature after a year, making them less likely to fade. Hence, the earlier a patient starts treatment, the better the outcome.

Although stretch marks are not a medical emergency, they may cause aesthetic concerns. Several topical formulations are available in the market for preventing stretch marks during pregnancy but there is limited evidence of their effectiveness. Although myriad treatment options are available to improve the appearance of stretch marks, only a few are based on true science. Stretch marks cannot be cured completely but there are several medically approved treatment options to help relieve the itch or make them less noticeable.

Laser-Based Treatments

Laser treatment is a nontoxic and noninvasive procedure using light energy at specific wavelengths to repair skin cells. It is the most effective treatment to reduce stretch marks and is recommended by the American Society for Dermatologic Surgery to improve the scars.

Most laser therapies, such as pulsed dye lasers, are more effective at improving the appearance of striae rubrae. Results of a recent study evaluating the improvements in stretch marks using a nonablative fractional Nd:YAG laser showed it to be a safe and effective treatment option with no long-term adverse effects.

Carbon dioxide lasers have a longer recovery period and are more painful than nonablative lasers but results of a study showed their use led to 50% to 70% improvements, especially in striae alba.

Although laser therapy is the most effective treatment option, it is expensive. A single session may cost $400 to $800, with up to 20 sessions required to show noticeable improvement.

Nonlaser Approaches

Retin-A

Tretinoin, also known by its brand name Retin-A, may help improve early stretch marks, though the evidence is limited. By penetrating the skin, tretinoin rebuilds collagen. It is effective for early stretch marks and may not produce any effects on older lesions.

Patients who experience adverse effects when using tretinoin may be able to use it when combined with a lipid-based moisturizer. It is important to note that Retin-A is not safe during pregnancy and should not be used by pregnant and lactating women because of concerns about its teratogenic effects.

A study published in the Journal of the European Academy of Dermatology and Venereology found no topical formulation that is most effective in improving or eradicating stretch marks.
Research suggests that women who get pregnant at a young age or those who gain weight quickly tend to have stretch marks more frequently than their counterparts.1

**Microdermabrasion**
Microdermabrasion is a noninvasive procedure that exfoliates the skin and scrubs off dead cells. In this procedure, an applicator with an abrasive surface removes the dead skin layer to rejuvenate it. Another microdermabrasion technique sprays fine particles of aluminum oxide or sodium carbonate using a suction/vacuum. According to results of a review conducted in 2017, microdermabrasion is found to be effective in improving early stretch marks. Moreover, another study suggested that when combined with topical platelet-rich plasma, microdermabrasion is more effective in enhancing the efficacy of the treatment.2

**Microneedling**
Microneedling is a minimally invasive collagen induction therapy that uses tiny needles to prick the skin to stimulate collagen production and naturally heal the targeted area, thereby improving the appearance of stretch marks. Unlike most treatments, microneedling is also effective in treating late stretch marks. Research revealed that microneedling is a more effective and tolerable treatment option for stretch marks than microdermabrasion with phenophoresis.3

**Chemoexfoliation**
Chemoexfoliation, also referred to as chemical peeling, is a skin resurfacing procedure in which certain caustic agents, such as glycolic acid, salicylic acid, or trichloroacetic acid, are applied to the skin surface. The main objective of the procedure is to remove the outer layer of the skin and promote new skin cell formation. **Platelet-rich plasma (PRP) combination therapies**
In this procedure, blood samples are collected from the individual’s body and placed in a centrifuge to separate platelets, which are then reinjected into the underlying layers of the skin. This initiates the skin’s natural repair cycle and improves the appearance of the stretch marks. Results of a study published in the Journal of Cosmetic and Laser Therapy showed that when combined with ultrasound treatment, PRP therapy may provide satisfactory results among individuals with stretch marks.4

**Radiofrequency therapy**
Radiofrequency (RF) therapy, a minimally invasive technique, delivers RF current that converts into heat energy when it reaches deep into the skin, stimulating collagen production. Evidence indicates radiofrequency therapy may improve the stretch marks’ appearance. RF therapy, when combined with microneedling, enhances the efficacy of the treatment by delivering energy waves deeper into the dermis, stimulating even deeper layers of collagen production.5

There is no single treatment for all, and not all treatment options are suitable for everyone, so it is important to speak with your patients about their options.6

**References**
INDICATION

ADBRY™ (tralokinumab-drzm) is indicated for the treatment of moderate-to-severe atopic dermatitis in adult patients whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. ADBRY can be used with or without topical corticosteroids.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATION

• ADBRY is contraindicated in patients who have known hypersensitivity to tralokinumab-drzm or any excipients in ADBRY.

WARNINGS AND PRECAUTIONS

• Hypersensitivity: Hypersensitivity reactions, including anaphylaxis and angioedema have occurred after administration of ADBRY. If a serious hypersensitivity reaction occurs, discontinue ADBRY immediately and initiate appropriate therapy.

• Conjunctivitis and Keratitis: Conjunctivitis and keratitis occurred more frequently in atopic dermatitis subjects who received ADBRY. Conjunctivitis was the most frequently reported eye disorder. Advise patients to report new onset or worsening eye symptoms to their healthcare provider.

• Parasitic (Helminth) Infections: Treat patients with pre-existing helminth infections before initiating treatment with ADBRY. If patients become infected while receiving ADBRY and do not respond to antihelminth treatment, discontinue treatment with ADBRY until the infection resolves.

• Risk of Infection with Live Vaccines: ADBRY may alter a patient’s immunity and increase the risk of infection following administration of live vaccines. Prior to initiating therapy with ADBRY, complete all age appropriate vaccinations according to current immunization guidelines. Avoid use of live vaccines in patients treated with ADBRY. Limited data are available regarding coadministration of ADBRY with non-live vaccines.

ADVERSE REACTIONS

• The most common adverse reactions (incidence ≥1%) are upper respiratory infections, conjunctivitis, injection site reactions, and eosinophilia.

Please see additional Important Safety Information and Brief Summary of Prescribing Information on following pages.
Adbry—For lasting control and itch relief

Patients experienced lasting improvement for up to 52 weeks with ADBRY

Visible Skin Clearance and Itch Relief With Adbry at Week 16

<table>
<thead>
<tr>
<th></th>
<th>ADDBRY MONOTHERAPY</th>
<th>COMBINATION THERAPY</th>
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<tbody>
<tr>
<td></td>
<td>ECZTRA 1</td>
<td>ECZTRA 2</td>
</tr>
<tr>
<td></td>
<td>Adbry 300 mg Q2W</td>
<td>placebo</td>
</tr>
<tr>
<td></td>
<td>601</td>
<td>197</td>
</tr>
<tr>
<td>IGA 0/1§</td>
<td>16% vs 7% (P=0.002)</td>
<td>21% vs 9% (P=0.001)</td>
</tr>
<tr>
<td>EASI-75§</td>
<td>25% vs 13% (P=0.001)</td>
<td>33% vs 10% (P=0.001)</td>
</tr>
<tr>
<td>No. of patients with baseline Worst Daily Pruritus NRS (weekly average) score ≥4</td>
<td>594</td>
<td>194</td>
</tr>
<tr>
<td>Worst Daily Pruritus NRS (24 point reduction)§</td>
<td>20% vs 10% (P=0.002)</td>
<td>25% vs 9% (P=0.001)</td>
</tr>
</tbody>
</table>

*Full Analysis Set (FAS) includes all subjects randomized and dosed.
§Subjects were defined as subjects with an IGA 0 or 1 (“clear” or “almost clear”).
† Percentages of patients who achieved response.

Nearly 9 out of 10 responders at Week 16 experienced lasting disease control at Week 32 with ADBRY 300 mg Q2W+TCS as needed†‡:

<table>
<thead>
<tr>
<th>ECZTRA 3</th>
<th>Adbry Q2W+TCS as needed</th>
<th>Percentage of patients who maintained response at Week 32</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 16</td>
<td></td>
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</tr>
<tr>
<td>Week 32</td>
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<tr>
<td></td>
<td></td>
<td>92% EASI-75 (60/65)</td>
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<tr>
<td></td>
<td></td>
<td>89% IGA 0/1 (40/45)</td>
</tr>
</tbody>
</table>

More than half of responders at Week 16 maintained response at Week 52 with Adbry Q2W monotherapy, without any TCS use†‡:

- **ECZTRA 1**: IGA 0/1 and EASI-75 response was maintained by 51% (20/39) and 60% (28/47) of patients on Adbry Q2W, respectively; 47% (9/19) and 33% (10/30) of patients on placebo maintained response.
- **ECZTRA 2**: IGA 0/1 and EASI-75 response was maintained by 60% (32/53) and 57% (43/76) of patients on Adbry Q2W, respectively; 23% (6/26) and 20% (8/40) of patients on placebo maintained response.

† Responders were defined as subjects with an IGA 0 or 1 or EASI-75 at Week 16. At Week 16, responders (defined as subjects with an IGA 0 or 1 or EASI-75 at Week 16) were rerandomized to Adbry 300 mg Q2W with TCS or Adbry Q4W with TCS for another 16 weeks.
‡ Responders were defined as subjects with an IGA 0 or 1 or EASI-75 at Week 16. At Week 16, responders (defined as subjects with an IGA 0 or 1 or EASI-75 at Week 16) were rerandomized to Adbry 300 mg Q2W, Adbry Q4W, or placebo Q2W for another 36 weeks.
§ Percentage of patients who achieved response.

Study designs

The efficacy and safety of Adbry were assessed in 3 randomized, double-blind, placebo-controlled trials with a total of 1934 patients 18 years of age and older, with moderate-to-severe atopic dermatitis not adequately controlled by topical medications. In ECZTRA 1, 2, and 3, subjects received subcutaneous injections of Adbry 600 mg or placebo on Day 0, followed by Adbry 300 mg or placebo Q2W for 16 weeks. In ECZTRA 3, patients received concomitant TCS as needed (mometasone furoate 0.1% cream was dispensed at each dosing visit). ECZTRA 1, 2, and 3 assessed the primary endpoints of the proportion of subjects with an IGA 0 or 1 at Week 16 and the proportion of subjects with EASI-75 at Week 16. Secondary endpoints included the reduction of Worst Daily Pruritus NRS (weekly average) of at least 4 points on the 11-point itch NRS from baseline to Week 16.

At Week 16, patients with an IGA 0/1 or EASI-75 response were re-randomized to Adbry Q2W, Q4W, or placebo for another 36 weeks (ECZTRA 1, 2) and Q2W or Q4W for another 16 weeks (ECZTRA 3).

Important Safety Information (cont’d)

Use in Specific Populations

- **Pregnancy**: There are limited data from the use of ADBRY in pregnant women to inform a drug-associated risk of adverse developmental outcomes. Human IgG antibodies are known to cross the placental barrier; therefore, ADBRY may be transmitted from the mother to the developing fetus.
- **Lactation**: There are no data on the presence of tralokinumab-lrdm in human milk, the effects on the breastfed infant, or the effects on milk production. Maternal IgG is present in breast milk. The effects of local gastrointestinal exposure and limited systemic exposure to ADBRY on the breastfed infant are unknown.
- **Pediatric Use**: The safety and effectiveness of ADBRY have not been established in pediatric patients.

Adbry™ (tralokinumab-lrdm)
Injection 150 mg/mL

The only biologic to exclusively target IL-13
multicentre, placebo-controlled phase III trials (ECZTRA 1 and ECZTRA 2).

ADBRY™ (tralokinumab-ldrm) injection, for subcutaneous use

Initial U.S. Approval 2021
Brief Summary of Prescribing Information

This Brief Summary does not include all the information needed to use ADBRY safely and effectively. Please see Full Prescribing Information.

For Only

INDICATIONS AND USAGE
ADBRY is indicated for the treatment of moderate-to-severe atopic dermatitis in adult patients whose disease is not adequately controlled with topical prescription corticosteroids when those therapies are not advisable. ADBRY can be used with or without topical corticosteroids.

CONTRAINDICATIONS
ADBRY is contraindicated in patients who have known hypersensitivity to tralokinumab-ldrm or any excipients in ADBRY.

WARNINGS AND PRECAUTIONS

Hypersensitivity
Hypersensitivity reactions including anaphylaxis and angioedema, have been reported with use of ADBRY.

It is a serious hypersensitivity reaction occurs, discontinue ADBRY immediately and initiate appropriate therapy.

Concomitants and Keratitis
Concomitants may occur more frequently in atopic dermatitis subjects who received ADBRY. Concomitants was the most frequently reported eye disorder. Most subjects with concomitants or keratitis recovered or were recovering during the treatment period.

Advise patients to report new or worsening eye symptoms to their healthcare provider.

Parotid (Salivary) Glands
Patients with known salivary gland infections were excluded from participation in clinical studies. It is unknown if ADBRY will influence the immune response against SARS-CoV-2 virus.

Treat patients with pre-existing salivary gland infections before initiating treatment with ADBRY. If patients become infected while receiving ADBRY and do not respond to antimicrobial treatment, discontinue treatment with ADBRY until the infection resolves.

Risk of Infection with Live Vaccines
ADBRY may alter a patient’s immunity and increase the risk of infection following administration of live vaccines. Prior to initiating therapy with ADBRY, compare all age-appropriate vaccinations according to current immunization recommendations when use of live vaccines in patients treated with ADBRY. Limited data are available regarding co-administration of ADBRY with non-live vaccines.

ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail elsewhere in this prescribing information:

• Hypersensitivity
• Concomitants and Keratitis

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.

The safety of ADBRY was evaluated in a pool of 5 randomized, double-blind, placebo-controlled trials in subjects with moderate-to-severe atopic dermatitis including three Phase 3 ECZTRA trials (ECZTRA 1, ECZTRA 2, ECZTRA 3), a dose-finding trial, and a vaccine response trial.

The safety profile had a mean age of 37 years; 41% of subjects were female. The majority of subjects were white (81%), and 5% were Black. In terms of co-morbid conditions, 39% of the subjects had asthma, 49% had hay fever, 36% had food allergy, and 27% had allergic conjunctivitis at baseline.

In these 5 atopic dermatitis trials, 1084 subjects were treated with subcutaneous injection of ADBRY with or without concurrent topical corticosteroids (TCS). A total of 807 subjects were treated with ADBRY for at least 1 year.

In ECZTRA 1 and ECZTRA 2 compared the safety of the ADBRY monotherapy to placebo through Week 52. ECZTRA 3 compared the safety of ADBRY + TCS to placebo + TCS through Week 32.

Weeks 0 to 16 (ECZTRA 1, ECZTRA 2, and ECZTRA 3), and that occurred at a rate of at least 1% in the ADBRY 300 mg every other week monotherapy group, and in the ADBRY 50 mg every week + TCS group, all at a higher rate than placebo during the first 16 weeks of treatment.

Table 1: Adverse Reactions Occurring in 1% of the ADBRY Monotherapy Group or the ADBRY + TCS Group in the Atopic Dermatitis Trials Through Week 52

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>ADBRY Monotherapy</th>
<th>ADBRY + TCS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper respiratory tract infections</td>
<td>281 (23.9) 279 (23.8)</td>
<td>281 (23.9) 279 (23.8)</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>34 (2.7) 33 (2.7)</td>
<td>34 (2.7) 33 (2.7)</td>
</tr>
<tr>
<td>Injection site reactions</td>
<td>87 (7.4) 61 (4.6)</td>
<td>87 (7.4) 61 (4.6)</td>
</tr>
</tbody>
</table>

Table 2: Upper respiratory tract infections cluster includes pharyngitis, rhinitis, and sinusitis, mainly reported as common cold.

Table 3: Injection site reactions cluster includes pain, edema, and swelling. Conjunctivitis cluster includes conjunctivitis and allergic conjunctivitis.

**Immunogenicity**

In the monotherapy trials (ECZTRA 1 and ECZTRA 2), through Week 16, the proportion of subjects with Anti-Drug-Antibodies (ADA) during treatment was 0.7% in the ADBRY 300 mg every other week group, and 0.8% in the ADBRY 300 mg every other week + TCS group. In the placebo group + TCS group, the ADA incidence was 0.8%.

In the ECZTRA 3 trial, ADA incidences were 0.6% in the ADBRY 300 mg every other week group and 0.7% in the ADBRY 300 mg every other week + TCS group. In the placebo group + TCS group, the ADA incidence was 0.8%.

In the monotherapy trials (ECZTRA 1 and ECZTRA 2), through Week 16, the proportion of subjects with Anti-Drug-Neutralizing Antibodies (ADNAB) during treatment was 0.8% in the ADBRY 300 mg every other week group and 0.9% in the ADBRY 300 mg every other week + TCS group. In the placebo group + TCS group, the ADNAB incidence was 1.0%.

In the ECZTRA 3 trial, ADNAB incidences were 0.7% in the ADBRY 300 mg every other week group and 1.0% in the ADBRY 300 mg every other week + TCS group. In the placebo group + TCS group, the ADNAB incidence was 0.8%.

Across all trials, the ADA incidence for subjects who received ADBRY was 4.6%; 0.9% had persistent ADA and 1.0% had neutralizing antibodies.

There is no clinical meaningful differences in the pharmacokinetics, safety, or efficacy of tralokinumab-ldrm were observed in patients who tested positive for anti-tralokinumab-ldrm antibody (including neutralizing antibodies).

USE IN SPECIFIC POPULATIONS

Pregnancy

There are no adequate data on the use of ADBRY in pregnant women to inform a drug-associated risk of adverse developmental outcomes. Human IgG antibodies are known to cross the placental barrier; therefore, ADBRY may be transmitted from the mother to the developing fetus.

In an enhanced pre- and post-natal developmental study, no adverse developmental effects were observed in offspring born to pregnant monkeys after intravenous administration of tralokinumab-ldrm during organogenesis through parturition at doses up to 10 times the maximum recommended human dose (MRHD).

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defects, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects is 2% to 4% and 1% to 2% in women over 35 years of age.

Lactation

There are no data on the presence of tralokinumab-ldrm in human milk, as measured by radioimmunoassay. The effect of ADBRY on nursing infants is unknown. The development and health benefits of breastfeeding should be considered along with the mother’s clinical need for ADBRY and any potential adverse effects on the breastfed child from ADBRY or from the underlying maternal condition.

Pediatric Use

The safety and effectiveness of ADBRY have not been established in pediatric patients.

Geriatric Use

Of the 1653 subjects exposed to ADBRY in 5 atopic dermatitis trials in the initial treatment period of up to 16 weeks, 77 subjects were 65 years or older. Clinical studies did not include sufficient numbers of subjects aged 65 years and over to determine whether they respond differently than younger subjects.

OVERDOSAGE

There is no specific treatment for ADBRY overdose. In the event of overdose, contact Poison Control (1-800-222-1222) for latest recommendations and monitor the patient for any signs or symptoms of adverse reactions and institute appropriate supportive treatment immediately.

PATIENT COUNSELING INFORMATION

Advise patients to avoid concurrent use of immunosuppressants and ADBRY, as the concurrent use of immunosuppressants and ADBRY may increase the potential for infection-related adverse effects on embryofetal toxicity or malformations.

Advise patients to inform their healthcare provider that they are taking ADBRY prior to a scheduled vaccination.

There is no specific treatment for ADBRY overdose. In the event of overdose, contact Poison Control (1-800-222-1222) for latest recommendations and monitor the patient for any signs or symptoms of adverse reactions and institute appropriate supportive treatment immediately.

PATIENT COUNSELING INFORMATION

Advise patients to avoid concurrent use of immunosuppressants and ADBRY, as the concurrent use of immunosuppressants and ADBRY may increase the potential for infection-related adverse effects on embryofetal toxicity or malformations.

Advise patients to inform their healthcare provider that they are taking ADBRY prior to a scheduled vaccination.

Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity with ADBRY. 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 the incidence of antibodies in the studies described below with the incidence of antibodies in other studies or to other tralokinumab products may not be meaningful.

In ECZTRA 1, ECZTRA 2, and the vaccine response trial, the incidence of Anti-Di-Antibody (ADA) during the initial 16 week treatment period was 1.4% for subjects treated with ADBRY 300 mg every other week, and 1.3% for subjects treated with placebo. Neutralizing antibodies were seen in 0.7% of subjects treated with ADBRY and 0.2% of subjects treated with placebo.

In ECZTRA 3, the ADA incidence was 1.6% in the ADBRY treated subjects, and in the placebo treated subjects.

In all treatment periods, the ADA incidence for subjects who received ADBRY was 4.6%; 0.9% had persistent ADA and 1.0% had neutralizing antibodies.

In clinical meaningful differences in the pharmacokinetics, safety, or efficacy of tralokinumab-ldrm were observed in patients who tested positive for anti-tralokinumab-ldrm antibody (including neutralizing antibodies).

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Managing Postpregnancy Hormonal Skin Issues in Breastfeeding Women

Being a new mother has many challenges, including dermatological changes.

Fazila Rajab, Staff Correspondent

During pregnancy, a woman’s body produces approximately 50% more blood, which makes the skin appear vibrant. After enjoying the period of pregnancy glow, many women may experience postpartum skin issues. Most of these skin conditions occur due to hormonal fluctuations. The levels of hormones, such as progesterone and estrogen responsible for maintaining healthy pregnancy suddenly drop after childbirth, causing changes in the body, especially in the skin. The good news is there are various treatments available to make the skin changes appear less noticeable.

Melasma
Melasma, also known as the mask of pregnancy, is a skin condition characterized by patches and spots similar to freckles. It primarily appears on the sun-exposed parts of the face, affecting cheeks, chin, temples, and nose. The condition is more prevalent in women with medium to darker skin tones and is caused by increased melanin production due to a combination of hormonal and genetic factors as well as photo exposure. Pregnancy, use of oral contraceptives, and sun exposure are the most common triggering factors.

Dermatologists can diagnose the condition by looking closely at the affected area or using a dermatoscope for a closer look. A Wood’s lamp can be used to diagnose the type of melasma by estimating the depth of melanin pigmentation in the skin. Occasionally, a skin biopsy will be required to rule out any serious skin conditions.

Although melasma does not cause pain or itchiness and may go away on its own, it may cause cosmetic distress for patients. Dermatologists recommend treating the condition at its earliest since it can be challenging to treat the disease at its late stage. The condition is best controlled by applying sunscreen and avoiding sun exposure, LED screens, and tanning beds.

Topical therapy with ingredients such as azelaic acid can help improving melasma in breastfeeding women. It is important to note that products containing tretinoin and hydroquinone should be avoided in breastfeeding mothers.

Hormonal Acne
Postpartum acne can appear in many forms, including whiteheads, blackheads, pustules, and painful cysts. Most women develop acne during their pregnancy that disappears following childbirth. However, for some women, it continues even in the postpartum period. Developing acne during pregnancy is normal and is mainly caused by an increase in progesterone levels, which increase sebum production, thus triggering breakouts.

After pregnancy, progesterone levels return to normal and acne disappears. However, it takes longer for some women to normalize their hormonal levels; hence, they continue to have acne even after childbirth.

It is important to note that breastfeeding increases hormone levels, so hormonal acne may take more time to disappear in breastfeeding women.

Topical therapy is recommended as the first line of treatment for hormonal acne in breastfeeding women, and birth control pills can be prescribed in case of severe breakouts to lower hormone levels. Benzoyl peroxide and azelaic acid may help unclog pores and manage acne; they are the safest options for breastfeeding women.
Telogen Effluvium
In women, transient hair loss, also known as telogen effluvium, commonly occurs after giving birth. During pregnancy, the high levels of estrogen prevent usual hair loss. The estrogen level falls as soon as the baby is delivered, and the hair makes up for lost time by falling out in clumps.

For diagnosis, a dermatologist may conduct trichogram (hair pull test); more than 25% of telogen hairs in a trichogram strongly suggest telogen effluvium. However, in rare cases, a scalp biopsy is needed. Although the condition can be quite distressing, the good news is it is self-limiting and can go away within 6 months of childbirth.

There are no medical treatments for preventing or stopping telogen effluvium. Having patients avoid hairstyling products, take vitamin supplements, and eat a balanced and healthy diet may help them fasten new hair growth. However, other possible causes should be ruled out in case of consistent hair loss.

Spider Veins
Varicose veins, also known as spider veins, are a postpartum skin condition characterized by abnormally swollen, painful veins. Varicose veins are associated with increased estrogen levels and often appear in the third trimester of pregnancy. They sometimes persist for several months to a year after childbirth. The increased blood volume in the body during pregnancy creates pressure in the blood vessels, causing blood to get backed up in the veins. The constant pressure may enlarge veins in the lower extremities, making the skin appear flaky and dry.

Although varicose veins are a cosmetic concern, they can be a medical emergency due to their potential to cause pain and increase the risk of blood clots. It is recommended that patients wait for 4 to 6 months after childbirth before going for any treatment as varicose veins mostly disappear within this period. Initial treatment for most patients is conservative and includes limb elevation, exercise, and compression therapy.

Dry Skin
During the postpartum period, hormonal fluctuations and increased water demand by the body due to breastfeeding may change the skin texture and cause dry skin. Low levels of estrogen during the postpartum and lactating period affect the production of hyaluronic acid, collagen, and elastin in the body. The low levels further contribute to transepidermal water loss, which subsequently leads to dehydration, making the skin appear flaky and dry.

The best way to treat postpartum dryness is to invest in a good moisturizer containing 3 components: emollients, occlusives, and humectants. A good moisturizer helps to protect the skin barrier, prevents transepidermal water loss, and maintains hydration levels. Furthermore, serums containing ingredients such as hyaluronic acid and vitamin C help the skin retain moisture and promote collagen formation.

References
Introducing ZORYVE, a next-generation topical PDE4i designed to simplify management of plaque psoriasis\textsuperscript{1,3}

The first and only topical PDE4i for plaque psoriasis—a once-daily cream without steroids for all affected areas of the body*\textsuperscript{1,3}

*Scalp excluded. Treatment of palms and soles excluded from efficacy analysis.

PDE4i = phosphodiesterase 4 inhibitor

Introducing ZORYVE, a next-generation topical PDE4i designed to simplify management of plaque psoriasis.

See the data at zoryvehcp.com

The first and only topical PDE4i for plaque psoriasis—a once-daily cream without steroids for all affected areas of the body.*

*Scalp excluded. Treatment of palms and soles excluded from efficacy analysis.

PDE4i = phosphodiesterase 4 inhibitor

References:

Indication
ZORYVE is indicated for topical treatment of plaque psoriasis, including intertriginous areas, in patients 12 years of age and older.

Important Safety Information
The use of ZORYVE is contraindicated in patients with moderate to severe liver impairment (Child-Pugh B or C).

The most common adverse reactions (≥1%) include diarrhea (3%), headache (2%), insomnia (1%), nausea (1%), application site pain (1%), upper respiratory tract infection (1%), and urinary tract infection (1%).

Please see brief summary of full Prescribing Information for ZORYVE on the following page.
ZORYVE is indicated for topical treatment of plaque psoriasis, including intertriginous areas, in patients 12 years of age and older.

**DOSAGE AND ADMINISTRATION**

Apply ZORYVE to affected areas once daily and rub in completely. Wash hands after application, unless ZORYVE is for treatment of the hands.

**CONTRAINDICATIONS**

The use of ZORYVE is contraindicated in the following condition:
- Moderate to severe liver impairment (Child-Pugh B or C)

**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 two multicenter, randomized, double-blind, vehicle-controlled trials (DERMIS-1 and DERMIS-2), 881 subjects 2 years of age or older with plaque psoriasis were treated with ZORYVE or vehicle once daily for 8 weeks.

The median age was 47 years (range 6 to 88). The majority of the subjects were male (64%) and White (82%). The median body surface area (BSA) affected was 5.5% (range 2% to 25%).

The proportion of subjects who discontinued treatment due to adverse reaction was 1.0% for subjects treated with ZORYVE and 1.3% for subjects treated with vehicle. The most common adverse reactions that led to discontinuation of ZORYVE was application site urticaria (0.3%).

Table 1 presents adverse reactions that occurred in at least 1% of subjects treated with ZORYVE, and for which the rate exceeded the rate for vehicle.

**Table 1. Adverse Reactions Reported in ≥1% of Subjects Treated with ZORYVE for 8 Weeks**

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>ZORYVE (N=576) n (%)</th>
<th>Vehicle (N=305) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>18 (3.1)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Headache</td>
<td>14 (2.4)</td>
<td>3 (1.0)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>8 (1.4)</td>
<td>2 (0.7)</td>
</tr>
<tr>
<td>Nausea</td>
<td>7 (1.2)</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Application site pain</td>
<td>6 (1.0)</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>6 (1.0)</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>6 (1.0)</td>
<td>2 (0.7)</td>
</tr>
</tbody>
</table>

In 594 subjects who continued treatment with ZORYVE for up to 64 weeks in open-label extension trials, the adverse reaction profile was similar to that observed in vehicle-controlled trials.

**USE IN SPECIFIC POPULATIONS**

**Pregnancy**

**Risk Summary**

There are no randomized clinical trials of oral or topical roflumilast in pregnant women. In animal reproduction studies, roflumilast administered orally to pregnant rats and rabbits during the period of organogenesis produced no fetal structural abnormalities at doses up to 9 and 8 times the maximum recommended human dose (MRHD), respectively. Roflumilast induced post-implantation loss in rats at oral doses greater than or equal to 3 times the MRHD. Roflumilast induced stillbirth and decreased pup viability in mice at oral doses 5 and 15 times the MRHD, respectively. Roflumilast has been shown to adversely affect pup post-natal development when dams were treated with an oral dose 15 times the MRHD during pregnancy and lactation periods in mice.

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

**Clinical Considerations**

**Labor and delivery**

ZORYVE should not be used during labor and delivery. There are no human studies that have investigated effects of ZORYVE on preterm labor or labor at term; however, animal studies showed that oral roflumilast disrupted the labor and delivery process in mice.

**Data**

**Animal data**

In an embryo-fetal development study, pregnant rats were dosed orally during the period of organogenesis with up to 1.8 mg/kg/day roflumilast (9 times the MRHD on a mg/m² basis). No evidence of structural abnormalities or effects on survival rates were observed. Roflumilast did not affect embryo-fetal development at a maternal oral dose of 0.2 mg/kg/day (equivalent to the MRHD on a mg/m² basis).

Roflumilast did not affect embryo-fetal development at a maternal oral dose of 0.2 mg/kg/day (equivalent to the MRHD on a mg/m² basis).

In an embryo-fetal development study in rabbits, pregnant does were treated with 0.8 mg/kg/day roflumilast during the period of organogenesis and lactation. Roflumilast did not cause fetal structural abnormalities at maternal oral doses up to 1.8 mg/kg/day (9 times the MRHD on a mg/m² basis).

In a fertility and embryo-fetal development study, male rats were dosed orally with up to 1.8 mg/kg/day roflumilast for 10 weeks and females for 2 weeks prior to pairing and throughout the organogenesis period. Roflumilast induced pre- and post-implantation loss at maternal oral doses greater than or equal to 0.6 mg/kg/day (3 times the MRHD on a mg/m² basis). Roflumilast did not cause fetal structural abnormalities at maternal oral doses up to 1.8 mg/kg/day (9 times the MRHD on a mg/m² basis).

In an embryo-fetal development study in rabbits, pregnant does were dosed orally with 0.8 mg/kg/day roflumilast during the period of organogenesis and lactation. Roflumilast did not cause fetal structural abnormalities at maternal oral doses up to 1.8 mg/kg/day (9 times the MRHD on a mg/m² basis).

In a pre- and post-natal developmental studies in mice, dams were dosed orally with up to 12 mg/kg/day roflumilast during the period of organogenesis and lactation. Roflumilast induced stillbirth and decreased pup viability at maternal oral doses greater than 2 mg/kg/day and 6 mg/kg/day, respectively (5 and 15 times the MRHD on a mg/m² basis, respectively).

Roflumilast induced delivery retardation in pregnant mice at maternal oral doses greater than 2 mg/kg/day (5 times the MRHD on a mg/m² basis). Roflumilast decreased pup rearing frequencies at a maternal oral dose of 6 mg/kg/day during pregnancy and lactation (15 times the MRHD on a mg/m² basis). Roflumilast also decreased survival and forelimb grip reflex and delayed pinna detachment in mouse pups at a maternal oral dose of 12 mg/kg/day (29 times the MRHD on a mg/m² basis).

**Lactation**

**Risk Summary**

There is no information regarding the presence of ZORYVE in human milk, the effects of breastfeeding on the breastfed infant, or the effects on milk production.

Roflumilast and/or its metabolites are excreted into the milk of lactating rats. When a drug is present in human milk, it is likely that the drug will present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for ZORYVE and any potential adverse effects on the breastfed infant from ZORYVE or from the underlying maternal condition.

**Clinical Considerations**

To minimize potential exposure to the breastfed infant via breast milk, use ZORYVE on the smallest area of skin and for the shortest duration possible while breastfeeding. Advise breastfeeding women not to apply ZORYVE directly to the nipple and areola to avoid direct infant exposure.

**Data**

**Animal data**

Roflumilast and/or its metabolite concentrations measured 8 hours after an oral dose of 1 mg/kg given to lactating rats were 0.32 and 0.02 mcg/g in the milk and pup liver, respectively.

**Pediatric Use**

The safety and effectiveness of ZORYVE have been established in pediatric patients ages 12 years and older for the treatment of plaque psoriasis. Use of ZORYVE in this age group is supported by data from two 8-week vehicle-controlled safety and efficacy trials with 7 and 6 adolescent patients aged 12 to 17 years, of whom 8 received ZORYVE. Eighteen adolescent patients were treated with ZORYVE in open-label trials of 2- and 24-weeks duration. The adverse reaction profile was similar to that observed in adults.

The safety and effectiveness of ZORYVE in pediatric patients below the age of 12 years have not been established.

**Geriatric Use**

Of the 881 subjects with psoriasis exposed to ZORYVE or vehicle for up to 8 weeks in 2 controlled clinical trials, 106 were 65 years of age or older. No overall differences in safety or effectiveness were observed between these subjects and younger subjects. Other reported clinical experience has not identified differences in responses between the geriatric and younger patients, but greater sensitivity of some older individuals cannot be ruled out. Based on available data for roflumilast, no adjustment of dosage in geriatric patients is warranted.

**Hepatic Impairment**

Oral roflumilast 250 mcg once daily for 14 days was studied in subjects with hepatic impairment. The AUC and Cmax values of roflumilast and roflumilast N-oxide were increased in subjects with moderate (Child-Pugh B) hepatic impairment. ZORYVE is contraindicated in patients with moderate to severe liver impairment (Child-Pugh B or C).

**PATIENT COUNSELING INFORMATION**

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

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Penn State Health Lead Physician Recruiter
Email: hpeffley@pennstatehealth.psu.edu
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¹One or more studies may be required by the FDA to demonstrate Interchangeability.