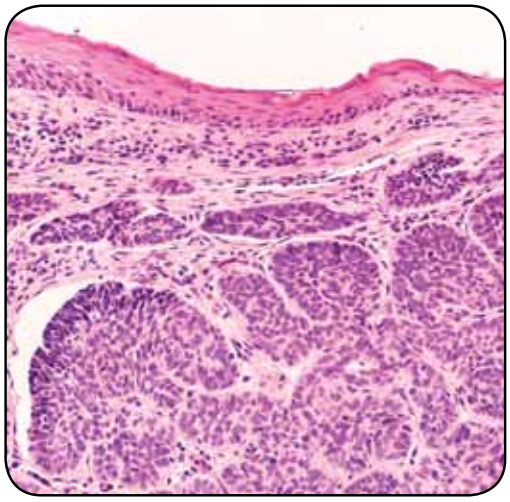
VOLUME 12 • NUMBER 2 • SUMMER 2018 • www.jdpa.org

JDPA

Journal of Dermatology for Physician Assistants



» Earn CME credit with this issue

CME

Official Journal of the Society of Dermatology Physician Assistants

Dermcast.tv: The Official Online Media Resource of the SDPA.
dermcast.tv | dermpa.org | sdpaconferences.org | hireadermpa.org

SOCIETY OF DERMATOLOGY PHYSICIAN ASSISTANTS
SDPA
•EST 1994•

JDPA Journal of Dermatology for Physician Assistants

EDITORIAL MISSION: The JDPA is the official clinical journal of the Society of Dermatology Physician Assistants. The mission of the JDPA is to improve dermatological patient care by publishing the most innovative, timely, practice-proven educational information available for the physician assistant profession.

PUBLISHED CONTENT IN THE JDPA: Statements and opinions expressed in the articles and communications herein are those of the authors and not necessarily those of the Publisher or the Society of Dermatology Physician Assistants (SDPA). The Publisher and the SDPA disclaim any responsibility or liability for such material, including but not limited to any losses or other damage incurred by readers in reliance on such content. Neither Publisher nor SDPA verify any claims or other information appearing in any of the advertisements contained in the publication and cannot take responsibility for any losses or other damage incurred by readers in reliance on thereon. Neither Publisher nor SDPA guarantees, warrants, or endorses any product or service advertised in this publication, nor do they guaranty any claim made by the manufacturer of such product or service.

THIS ISSUE: The JDPA includes articles that have been reviewed and approved for Category I (Preapproved) CME credit by the American Academy of Physician Assistants. Approval is valid for 1 year from the issue date, and participants may submit the self-assessment at any time during that period. Category I CME articles included in JDPA are planned and developed in accordance with AAPA's CME Standards for Journal Articles and for Commercial Support of Journal Articles.

GOING GREEN: Since its inception, the JDPA has utilized eco-friendly printing practices. The JDPA is printed on paper obtained from sustainable forests that meet strict environmental standards. Soy-based inks that have a low environmental impact are used during printing of the journal and the journal is printed using 100% renewable energy. SDPA members may join us in our efforts and opt to receive the JDPA in digital format.

PUBLISHING STAFF

Managing Editor Jennifer M. Hayden, M.Ed
Copy Editor Douglas Morris
Art Director Angela Simiele
Website Design Terry Scanlon

SALES OFFICE

Physician Assistant Communications, LLC
P.O. Box 416, Manlius NY 13104-0416
Phone (315) 663-4147
PAC@pacommunications.org
www.pacommunications.org

Cover Image: iStockphoto

To read the JDPA publication's Ethics and Malpractice Statement, please visit www.jdpa.org/write.html.

KEEP CURRENT WITH THE SDPA:

JDPA.org

JDPA/Journal of Dermatology for Physician Assistants (ISSN 1938-9574) is published quarterly (4 issues per volume, one volume per year) by Physician Assistant Communications, LLC, P.O. Box 416, Manlius NY 13104-0416. Volume 12, Number 2, Summer 2018. One year subscription rates: $40 in the United States and Possessions. Single copies (prepaid only): $10 in the United States (Include $6.50 per order plus $2 per additional copy for US postage and handling). Periodicals postage rate paid at New York, NY 10001 and additional mailing offices.

POSTMASTER: Send address changes to Society of Dermatology Physician Assistants, Inc., 8400 Westpark Drive, 2nd Floor, McLean, VA 22102 1-800-380-3992., email SDPA@dermpa.org, www.dermpa.org.

EDITOR'S **MESSAGE**

There is feeling of comfort and pride experienced in knowing you have handled situations with level headedness, consistency, and professionalism. This holds true not only relating to our personal relationships but our professional relationships as well. The dermatology PA profession has experienced various ups and downs this year revolving around dissemination of flawed information, assumptions, and misinterpreted conclusions.

The SDPA leadership has stayed the course for its members and has exercised professionalism, and maintained level headedness. In light of misinformed statements, the leadership has remained steadfast in maintaining consistency. They have remained committed to using facts and data to support their assertions. When we take it upon ourselves to provide accurate education about our profession the results are positive. The SDPA leaders, and in turn members rely on facts and data verses assumptions when enlightening the public about our role in the healthcare system. This positive education approach provides a better outcome for our patients, our profession, and our Society overall. The SDPA has taken the lead on taking the high road and sticking to this plan of action. As a result, the SDPA continues to be a shining example of what an elite specialty PA organization should strive to be.

As SDPA members, we should continue to welcome and embrace the opportunity to properly educate those we meet about our roles as dermatology PAs. We need to remember that our patients may be exposed to misinformation through the Internet and social media. By patiently providing education through facts, we will be raising awareness, and ultimately this is a win- win for PAs and our patients. When we work together we can make great strides and continue to achieve major accomplishments.

Travis Hayden, MPAS, PA-C
JDPA Editor in Chief
editor@jdpa.org

TABLE OF **CONTENTS**

DEPARTMENTS

HYPERHIDROSIS IS SPOILING MORE THAN JUST HER CLOTHES

For more than 15 million Americans, hyperhidrosis is more than just an inconvenience.[1,2]

Primary axillary hyperhidrosis impacts a patient's emotional and social well-being. Despite the embarrassment and low self-confidence sufferers feel, about 70% remain undiagnosed and untreated.[1,3]

85% EXPERIENCE EMBARRASSMENT[1]

70% REPORT IMPACT TO DAILY ACTIVITIES AND LACK OF TOLERABILITY[1]

63% SAY IT LIMITS THEM AT WORK[2]

It is hard for your patients to talk about sweat.[1]
Visit CheckTheirSweat.com for resources to manage hyperhidrosis.

References: 1. Doolittle J, Walker P, Mills T, Thurston J. Hyperhidrosis: an update on prevalence and severity in the United States. *Arch Dermatol Res.* 2016;308(10):743-749.
2. Hamm H, Naumann MK, Kowalski JW, Kütt S, Kozma C, Teale C. Primary focal hyperhidrosis: disease characteristics and functional impairment. *Dermatology.* 2006;212(4):343-353.
3. Kamudoni P, Mueller B, Halford J, Schouveller A, Stacey B, Salek MS. The impact of hyperhidrosis on patients' daily life and quality of life: a qualitative investigation. *Health Qual Life Outcomes.* 2017;15:121. doi:10.1186/s12955-017-0693-x.

Dermira

CALENDAR OF EVENTS

2018

NOVEMBER

SDPA 16th Annual Fall Dermatology Conference
November 1 - 4, 2018
Loews Portofino Bay Hotel
Orlando, FL

2019

MARCH

77th AAD Annual Academy Meeting
March 1 - 5, 2019
Washington, DC

JUNE

SDPA Summer Dermatology Conference
June 5 - 9, 2019
Marriott Marquis
Washington, DC

JULY

AAD Summer Meeting
July 25 - 28, 2019
New York, NY

Empower. Educate. Advance.

The Future of Dermatology

FROM THE SDPA
NEWS & CURRENT AFFAIRS

Greetings Colleagues,

It is a special honor and privilege to begin my term as President and represent the Society of Dermatology Physician Assistants. I would like to thank our outgoing President, Jane Mast, for her dedicated ongoing service to the Society. She has put in countless hours and effort to advocate for the dermatology profession for many years as an SDPA volunteer leader, culminating with this last year as she served as President. Jane now moves on to the role of Immediate Past President where she will graciously continue her advocacy efforts. It has been a challenging year for dermatology PAs in the political arena with continuing attacks on our profession and I am grateful to have Jane's leadership and counsel as we move forward.

I am optimistic that this will be a better year for the SDPA and dermatology PAs as a whole. Realizing the need to change the conversation about PAs, and dermatology PAs specifically, the SDPA Board of Directors (BOD) voted to hire a public relations (PR) firm. The PR firm will help guide us through the challenges that may present themselves and threaten our profession, as well as to better help us highlight the benefits we provide our patients and the healthcare profession as a whole.

There are also ways we can help as individuals. Now is the time that we all need to take strides to protect our profession by supporting local and state legislation. It is important to support our state PA societies as well as the AAPA Political Action Committee (PAC) as we fight in the trenches to pass Optimal Team Practice (OTP). I strongly encourage you to get involved at the local level and to donate to the AAPA PAC; it truly can make a difference in getting our voices heard in the halls of power.

Coming off of another amazing SDPA conference, I want to thank all those involved who help in ensuring that the SDPA provides the best dermatology education available. It was very rewarding to be sitting at the airport lounge on my way back from Seattle and overhearing a conversation from a nearby table about, "the best conference I have been to." We have some of the greatest leaders who make our conferences run seamlessly. A special thanks to the CME Committee and all of the SDPA leaders, you may not realize that they are all volunteers; PAs with full-time jobs who go the extra mile during their "off-time" to make all of this possible. I also want to thank our industry partners for their continued support, as well as the SDPA's staff and our conference management team for their commitment as well. All this would not be possible without each of you. Thank you.

I am looking forward to an exciting year. If you have an interest in getting involved in leadership, the SDPA BOD and leaders would like to help you find your fit, whether that be helping to develop new benefits and increase our membership, working to develop new CME content, or anything in between. We will be happy to help you find where you and your talent and passion can best help the SDPA. Please reach out to sdpa@dermpa.org for more information.

Sincerely,

Joleen M. Volz

Joleen M. Volz, MPAS, PA-C, DFAAPA
SDPA President

SOCIETY OF DERMATOLOGY PHYSICIAN ASSISTANTS

NOVEMBER 1 - 4, 2018

PRE-CONFERENCE DAY | FUNDAMENTALS OF DERMATOLOGY | OCTOBER 31, 2018

JOIN US NOVEMBER 1 – 4, 2018 FOR THE SDPA 16TH ANNUAL FALL DERMATOLOGY CONFERENCE, THE LEADING CME CONFERENCE FOR DERMATOLOGY PAS! THE EVENT WILL TAKE PLACE IN ORLANDO, FLORIDA, AT THE LOEWS PORTOFINO BAY HOTEL, IN THE HEART OF ALL THIS EXCITING AND FUN CITY HAS TO OFFER.

844-DERM-PAS, Ext. 1 SDPAConferences.org conferences@dermpa.org

Dermatology Market Watch

Ortho Dermatologics Announces Commercial Availability of Retin-A Micro® (Tretinoin) Gel Microsphere 0.06%

Topical Treatment for Acne Vulgaris

Ortho Dermatologics, a division of Valeant Pharmaceuticals North America, LLC, recently announced that Retin-A Micro® (tretinoin) gel microsphere 0.06% is now available commercially to health care professionals.

The U.S. Food and Drug Administration (FDA) approved the Supplemental New Drug Application (sNDA) for Retin-A Micro® (tretinoin) gel microsphere 0.06% for topical application in the treatment of can vulgaris in the Fall of 2017.

Clinical data provided to the U.S. FDA showed 98.7% (252/255) and 94% (210/224) of patients found Retin-A Micro® to be tolerable

- In the 0.04% study no severe irritation was reported at week 2, the typical peak of irritation, and only 1.3% (3/255) of subjects discontinued due to irritation
- In the 0.1% study no more than 3% of subjects reported severe irritation and only 6% (14/224) discontinued as a result

Acne is the most common skin disease in the United States and as many as 50 million people in the United States may have the disease. Recommended treatments include topical therapy, antibiotics, isotretinoin and oralcontraceptives.

Retin-A Micro® (tretinoin) gel microsphere 0.06% features a unique microsponge delivery system technology that helps to control the release of tretinoin and improves photostability, even when used in conjunction with benzoyl peroxide. A pump delivery system also allows for controlled dispensing and consistent dosing.

Tree to Tub *Who said soap doesn't grow on trees?*

Natural beauty brand Tree To Tub has a groundbreaking collection of ultra-gentle, organic body care products featuring the brand's unique ingredient, the soapberry, an exotic fruit that when rubbed, produces a gentle, nourishing lather.

Today, nearly 18 million tons of surfactants are produced annually; most are synthetic, many are known toxins. Tree To Tub is turning the body care industry on its head by replacing these chemicals with the gentle, nourishing lather of the soapberry, an ancient fruit hailing from India and Taiwan. For centuries, the berry has been hidden in Ayurvedic herbal tradition as a nourishing remedial for an assortment of skin and hair conditions. Since then, its benefits have been scientifically validated, and Tree To Tub is the first to make the soapberry available through its full body care collection.

The brand launched last November on Indiegogo, the global platform for entrepreneurs to bring their ideas to life. The brand was personally scouted by Sandy Diao, Director at Indiegogo, who believes the young beauty brand can bring about revolutionary change in the encumbered body care industry. The new collection is all organic, cruelty free, hypoallergenic, eco-friendly, vegan fair trade, including:

- **Soapberry Facial Cleanser:** a one-step wonder, this ultra-gentle cleanser wipes away grime and makeup while repairing dry and irritated skin with organic acai, aloe vera and chamomile
- **Soapberry Body Wash:** a cleansing massage for even the most delicate skin, this body wash locks in moisture for flawlessly healthy skin, powered by organic shea butter, cucumber and aloe vera
- **Soapberry Shampoo:** this color-safe, ultra-gentle shampoo restores hair to a magnificent shine and luster with a nourishing combination of organic olive leaf, gotu kola leaf, and chamomile
- **Argan Oil Conditioner:** an intensively hydrating conditioner that restores vibrant life to damaged hair and soothes dry, itchy scalps with organic pomegranate, shea butter, and coconut oil
- **Shea Butter Body Lotion:** this deeply moisturizing oasis repairs dry, damaged skin with a quick-absorb, non-greasy formula combining organic cocoa butter, aloe vera, and colloidal oatmeal

To connect with the brand on their official website visit www.treetotub.com.

Certification Review

All Those Things Inside the Skin You Might Have Forgotten

By James A. Van Rhee, MS, PA-C

Are you recertifying soon? Start your board review early. Each issue of the JDPA features one board question accompanied by a brief explanation of the answer along with any pertinent test taking tips. Best of luck!

QUESTION: A 35-year-old female has been coming to the clinic because over the past two years she has felt constantly edgy, tense, and vigilant. She complains of dizziness, sweating palms, ringing in the ears, and palpitations. She denies any nausea, vomiting, or diarrhea. These symptoms have been present most of the time and are not limited to discrete periods. Which of the following is the most likely diagnosis?

A. Generalized anxiety disorder
B. Post-traumatic stress disorder
C. Major depressive disorder
D. Agoraphobia with panic attacks
E. Obsessive-compulsive disorder

EXPLANATION: This patient presents with the presentation of generalized anxiety disorder. Generalized anxiety disorder presents with pervasive anxiety and worry about every aspect of life most days for at least 6 months. They have trouble controlling the worry and associated with at least three of the following: difficulty concentrating, easy fatigue, irritability, muscle tension, restlessness, and sleep disturbances. The patient will not have panic attacks, phobias, obsessions, or compulsions. Post-traumatic stress disorder would present with the history of a traumatic event; major depressive disorder presents with at least a two-week history of depressed mood or loss of interest or pleasure. Agoraphobia and panic attacks presents with fear of places in which escape may be difficult and signs of a panic attack. Obsessive-compulsive disorder presents with a history of have recurring, unwanted thoughts, ideas, or sensations (obsessions) that make them feel driven to do something repetitively (compulsions).

The correct answer is A.

James A. Van Rhee, MS, PA-C, *is the Program Director for the Yale School of Medicine Physician Assistant Online Program. Mr. Van Rhee has been involved in physician assistant education for over 20 years. He has served as project director and test item writer for the Physician Assistant Education Association's (PAEA) Physician Assistant Clinical Knowledge Rating Assessment Tool (PACKRAT) and is the author of the Physician Assistant: Certification and Re-certification Review Book, published by Elsevier. For the last fifteen years he has been course director and presenter of the Physician Assistant Board Review, which is now being produced live online by Kaplan Medical.*

Vismodegib as Neoadjuvant Therapy to Surgery for Basal Cell Carcinoma

By Megan Allison, DMSc, MPAS, PA-C

With basal cell carcinoma (BCC) being the most common form of skin cancer in the United States, it is important for healthcare professionals to stay current on the available treatment options for patients with BCC. Vismodegib (Erivedge) is an oral inhibitor of the hedgehog pathway, which is important in the development of BCC. This medication was approved by the Food and Drug Administration in 2012 as the first systemic treatment for patients with locally advanced or metastatic BCC. However, the majority of patients who develop BCC are not locally advanced or metastatic tumors. The initial clinical data with this medication was impressive, which led to the medication being rushed to market with poor clinical guidelines concerning the use and dosing of this medication. However, more information about the medication is needed in different treatment populations. The purpose of this review article is to discuss the use of vismodegib as neoadjuvant therapy prior to surgical removal (excision vs. Mohs surgery) of basal cell carcinoma while providing additional information about the dosage, use, efficacy, and safety of vismodegib.

» CME

This program has been reviewed and is approved for a maximum of .5 hours of AAPA Category I CME credit by the Physician Assistant Review Panel.

Approval is valid for 1 year from the issue date of August 2018. Participants may submit the self-assessment exam at any time during that period.

This program was planned in accordance with AAPA's CME Standards for Enduring Material Programs and for Commercial Support of Enduring Material Programs.

SDPA members may access the posttest at www.jdpa.org

Learning Objectives:

1. *Review the etiology and current treatment options for basal cell carcinoma (BCC).*
2. *Discuss the use of vismodegib (Erivedge) as neoadjuvant therapy prior to surgical removal of basal cell carcinoma.*
3. *Understand the mechanism of action, dosing, efficacy, and safety of vismodegib (Erivedge).*

OVERVIEW OF BASAL CELL CARCINOMA

Nature of the Problem

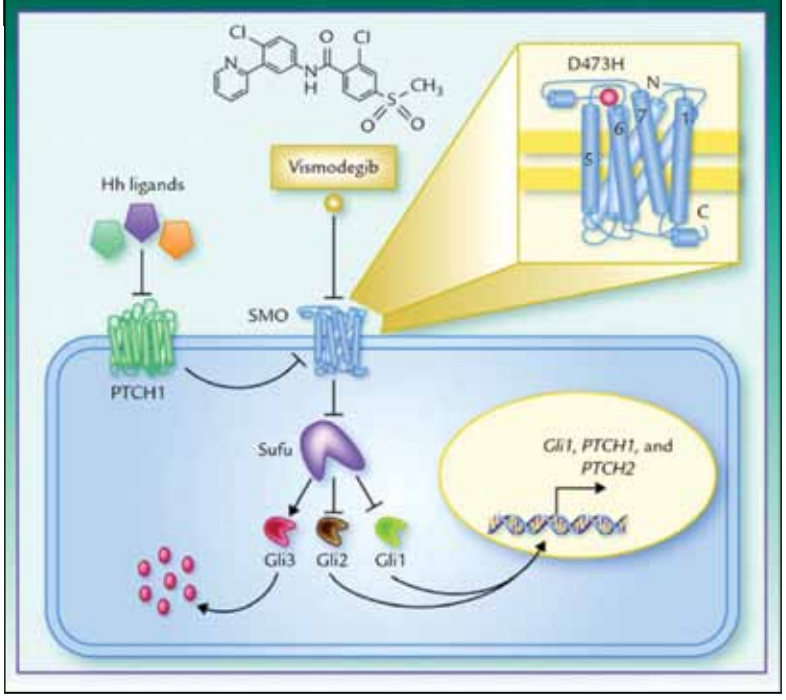
There are an estimated 1.2 to 1.5 million new cases of BCC diagnosed each year in the United States with incidence rising annually.[1] In 2006, more than 2.1 million patients were diagnosed with non-melanoma skin cancer in the United States. Approximately 80% of these non-melanoma skin cancers were BCCs.[2] Fortunately, this type of skin cancer is rarely fatal. Mutations in the tumor suppressor gene PATCHED (PTCH1) cause inappropriate activation in the hedgehog signaling pathway, which is important in the development of BCCs.[1] Patients with a history of basal cell nevus syndrome (also known as Gorlin syndrome) develop multiple BCCs because of a genetic mutation in the sonic hedgehog pathway.[1] The cause of BCC in non-Gorlin syndrome patients is almost always secondary to an up-regulated signaling of the hedgehog pathway.[3] The most important risk factor in the development of BCC is UV radiation.[4] Short-wavelength UVB radiation plays a greater role in BCC formation than long-wavelength UVA radiation. UVB radiation damages DNA and its repair system, which in turn alters the immune system. This results in progressive genetic alterations and formulation of BCC. UV-induced mutations in the TP53 tumor-suppressor gene have been found in approximately 50% of BCC cases. The mutations that activate the hedgehog intracellular signaling pathway genes, including PTCH, sonic hedgehog, and smoothened, play a significant role in the development of BCC *(see Figure 1)*.[4] Vismodegib is an oral hedgehog pathway inhibitor, which was approved by the Food and Drug Administration in 2012 for the treatment of locally advanced and metastatic BCCs.[2] However, the vast majority of patients with BCC do not have metastatic tumors, are not locally advanced, and are not in patients with basal cell nevus syndrome.[5] Most BCCs are approximately 1cm in longest diameter and can successfully be treated by in-office destructive modalities; radiation, topical chemotherapy, excision, or Mohs surgery.[5]

Summary of First-Line Treatments for Basal Cell Carcinoma

First-line therapies for BCC treatment are determined by location, size, and histologic features *(see Figure 2).* There are several different treatment options for BCC including excision (4mm margins), electrodessication and curettage (ED&C), and Mohs micrographic surgery. There are several distinct histologic subtypes of BCC. More aggressive subtypes are associated with a worse prognosis and higher risk of recurrence. Superficial and nodular BCCs are considered less aggressive, with lower recurrence rates.[6] Electrodessication and curettage is a fast and easily performed treatment for BCC. However, the treatment does not allow for histologic confirmation of the removed tumor. This treatment is most appropriate for small, low-risk superficial or nodular BCCs on the trunk or extremities, but is not recommended for BCCs with histologic features that suggest a higher risk for tumor recurrence.[6] Infiltrative and micronodular BCCs account for 20% of all BCCs and have more aggressive and destructive behaviors with high recurrence rates. Morpheaform or sclerosing BCCs also have high recurrence rates. Metatypical or basosquamous BCCs are an overlap tumor of both basal and squamous cell carcinoma, which account for about 2% of all BCCs.[6] Some tumors have multiple histologic subtypes. In these advanced cases, ED&C would not be an appropriate treatment for BCC. Other treatment options include surgical excision or Mohs micrographic surgery. Four millimeter surgical margins are commonly used for excision of these lesions, because surgical excision of truncal, extremity, and small facial BCCs on the head or neck with 4-5mm margins have been associated with 5-year cure rates exceeding ninety-five percent.[7] Mohs micrographic surgery is a specialized surgical technique that optimizes the chance of complete tumor removal.[8] Mohs surgery allows for histologic evaluation of 100% of the peripheral margin at the time of the surgical procedure, while remaining a tissue sparing treatment. Mohs surgery is indicated for the treatment of locally aggressive tumors at high risk for recurrence. The high risk nature of a cutaneous tumor is determined by the characteristics of the tumor, patient risk factors, and anatomic site. Mohs is indicated for the treatment of BCCs that are recurrent, morphoeic, or in locations at high risk for recurrence.[8]

Most BCCs are cured by surgery, but in some cases

Figure 1 - *Hedgehog Signaling Pathway*



Hedgehog (Hh) signaling, vismodegib action, and acquired resistance. SMO = Smoothened; PTCH = patched gene of human chromosome 9q22; Sufu = suppressor of fused; GLI = glioma-associated oncogene.[3]

Figure 2

Summary of First-Line Therapies for Basal Cell Carcinoma
Superficial BCC:
• Topical chemotherapy vs. Excision vs. ED&C
- ED&C – Avoid on face, scalp, and neck unless treatment plan discussed with surgeon
- ED&C & Topical - not advised for areas with high follicular density such as the scalp (even in areas of androgenic alopecia)
• Mohs surgery if meets criteria
Nodular BCC:
• Excision vs. ED&C
- If appropriate location such as trunk or proximal extremities
- ED&C – Avoid on face, scalp, and neck unless treatment plan discussed with surgeon
- Topical – avoid due to increased rates of recurrence
• Mohs surgery if meets criteria
Infiltrative BCC, Morpheaform BCC, & Micronodular BCC:
• Mohs (regardless of size or location – "aggressive histology")
- Excision – if patient declines Mohs surgery or is a poor candidate due to other factors
- ED&C & Topical – Avoid due to increased rates of recurrence

the cancer is unresectable, the procedure is considered too cosmetically disfiguring, or the patient is a poor surgical candidate. These are considered locally advanced BCCs, which may metastasize if not treated.[3] Until vismodegib, there was not a treatment option available for these cases. The median survival for metastatic disease was as little as 6 months to 3.6 years.[3] Vismodegib has been shown to clinically "cure" operable BCCs in patients with basal cell nevus syndrome, but the side effects often prevent long-term use of the medication.

OVERVIEW OF VISMODEGIB (ERIVEDGE)

Vismodegib was discovered in an unlikely location: Idaho's mountain pastures. In 1962, Binns, James, Shupe, and Thacker reported an epidemic of cyclopia in lambs. Sheep farmers noticed that pregnant ewes were giving birth to lambs with a single, central eye. After an 11-year investigation with the United States Department of Agriculture, it was discovered that the pregnant ewes were grazing on a plant of the lily family.[9] American corn lily is a mountain meadow plant that contains chemicals known to disrupt normal brain and facial development.[10] The corn lily contains two chemicals, cyclopamine and jervine, which were found to be potent inhibitors of the hedgehog signaling pathway resulting in teratogenic effects.[11] The hedgehog pathway is important in "regulating growth and development in embryogenesis, but it becomes almost dormant during adulthood, with activity limited to some regulation of tissue homeostasis, continuous renewal and repair of adult tissues, and stem cell maintenance."[3] Inappropriate activation of this pathway is associated with the development of BCC.3 A mutation in the hedgehog pathway inactivates PTCH1, causing an abnormal proliferation of cells leading to BCC. When PTCH1 is mutated, the signaling continues, which results in abnormal cell growth and proliferation creating tumor formation *(see Figure 1)*.[3] Patients with a history of basal cell nevus syndrome develop multiple BCCs because of a genetic mutation in the sonic hedgehog pathway.[1] The cause of BCC in non-Gorlin syndrome patients is almost always secondary to an up-regulated signaling of the hedgehog pathway.[3] Vismodegib is an oral hedgehog pathway inhibitor, which was approved by the Food and Drug Administration in 2012 for the treatment of locally advanced and metastatic BCCs.[2]

REVIEW OF THE LITERATURE

In 2014, Ally et al. performed a study to evaluate the reduction in BCC surgical defect area after three and six months of neoadjuvant vismodegib. The goal of this study was to create a change in the surgical defect area pre- and post- vismodegib treatment of BCC tumors of any histologic subtype.[5] This study was an open-label single-arm clinical trial. This study included fifteen patients over 18 years old with at least one biopsy confirmed BCC of any histologic subtype. The BCC had to be more than 5mm in diameter and eligible for surgical removal. Patients with recurrent BCCs were also eligible for this study. Patients enrolled in this study were to receive three to six months of vismodegib 150mg daily. One patient received nine months of therapy, as the patient desired to further reduce the tumor size before surgery. Response to treatment was assessed per tumor and each tumor was evaluated independently. The Image J software program was used to measure the tumor size. For tumor undergoing standard excision, a 4mm margin was added to the tumor size in order to estimate surgical defect. Of the fifteen patients enrolled in the study, eleven patients completed the trial and had their target BCCs surgically excised. Ten BCCs were treated with Mohs surgery and one by standard excision. One patient was lost to follow-up and two patients withdrew from the study secondary to side effects, including elevated creatinine phosphokinase and fatigue. One patient withdrew because of unrelated adverse events. There were a total of forty-three BCCs being evaluated throughout the course of the study, as six of the eleven patients had multiple BCCs. Vismodegib reduced the size of most of the BCCs (38 of the 43) over the course of about four months of treatment. Of the eleven patients that completed the trial, all experienced mild side effects including dysgeusia, muscle cramps, fatigue, diarrhea, weight loss (less than 5% body weight), depressed mood, and amenorrhea. Interestingly, all of the patients experienced alopecia. However, all side effects resolved after two months of stopping the medication. For the thirteen targeted BCCs selected for surgery, vismodegib reduced the surgical defect area by 27% (95% confidence interval -45.7% to -7.9%, $p = 0.006$). If patients completed less than three months of treatment with vismodegib, they did not have a significant reduction in surgical defect (mean -12%, 95% confidence interval -55.0% to 33.0%, $p = 0.1$). Fifty-percent of the vismodegib pre-treated BCCs cleared after one Mohs stage despite being larger and more aggressive in histology. BCCs pretreated with vismodegib required a mean number of two Mohs stages for clearance in this study. Recurrence occurred in one of thirteen tumors in this study (in a patient with previously recurrent BCC) who was treated with vismodegib for only two months.[5]

The authors of the previous study provided an update of patient outcomes and tumor recurrence two years after the trial.[12] Eleven patients completed the trial and a total of thirteen BCC tumors were surgically treated. All vismodegib related side effects resolved after two months of stopping the medication.[12] Eight patients agreed to a long-term follow-up period of about twenty-two months. Neoadjuvant treatment with vismodegib

was found to decrease the surgical defect size by 34.8% when compared with baseline and allowed for clearance of the tumor with an average of two Mohs stages. One BCC tumor recurred after seventeen months post-Mohs surgery. However, this patient had only completed two months of vismodegib treatment and the tumor was a recurrent, infiltrative BCC.[12] After a longer follow-up period (twenty-two months) post-Mohs, no further recurrences have been evaluated. There are no long term side effects from vismodegib. This study concluded that the update supports the use of vismodegib as neoadjuvant to surgery in the treatment of large, high-risk BCCs.[12]

In 2017, Dreno et al. performed a study titled MIKIE, which sought to evaluate the safety and efficacy of two long-term, intermittent vismodegib dosing regimens in patients with multiple BCCs. MIKIE was a randomized, double-blind, placebo controlled, phase II trial of vismodegib. The study was performed in 52 hospitals and clinics in ten countries. Eligible patients were adults (aged 18 years or older) with multiple BCCs amenable to surgery. The study did include patients with basal cell nevus syndrome. The study excluded patients who had locally advanced BCCs unsuitable for surgery or radiation and patients who had metastatic BCC. Patients had to have six or more BCCs, with three BCCs measuring 5mm in diameter or greater and one or more histologically confirmed BCCs. There were two treatment groups in this study, Group A and Group B. Group A received 150mg of vismodegib daily for twelve weeks, then three rounds of eight weeks of placebo daily, followed by twelve weeks of 150mg of vismodegib daily.[13] This dosing was based off of a study of patients with basal cell nevus syndrome performed by Tang et al. (2012), which showed that more than 90% of patients tolerated twelve weeks of vismodegib therapy and had minimal regrowth of BCCs after eight weeks post-treatment.[14] Group B received 150 mg of vismodegib per day for 24 weeks, then three rounds of eight weeks of placebo daily, followed by eight weeks of 150mg of vismodegib daily. The primary outcome was percentage reduction from baseline in the number of clinically evident BCCs at week seventy-three. A total of 229 patients were randomly assigned to either Group A (n=116) or Group B (n=113). The mean relative reduction of BCCs from baseline to the end of the study was 62.7% (95% confidence interval, 53.0 to 72.3) in Group A and 54% (95% confidence interval 43.6 to 64.4) in Group B. Overall, 53 (23%) of 229 patients discontinued treatment because of side effects related to vismodegib. This occurred in more patients in Group B than in Group A (30 patients vs. 23 patients). The most commonly reported adverse events during the study were muscle spasms, dysgeusia, and alopecia. Overall, 107 patients (94%) in Group A and 109 (97%) of patients in Group B had an adverse effect related to vismodegib. Other common adverse effects included: muscle spasms (4 patients in Group A vs. 12 patients in Group B), increase blood creatinine phosphokinase (1 vs. 4), and hypophosphatemia (0 vs. 3). The two most frequently reported side effects leading to discontinuation of the study included muscle spasms (7 vs. 14) and dysgeusia (4 vs. 9). Four patients died from adverse events (two patients from each group). Emergent adverse events in the study included: increase liver enzyme concentration, increased platelet count, acute pancreatitis, asthenia, arthralgia, pulmonary embolism, pseudolymphoma, dehydration, and lethargy. The causes of death were pulmonary embolism (one in each treatment group), cardiogenic shock (Group B), and pneumonia (Group A – which occurred 70 days after completing treatment). The authors concluded that the primary endpoint did not differ significantly between treatment groups.[13] Overall, both dosing schedules of vismodegib seemed to show good activity in long-term regimens for patients with multiple BCCs. Both dosing regimens had similar activity and tolerability. Though not the intent of the study, the authors concluded that the data suggests that intermittent dosing schedules could be a useful strategy for patients with multiple BCCs who need long-term treatment.[13]

In 2015, Sofen et al. performed a study evaluating the efficacy of vismodegib in patients with smaller, operable, nodular BCCs by measuring the rate and durability of complete histologic clearance (CHC) of the lesions. Complete histologic clearance is defined as absence of BCC in excised target site by histology.[15] The following was a non-randomized, open-label, 3-cohort, phase II study. The study included patients aged 21 years or older with new, operable, nodular BCCs. Patients with other histologic subtypes other than nodular BCC, history of Gorlin syndrome, history of prior treatment with any hedgehog pathway inhibitor, or currently pregnant or lactating were excluded from the trial. This study also evaluated safety with different durations of treatment and resolution of adverse effects related to the medication. The study participants were divided into three cohorts titled Cohort 1 (n=24), Cohort 2 (n=25), and Cohort 3 (n=25). Cohort 1 patients were to receive 150mg daily of vismodegib for twelve weeks. Cohort 2 patients were to receive 150mg daily of vismodegib for twelve weeks, then undergo twenty-four weeks of observation before Mohs surgery. Cohort 3 patients were to receive 150mg daily of vismodegib for eight weeks, followed by a four-week drug holiday, then to receive eight more weeks of treatment. Cohorts 1 and 3 underwent excision followed by Mohs surgery (to ensure

clear margins) within two weeks of discontinuing the medication. Cohort 2 underwent excision in a similar time frame as the previous cohorts, but Mohs surgery was not performed until after completing a twenty-four-week observation period. Of the seventy-four patients enrolled in the study, twenty-five discontinued treatment early. Only four patients (5%) discontinued secondary to adverse events. The most frequently reported side effects included muscle spasms (76%), alopecia (58%), dysgeusia (50%), and ageusia (30%). No deaths were reported in this study. One patient experienced hepatitis, which was considered related to the vismodegib and resolved within two months of discontinuing treatment. The study concluded that the safety profile of vismodegib (150mg daily) was comparable when dosed as a short-term continuous regimen or dosed intermittently. The adverse side effects reported resolved within six to twelve weeks after the medication was discontinued. Throughout the course of the study, there were several differences in adverse events among the cohorts, including onset of symptoms and number of adverse events.[15]

CONCLUSION

Basal cell carcinoma is the most common form of skin cancer in the United States, making it crucial for healthcare professionals to stay current on the available treatment options for patients with BCC. Vismodegib (Erivedge) is an oral inhibitor of the hedgehog pathway, which is important in BCC development. This is an exciting era for dermatology with the availability of multiple treatment options for patients with various types of BCC. It is important to understand the mechanism of action, effectiveness, and safety profile of vismodegib as neoadjuvant therapy prior to surgical removal (excision vs. Mohs surgery) of basal cell carcinoma in order to individualize therapy, properly counsel patients, and monitor for adverse events.

REFERENCES:

1. Lee PK. Actinic Keratosis, Basal, and Squamous Cell Carcinoma. In: Soutor C, Hordinsky MK. eds. Clinical Dermatology. New York, NY: McGraw-Hill; http://accessmedicine.mhmedical.com.ezproxy.lynchburg.edu/content.aspx?bookid=2184&sectionid=165460313. Accessed March 24, 2018.
2. Sekulic A, Migden M, Oro A, et al. Efficacy and safety of vismodegib in advanced basal-cell carcinoma. The New England Journal of Medicine. 2012;366(23):2171-2179. Available from: http://dx.doi.org.ezproxy.lynchburg.edu/10.1056/NEJMoa1113713. Accessed March 24, 2018.
3. Cirrone F, Harris CS. Vismodegib and the hedgehog pathway: a new treatment for basal cell carcinoma. Clin Ther. 2012;34(10):2039-50. Available from: http://dx.doi.org/10.1016/j.clinthera.2012.08.011. Accessed March 24, 2018.
4. Situm M, Buljan M, Bulat V, Lugovic Mihic L, Bolanca Z, Simic D. The role of UV radiation in the development of basal cell carcinoma. Collegium Antropologicum. 2008;32(2):167-170. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19138022. Accessed March 24, 2018.
5. Ally MS, Aasi S, Wysong A, et al. An investigator-initiated open-label clinical trial of vismodegib as a neoadjuvant to surgery for high-risk basal cell carcinoma. J Am Acad Dermatol. 2014;71(5):904-911.e1. Available from: http://dx.doi.org/10.1016/j.jaad.2014.05.020. Accessed March 24, 2018.
6. Blixt E, Nelsen D, Stratman E. Recurrence rates of aggressive histologic types of basal cell carcinoma after treatment with electrodessication and curettage alone. Dermatologic Surgery. 2013;39(5):719-725. Available from: https://doi.org/10.1111/dsu.12122. Accessed March 24, 2018.
7. Silverman M, Kopf A, Bart R, Grin C, Levenstein M. (1992). Recurrence rates of treated basal cell carcinomas. Part 3: Surgical excision. The Journal of Dermatologic Surgery and Oncology. 1992;18(6):471-476. Available from: http:/doi.org/10.1111/j.1524-4725.1992.tb03307.x. Accessed March 24, 2018.
8. Muller F, Dawe R, Moseley H, Fleming C. Randomized comparison of Mohs micrographic surgery and surgical excision for small nodular basal cell carcinoma: Tissue-sparing outcome. Dermatologic Surgery. 2009;35(9):1349-1354. Available from: https://doi.org/10.1111/j.1524-4725.2009.01240.x. Accessed March 24, 2018.
9. Binns W, James L, Shupe J, Thacker E. Cyclopian-type of malformation in lambs. Archives of Environmental Health. 1962;5:106-108. Available from: https://www.tandfonline.com/doi/abs/ 10.1080/00039896.1962.1066325. Accessed March 24, 2018.
10. Savoie K. More than skin deep: Interdisciplinary investment in dermatology research is now paying dividends for patients. Columbia Medicine. 2014. Available from: http://www.columbiamedicinemagazine.org/features/fall-2014/more-skin-deep. Accessed March 24, 2018.
11. Low J, de Sauvage F. Clinical experience with hedgehog pathway inhibitors. Journal of Clinical Oncology. 2010;28(36):5321-5326. Available from: http://dx.doi.org.ezproxy.lynchburg.edu/10.1200/JCO.2010.27.9943. Accessed March 24, 2018.
12. Ally M, Aasi S, Wysong A, et al. Update to an open-label clinical trial of vismodegib as neoadjuvant before surgery for high-risk basal cell carcinoma (BCC). J Am Acad Dermatol. 2016;75(1):213-5. Available from: http://dx.doi.org/10.1016/j.jaad.2016.02.1235. Accessed March 24, 2018.
13. Dreno B, Kunstfeld R, Hauschild A, et al. Two intermittent vismodegib dosing regimens in patients with multiple basal-cell carcinomas (MIKIE): A randomised, regimen-controlled, double-blind, phase 2 trial. Lancet Oncology. 2017;18:404-412. Available from: https://doi.org/10.1016/S1470-2045(17)30072-4. Accessed March 24, 2018.
14. Tang J, Mackay-Wiggan J, Aszterbaum M, et al. Inhibiting the hedgehog pathway in patients with the basal-cell nevus syndrome. The New England Journal of Medicine. 2012;366(23):2180-2188. Available from: http://dx.doi.org.ezproxy.lynchburg.edu/10.1056/NEJMoa1113538. Accessed March 24, 2018.
15. Sofen H, Gross K, Goldberg L, et al. A phase II, multicenter, open-label, 3-cohort trial evaluating the efficacy and safety of vismodegib in operable basal cell carcinoma. The Journal of the American Academy of Dermatology. 2015;73(1):99-105.e1. Available from: http://dx.doi.org/10.1016/j.jaad.2015.03.013. Accessed March 24, 2018.

Megan Allison, DMSc, MPAS, PA-C *received her Master's Degree in Physician Assistant Studies from Jefferson College of Health Sciences in Roanoke, Virginia. She recently received her Doctor of Medical Science Degree from the University of Lynchburg in Lynchburg, Virginia. After graduating from PA school, Megan started working at a dermatology office in Lynchburg, Virginia. Since this time, she has enjoyed treating a variety of skin conditions in patients of all ages as well as performing several different cosmetic procedures. She is a member of the American Academy of Physician Assistants and the Society of Dermatology Physician Assistants. She enjoys public speaking and is the author of four books. She has indicated no relationships to disclose relating to the content of this article.*

From The Patient's Perspective

For Tracy Welge, The Cure Is In The Bag

Meet Tracy Welge, a 41-year-old wife, mother, and melanoma survivor from Naperville, Illinois.

Two melanoma diagnoses, an entrepreneurial spirit, and a desire to do more converged in Tracy in 2012 and led her to start a business called **The Cure is in the Bag.** Since founding her business, she has donated all proceeds to melanoma research, and this month she will begin donating her proceeds to AIM at Melanoma. Thank you, Tracy!

What is your diagnosis?

I was first diagnosed in 2005 at age 28 with Stage I melanoma. I had a black mole on my right arm removed because it was itchy and bothering me. It was a very thin melanoma, and the dermatologist told me I was lucky to have caught it so early. In 2009, I had a lump in my right armpit of the same arm, and it hurt whenever I extended my arm. My daughter was four months old at the time and I thought maybe I had a clogged milk duct from nursing her. My doctor explained that I didn't have milk ducts in my armpit (LOL) and referred me to a surgeon. It turned out that I had locally metastasized melanoma, Stage III with lymph node involvement. After completing surgery, I did a year of interferon at our local hospital. In 2014, my dermatologist found another melanoma, this time Stage 0, on my upper leg, which was removed with surgery and without further treatment.

How did you feel when you were first diagnosed?

With my first diagnosis, I was scared and did a lot of research on the Internet, which made me feel even more worried. My dermatologist seemed optimistic, stating I had a 5% chance of recurrence. That made me feel better, but I later learned statistics don't always define us. With my recurrence to my lymph nodes, I was terrified that I wouldn't see my daughter grow up and felt like I should pull away from my family so it would be less difficult for them if I died from melanoma. I developed severe anxiety and depression.

What did you know about melanoma when you received your first diagnosis?

I was aware that melanoma was a serious skin cancer, but I thought it was something that affected elderly people. I also didn't realize it could keep popping up once it was removed.

How did you tell your family about your diagnosis?

My husband was with me when the doctor told me it had become Stage III, and he was very supportive. It wasn't until several months after I had finished the interferon treatments he told me how scared he had been. I told my parents over the phone and they tried to be optimistic (probably for as much for their sake as mine). My daughter was an infant so she didn't know any different.

Do you have a good support system?

My friends, family, and coworkers were a huge support to us while I was going through interferon. My

AIM AT MELANOMA FOUNDATION

Melanoma is one of the fastest growing cancers in the United States and worldwide. It's one of the most complex forms of cancer and has the most mutations of all solid cancers. Founded in 2004, AIM at Melanoma is the largest international melanoma foundation focused on the discovery of the cure for melanoma. AIM's global research initiatives include The International Melanoma Tissue Bank Consortium, The Melanoma International Collaboration for Adaptive Trials, and the International Melanoma Working Group. AIM at Melanoma also provides education, connection to resources, and opportunitieas for meaningful engagement to help patients, caregivers, and families better face the challenges of melanoma. For more information, visit www.AIMatMelanoma.org and follow our groundbreaking initiatives on Facebook, Twitter, and YouTube.

AIM at Melanoma
3217 Bob O Link Court
Plano, TX 75093
www.aimatmelanoma.org
Email: info@AIMatMelanoma.org

parents drove me to and sat with me at every infusion appointment. My boss was very understanding and supportive when I missed work for appointments, and my coworkers set up a meal plan for us. Some friends stepped up to be by my side and others drifted away, which was both disappointing and surprising to me. I joined an online patient forum, which probably did more harm than good for my anxiety because it seemed like warriors in the forum were losing their battles left and right.

I met a survivor named Kerri through the forum and she had gone through the exact same diagnosis as me a few years earlier. She graciously offered to let me call her and we talked for over an hour. I was struggling with the decision on whether to do interferon with an infant at home. She shared her story with me about how it was a really difficult decision for her because she also had young children at home. Her encouragement gave me the strength to make the decision that I knew was best for me.

My husband and I went to a volunteer training in Chicago to learn about fundraising for melanoma research where we met other melanoma patients and their families. We became very close to one Stage III melanoma survivor and another advocate who had lost his best friend to melanoma, and we all started working together to raise awareness and funds for melanoma. We're still very good friends to this day.

What do you find was your biggest challenge during cancer treatment and into survivorship?

My biggest challenge was mentally dealing with the unknown. It's true that something bad can happen at any moment to any of us, but when you've already personally experienced something that could kill you, it's hard to not think about how it could come back again. Even now, almost ten years after my the melanoma spread to my lymph nodes, the unknown still scares me and I'm reminded that I'm not invincible every time I learn of a melanoma warrior losing their battle. But I cannot live my life in fear, and so I try to make a difference and I try to appreciate this life I'm given.

Where are you now in your melanoma journey?

I'm NED (No Evidence of Disease) and am focused on raising money to find a cure for melanoma.

What is The Cure is in the Bag?

The Cure is in The Bag is my Thirty-One business that I use as a vehicle to educate people about sun safety, create melanoma awareness, and raise money for foundations who support melanoma research. It's something I started in 2012 as a way to give back and to give myself a feeling of fighting against something I really have no control over. I work through Facebook parties and also go to people's homes to sell Thirty-One products so that I can share with everyone my melanoma story and explain to them that there is no cure. It's amazing how many new people I meet who have been affected by melanoma in some way and they connect with my story. Thirty-One pays me a 25% commission of sales and my customers know I donate all of my proceeds to melanoma research. As of today, I've donated over $21,000 to melanoma research just by selling some cute bags and sharing my melanoma journey.

I also have a Facebook page and group named The Cure is in The Bag where I share melanoma stories and talk about sunscreen, getting skin checks, and staying safe in the sun in addition to information about my Thirty-One products. It's nice because people will share in the group what sunscreens have worked for them and ask me questions. Sometimes melanoma warriors will share their personal stories in the group to help raise awareness. Friends will comment on how the group has encouraged them to get their skin checked and be more vigilant when it comes to sun protection. It's a nice little community.

How has sharing your story has impacted your melanoma journey?

Sharing my story has made me feel like I can turn a very bad experience into a story of encouragement. I've met many warriors who are currently fighting or have been NED for several years. I've met families who have lost loved ones to melanoma or their loved one has just been diagnosed. These people have become my close friends and they've joined me in fundraising for melanoma research. It's like having a bigger family.

I also have a full-time job as an HR Manager at a park district. We hire over 200 summer employees (mostly high school and college kids) who will be working outside under the sun for three months. Every year we have a big orientation for all the summer employees and I tell them my story in detail to educate them about how important it is they practice good sun protection and they don't tan. Even if only one kid takes me seriously, it's worth it. My family and I were walking out of a restaurant one day and I heard one of the employees say to her coworker, "Do you see that lady? She's the reason I don't go tanning

> My family and I were walking out of a restaurant one day and I heard one of the employees say to her coworker, "do you see that lady? She's the reason I don't go tanning anymore." Wow, to know I made a difference with her made me feel such joy!
>
> **Tracy Welge, Stage III Survivor**
> **Founder, The Cure is in the Bag**

anymore." Wow, to know I made a difference with her made me feel such joy!

How important is it to you to promote beautiful, naturally healthy skin?

It is so important! People need to know just how dangerous tanning can be to their health, that it can cost them their lives. It's up to me to be a good role model for my young daughter and her friends to show them how beautiful our natural skin is and that we need to protect it. We need to show that we are confident in the skin we were born with.

Have you been involved in other melanoma fundraisers, besides The Cure is in the Bag?

Yes! For the past eight years, I have organized a fundraiser called MelaNoNo benefiting melanoma research. It's a nice grass-roots event where we celebrate life and honor those who have lost their melanoma fight. We have food, drinks, raffle prizes, and entertainment.

What do you do in your spare time?

I work full time in human resources, spend time with my husband, daughter, and two dogs, and enjoy yoga.

What advice would you share with someone facing melanoma?

I would tell that person You are not a statistic. *Your* melanoma journey is not written in stone, and there are new breakthroughs happening in melanoma research. I would also tell that person You need to be an advocate for yourself and speak up to your doctor.

You can follow Tracy on Facebook and join her Facebook group, "The Cure Is In The Bag VIP."

CLINICAL snapshots

Treatment of Partial Tissue Necrosis of the Ear Due to Presumptive Brown Recluse Spider Bite

"In the cup, a spider steep'd"

By John Ramos, PA-C and John H. Hall, Jr., MD, FAAD

INTRODUCTION

A 58 year-old Caucasian female presented with a spider bite complaint that had occurred twenty-one days ago. The patient states three weeks ago she awoke in the morning with external right ear pain and found a dead, "brown," penny sized spider in her bed. Later, as her ear became more red, painful, and swollen, she sought treatment at a local emergency department. Although she saved the spider, the emergency department provider was unable to identify the spider as a brown recluse, and patient later discarded the spider. At the emergency department she was diagnosed with a spider bite, and discharged with conservative treatment (rest, ice, elevation, and compression) in addition to 100mg doxycycline once a day for 12 days, naproxen 200mg (per patient NSAID preference) as needed for pain, and a 9 day prednisone taper.

She presented on day 21 to her dermatologist for follow up of the lesion *(see Figures 1 & 2)*. She described the ear as slightly painful (pain scale 2/10), with an intermittent burning and tingling sensation, and noticed worsening bruising and discoloration of the skin since day 9. Patient was afebrile and in no acute distress. Physical examination of the anterior and posterior ear showed a 1.5cm x 3cm erythematous erosion with eschar on the superior and mid helix extending to the posterior auricle, that was slightly tender to palpation. She was prescribed cephalexin 500mg x 21 days, a second 9 day prednisone taper, diphenhydramine 25mg once a day, and topical lidocaine jelly as needed for pain. On day 28, she followed up with her dermatologist and had no complaints, other than concern for the lesion's appearance *(see Figure 3)*. The eschar decreased in size, and although no longer painful, was not completely healed. She completed the second prednisone taper and continued taking cephalexin. She was advised to follow up in one month if the necrotic tissue was unresolved. Potential surgical treatment was discussed with the patient, and she wished to avoid surgical interventions if possible.

Figure 1

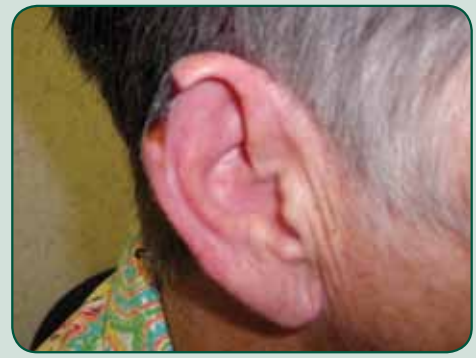


Figure 2

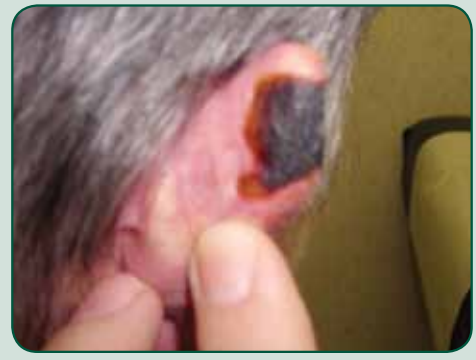
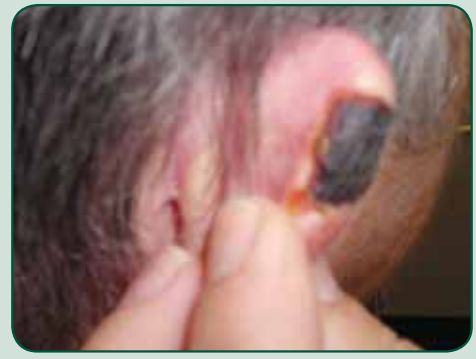


Figure 3



...Continued on page 21

Aktipak™
(erythromycin and benzoyl peroxide) Gel, 3%/5%

PATIENT-BLENDED
ACNE THERAPY

MIXES FRESH

Pocket-sized, dual-chamber pouch[1] with an 18-month shelf life from the date of manufacture.[2]

PRESCRIBE AKTIPAK™ FOR YOUR ACTIVE ACNE PATIENTS

INDICATIONS AND USAGE

AKTIPAK™ (erythromycin and benzoyl peroxide) Gel, 3%/5% is indicated for the topical treatment of acne vulgaris.

IMPORTANT SAFETY INFORMATION

Contraindications: AKTIPAK™ is contraindicated in those individuals who have shown hypersensitivity to any of its components.

Precautions: For topical use only; not for ophthalmic use. Concomitant topical acne therapy should be used with caution because a possible cumulative irritancy effect may occur, especially with the use of peeling, desquamating or abrasive agents. If severe irritation develops, discontinue use and institute appropriate therapy. The use of antibiotic agents may be associated with the overgrowth of nonsusceptible organisms. If this occurs, discontinue use and take appropriate measures. Avoid contact with eyes and all mucous membranes.

Pregnancy: It is not known whether **AKTIPAK™** can cause fetal harm when administered to a pregnant woman. **AKTIPAK™** should be given to a pregnant woman only if clearly needed. It is not known whether the ingredients of **AKTIPAK™** are excreted in human milk. Therefore, caution should be exercised when erythromycin is administered to a nursing woman.

Pediatric Use: The safety and effectiveness of **AKTIPAK™** in pediatric patients below 12 years of age have not been established.

Adverse Reactions: The most frequently reported adverse events reported in clinical trials include: dry skin, application site reaction, blepharitis, pruritus, and photosensitivity.

Please see the Brief Summary of Full Prescribing Information on the next page. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit http://www.fda.gov/Safety/MedWatch/default.htm or call 1-800-FDA-1088.

To learn more about how AKTIPAK™ is patient-blended, visit aktipak.com.

60
SINGLE-DOSE
POUCHES
PER CARTON

Cutanea™

References: 1. Aktipak™ (erythromycin and benzoyl peroxide) Gel, 3%/5% [package insert]. Wayne, PA: Cutanea Life Sciences, Inc.; 2017. **2.** Data on file, Cutanea Life Sciences, Inc. 2017.

Aktipak™
(erythromycin and benzoyl peroxide) Gel, 3%/5%

BRIEF SUMMARY OF PRESCRIBING INFORMATION

This Brief Summary does not include all the information needed to use AKTIPAK™ safely and effectively. See full prescribing information for AKTIPAK™.

AKTIPAK™ (erythromycin and benzoyl peroxide) Gel, 3%/5% - For Dermatological Use Only – Not for Ophthalmic Use

INDICATIONS AND USAGE
Aktipak™ is indicated for the topical treatment of acne vulgaris.

CONTRAINDICATIONS
Aktipak™ is contraindicated in those individuals who have shown hypersensitivity to any of its components.

PRECAUTIONS
General: For topical use only; not for ophthalmic use. Concomitant topical acne therapy should be used with caution because a possible cumulative irritancy effect may occur, especially with the use of peeling, desquamating or abrasive agents. If severe irritation develops, discontinue use and institute appropriate therapy. The use of antibiotic agents may be associated with the overgrowth of nonsusceptible organisms. If this occurs, discontinue use and take appropriate measures. Avoid contact with eyes and all mucous membranes.

Information for Patients: Patients using Aktipak™ should receive the following information and instructions:

1. Patients should be informed that they will need to mix this medication prior to use. The medication will be dispensed in one foil pouch which contains medication in two separated compartments.
2. The contents must be mixed thoroughly by the patient (in the palm of the hand), prior to application.
3. Patients should apply the product immediately after mixing, then the hands should be washed.
4. Do not mix or apply near an open flame.
5. Aktipak™ may bleach hair or colored fabric.
6. Excessive or prolonged exposure to sunlight should be limited. To minimize exposure to sunlight, a hat or other clothing should be worn.
7. This medication is to be used as directed by a physician. It is for external use only. Avoid contact with the eyes, mouth, and all mucous membranes as this product may be irritating.
8. Patients should report to their physician any signs of local adverse reactions.
9. This medication should not be used for any disorder other than that for which it was prescribed.
10. Patients should not use any other topical acne preparation unless otherwise directed by physician.
11. Patients should be instructed to review the instructions for use on the product carton.
12. This medication should be stored at room temperature away from heat and any open flame.

Carcinogenesis, Mutagenesis, Impairment of Fertility:
The combination of benzoyl peroxide and erythromycin in Aktipak™ has not been evaluated for its carcinogenic or mutagenic potential or for its effects on fertility.

Benzoyl peroxide has been shown to be a tumor promoter and progression agent in a number of animal studies. The clinical significance of this is unknown.

Benzoyl peroxide in acetone at doses of 5 and 10 mg administered twice per week induced skin tumors in transgenic Tg.AC mice in a study using 20 weeks of topical treatment.

Benzoyl peroxide has been found to cause DNA strand breaks in a variety of mammalian cell types, to be mutagenic in *Salmonella typhimurium* tests by some but not all investigators, and to cause sister chromatid exchanges in Chinese hamster ovary cells.

No animal studies have been performed to evaluate the carcinogenic potential or effects on fertility of topical erythromycin. However, long-term (2-year) oral studies in rats with erythromycin base and erythromycin ethylsuccinate and in rats and mice with erythromycin stearate did not provide evidence of tumorigenicity.

The genotoxicity of erythromycin stearate has been evaluated in the *Salmonella typhimurium* reverse mutation assay, the mouse L5178Y lymphoma cell assay, and for sister chromatid exchanges and chromosomal aberrations in CHO cells. These studies indicated that erythromycin stearate was not genotoxic. There was no apparent effect on male or female fertility in rats fed erythromycin base at levels up to 0.25% of diet.

Pregnancy: Teratogenic Effects: Pregnancy CATEGORY C: Animal reproduction studies have not been conducted with Aktipak™ or benzoyl peroxide.

There was no evidence of teratogenicity or any other adverse effect on reproduction in female rats fed erythromycin base (up to 0.25% diet) prior to and during mating, during gestation and through weaning of two successive litters.

There are no well-controlled trials in pregnant women with Aktipak™. It is also not known whether Aktipak™ can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Aktipak™ should be given to a pregnant woman only if clearly needed.

Nursing Women: It is not known whether the ingredients of Aktipak™ are excreted in human milk after topical application. However, erythromycin is excreted in human milk following oral and parenteral erythromycin administration. Therefore, caution should be exercised when erythromycin is administered to a nursing woman.

Pediatric Use: Safety and effectiveness of this product in pediatric patients below 12 years of age have not been established.

ADVERSE REACTIONS
During clinical trials, 550 acne patients were studied. Of these patients, 236 were treated with Aktipak™. The most frequently reported adverse event considered at least possibly related was dry skin (7.6%) as compared to Vehicle (3.9%). Application site reactions (stinging, burning sensation, tingling, erythema) were reported in 2.5% of patients versus 1.3% of Vehicle patients. Blepharitis, pruritus and photosensitivity reactions were reported in <2% of patients who used the dual pouch product.

Treatment Groups Summaries
Number of Patients (%)

COSTART Term	Aktipak™ N = 236	Aktipak™ Vehicle N = 153	Benzamycin Topical Gel N = 121	Benzamycin Topical Gel Vehicle N = 40
DRY SKIN	18 (7.6%)	6 (3.9%)	6 (5.0%)	0
APPLICATION SITE REACTION (stinging, erythema, and burning)	6 (2.5%)	2 (1.3%)	1 (0.8%)	0
BLEPHARITIS	4 (1.7%)	1 (0.7%)	0	1 (2.5%)
PRURITUS	4 (1.7%)	2 (1.3%)	3 (2.5%)	0
PHOTO-SENSITIVITY REACTION (Sunburn, stinging with sun exposure)	3 (1.3%)	0	0	0
PEELING	1 (0.5%)	1 (0.7%)	0	0

Cutanea™

Manufactured for:
Cutanea Life Sciences, Inc.
Wayne, PA 19087
Revised: December 2016

AKT013

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

LITERATURE REVIEW

The brown recluse spider (loxosceles reclusa) is more common in South Central regions of the United States and bites occur more frequently between the months of May and August.[1,2] Among spider bites in the United States, those of the brown recluse and black widow spiders are the most common causes of tissue damage and necrosis.[3] A diagnosis of a brown recluse spider bite is made with identification of the spider that was observed to cause the bite; the unique physical characteristics include six eyes and a fiddle shaped mark on the back.[3] In many cases a presumptive diagnosis is made based on a patient's history and physical exam, ruling out other causes of tissue damage or necrosis including microbial infections or diabetes mellitus.[1,2]

TREATMENT

In addition to preserving skin integrity and circulation, major goals in treatment of the lesion include preventing secondary infection, tissue necrosis caused by lexosceles venom, and the onset of systemic loxoscelism, which can lead to kidney damage.[1-3] For mild lesions presenting within 72 hours of the bite, the recommended treatment is conservative: rest, ice, compression, and elevation, and symptomatic treatment with oral antihistamines and nonsteroidal anti inflammatory drugs. In addition, tetanus immunization should be up to date and antibiotic treatment for cellulitis should be considered.[1-3] Surgical intervention within 6 to 8 weeks of the initial injury is not warranted, as a new eschar is likely to form post operatively, and most lesions heal with conservative treatment.[3] A recent and noteworthy case of surgical intervention with skin grafting for a necrotic ear lesion caused by a Mediterranean recluse spider proved cosmetically successful.[4] Additional therapeutic measures, many of which are anecdotal or experimental, include Dapsone for rapidly progressing wounds, oral steroid prophylaxis, hyperbaric oxygen, topical nitroglycerin, and oral tetracyclines.[3,5]

DISCUSSION

A challenging aspect of the brown recluse spider bite diagnosis is identifying the spider, often leading to a false diagnosis of a recluse spider bite.[1-3] Although, in this case, the spider was not identified as a brown recluse, the description of the spider and the progression of the lesion are incredibly similar to a brown recluse spider bite. Adequate treatment and preventing tissue necrosis associated with loxosceles reclusa is highly dependent on the time of presentation. This patient presented early, and although treated sufficiently with conservative measures, still developed tissue necrosis of the ear. When she presented on day 21, treatment for cellulitis with a cephalosporin was warranted. Patient education is important to ensure understanding of wound healing time, pharmacologic management, and the risks of early surgical intervention.

REFERENCES:

1. Rhoads J. Epidemiology of the brown recluse spider bite. J Am Acad Nurse Pract. 2007; 19: 79–85.
2. Norris K, Misra S. Brown recluse spider bite on the breast. JAAPA. 2014; 27: 32-34.
3. Andersen RJ, Campoli J, Johar SK, et al. Suspected brown recluse envenomation: a case report and review of different treatment modalities. J Emerg Med. 2011; 41:e31–e37.
4. Holtslag I . Partial ear necrosis due to recluse spider bite. Journal of plastic, reconstructive & aesthetic surgery. 2014; 67: 419-421.
5. Paixão-Cavalcante D, van den Berg CW, Gonçalves-de-Andrade RM, et al. Tetracycline protects against dermonecrosis induced by Loxosceles spider venom. J Invest Dermatol 2007; 127:1410.

John Ramos, PA-C *graduated from the Physician Assistant Program at Wake Forest School of Medicine in 2016. Mr. Ramos completed his Bachelor of Science in Dietetics at California State University, Sacramento in 2014. Mr. Ramos is an assistant professor at Dominican University of California and practices emergency medicine at Marin General Hospital in Greenbrae, CA. He has indicated no relationships to disclose relating to the content of this article.*

John H. Hall, Jr. MD, FAAD *achieved his Doctorate of Medicine in 1988 from Wake Forest School of Medicine, and completed his dermatology residency at Medical College of Georgia in 1992. He currently practices clinical dermatology in Greensboro, NC. He has indicated no relationships to disclose relating to the content of this article.*

Journal Club: *Practice Changing Articles for Dermatology PAs*

Hydrochlorothiazide use and risk of nonmelanoma skin cancer: A nationwide case-control study from Denmark.

J Am Acad Dermatol. 2018 Apr; 78(4):673-681

Pedersen SA[1], Gaist D[2], Schmidt SAJ[3], Hölmich LR[4], Friis S[5], Pottegård A[6]

1. Department of Neurology, Odense University Hospital, Odense, Denmark; Department of Clinical Research, Faculty of Health Sciences, Odense, Denmark; Clinical Pharmacology and Pharmacy, Department of Public Health, University of Southern Denmark, Odense, Denmark.
2. Department of Neurology, Odense University Hospital, Odense, Denmark; Department of Clinical Research, Faculty of Health Sciences, Odense, Denmark.
3. Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus, Denmark.
4. Department of Plastic Surgery, Herlev-Gentofte Hospital, Herlev, Denmark.
5. Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus, Denmark; Danish Cancer Society Research Center, Danish Cancer Society, Copenhagen, Denmark; Department of Public Health, University of Copenhagen, Copenhagen, Denmark.
6. Clinical Pharmacology and Pharmacy, Department of Public Health, University of Southern Denmark, Odense, Denmark.

Background

Hydrochlorothiazide, one of the most frequently used diuretic and antihypertensive drugs in the United States and Western Europe, is photosensitizing and has previously been linked to lip cancer.

Objective

To examine the association between hydrochlorothiazide use and the risk of basal cell carcinoma (BCC) and squamous cell carcinoma (SCC).

Methods

From the Danish Cancer Registry, we identified patients (cases) with nonmelanoma skin cancer (NMSC) during 2004-2012. Controls were matched 1:20 by age and sex. Cumulative hydrochlorothiazide use (in 1995-2012) was assessed from the Danish Prescription Registry. Using conditional logistic regression, we calculated odds ratios (ORs) for BCC and SCC associated with hydrochlorothiazide use.

Results

High use of hydrochlorothiazide (≥50,000 mg) was associated with ORs of 1.29 (95% confidence interval [CI], 1.23-1.35) for BCC and 3.98 (95% CI, 3.68-4.31) for SCC. We found clear dose-response relationships between hydrochlorothiazide use and both BCC and SCC; the highest cumulative dose category (≥200,000 mg of HCTZ) had ORs of 1.54 (95% CI, 1.38-1.71) and 7.38 (95% CI, 6.32-8.60) for BCC and SCC, respectively. Use of other diuretics and antihypertensives was not associated with NMSC.

Limitations

No data on sun exposure were available.

Conclusion

Hydrochlorothiazide use is associated with a substantially increased risk of NMSC, especially SCC.

From MEDLINE®/PubMed®, a database of the U.S. National Library of Medicine. PreMedline Identifier: 29217346

Journal clubs are a great way to review and critically evaluate the most current literature impacting the practice of dermatology. For physician assistants who are new to the practice of dermatology, journal clubs can assist them to become more familiar with advanced medical literature and improve their understanding of current issues within the field. The articles selected for the JDPA Journal Club are meant to be shared and discussed with your colleagues, peers, and supervising physicians. If you have any articles to recommend for the JDPA Journal Club, please email them to editor@jdpa.org.

TOP 9 REASONS

Dermatology PAs

[or those PAs interested in dermatology]

Should Become a Member of the SDPA

The largest of 26 specialty organizations under the American Academy of Physician Assistants (AAPA), the Society of Dermatology Physician Assistants (SDPA) is a non-profit professional association focused on empowering, educating and advancing PAs currently working in the field of dermatology and those who would like to work in the field.

SOCIETY OF DERMATOLOGY PHYSICIAN ASSISTANTS
SDPA
• EST 1994 •

Empower. Educate. Advance.

The Future of Dermatology

Elevate your career by joining the only association advocating for PAs in dermatology.

BECOME A MEMBER

Dermcast.tv Blog -

Can Vitiligo Be Treated with Surgery?

By Martha L. Sikes, MS, RPh, PA-C

Epidermal cell suspension (ECS) is an effective surgical method for repigmenting stable vitiligo. Complete and quick repigmentation on face and trunk regions and in focal and segmental vitiligo is usually achieved through ECS, but vitiligo that occurs at elbows, knees, iliac crests, and malleoli and/or vitiligo types, such as generalized and acrofacial vitiligo tend to be more resistant and difficult to treat.

A recent study looked at the addition of follicular cell suspension (FCS) to determine whether that improved outcomes. The study was a randomized trial that compared the efficacy of ECS + FCS and used ECS as an active control method. The authors matched vitiligo patches based on their anatomic locations, and participants were then randomized to either ECS + FCS (group A) or ECS alone (group B). They were able to compare a total of eighty-four target lesions (42 pairs); seventy-four percent of the lesions were difficult-to-treat vitiligo.

The results showed that the repigmentation outcome of ECS + FCS was superior to ECS even at acral or bony sites and in generalized or acrofacial vitiligo. There was faster repigmentation and a superior color match, which resulted in better patient satisfaction.

The authors conclude that this novel approach (that can be done in the clinical setting) achieves optimal repigmentation with fast results and a good color match in difficult-to-treat vitiligo patients.

Dermcast.tv Blog Post: May 2, 2018
Source: JAMA Network
Adapted from the original article.

Dermcast.tv is the official online media resource of the SDPA and is your free source for the latest SDPA-related audio podcasts, current dermatology news and research, and videos featuring thought-leaders, procedures, conference highlights, and much more. In addition, Dermcast is the #1 dermatology-related podcast on iTunes! To read more Dermcast.tv Blogs and/or to follow the next live blog from an upcoming SDPA dermatology conference, please visit the Dermcast.tv website at www.dermcast.tv and subscribe today.

Ortho | Dermatologics

FOR MODERATE TO SEVERE INFLAMMATORY ACNE

SOLODYN®
(MINOCYCLINE HCl, USP) EXTENDED RELEASE TABLETS

MATCH THE POWER TO THE PATIENT[1]

THREE CUSTOMIZED, WEIGHT-BASED STRENGTHS

LEARN MORE AT SOLODYN.COM

Indication and Usage

SOLODYN® is indicated to treat only inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients 12 years of age and older.

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

Important Safety Information for SOLODYN Tablets

- This drug is contraindicated in persons who have shown hypersensitivity to any of the tetracyclines
- MINOCYCLINE, LIKE OTHER TETRACYCLINE-CLASS DRUGS, CAN CAUSE FETAL HARM WHEN ADMINISTERED TO A PREGNANT WOMAN. Should not be used during pregnancy or by individuals of either gender who are attempting to conceive a child; concurrent use of tetracyclines with oral contraceptives may render oral contraceptives less effective.
- TETRACYCLINE DRUGS SHOULD NOT BE USED DURING TOOTH DEVELOPMENT (LAST HALF OF PREGNANCY AND UP TO 8 YEARS OF AGE) AS THEY MAY CAUSE PERMANENT DISCOLORATION OF TEETH.
- Pseudomembranous colitis has been reported with nearly all antibacterial agents and may range from mild to life-threatening; therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents
- Dose adjustments may be necessary in patients with renal impairment to avoid liver toxicity
- Central nervous system side effects, including light-headedness, dizziness, and vertigo, have been reported with minocycline therapy
- Pseudotumor cerebri (benign intracranial hypertension) and autoimmune syndromes have been associated with the use of tetracyclines
- Cases of anaphylaxis, serious skin reactions, erythema multiforme, and drug rash with eosinophilia and systemic symptoms have been reported postmarketing with minocycline use. Discontinue SOLODYN immediately if symptoms occur. In rare cases, photosensitivity has been reported.
- The most commonly observed adverse reactions are headache, fatigue, dizziness, and pruritus

To report SUSPECTED ADVERSE REACTIONS contact Ortho Dermatologics at 1-800-321-4576 or FDA at 1-800-FDA-1088 or visit www.fda.gov/medwatch.

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

Reference: 1. SOLODYN Tablets Package Insert. Valeant Pharmaceuticals North America LLC.

SOLODYN® (MINOCYCLINE HCl, USP) EXTENDED RELEASE TABLETS

SUMMARY OF PRESCRIBING INFORMATION

This Brief Summary does not include all the information needed to use SOLODYN safely and effectively.

See full Prescribing Information.

SOLODYN®

(minocycline HCl, USP) Extended Release Tablets

Rx Only

KEEP OUT OF REACH OF CHILDREN

INDICATIONS AND USAGE

Indication

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

Limitations of Use

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

(see Warnings and Precautions).

CONTRAINDICATIONS

This drug is contraindicated in persons who have shown hypersensitivity to any of the tetracyclines.

Warnings and Precautions

Teratogenic Effects

A. MINOCYCLINE, LIKE OTHER TETRACYCLINE-CLASS DRUGS, CAN CAUSE FETAL HARM WHEN ADMINISTERED TO A PREGNANT WOMAN. IF ANY TETRACYCLINE IS USED DURING PREGNANCY OR IF THE PATIENT BECOMES PREGNANT WHILE TAKING THESE DRUGS, THE PATIENT SHOULD BE APPRISED OF THE POTENTIAL HAZARD TO THE FETUS.

SOLODYN should not be used during pregnancy or by individuals of either gender who are attempting to conceive a child *(see Use in Specific Populations & Nonclinical Toxicology).*

B. THE USE OF DRUGS OF THE TETRACYCLINE CLASS DURING TOOTH DEVELOPMENT (LAST HALF OF PREGNANCY, INFANCY, AND CHILDHOOD UP TO THE AGE OF 8 YEARS) MAY CAUSE PERMANENT DISCOLORATION OF THE TEETH (YELLOW-GRAY-BROWN).

This adverse reaction is more common during long-term use of the drug but has been observed following repeated short-term courses. Enamel hypoplasia has also been reported. TETRACYCLINE DRUGS, THEREFORE, SHOULD NOT BE USED DURING TOOTH DEVELOPMENT.

C. All tetracyclines form a stable calcium complex in any bone-forming tissue. A decrease in fibula growth rate has been observed in premature human infants given oral tetracycline in doses of 25 mg/kg every 6 hours. This reaction was shown to be reversible when the drug was discontinued.

Results of animal studies indicate that tetracyclines cross the placenta, are found in fetal tissues, and can cause retardation of skeletal development on the developing fetus. Evidence of embryotoxicity has been noted in animals treated early in pregnancy *(see Use in Specific Populations).*

Pseudomembranous Colitis

Clostridium difficile associated diarrhea (CDAD) has been reported with nearly all antibacterial agents, including minocycline, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile.*

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated.

Hepatotoxicity

Post-marketing cases of serious liver injury, including irreversible drug-induced hepatitis and fulminant hepatic failure (sometimes fatal) have been reported with minocycline use in the treatment of acne.

Metabolic Effects

The anti-anabolic action of the tetracyclines may cause an increase in BUN. While this is not a problem in those with normal renal function, in patients with significantly impaired function, higher serum levels of tetracycline-class drugs may lead to azotemia, hyperphosphatemia, and acidosis. If renal impairment exists, even usual oral or parenteral doses may lead to excessive systemic accumulations of the drug and possible liver toxicity. Under such conditions, lower than usual total doses are indicated, and if therapy is prolonged, serum level determinations of the drug may be advisable.

Central Nervous System Effects

Central nervous system side effects including light-headedness, dizziness or vertigo have been reported with minocycline therapy. Patients who experience these symptoms should be cautioned about driving vehicles or using hazardous machinery while on minocycline therapy. These symptoms may disappear during therapy and usually rapidly disappear when the drug is discontinued.

Benign Intracranial Hypertension

Pseudotumor cerebri (benign intracranial hypertension) in adults and adolescents has been associated with the use of tetracyclines. Minocycline has been reported to cause or precipitate pseudotumor cerebri, the hallmark of which is papilledema. Clinical manifestations include headache and blurred vision. Bulging fontanels have been associated with the use of tetracyclines in infants. Although signs and symptoms of pseudotumor cerebri resolve after discontinuation of treatment, the possibility for permanent sequelae such as visual loss that may be permanent or severe exists. Patients should be questioned for visual disturbances prior to initiation of treatment with tetracyclines. If visual disturbance occurs during treatment, patients should be checked for papilledema. Concomitant use of isotretinoin and minocycline should be avoided because isotretinoin, a systemic retinoid, is also known to cause pseudotumor cerebri.

Autoimmune Syndromes

Tetracyclines have been associated with the development of autoimmune syndromes. The long-term use of minocycline in the treatment of acne has been associated with drug-induced lupus-like syndrome, autoimmune hepatitis and vasculitis. Sporadic cases of serum sickness have presented shortly after minocycline use. Symptoms may be manifested by fever, rash, arthralgia, and malaise. In symptomatic patients, liver function tests, ANA, CBC, and other appropriate tests should be performed to evaluate the patients. Use of all tetracycline-class drugs should be discontinued immediately.

Photosensitivity

Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking tetracyclines. This has been reported rarely with minocycline. Patients should minimize or avoid exposure to natural or artificial sunlight (tanning beds or UVA/B treatment) while using minocycline. If patients need to be outdoors while using minocycline, they should wear loose-fitting clothes that protect skin from sun exposure and discuss other sun protection measures with their physician.

Serious Skin/Hypersensitivity Reaction

Cases of anaphylaxis, serious skin reactions (e.g. Stevens Johnson syndrome), erythema multiforme, and drug rash with eosinophilia and systemic symptoms (DRESS) syndrome have been reported postmarketing with minocycline use in patients with acne. DRESS syndrome consists of cutaneous reaction (such as rash or exfoliative dermatitis), eosinophilia, and one or more of the following visceral complications such as: hepatitis, pneumonitis, nephritis, myocarditis, and pericarditis. Fever and lymphadenopathy may be present. In some cases, death has been reported. If this syndrome is recognized, the drug should be discontinued immediately.

Tissue Hyperpigmentation

Tetracycline-class antibiotics are known to cause hyperpigmentation. Tetracycline therapy may induce hyperpigmentation in many organs, including nails, bone, skin, eyes, thyroid, visceral tissue, oral cavity (teeth, mucosa, alveolar bone), sclerae and heart valves. Skin and oral pigmentation has been reported to occur independently of time or amount of drug administration, whereas other tissue pigmentation has been reported to occur upon prolonged administration. Skin pigmentation includes diffuse pigmentation as well as over sites of scars or injury.

Development of Drug Resistant Bacteria

Bacterial resistance to the tetracyclines may develop in patients using SOLODYN, therefore, the susceptibility of bacteria associated with infection should be considered in selecting antimicrobial therapy. Because of the potential for drug-resistant bacteria to develop during the use of SOLODYN, it should be used only as indicated.

Superinfection

As with other antibiotic preparations, use of SOLODYN may result in overgrowth of nonsusceptible organisms, including fungi. If superinfection occurs, SOLODYN should be discontinued and appropriate therapy instituted.

Laboratory Monitoring

Periodic laboratory evaluations of organ systems, including hematopoietic, renal and hepatic studies should be performed. Appropriate tests for autoimmune syndromes should be performed as indicated.

ADVERSE REACTIONS

Clinical Trial Experience

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

The following table summarizes selected adverse reactions reported in clinical trials at a rate of ≥1% for SOLODYN.

Selected Treatment-Emergent Adverse Reactions in at least 1% of Clinical Trial Subjects

Adverse Reactions	SOLODYN (1 mg/kg) N=674 (%)	PLACEBO N=364 (%)
At least one treatment-emergent event	379 (56)	197 (54)
Headache	152 (23)	83 (23)
Fatigue	62 (9)	24 (7)
Dizziness	59 (9)	17 (5)
Pruritus	31 (5)	16 (4)
Malaise	26 (4)	9 (3)
Mood alteration	17 (3)	9 (3)
Somnolence	13 (2)	3 (1)
Urticaria	10 (2)	1 (0)
Tinnitus	10 (2)	5 (1)
Arthralgia	9 (1)	2 (0)
Vertigo	8 (1)	3 (1)
Dry mouth	7 (1)	5 (1)
Myalgia	7 (1)	4 (1)

Postmarketing Experience

Adverse reactions that have been reported with minocycline hydrochloride use in a variety of indications include:

Skin and hypersensitivity reactions: fixed drug eruptions, balanitis, erythema multiforme, Stevens-Johnson syndrome, anaphylactoid purpura, photosensitivity, pigmentation of skin and mucous membranes, hypersensitivity reactions, angioneurotic edema, anaphylaxis, DRESS syndrome *(see Warnings and Precautions).*

Autoimmune conditions: polyarthralgia, pericarditis, exacerbation of systemic lupus, pulmonary infiltrates with eosinophilia, transient lupus-like syndrome.

Central nervous system: pseudotumor cerebri, bulging fontanels in infants, decreased hearing.

Endocrine: brown-black microscopic thyroid discoloration, abnormal thyroid function.

Oncology: thyroid cancer.

Oral: glossitis, dysphagia, tooth discoloration.

Gastrointestinal: enterocolitis, pancreatitis, hepatitis, liver failure.

Renal: reversible acute renal failure.

Hematology: hemolytic anemia, thrombocytopenia, eosinophilia. Preliminary studies suggest that use of minocycline may have deleterious effects on human spermatogenesis

(see Nonclinical Toxicology).

DRUG INTERACTIONS

Anticoagulants

Because tetracyclines have been shown to depress plasma prothrombin activity, patients who are on anticoagulant therapy may require downward adjustment of their anticoagulant dosage.

Penicillin

Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, it is advisable to avoid giving tetracycline-class drugs in conjunction with penicillin.

Methoxyflurane

The concurrent use of tetracycline and methoxyflurane has been reported to result in fatal renal toxicity.

Antacids and Iron Preparations

Absorption of tetracyclines is impaired by antacids containing aluminum, calcium or magnesium and iron-containing preparations.

Low Dose Oral Contraceptives

In a multi-center study to evaluate the effect of SOLODYN on low dose oral contraceptives, hormone levels over one menstrual cycle with and without SOLODYN 1 mg/kg once-daily were measured. Based on the results of this trial, minocycline-related changes in estradiol, progestinic hormone, FSH and LH plasma levels, of breakthrough bleeding, or of contraceptive failure, cannot be ruled out. To avoid contraceptive failure, female patients are advised to use a second form of contraceptive during treatment with minocycline.

Drug/Laboratory Test Interactions

False elevations of urinary catecholamine levels may occur due to interference with the fluorescence test.

USE IN SPECIFIC POPULATIONS

Pregnancy

Teratogenic Effects: Pregnancy category D (see Warnings and Precautions)

SOLODYN should not be used during pregnancy. If the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus and stop treatment immediately.

There are no adequate and well-controlled studies on the use of minocycline in pregnant women. Minocycline, like other tetracycline-class drugs, crosses the placenta and may cause fetal harm when administered to a pregnant woman.

Rare spontaneous reports of congenital anomalies including limb reduction have been reported with minocycline use in pregnancy in post-marketing experience. Only limited information is available regarding these reports; therefore, no conclusion on causal association can be established.

Minocycline induced skeletal malformations (bent limb bones) in fetuses when administered to pregnant rats and rabbits in doses of 30 mg/kg/day and 100 mg/kg/day, respectively, (resulting in approximately 3 times and 2 times, respectively, the systemic exposure to minocycline observed in patients as a result of use of SOLODYN). Reduced mean fetal body weight was observed in studies in which minocycline was administered to pregnant rats at a dose of 10 mg/kg/day (which resulted in approximately the same level of systemic exposure to minocycline as that observed in patients who use SOLODYN).

Minocycline was assessed for effects on peri- and post-natal development of rats in a study that involved oral administration to pregnant rats from day 6 of gestation through the period of lactation (postpartum day 20), at dosages of 5, 10, or 50 mg/kg/day. In this study, body weight gain was significantly reduced in pregnant females that received 50 mg/kg/day (resulting in approximately 2.5 times the systemic exposure to minocycline observed in patients as a result of use of SOLODYN). No effects of treatment on the duration of the gestation period or the number of live pups born per litter were observed. Gross external anomalies observed in F1 pups (offspring of animals that received minocycline) included reduced body size, improperly rotated forelimbs, and reduced size of extremities. No effects were observed on the physical development, behavior, learning ability, or reproduction of F1 pups, and there was no effect on gross appearance of F2 pups (offspring of F1 animals).

Nursing Mothers

Tetracycline-class antibiotics are excreted in human milk. Because of the potential for serious adverse effects on bone and tooth development in nursing infants from the tetracycline-class antibiotics, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother *(see Warnings and Precautions).*

Pediatric Use

SOLODYN is indicated to treat only inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients 12 years and older. Safety and effectiveness in pediatric patients below the age of 12 has not been established.

Use of tetracycline-class antibiotics below the age of 8 is not recommended due to the potential for tooth discoloration *(see Warnings and Precautions).*

Geriatric Use

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

OVERDOSAGE

In case of overdosage, discontinue medication, treat symptomatically and institute supportive measures. Minocycline is not removed in significant quantities by hemodialysis or peritoneal dialysis.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis—In a carcinogenicity study in which minocycline HCl was orally administered to male and female rats once daily for up to 104 weeks at dosages up to 200 mg/kg/day, minocycline HCl was associated in both genders with follicular cell tumors of the thyroid gland, including increased incidences of adenomas, carcinomas and the combined incidence of adenomas and carcinomas in males, and adenomas and the combined incidence of adenomas and carcinomas in females. In a carcinogenicity study in which minocycline HCl was orally administered to male and female mice once daily for up to 104 weeks at dosages up to 150 mg/kg/day, exposure to minocycline HCl did not result in a significantly increased incidence of neoplasms in either males or females.

Mutagenesis—Minocycline was not mutagenic *in vitro* in a bacterial reverse mutation assay (Ames test) or CHO/HGPRT mammalian cell assay in the presence or absence of metabolic activation. Minocycline was not clastogenic *in vitro* using human peripheral blood lymphocytes or *in vivo* in a mouse micronucleus test.

Impairment of Fertility—Male and female reproductive performance in rats was unaffected by oral doses of minocycline of up to 300 mg/kg/day (which resulted in up to approximately 40 times the level of systemic exposure to minocycline observed in patients as a result of use of SOLODYN). However, oral administration of 100 or 300 mg/kg/day of minocycline to male rats (resulting in approximately 15 to 40 times the level of systemic exposure to minocycline observed in patients as a result of use of SOLODYN) adversely affected spermatogenesis. Effects observed at 300 mg/kg/day included a reduced number of sperm cells per gram of epididymis, an apparent reduction in the percentage of sperm that were motile, and (at 100 and 300 mg/kg/day) increased numbers of morphologically abnormal sperm cells. Morphological abnormalities observed in sperm samples included absent heads, misshapen heads, and abnormal flagella.

Limited human studies suggest that minocycline may have a deleterious effect on spermatogenesis.

SOLODYN should not be used by individuals of either gender who are attempting to conceive a child.

HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

SOLODYN (minocycline HCl, USP) Extended Release Tablets are supplied as aqueous film coated tablets containing minocycline hydrochloride equivalent to 55 mg, 65 mg, 80 mg, 105 mg or 115 mg minocycline, are supplied as follows.

The 55 mg extended release tablets are pink, unscored, coated, and debossed with "DYN-055" on one side. Each tablet contains minocycline hydrochloride equivalent to 55 mg minocycline, supplied as follows:

NDC 99207-465-30 Bottle of 30

The 65 mg extended release tablets are blue, unscored, coated, and debossed with "DYN-065" on one side. Each tablet contains minocycline hydrochloride equivalent to 65 mg minocycline, supplied as follows:

NDC 99207-463-30 Bottle of 30

The 80 mg extended release tablets are dark gray, unscored, coated, and debossed with "DYN-080" on one side. Each tablet contains minocycline hydrochloride equivalent to 80 mg minocycline, supplied as follows:

NDC 99207-466-30 Bottle of 30

The 105 mg extended release tablets are purple, unscored, coated, and debossed with "DYN-105" on one side. Each tablet contains minocycline hydrochloride equivalent to 105 mg minocycline, supplied as follows:

NDC 99207-467-30 Bottle of 30

The 115 mg extended release tablets are green, unscored, coated, and debossed with "DYN-115" on one side. Each tablet contains minocycline hydrochloride equivalent to 115 mg minocycline, supplied as follows:

NDC 99207-464-30 Bottle of 30

Storage

Store at 25ºC (77ºF); excursions are permitted to 15º-30ºC (59º-86ºF) [See USP Controlled Room Temperature].

Handling

Keep out of reach of children

Protect from light, moisture, and excessive heat.

Dispense in tight, light-resistant container with child-resistant closure.

PATIENT COUNSELING INFORMATION

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

Distributed by:
Valeant Pharmaceuticals
North America LLC
Bridgewater, NJ 08807 USA
U.S. Patent Numbers: 5,908,838; 7,790,705; 7,919,483; 8,252,776; 8,268,804; 8,722,650 and 9,192,615

VALEANT
Pharmaceuticals North America LLC

Based on 9387304 Rev 09/2017
SDN.0068.USA.17

FDA Warns About Laser Devices for "Vaginal Rejuvenation"

By Scott Gottlieb, MD
FDA Commissioner

Statement from FDA Commissioner Scott Gottlieb, MD on efforts to safeguard women's health from deceptive health claims and significant risks related to devices marketed for use in medical procedures for "vaginal rejuvenation."

Our most fundamental obligation to the American public is providing patients with access to safe and effective medical products to meet their health care needs as well as protecting them from harmful products and deceptive medical claims. A large part of our work focuses on efforts to bring forth innovative, new products. But we're equally dedicated to monitoring the landscape to ensure products are delivering on their intended benefits and to ensure that if new health risks arise, we take appropriate action.

Delivering on this complementary mission is a key aim of our Medical Device Safety Action Plan. The plan outlines how the FDA will encourage innovation to improve safety, detect safety risks earlier and keep healthcare providers and patients better informed. Our plan would establish a robust medical device patient safety net in the U.S. We are taking steps to streamline and modernize how we implement post-market actions to address device safety issues to make our response to risks more timely and effective.

Advancing the health of women is a priority for the FDA. As part of our action plan, we're working to improve evidence generation about the safety and effectiveness of health technologies in clinical areas that are unique to women. And as part of these efforts, we also watch for, and take action against, bad actors who unfortunately take advantage of unsuspecting consumers by marketing unapproved, deceptive products that may pose safety risks and violate the trust of American consumers.

That's what we're doing today.

We've recently become aware of a growing number of manufacturers marketing "vaginal rejuvenation" devices to women and claiming these procedures will treat conditions and symptoms related to menopause, urinary incontinence or sexual function. The procedures use lasers and other energy-based devices to destroy or reshape vaginal tissue. These products have serious risks and don't have adequate evidence to support their use for these purposes. We are deeply concerned women are being harmed.

As part of our efforts to promote women's health, the FDA has cleared or approved laser and energy-based devices for the treatment of serious conditions like the destruction of abnormal or pre-cancerous cervical or vaginal tissue, as well as condylomas (genital warts). But the safety and effectiveness of these devices hasn't been evaluated or confirmed by the FDA for "vaginal rejuvenation." In addition to the deceptive health claims being made with respect to these uses, the "vaginal rejuvenation" procedures have serious risks. In some cases, these devices are being marketed for this use to women who have completed treatment for breast cancer and are experiencing symptoms caused by early menopause. The deceptive marketing of a dangerous procedure with no proven benefit, including to women who've been treated for cancer, is egregious.

In reviewing adverse event reports and published literature, we have found numerous cases of vaginal burns, scarring, pain during sexual intercourse, and recurring or chronic pain.

We haven't reviewed or approved these devices for use in such procedures. Thus, the full extent of the risks is unknown. But these reports indicate these procedures can cause serious harm.

Today, we're warning women and their healthcare providers that the FDA has serious concerns about the use of these devices to treat gynecological conditions beyond those for which the devices have been approved or cleared.

We recently notified seven device manufacturers of our concerns about inappropriate marketing of their

devices for "vaginal rejuvenation" procedures. They are: Alma Lasers, BTL Industries, Cynosure, InMode, Sciton, Thermigen, and Venus Concept. We requested that the manufacturers address our concerns within 30 days. If our concerns are not addressed, then the FDA will consider what next actions, including potential enforcement actions, are appropriate. This matter has the full attention of our professional staff.

The deceptive marketing of unproven treatments may not only cause injuries but may also keep some patients from accessing appropriate, recognized therapies to treat severe medical conditions. These products may be particularly appealing to women who may not be candidates for certain FDA-approved treatments to relieve vaginal dryness, and thus are seeking alternative, non-hormonal options. Women considering treatment for vaginal symptoms should speak to their healthcare provider about the potential and known benefits and risks of all available treatment options. FDA is committed to helping advance the development of safe, effective treatment options for these conditions.

We've been focused on advancing new policies to improve our oversight of device safety. As part of our Medical Device Safety Action Plan and our ongoing commitment to advancing women's health, we've begun building out important device safety registries. We've also established the Women's Health Technologies Strategically Coordinated Registry Network (CRN) to provide more complete evidence in clinical areas that are unique to women, such as uterine fibroids and pelvic floor disorders.

As part of this critical work, we remain dedicated to closely monitoring reports of adverse events associated with "vaginal rejuvenation" procedures. We will keep the public informed if significant new information becomes available. We'd also like to learn more about patients' experiences with these procedures. We encourage those who've had an adverse event associated with the use of these devices to report their problem to MedWatch, the FDA Safety Information and Adverse Event Reporting program.

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

COSMETIC pearls

Dermcast.tv Blog

Does Microneedling with Platelet-Rich Plasma Injections Improve Androgenic Alopecia?

By Martha L. Sikes, MS, RPh, PA-C

Androgenic alopecia (AGA) is typically treated with a combination of finasteride and minoxidil, which targets androgens, but even with this treatment 40% of patients go bald. A recent study used dermoscopy to evaluate the effectiveness of using microneedling in combination with injections of platelet-rich plasma (PRP) as a treatment modality.

Twenty patients participated in the study. Dermoscopic evaluation assessed the number of yellow dots, hair shaft diameter, and number of vellus hairs after each treatment. New hair growth began immediately after the first treatment leading to high patient satisfaction scores. Dermoscopy showed an increase in the number of vellus and total hairs, increased hair shaft diameter, and dramatic reduction or disappearance of black/yellow dots after twelve weeks of three sessions of PRP.

The authors conclude that the study supports the use of dermoscopy in evaluating the pre- and post-treatment response and demonstrates an excellent response to PRP with microneedling in patients not responding to conventional therapy.

Dermcast.tv Blog Post: June 10, 2018
Source: Wiley Online
Adapted from the original article.

Dermcast.tv is the official online media resource of the SDPA and is your free source for the latest SDPA-related audio podcasts, current dermatology news and research, and videos featuring thought-leaders, procedures, conference highlights, and much more. In addition, Dermcast is the #1 dermatology-related podcast on iTunes! To read more Dermcast.tv Blogs and/or to follow the next live blog from an upcoming SDPA dermatology conference, please visit the Dermcast.tv website at www.dermcast.tv and subscribe today.

NOTES from your **Office Manager**

Communicating with Low Health Literacy Patients

THE RISK:

The lay public often has limited knowledge and understanding of medical terminology. A patient's ability to understand medical information may be compounded by stress, age, illness, and language or cultural barriers. Effective communication with patients may improve compliance with treatment regimens, enhance the informed consent process, and increase safe medication use. Physician office practices can improve the patient experience, and reduce potential liability exposure, by employing the following recommendations.

RECOMMENDATIONS:

1. Use lay terminology whenever possible. Define technical terms with simple language. Patient education materials should be written in plain language, avoiding the use of medical jargon.
2. Verbal instructions may be reinforced with visual aids and printed materials that are easy to read and include pictures, models, and illustrations. Consider using non-printed materials, such as videos and audio recordings, as indicated.
3. Offer to assist your patients when completing new patient information or any other practice documents. Provide this help in a confidential way, preferably in an area that is private and conducive to this type of information exchange. Encourage your patients to contact you with any further questions.
4. The use of interpreters may be indicated for patients who are not fluent in the English language.
5. At the end of the encounter, use open-ended questions rather than yes/no questions to further assess patient understanding. Instead of asking "Do you have any questions?" try asking, "What questions do you have for me?"
6. Providers and staff should be familiar with and utilize the principles of the "teach back method" when reviewing new medications or treatment plans with patients. First teach a concept, then ask patients to repeat back the information they just heard using their own words.
7. Patients and family members may be embarrassed by, or unaware of, their healthcare literacy deficits. An empathetic approach to understanding patient health literacy will enhance your physician-patient relationship.

Outside & Inside the 9 to 5...

How Jennifer Conner, PA-C Makes a Difference

The National Commission on Certification of Physician Assistants (NCCPA) has been spotlighting Certified PAs in the community who are making a difference. The goal was to celebrate the achievements of the profession and the individuals who exemplify the many ways Certified PAs have a positive impact on patients' lives every day. The chosen PAs embody what it means to be a PA, demonstrating that when it comes to providing high quality health care, promoting wellness, impacting communities, and saving and changing lives…#PAsDoThat!

Our very own former SDPA President, Jennifer Conner was one of the highlighted PAs. We congratulate Jennifer for the many ways she embodies what it truly means to be a PA making a difference. We also want to share the original article (printed below) with our members.

Jennifer Conner, PA-C, strives to enhance the face of PAs in dermatology through meaningful patient interactions and service to the dermatology community. Since beginning her PA career in 2006, she has emerged as a talented clinician and thought leader in the profession, and she continuously chases ways to expand community outreach, the footprint of PAs in dermatology, and improve professional standards.

Jennifer Conner, PA-C

Conner's unconventional path into dermatology began in the Army National Guard. After working as a medic and Medical Service Corps officer, she entered the U.S. Army Interservice PA program where she completed rotations under a dermatologist who imparted invaluable lessons and sparked her interest in the specialty. "He was an amazing mentor but tough," she said. "I was drawn to dermatology because it's an area of medicine that allows patients to physically see their transformations and involves a number of minor procedures as well."

Conner now practices at Dawes-Fretzin Dermatology in Indianapolis, where she performs a wide range of general dermatology and surgical procedures alongside her collaborating physician. But her impact doesn't stop there. Her clinical career intersects with some of her philanthropic work for communities, children, and fellow PAs in dermatology.

To open opportunities for PAs to get involved in supporting critical research for viable melanoma treatments, in 2012, she spearheaded the Society of Dermatology PAs partnership with the Melanoma Research Foundation (MRF) for the Miles for Melanoma 5K program. She also served as President of the Society of Dermatology Physician Assistants (SDPA) and acted as a founding trustee of the Dermatology PA Foundation. She served as an MRF volunteer, offering free skin cancer screenings to Iron Man triathletes to bring awareness to the dermatology PA community; and she connected athletes, fans, and spectators to the organization. Her involvement with MRF led her to establish an annual Miles for Melanoma race in San Antonio (where she practices) and in several cities across the country in coordination with SDPA conferences.

IMPACT

During her tenure as SDPA president, she oversaw the development and launch of its Diplomate Fellowship program, which is designed

to offer new and seasoned dermatology PAs the full knowledge base needed to best serve patients in their specialty and complement training they receive from dermatologists. Under her leadership, fellow SDPA leaders launched a task force to investigate corporate buyouts in dermatology and the impact it has on PAs. She also helped to develop two PI-CME programs for dermatology PAs to conduct in their clinics. She has championed efforts to promote philanthropy, research and education – three main missions of the Dermatology PA Foundation (DPAF). Initiatives achieved thus far with the DPAF have included researching ways to ease patient access to care, increase dermatology PA involvement in local communities and patient advocacy groups, as well as hosting an inaugural silent auction that raised about $14,000 to send children with skin diseases to Camp Wonder in California.

"Jennifer goes above and beyond for the profession," said colleague Joleen Volz, PA-C. "Despite having a family, she works tirelessly on multiple tasks and devotes a substantial amount of time to the national society. She solicits the opinions and expertise of her colleagues to inform her decisions, and that makes her a great leader.

Conner credits much of that capacity for leadership to personal and educational development opportunities in the military, but also a passion to enhance opportunities for PAs in a medical specialty she respects and enjoys.

"I love that our profession has grown and more patients understand what we do," she said. "It's great that we can offer better access to care for patients, educate patients and employers about what we do and offer a true extension of the healthcare team in collaboration with dermatologists."

Through her platform, Conner will continue to rejuvenate ways to serve patients and the dermatology community.

NCCPA salutes Jennifer Conner, PA-C, for her efforts in strengthening the presence of dermatology PAs.

Reprinted with permission from NCCPA

Workplace Excellence

Coaching on Goal Achievement Process - Part 2 of 2

By Matthew Davidson, PhD

In my work as President of the Institute for Excellence & Ethics (IEE) I have had the opportunity to work with diverse individuals and organizations in their quest to achieve excellence. This column dedicated to workplace excellence explores the organizational, interpersonal, and ethical issues that contribute to (or detract from) individual or organizational excellence within the physician assistant profession. If you have any workplace topics you would like to see covered in the JDPA please feel free to share them with us. Email editor@jdpa.org with any topic ideas or questions concerning the workplace.

GETTING FROM HERE TO THERE

Goal setting is essentially a "how do you get from here to there" process.

Sometimes getting from point A to point B is straightforward. However, often getting from where we are currently to where we want to be, can be a difficult and frustrating, even demoralizing experience.

Usually when we think of goals, we think and talk about setting them. But anybody can set goals; we want to figure out what it takes to achieve our goals. For centuries people have developed different tools to help us navigate our way from here to there. Early travelers used the stars as a navigation guide. Explorers developed detailed maps so that others could follow their paths. Today Global Positioning Systems (GPS) allow a Garmin or Google Maps on your phone to help guide us from here to there. The *Excellence with Integrity Goal Achievement Process* is like a GPS for goals.

The Excellence with Integrity Goal Achievement Process can be summarized as follows: No matter what you're trying to achieve, no matter what challenge you're trying to overcome, it begins by figuring out your starting point and your desired end goal. Then you need to identify the action steps to get you from your starting point to your end goal, breaking them into small steps.

Once the plan is put into action, you must continuously measure and monitor your progress and make changes as needed. You also need to seek out support and challenge from individuals who are able to provide you with expertise, accountability, and encouragement.

IT AIN'T SMART IF IT DON'T WORK

There are lots of goal setting frameworks out there. The SMART goal acronym is often recommended. (Our design team fought for weeks about the different versions of it and whether they

were logical and useful, measureable versus results-oriented, versus reasonable, etc.). In our experience, even if the SMART goal template works, and I think it's only so-so, it only works for goal setting, not goal achievement. Primarily because it doesn't address two essential elements of goal achievement: (1) the need to measure, monitor and revise accordingly and continuously; and (2) the essential need for support and challenge necessary to help us achieve our goals. Very few people achieve challenging and important goals in isolation. The expertise, encouragement, and accountability are essential. We need the new knowledge and strategies, motivation and accountability to achieve our goals.

DON'T JUST MAKE A LIST OF PLACES YOU'D LIKE TO VISIT (GOALS); MAKE A MAP TO GET THERE

The Excellence with Integrity Goal Map provides the template for creating a customized goal map for any goal you're seeking to achieve. Goal maps are no different than any other kind of map: they depend on accurate calibration, it must be accurate and provide the right level of detail. The most accurate map of the earth still won't get you from your house to a location across town. Just like Google Maps or any other map, sometimes we want a map that pans from a wide view (e.g., the entire world, country, or state) to guide a certain kind of planning. But then we often need to create a customized map that provides a more focused view with more specific details (e.g., the possible roads and routes we might take to get from our home to the mall across town).

Thus, a goal map for your life would look very different than a goal map on how to finish your first marathon, or go from seeing 20 patients to 30 patients efficiently a day, or provide your community with free skin cancer screenings as a community service project next year. Each goal requires a specific map calibrated to guide you on the journey from your current starting point to your desired end-goal. Once a goal map has been created, we want to check to make sure it is as strong as it can be.

First, we should be sure that the desired goal we're going after is specific and measureable. Second, we must be sure that we have an accurate understanding of our current position. If we know where we're starting from, no matter how bad it might seem, we can create a detailed plan of action. If you're not honest or accurate, you will ignore or miss out on key action steps that are needed. Finally, with a specific end-goal and a clear starting position, we need to make sure we have identified the major action steps required, and that we have broken them down into doable, smaller steps.

THE DEVIL IS IN THE DETAILS—OR LACK THEREOF

When we set goals, most people simply write down their desired goal; doing that is important, but reaching that goal depends on the detailed breakdown of the action steps from the starting point to the desired destination. When we do an autopsy of a goal failure, we often find that the action steps are not sufficiently broken down into smaller, concrete steps (or there are action steps that are altogether missing). For example, my diet goal: lose 10 pounds. My first major action step: Eat Good Food. My breakdown of this: eat a balance of carbohydrates, proteins, and fats. Analysis: all carbs, proteins, and fats are NOT created equal. Also, what about the importance of what and how much you drink? This could be another major action step, or part of the breakdown of Eat Good Food. Either way, you must

include it because too much soda (or even Gatorade) could be preventing your goal achievement. Also, what about what you're NOT going to eat? Maybe an action step that addresses the "don't eat junk" is missing or needs to be more detailed in outlining what you plan to do and how you plan to do it. The bottom line is: the breakdown of action steps into smaller steps that are sufficiently thorough and detailed is essential. Goal setting is about taking control of the details that are within our control. The devil is in the details, and as the saying goes, "Details are what stand between most people and the accomplishment of their goals."

MEASURE, MONITOR, REVISE, GROW AND LET GO

Like the GPS system, the Goal Achievement Process encourages you to regularly measure and monitor as you begin to put your plan into action, and to quickly revise your plan as needed. This is one of the important differences between goal-setting, and the Goal Achievement Process. Anybody can set goals, but achieving your goals requires that you continuously measure and monitor progress to see what changes need to be made along the way. Actions steps are the WHAT of goal achievement, measuring and monitoring goes after the WHAT BY WHEN? HOW MUCH OR HOW MANY FOR HOW LONG?

Some monitoring can be done through the use of a simple YES/NO checklist. For example, "Incorporate new check-in process by March 15th." Accomplished? Yes or No? Some monitoring can be done by COUNTS (for example, Past Personal Best = 5 charts completed before lunch; Future Best Goal = 10 charts completed before lunch). Some monitoring can be done by CLOCKS (for example, Past Personal Best = 20 minutes wait time after check-in; Future Best Goal = 10 minutes wait time after check in). When you monitor those measurements you are then able to revise (missed the mark so I'll knock it back to a goal of 15 minutes or hit it easily so I'll bump it up to 8 minutes); sometimes revising means trying an entirely different approach, recalibrate. An autopsy of a failed goal often reveals a lack of measuring, monitoring, and revising. It's a constant process of keeping our eyes on the end-goal and then working on continuous growth and improvement. Keeping in mind that a "normal" day in the clinic isn't always predictable or normal- so adjustments will need to be made.

YOUR GOAL MAP WON'T WORK IF YOU DON'T!

The best map in town won't get you to your destination; it provides the route, you must follow it. You can walk, drive, bike, or fly but no matter what you do it takes energy and effort. Attitude and effort are the fuel for achievement. We choose our attitude and effort. We can choose to reframe a failure or setback and use it to improve. We can choose to keep going after it, to keep revising, to keep our eye on the prize. What it ultimately comes down to is, how badly you want it. You can have a bad map and a poor means of transportation, but if you want it badly enough you'll get there.

There is a video, entitled *From Homeless to Harvard* that tells the story of Zack Hodges who overcame unbelievable hardship in his life to achieve his goal of being a student-athlete at Harvard University. It is a great example of the overall goal achievement process, showing the journey from the starting point to a desired end-goal. We see the major action steps with their detailed specifics that he must accomplish to reach his goal. It shows how he overcomes hunger, homelessness, and the loss of his parents. It especially shows the importance of attitude and effort. Again, when we study an autopsy of a failed goal, sometimes it's because we just don't have enough talent or ability; often it's because we don't work hard enough or long enough even though our plans are good enough.

SUPPORT AND CHALLENGE ON THE WAY TO YOUR DESTINATION

To stay with our "how do you get from here to there" approach to goal achievement, the support and challenge element basically asks you to consider who is traveling with you as you try to get from your current position to your desired goal. These won't always be the same individuals. Depending on your goal, your companions on your journey may change. In fact, sometimes the success of our journey requires that we ask somebody to hop out for a particular trip. That doesn't mean they're not good people, just that they might not be the best match for the challenges of the particular journey you are on.

No matter how big or small your goals, the process for achieving them is still the same. Create a goal map to mark your starting point and identify your desired destination. Write down the major action steps required to get you to your goal, and

break those down into smaller, doable steps. Measure and monitor your progress, and revise as needed. Seek support and challenge from individuals who can provide you with expertise, accountability, and encouragement.

When we feel lost or unsure about where we're going, it can be difficult to see a way out. But, it's important to remember that, "the journey of a thousand miles begins with a first step." So figure out where you are and where you need to get to, and get yourself moving. Whether your goal is to decrease patient wait time, make patient check-in more efficient, or, improve continuity of care amongst the healthcare team in your office, the goal achievement process is the same. Simple, but not easy. Pick a goal today and get started. And remember, "What you get by achieving your goals is not as important as what you become by achieving your goals."

Matthew L. Davidson, Ph.D. *is the Founder, President, and Director of Education for the Institute for Excellence & Ethics (IEE), a 501(c)3 nonprofit corporation dedicated to helping individuals and organizations achieve excellence. He is a National Spokesperson for the Business Bureau National Center for Character Ethics. The IEE specializes in the development and dissemination of research-based tools for developing the culture and competencies of excellence and ethics in schools, athletics, the workplace, and the home; this is done through professional development workshops & academies, teaching & learning resources, assessment, and consulting services. He is a frequent national presenter and is available for keynote lectures, professional development, retreats, and organizational consulting. He has indicated no relationships to disclose relating to the content of this article. For additional information or to contact the IEE, please visit www.excellenceandethics.org.*

The Only FDA Approved Clobetasol Propionate 0.025%

IMPOYZ™ (clobetasol propionate) Cream 0.025% is indicated for the treatment of moderate to severe plaque psoriasis in patients 18 years of age and older.[1]

impoyz™
(clobetasol propionate)
Cream, 0.025%

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

Topical corticosteroids, including IMPOYZ Cream can cause reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency. This may occur during treatment or after withdrawal of treatment. This may require that patients be evaluated periodically for evidence of HPA axis suppression. Factors that predispose to HPA axis suppression include, use of high-potency steroids, large treatment surface areas, prolonged use, use of occlusive dressings, altered skin barrier, liver failure, and young age. If HPA axis suppression occurs, gradually withdraw the drug, reduce frequency of application, or substitute with a less potent corticosteroid. If signs and symptoms of withdrawal occur, systemic corticosteroids may be required. Recovery of HPA axis function is generally prompt and complete upon discontinuation of topical corticosteroids. Although rare, systemic effects of topical corticosteroids may manifest as Cushing's syndrome, hyperglycemia, and glucosuria. Pediatric patients may be more susceptible to systemic toxicity because of their larger skin surface to body mass ratios. **Local Adverse Reactions with Topical Corticosteroids -** Local adverse reactions from topical corticosteroids may be more likely to occur with occlusion, prolonged use, or use of higher potency corticosteroids. Some local adverse reactions may be irreversible. **Concomitant Skin Infections -** Use an appropriate antimicrobial agent if a skin infection is present or develops. If appropriate, discontinue use of IMPOYZ Cream. **Allergic Contact Dermatitis -** Allergic contact dermatitis with corticosteroids is usually diagnosed by observing failure to heal rather than noting a clinical exacerbation. **Adverse Events -** The adverse reaction that occurred in at least 1% of subjects treated with IMPOYZ Cream and at a higher incidence than in subjects treated with vehicle cream was application site discoloration (2% versus 1%). Less common local adverse events occurring in < 1% of subjects treated with IMPOYZ Cream were application site atrophy, telangiectasia and rash.

1. Impoyz Cream full Prescribing Information.

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

CLB1214 4/18

This Brief Summary does not include all the information needed to use IMPOYZ safely and correctly. See full Prescribing Information.
IMPOYZ (clobetasol propionate) Cream, 0.025%, for topical use

INDICATIONS AND USAGE

IMPOYZ Cream 0.025% is indicated for the treatment of moderate to severe plaque psoriasis in patients 18 years of age and older.

DOSAGE AND ADMINISTRATION

Apply a thin layer of IMPOYZ Cream to the affected skin areas twice daily and rub in gently and completely. Use IMPOYZ Cream for up to 2 consecutive weeks of treatment. Treatment beyond 2 consecutive weeks is not recommended, and the total dosage should not exceed 50 g per week because of the potential for the drug to suppress the hypothalamic-pituitary-adrenal (HPA) axis [see Warnings and Precautions (5.1)]. Discontinue IMPOYZ Cream when control is achieved. Do not use if atrophy is present at the treatment site. Do not bandage, cover, or wrap the treated skin area unless directed by a physician. Avoid use on the face, scalp, axilla, groin, or other intertriginous areas. IMPOYZ Cream is for topical use only. It is not for oral, ophthalmic, or intravaginal use. Wash hands after each application.

DOSAGE FORMS AND STRENGTHS

Cream, 0.025%: each gram contains 0.25 mg of clobetasol propionate in a white to off-white cream base.

CONTRAINDICATIONS. None

WARNINGS AND PRECAUTIONS

Effects on the Endocrine System: IMPOYZ Cream can cause reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency. This may occur during treatment or after withdrawal of treatment. Because of the potential for systemic absorption, use of topical corticosteroids, including IMPOYZ Cream, may require that patients be evaluated periodically for evidence of HPA axis suppression. Factors that predispose a patient to HPA axis suppression include the use of high-potency steroids, large treatment surface areas, prolonged use, use of occlusive dressings, altered skin barrier, liver failure, and young age. Evaluation for HPA axis suppression may be done by using the adrenocorticotropic hormone (ACTH) stimulation test. In a trial evaluating the effects of IMPOYZ Cream on the HPA axis, subjects with plaque psoriasis applied IMPOYZ Cream twice daily to at least 20% of involved Body Surface Area (BSA) for 15 days. Abnormal ACTH stimulation tests suggestive of HPA axis suppression were seen in 3 of 24 (12.5%) subjects on IMPOYZ Cream [see Clinical Pharmacology (12.2)]. In another trial to evaluate the effects of IMPOYZ Cream on the HPA axis, subjects with moderate to severe plaque psoriasis applied IMPOYZ Cream twice daily to at least 25% of involved BSA for 28 consecutive days. Abnormal ACTH stimulation test suggestive of HPA axis suppression was seen in 8 of 26 (30.8%) of subjects on IMPOYZ Cream. If HPA axis suppression is documented, gradually withdraw the drug, reduce the frequency of application, or substitute with a less potent corticosteroid. If signs and symptoms of steroid withdrawal occur, supplemental systemic corticosteroids may be required. Recovery of HPA axis function is generally prompt and complete upon discontinuation of topical corticosteroids. Systemic effects of topical corticosteroids may also manifest as Cushing's syndrome, hyperglycemia, and glucosuria. These complications are rare and generally occur after prolonged exposure to larger than recommended doses, particularly with high-potency topical corticosteroids. Use of more than one corticosteroid-containing product at the same time may increase the total systemic exposure to topical corticosteroids. Minimize the unwanted risks from endocrine effects by mitigating risk factors favoring increased systemic bioavailability and by using the product as recommended [see Dosage and Administration (2)]. Pediatric patients may be more susceptible to systemic toxicity because of their larger skin surface to body mass ratios [see Use in Specific Populations (8.4)].

Local Adverse Reactions with Topical Corticosteroids

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

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

Allergic Contact Dermatitis: Allergic contact dermatitis with corticosteroids is usually diagnosed by observing failure to heal rather than noting a clinical exacerbation. Such an observation should be corroborated with appropriate diagnostic patch testing. If irritation develops, discontinue the topical corticosteroid and institute appropriate therapy.

ADVERSE REACTIONS

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug, and may not reflect the rates observed in practice. IMPOYZ Cream was evaluated in two randomized, multicenter, prospective, vehicle-controlled clinical trials in subjects with moderate to severe plaque psoriasis. Subjects applied IMPOYZ Cream or vehicle cream twice daily for 14 days. A total of 354 subjects applied IMPOYZ Cream and 178 subjects applied vehicle. The adverse reaction that occurred in at least 1% of subjects treated with IMPOYZ Cream and at a higher incidence than in subjects treated with vehicle cream was application site discoloration (2% versus 1%). Less common local adverse events occurring in < 1% of subjects treated with IMPOYZ Cream were application site atrophy, telangiectasia and rash.

Postmarketing Experience

The following adverse reactions have been identified during post-approval use of clobetasol propionate: striae, irritation, dryness, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, hypertrichosis, and miliaria. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

USE IN SPECIFIC POPULATIONS

Pregnancy: Risk Summary There are no available data on IMPOYZ Cream in pregnant women to inform a drug-associated risk for adverse developmental outcomes. Published data report a significantly increased risk of low birthweight with the use of greater than 300 grams of potent or very potent topical corticosteroid during a pregnancy. Advise pregnant women of the potential risk to a fetus and to use IMPOYZ Cream on the smallest area of skin and for the shortest duration possible (see Data). In animal reproduction studies, increased malformations, such as cleft palate and skeletal abnormalities, were observed after subcutaneous administration of clobetasol propionate to pregnant mice and rabbits. No comparisons of animal exposure with human exposure are provided due to minimal systemic exposure noted after topical administration of IMPOYZ Cream [see Clinical Pharmacology (12.3)]. The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Human Data

Multiple observational studies found no significant associations between maternal use of topical corticosteroids of any potency and congenital malformations, preterm delivery, or fetal mortality. However, when the dispensed amount of potent or very potent topical corticosteroid exceeded 300 g during the entire pregnancy, use was associated with an increase in low birth weight infants [adjusted RR, 7.74 (95% CI, 1.49–40.11)]. In addition, a small cohort study, in which 28 sub-Saharan women using potent topical corticosteroids (27/28 used clobetasol propionate 0.05%) for skin lightening during pregnancy, noted a higher incidence of low birth weight infants in the exposed group. The majority of exposed subjects treated large areas of the body (a mean quantity of 60 g/month (range, 12–170g) over long periods of time.

Animal Data

In an embryo fetal development study in mice, subcutaneous administration of clobetasol propionate resulted in fetotoxicity at the highest dose tested (1 mg/kg) and malformations at the lowest dose tested (0.03 mg/kg). Malformations seen included cleft palate and skeletal abnormalities. In an embryofetal development study in rabbits, subcutaneous administration of clobetasol propionate resulted in malformations at doses of 0.003 and 0.01 mg/kg. Malformations seen included cleft palate, cranioschisis, and other skeletal abnormalities.

Lactation: Risk Summary There is no information regarding the presence of clobetasol propionate in breast milk or its effects on the breastfed infant or on milk production. Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. It is not known whether topical administration of clobetasol propionate could result in sufficient systemic absorption to produce detectable quantities in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for IMPOYZ Cream and any potential adverse effects on the breastfed infant from IMPOYZ Cream or from the underlying maternal condition. Clinical Considerations: To minimize potential exposure to the breastfed infant via breast milk, use IMPOYZ Cream on the smallest area of skin and for the shortest duration possible while breastfeeding. Advise breastfeeding women not to apply IMPOYZ Cream directly to the nipple and areola to avoid direct infant exposure.
Pediatric Use: The safety and effectiveness of IMPOYZ Cream in patients younger than 18 years of age have not been established; therefore, use in children younger than 18 years is not recommended. Because of a higher ratio of skin surface area to body mass, pediatric patients are at a greater risk than adults of systemic toxicity, including HPA axis suppression, when treated with topical drugs [see Warnings and Precautions (5.1)]. Rare systemic toxicities such as Cushing's syndrome, linear growth retardation, delayed weight gain, and intracranial hypertension have been reported in pediatric patients, especially those with prolonged exposure to large doses of high potency topical corticosteroids. Local adverse reactions including striae and skin atrophy have also been reported with use of topical corticosteroids in pediatric patients. Avoid use of IMPOYZ Cream in the treatment of diaper dermatitis.
Geriatric Use: Clinical studies of IMPOYZ Cream did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience with topical corticosteroids has not identified differences in responses between the elderly and younger patients.
NONCLINICAL TOXICOLOGY Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term animal studies have not been performed to evaluate the carcinogenic potential of clobetasol propionate cream. In a 13-week repeat dose toxicity study in rats, topical administration of clobetasol propionate cream, 0.001, 0.005 and 0.025 % at corresponding doses of 0.004, 0.02 and 0.1 mg/kg/day resulted in corticosteroid class-related systemic effects such as reductions in body weight gain, reductions in total leukocytes and individual white cells, decrease in weight of adrenals, thymus, spleen, liver and lung. Histologically, there were decreased hematopoiesis in the bone marrow, thymic atrophy and mast cell infiltration of the mesenteric lymph nodes. All these effects were indicative of severe immune suppression consistent with long-term exposure to corticosteroids. A no observable adverse effect level (NOAEL) was determined to be clobetasol propionate cream, 0.001% (0.004 mg/kg/day) in male rats while a NOAEL could not be determined in females. The clinical relevance of the findings in animals to humans is not clear, but sustained glucocorticoid-related immune suppression may increase the risk of infection and possibly the risk of carcinogenesis. Clobetasol propionate was not mutagenic in three different test systems: the Ames test, the Saccharomyces cerevisiae gene conversion assay, and the E. coli B WP2 fluctuation test. Fertility studies conducted in the rat following subcutaneous administration of clobetasol propionate at dosage levels up to 0.05 mg/kg/day revealed that females exhibited an increase in the number of resorbed embryos and a decrease in the number of living fetuses at the highest dose.

Manufactured by DPT Laboratories Ltd., San Antonio, TX 78215 For Encore Dermatology, Inc., Scottsdale, AZ 85254

www. encorederm.com

Encore™ Dermatology

CLB1214 4/18

Listening To Patients

Fake Medical News: The Black Salve and the Black Arte

By Alan Rockoff, MD

Jake clearly needed a biopsy. When I suggested that we had to find out what that new growth on his cheek was, he responded with fear. "Do I really need to have it tested?" he asked. Then he proposed an alternative. "I had another spot last year," he said. "This European doctor I saw in somebody's home put a special black salve on it, and it went away." "Who was this doctor?" I asked. "At the time I was a raw vegan," he said. "One of our group members gave me the doctor's name. He has a big reputation in Europe. He treated people locally in someone's living room." "Do you recall his name?" I asked him. Jake didn't. But I did.

About three years ago, a frightened, middle-aged woman named Josie came to see me with ugly scarring all over her face. Josie's story was similar to Jake's: A famous European doctor. Somebody's living room. "He had me lie on the floor," she recalled, "and he put on some kind of salve. It burned horribly. I was screaming in pain. He washed it off, but it still burned for a long time. This is what it left," she said, pointing to scarring and discoloration on both her cheeks and her upper lip. She remembered the doctor's name. It took just a few clicks to find him. He wasn't a licensed doctor, and he'd fled his home country ahead of fraud charges for illegal and harmful practice.

I couldn't offer Josie much, beyond advising her to avoid getting treated on living room floors by strange practitioners with painful salves. If you don't know about the treatment Josie and Jake underwent - it's called "escharotic treatment." You can look it up at https://en.wikipedia.org/wiki/Black_salve.

Escharotic treatment has been around a long time. It is used for cancers of the skin and cervix, among others. The principle behind it is the same as that behind "drawing salves" (available at CVS and WalMart, www.healthguidance.org/entry/15685/1/Drawing-Salve.html), sometimes known as "the black salve." The idea behind both is to apply something that blisters the skin and causes a scab to form. This is supposed to draw the evil out of the body and bring cure. You can smile at this idea if you want, but it's been around forever and will probably outlast a lot of the treatments doctors now use. Fake news is old news, and it doesn't need social media to spread (though Facebook helps).

Apparently ordinary people believe amazing things, irrational things, and harmful things. Why? Why on earth would Jake and Josie let somebody they don't know put black goop that hurts like hell on their faces as they lie on a stranger's living room floor? Here are some thoughts: Fear. They think they have cancer and are afraid to find out. Suspicion. They think the medical establishment is corrupt and self-serving. People they trust tell them to. The folks they hang with encourage them. Some groups share a touchy, suspicious, even hostile stance toward conventional medicine, convinced that its principles are unnatural and its practitioners are more concerned with profit and prestige than with the good of their patients. Those who hold such beliefs, along with various conspiracy theorists, span the political and social spectrum, from left to right, and they've been around forever.

I don't plan to try convincing them otherwise. No one can convince them. Citing facts and authority gets you nowhere. As Jonathan Swift said, "You cannot reason someone out of something they did not reason themselves into."

Fake political news is a problem for society. Fake medical news can be a problem for doctors. A pediatrician confronting an anti-vaxer family has to decide whether to try negotiating (giving their kid vaccines a little at a time) or whether to give up and send them elsewhere.

It takes effort for physicians to have patience with people who let unscrupulous strangers etch and mutilate their faces. However, since as professionals, doctors are obligated to care for people they may not like or agree with, they should try to understand why such people think the way they do. Often, what these patients, the ones who undertake dangerous and irrational treatment mainly are, is afraid. Still, the ones who actually come to doctors' offices are willing to at least consider medical opinion. Those who aren't willing to consider medical opinion never show up there. Jake had enough faith in me to let me calm him down enough to do the biopsy. It was benign.

Alan Rockoff, MD *practices dermatology in Boston, MA. He graduated with his medical degree in 1972 from the Albert Einstein College of Medicine in New York and then completed a pediatric internship and residency at Bronx Municipal Hospital Center. Continuing his education, Dr. Rockoff completed a dermatology residency program at the combined program at Boston University and Tufts University. Dr. Rockoff is a Clinical Assistant Professor of Dermatology at Tufts University School of Medicine. He has taught senior medical students and other trainees for over thirty-five years.*

Dr. Rockoff has been named one of Boston's Top Doctors by Boston Magazine for five years. Dr. Rockoff is board certified by the American Board of Pediatrics and the American Board of Dermatology. Dr. Rockoff is a Fellow of the American Academy of Dermatology and a member of the Massachusetts Medical Society and the Massachusetts Academy of Dermatology.

Dr. Rockoff's publications have appeared in a number of journals. He writes a monthly column for his dermatologic colleagues in Dermatology News as well as a blog for the magazine Psychology Today. His first book, "Under My Skin: A Dermatologist Looks at His Profession and His Patients" is available on Amazon and is his second book, "Act Like a Doctor, Think Like a Patient: Teaching Patient-focused Medicine" is available on Amazon and at Barnes and Noble.

From the Desk of...

Susan R. Hammerling, MPAS, PA-C

Advocacy: Now More Than Ever, We Must *Advocate* For The PA Profession

Advocating for the dermatology PA profession is one of the core tenets of the SDPA. We do that by supporting the legislative efforts of the AAPA as well as taking positions on various issues that could have an impact on PAs. You can help in these efforts by actively monitoring PA-related legislation in your states and at the federal level and by writing to your legislators.

One of your greatest responsibilities as a U.S. citizen is to help elect legislators who represent you and those in your community. By sharing your opinions and ideas with your elected representatives and senators, you can help them to decide what to do about certain issues or pending legislation that affects everyone by making suggestions to them or their staff.

How can you be sure your voice is heard? How do you communicate effectively with your legislators? Below are several tips to help you get started and to get the most impact out of your communications with your legislators. Remember, the more voices the better when it comes to advocating for the PA profession!

GENERAL TIPS:

- Know who your legislators are and how to contact them.
- Review how the legislative process works and understand how an idea becomes a law. This will help you effectively express your own ideas.
- Contact your legislator about a particular issue before the legislature takes action on it.
- Use a variety of communication methods. You may choose to contact your legislator by phone, letter, email, fax, social media, or visit in person.
- Give testimony at public hearings held by the legislature. To give testimony, you need to contact the appropriate committee administrative assistant to sign up.
- Be concise. Tell your legislator what effect you think a particular issue or bill, if it becomes law, will have on you, your children, business, or community. Also, suggest a course of action and offer assistance.

WRITING EFFECTIVE LETTERS:

- Address letters to members of the legislature as follows: The Honorable John Doe State Senator, District # The Capitol Boston, MA.
- Use the right address and spell your legislator's name correctly. Type or print legibly. Sign your name neatly and give your address correctly so the legislator can respond to your letter.
- Keep letters, email, and faxes as brief as possible. Concisely written correspondence is more likely to grab and keep the reader's attention.
- Identify your issue or opinion at the beginning of the letter; don't bury your main point.
- Cover only one issue per letter. If you have another issue to address, write another letter.
- Back up your opinions with supporting facts. Your letter should inform the reader, and facts make an argument more tangible and convincing.
- Avoid abbreviations or acronyms, and don't use technical jargon.
- Don't send the same letter to more than one legislator. Personalized letters have a greater impact.
- Be courteous and include key information, using examples to support your position. Explain how the legislation would affect your profession, your colleagues, and the community in which you live.
- Ask your elected officials to explain their position on the issue in their reply so you do not get the typical form letter response. "I'll keep your views in mind should this legislation come up for a vote." As a constituent, you are entitled to know why your elected officials think as they do.
- Thank your elected officials if they vote your way. They appreciate compliments and remember positive feedback.
- Do not hesitate to state your displeasure. However, that too will be remembered, so be polite if your elected officials oppose your position.
- State the reasons for your support or opposition to the bill. Ask for your Senator's or Representative's position on the bill.

NATIONAL PSORIASIS FOUNDATION®

Screening Tool for Psoriatic Arthritis

Psoriatic arthritis is a form of arthritis that can affect almost one-third of people with psoriasis and lead to lasting damage to your joints and bones. But getting diagnosed and treated as soon as possible can prevent that damage and help you stay healthy.

Answer the following five questions to find out if you're at risk for psoriatic arthritis. Then put a check mark next to the places on the diagram where your body feels tender or sore. Bring this handout with you to your doctor's appointment.

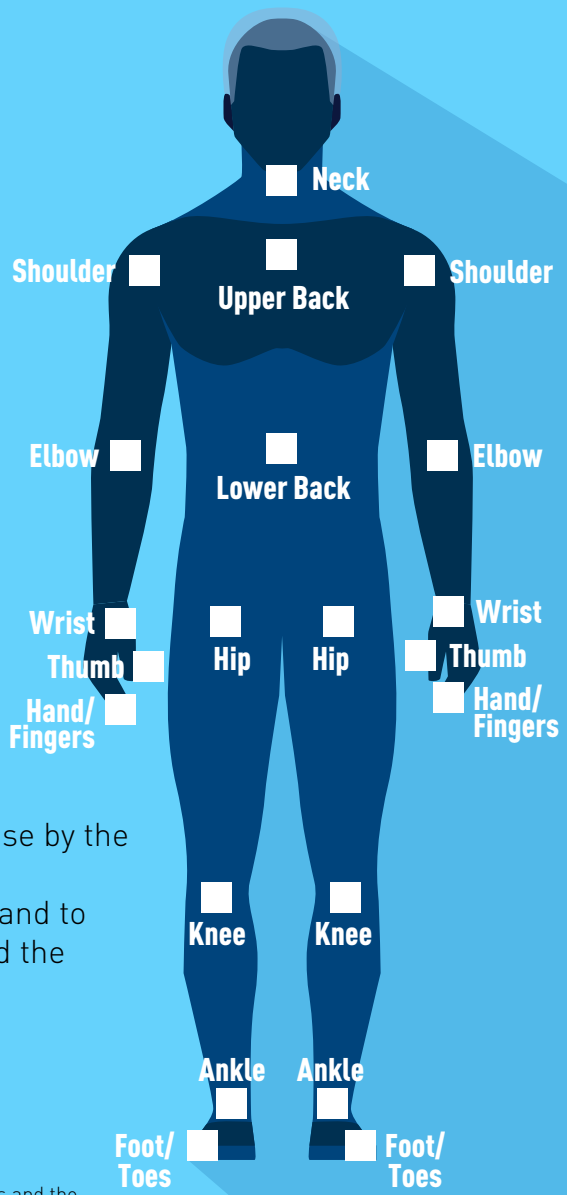
1. Have you ever had a swollen joint (or joints)?
   ☐ Yes ☐ No

2. Has a doctor ever told you that you have arthritis?
   ☐ Yes ☐ No

3. Do your fingernails or toenails have holes or pits?
   ☐ Yes ☐ No

4. Have you had pain in your heel?
   ☐ Yes ☐ No

5. Have you had a finger or toe that was completely swollen and painful for no apparent reason?
   ☐ Yes ☐ No



This validated screening tool was approved for use by the National Psoriasis Foundation (NPF). For more information on psoriasis and psoriatic arthritis, and to learn about NPF's Patient Navigation Center and the many services it offers, visit www.psoriasis.org.

Ibrahim GH, Buch MH, Lawson C, Waxman R, Helliwell PS. Evaluation of an existing screening tool for psoriatic arthritis in people with psoriasis and the development of a new instrument: the Psoriasis Epidemiology Screening Tool (PEST) questionnaire. Clin Exp Rheumatol. 2009 May-June; 27(3): 469-474.

Collaborating Physician **CORNER**

A Critical Evaluation of the Methodology of "Accuracy of Skin Cancer Diagnosis by Physician Assistants Compared with Dermatologists in a Large Health Care System"

By Ryan M. Svoboda, MS, MD, Marianne Pistilli, MBA, PA-C, Alex M. Glazer, MD, and Darrell S. Rigel, MS, MD

JAMA Dermatology recently published an article by Anderson et al. comparing accuracy of skin cancer diagnosis by physician assistants (PAs) versus dermatologists.[1] In this study, the authors found that, in a single institution over a five year period, dermatology PAs performed more skin biopsies per case of skin cancer diagnosed and were less likely to diagnose melanoma in situ when compared to dermatologists. Although the issue of comparing outcomes between providers with different training backgrounds is important, there are multiple methodological flaws in this study, which we believe limit any conclusions that can be drawn.

A material flaw in the research methods employed by Anderson and co-authors is the failure to properly adjust for confounding variables - covariates which could have created an apparent association between provider type and diagnostic acumen. One such potential confounder is disparate patient mix. For example, the authors acknowledge that dermatologists were more likely than PAs to see patients with a history of melanoma, and they stratified their results by this factor. This showed no significant difference in the number needed to biopsy (NNB) between dermatologists and PAs to diagnose melanoma in those with a history of melanoma. Despite this finding, the authors did not attempt to adjust the overall results for this confounder using multivariable regression.

Another, potentially even more impactful confounder is provider experience. Physicians in this sample, on average, had 6.6 more years of dermatologic experience than PAs (even more if residency training is considered). An equally plausible explanation for the finding of increased diagnostic accuracy of dermatologists versus PAs in this sample could be this difference in experience (as opposed to provider type). Failure to adjust for confounding variables weakens the authors' conclusions.

An additional issue with the methodology of this study is use of NNB as the primary outcome. NNB has been called into question as a valid performance metric as it is impacted by factors other than diagnostic accuracy, such as disease prevalence.[2] If the PAs in this study saw a mix of patients with a lower skin cancer prevalence, this could have led to a higher NNB in and of itself.[2]

The authors' improper framing of sample size also has significant bearing on the validity of their findings. The vital comparison of this study is between dermatologists and PAs, of which there were only 15 each. Because the authors analyzed the data such that the individual patient visit, rather than the clinician was the unit of observation, the sample size was inflated, leading to detection of statistical significance possibly without clinical relevance. In fact, the authors mistakenly cite their sample size of 20,270 patients as a strength of this study, while in reality the truly relevant sample size of providers (n = 30) is quite small.

More importantly, this small provider sample severely limits generalizability. With only 15 PAs and 15 dermatologists, a few outliers could significantly impact the overall findings. It is difficult to claim that any difference seen between two groups of 15 clinicians from a single institution extrapolates to all providers of dermatologic care.

Finally, we are concerned Anderson's conclusions, methodological errors notwithstanding, might pressure PAs to biopsy fewer lesions. If a given provider does actually have lower diagnostic accuracy (notwithstanding the fact that this article does not allow for this conclusion to be drawn in terms of

PAs versus dermatologists), we should then actually encourage them to have a lower biopsy threshold, given that the societal costs of missed melanomas greatly exceed those of negative biopsies.[3] We would espouse this strategy to less experienced physicians just as we would to any other providers with less experience, irrespective of their training or credentials.

While examining diagnostic accuracy between different providers is worthwhile, this study's shortcomings prevent drawing definitive conclusions. We hope that future studies take into consideration the methodological concerns we note.

REFERENCES:

1. Anderson AM, Matsumoto M, Saul MI, Secrest AM, Ferris LK. Accuracy of Skin Cancer Diagnosis by Physician Assistants Compared With Dermatologists in a Large Health Care System. JAMA Dermatol. 2018.
2. Marchetti MA, Dusza SW, Halpern AC. A Closer Inspection of the Number Needed to Biopsy. JAMA Dermatol. 2016;152(8):952-953.
3. Goldsmith SM. Cost analysis suggests overemphasis on biopsy rate for melanoma diagnosis. J Am Acad Dermatol. 2013;68(3):517-519.

Ryan Svoboda, MS, MD *is completing a Clinical Research Fellowship in cutaneous malignancy, sponsored by the National Society of Cutaneous Medicine. He earned a Master of Science in Healthcare Research from The Dartmouth Institute for Health Policy and Clinical Practice and is particularly interested in observational and clinical outcomes research methodology. He has indicated no relationships to disclose relating to the content of this article.*

Marianne Pistilli, MBA, PA-C *graduated from the Physician Assistant program at Weill Cornell Medical College and has over 11 years of dermatologic experience. She is a member of the Society of Dermatology Physician Assistants as well as the American Society for Laser Medicine and Surgery. She has indicated no relationships to disclose relating to the content of this article.*

Alex Glazer, MD *is a Dermatology Resident at the University of Arizona, with interests in general dermatology and dermatopathology. He has a research background and has authored multiple publications in leading journals. He has indicated no relationships to disclose relating to the content of this article.*

Darrell Rigel, MS, MD *is a world expert in the diagnosis and treatment of melanoma and was involved in the original development of the ABCDE algorithm and the concept of skin self-examination. He is a Clinical Professor of Dermatology at New York University's Langone School of Medicine. He has indicated no relationships to disclose relating to the content of this article.*

JDPA Journal of Dermatology for Physician Assistants

INFORMATION FOR AUTHORS – The JDPA is a peer-reviewed publication that delivers innovative clinical, surgical, cosmetic, and professional content exclusively for dermatology PAs. Submissions to the JDPA are peer-reviewed by a panel of experienced dermatology PAs, educational PAs, and dermatologists before articles are accepted for publication.

Manuscripts submitted for publication will be reviewed with the understanding that they are original and have not been submitted elsewhere nor are being considered by other journals. Electronic submissions are accepted and should be sent to editor@jdpa.org.

The five main sections featured in each issue of the JDPA are listed below along with a brief description of the various topics that authors can contribute to. Regardless of the section, all articles must follow the following criteria:

- ***Formatting*** - Times New Roman font, 12 point, double-spaced, left aligned.
- ***Article Order*** - Title, Author(s), Author bios (including disclosures), Text of Article, References, Tables, and Figures
- ***Reference Citations*** - Utilize the AMA Manual of Style, 10th Edition.

DERMATOLOGY PA NEWS AND NOTES

Feature Articles

Write a review about a new or innovative dermatological procedure, device, and/or approach to patient care (500-1000 words).

From The Desk Of…

Write an opinion essay sharing your insight regarding a current "hot item" issue *(e.g., specialty PA credentialing, dermatology access to care, supervising physician relationships, etc.)* or any other topic regarding the field of dermatology (250-1000 words).

CLINICAL DERMATOLOGY

CME articles

Content should be specific to the field of dermatology following any of the following formats:

Study – Original research (clinical or basic science).
Professional issues or health policy papers.
Review – Scholarly review of a topic.

Content length:

6 pages (requires 4 self-assessment Q&A) = .5hr of Cat. I CME.
12 pages (requires 8 self-assessment Q&A) = 1hr of Cat. I CME.

Article should include written learning objectives (3-4 required).

Dermatology Case Report

Write a report and discuss a case(s) that illustrate an important or interesting observation (500-1500 words).

Journal Club: Dermatology PA Perspectives

Write a review of an already published article from an established dermatology journal *(e.g., JAAD, Cos Dermatol, Dermatol Surg, etc.),* summarizing the practical thoughts and clinical issues (250-1000 words).

From the Patient's Perspective

Patients' stories published in their own words. JDPA staff can even assist patients with writing their stories (250-1000 words).

Clinical Snapshots

Write a brief written description and clinical facts about an interesting cutaneous anomaly (250-500 words).

Drugs in Dermatology

Write about the current information regarding a particular dermatological medication, drug interaction, or medication side effect/adverse reaction (250-1000 words).

Dermatology Evidence-Based Medicine (derm EBM)

Write a brief, evidence-based assessment of the one or two most relevant studies retrieved to answer a focused clinical question that may have arisen from a real-life situation. A derm EBM is not a comprehensive review of a subject or a synthesis of all the available knowledge (500–1500 words).

SURGICAL DERMATOLOGY

Feature Articles

Write a review about a new or innovative surgical procedure, device, and/or approach to patient care (500-1000 words).

Surgical Wisdom

Write a brief article on a fact or pearl for the surgical setting (250-500 words).

Surgical Dermatology Case Report

Write a report and discuss a case(s) that illustrate an important or interesting observation (500-1500 words).

Journal Club: Dermatology PA Perspectives

Write a review of an already published article from an established dermatology journal *(e.g., JAAD, Cos Dermatol, Dermatol Surg, etc.),* summarizing the practical thoughts and clinical issues (250-1000 words).

COSMETIC DERMATOLOGY

Feature Articles

Write a review about a new or innovative cosmetic procedure, device, and/or approach to patient care (500-1000 words).

Cosmetic Pearls

Write a brief article on a fact or pearl for the cosmetic setting (250-500 words).

Cosmetic Dermatology Case Report

Write a report and discuss a case(s) that illustrate an important or interesting observation (500-1500 words).

Journal Club: Dermatology PA Perspectives

Write a review of an already published article from an established dermatology journal *(e.g., JAAD, Cos Dermatol, Dermatol Surg, etc.),* summarizing the practical thoughts and clinical issues (250-1000 words).

PROFESSIONAL DEVELOPMENT

Feature Articles

Write an article that explores the professional issues dermatology PAs face such as reimbursement, education, medical trends, contracts, office management, etc. (500-1500 words).

Outside & Inside the 9 to 5

Allow us to share your story of the good work that you do either outside or inside your practice of dermatology. You can write this article yourself or the JDPA staff can interview you to write the article (250-1000 words). **Notes From Your Office Manager**
Write a brief article on a fact or pearl for the office setting (250-500 words).

Judicial and Ethical Affairs

Write an article that explores the complex or multifaceted ethical or judicial professional issues that affect the practice of dermatology for PAs (250-1000 words).

To read the JDPA publication's Ethics and Malpractice Statement, please visit www.jdpa.org/write.html.

ADVERTISER **INDEX**

For more information on advertising opportunities in the JDPA, please log on to www.jdpa.org

BRIEF SUMMARY OF PRESCRIBING INFORMATION

This Brief Summary does not include all the information needed to use RETIN-A MICRO safely and effectively. See full prescribing information for RETIN-A MICRO.

RETIN-A MICRO® (tretinoin) gel microsphere, 0.1%, 0.08%, 0.06% and 0.04%, for topical use
Initial U.S. Approval: 1971

INDICATIONS AND USAGE
Retin-A Micro® is a retinoid indicated for topical application in the treatment of acne vulgaris.

CONTRAINDICATIONS
None.

WARNINGS AND PRECAUTIONS
Local Irritation
The skin of certain individuals may become excessively dry, red, swollen, or blistered.

Tretinoin has been reported to cause severe irritation on eczematous skin and should be used with utmost caution in patients with this condition.

If the degree of irritation warrants, patients should be directed to temporarily reduce the amount or frequency of application of the medication, discontinue use temporarily, or discontinue use all together. Efficacy at reduced frequencies of application has not been established. If a reaction suggesting sensitivity occurs, use of the medication should be discontinued.

To help limit skin irritation, patients must

- wash the treated skin gently, using a mild, non-medicated soap, and pat it dry, and
- avoid washing the treated skin too often or scrubbing it hard when washing.

Patients should apply a topical moisturizer if dryness is bothersome.

Exposure to Ultraviolet Light or Weather Extremes
Unprotected exposure to sunlight, including sunlamps (UV light) should be avoided or minimized during the use of Retin-A Micro and patients with sunburn should be advised not to use the product until fully recovered because of heightened susceptibility to sunlight as a result of the use of tretinoin. Patients who may be required to have extended periods of UV exposure (e.g., due to occupation or sports), or those with inherent sensitivity to the sun, or those using medications that cause photosensitivity, should exercise particular caution. Use of sunscreen products (SPF 15 or higher) and protective clothing over treated areas are recommended when exposure cannot be avoided *[see Nonclinical Toxicology]*.

Weather extremes, such as wind or cold, also may be irritating to tretinoin-treated skin.

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.

Clinical Trials in Subjects with Acne
In separate clinical trials for each concentration, acne subjects treated with Retin-A Micro (tretinoin) Gel microsphere, 0.1% or 0.04%, over the twelve-week period showed that cutaneous irritation scores for erythema, peeling, dryness, burning/stinging, or itching peaked during the initial two weeks of therapy, decreasing thereafter.

Approximately half of the subjects treated with Retin-A Micro, 0.04%, had cutaneous irritation at Week 2. Of those subjects who did experience cutaneous side effects, most had signs or symptoms that were mild in severity (severity was ranked on a 4-point ordinal scale: 0=none, 1=mild, 2=moderate, and 3=severe). Less than 10% of patients experienced moderate cutaneous irritation and there was no severe irritation at Week 2.

In trials of Retin-A Micro (tretinoin) Gel microsphere, 0.04%, throughout the treatment period the majority of subjects experienced some degree of irritation (mild, moderate, or severe) with 1% (2/225) of subjects having scores indicative of a severe irritation; 1.3% (3/225) of subjects treated with Retin-A Micro (tretinoin) Gel microsphere, 0.04%, discontinued treatment due to irritation, which included dryness in one patient and peeling and urticaria in another.

In trials of Retin-A Micro (tretinoin) Gel microsphere, 0.1%, no more than 3% of subjects had cutaneous irritation scores indicative of severe irritation; 6% (14/224) of subjects treated with Retin-A Micro (tretinoin) Gel microsphere, 0.1%, discontinued treatment due to irritation. Of these 14 subjects, four had severe irritation after 3 to 5 days of treatment, with blistering in one subject.

In a double-blind trial with 156 acne subjects comparing 12 weeks of treatment with Retin-A Micro (tretinoin) Gel, 0.04% or 0.1%, (78 subjects each group), the most frequently reported adverse events affected the skin and subcutaneous tissue (15.4% in the 0.04% group, and 20.5% in the 0.1% group). The most prevalent of the dermatologic adverse events in the 0.04% group was skin irritation (6.4%); and in the 0.1% group skin burning (7.7%), erythema (5.1%), skin irritation (3.8%), and dermatitis (3.8%). Most adverse events were of mild intensity (63.4%), and 34.4% were moderate. One subject in each group had adverse events characterized as severe, neither were dermatologic findings and neither was characterized as related to drug by the investigator.

Trials in Subjects without Acne
In a half-face comparison trial conducted for up to 14 days in women with sensitive skin, but without acne, Retin-A Micro (tretinoin) Gel microsphere, 0.1%, was statistically less irritating than tretinoin cream, 0.1%. In addition, a cumulative 21-day irritation evaluation in subjects with normal skin showed that Retin-A Micro (tretinoin) Gel microsphere, 0.1%, had a lower irritation profile than tretinoin cream, 0.1%. The clinical significance of these irritation studies for patients with acne is not established. Comparable effectiveness of Retin-A Micro (tretinoin) Gel microsphere, 0.1%, and tretinoin cream, 0.1%, has not been established. The lower irritancy of Retin-A Micro (tretinoin) Gel microsphere, 0.1%, in subjects without acne may be attributable to the properties of its vehicle. The contribution of decreased irritancy by the MICROSPONGE System has not been established. No irritation trials have been performed to compare Retin-A Micro (tretinoin) Gel microsphere, 0.04%, with either Retin-A Micro (tretinoin) Gel microsphere, 0.1%, or tretinoin cream, 0.1%.

Postmarketing Experience
The following adverse reactions have been identified during post-approval use of Retin-A Micro Gel. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Temporary hyper- or hypopigmentation has been reported with repeated application of tretinoin.

USE IN SPECIFIC POPULATIONS
Pregnancy
Pregnancy Category C

There are no adequate and well-controlled studies in pregnant women. Retin-A Micro should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Thirty human cases of temporally associated congenital malformations have been reported during two decades of clinical use of tretinoin products. Although no definite pattern of teratogenicity and no causal association has been established from these cases, five of the reports describe the rare birth defect category holoprosencephaly (defects associated with incomplete midline development of the forebrain). The significance of these spontaneous reports in terms of risk to the fetus is not known.

For purposes of comparison of the animal exposure to systemic human exposure, the MRHD applied topically is defined as 1 gram of Retin-A Micro (tretinoin) Gel microsphere, 0.1%, applied daily to a 60 kg person (0.017 mg tretinoin/kg body weight).

Pregnant rats were treated with Retin-A Micro (tretinoin) Gel microsphere, 0.1%, at daily dermal doses of 0.5 to 1.0 mg/kg/day tretinoin on gestation days 6-15. Alterations were seen in vertebrae and ribs of offspring at 5 to 10 times the MRHD based on the body surface area (BSA) comparison.

Pregnant New Zealand White rabbits were treated with Retin-A Micro (tretinoin) Gel microsphere, 0.1%, at daily dermal doses of 0.2, 0.5, and 1.0 mg/kg/day tretinoin on gestation days 7-19. Doses were administered topically for 24 hours a day while wearing Elizabethan collars to prevent ingestion of the drug. Increased incidences of certain alterations, including domed head and hydrocephaly, typical of retinoid-induced fetal malformations in this species, were observed at 0.5 and 1.0 mg/kg/day. Similar malformations were not observed at 0.2 mg/kg/day, 4 times the MRHD based on BSA comparison. Other pregnant rabbits exposed topically for six hours per day to 0.5 or 1.0 mg/kg/day tretinoin while restrained in stocks to prevent ingestion, did not show any malformations at doses up to 19 times (1.0 mg/kg/day) the MRHD based on BSA comparison, but fetal resorptions were increased at 0.5 mg/kg (10 times the MRHD based on BSA comparison).

Oral tretinoin has been shown to cause malformations in rats, mice, rabbits, hamsters, and nonhuman primates.

Tretinoin induced fetal malformations in Wistar rats when given orally at doses greater than 1 mg/kg/day (10 times the MRHD based on BSA comparison). In the cynomolgus monkey, fetal malformations were reported for doses of 10 mg/kg/day but none were observed at 5 mg/kg/day (95 times the MRHD based on BSA comparison), although increased skeletal variations were observed at all doses. Dose-related increases in embryolethality and abortion also were reported. Similar results have also been reported in pigtail macaques.

In oral peri- and postnatal development studies in rats with tretinoin, decreased survival of neonates and growth retardation were observed at doses in excess of 2 mg/kg/day (19 times the MRHD based on BSA comparison).

Nonteratogenic effects on fetus
Oral tretinoin has been shown to be fetotoxic in rats when administered at doses 24 times the MRHD based on BSA comparison.

Topical tretinoin has been shown to be fetotoxic in rabbits when administered at doses 10 times the MRHD based on BSA comparison.

Nursing Mothers
It is not known whether tretinoin and/or its metabolites are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Retin-A Micro is administered to a nursing woman.

Pediatric Use
Safety and effectiveness in children below the age of 12 have not been established.

Geriatric Use
Safety and effectiveness in a geriatric population have not been established. Clinical trials of Retin-A Micro (tretinoin) Gel microsphere, 0.1% and 0.04%, did not include sufficient numbers of subjects aged 65 and over to determine whether they responded differently from younger subjects.

OVERDOSAGE
Oral ingestion of large amounts of the drug may lead to the same side effects as those associated with excessive oral intake of Vitamin A.

NONCLINICAL TOXICOLOGY
Carcinogenesis, Mutagenesis, Impairment of Fertility
Dermal carcinogenicity testing has not been performed with Retin-A Micro (tretinoin) Gel microsphere, 0.1%, 0.08%, 0.06% or 0.04%.

In a 91-week dermal study in which CD-1 mice were administered 0.017% and 0.035% formulations of tretinoin, cutaneous squamous cell carcinomas and papillomas in the treatment area were observed in some female mice. These concentrations are near the tretinoin concentration of the 0.04% and 0.1% clinical formulations. A dose-related incidence of liver tumors in male mice was observed at those same doses. The maximum systemic doses associated with the administered 0.017% and 0.035% formulations are 0.5 and 1.0 mg/kg/day tretinoin, respectively. These doses are two and four times the MRHD based on BSA comparison.

The biological significance of these findings is not clear because they occurred at doses that exceeded the dermal maximally tolerated dose of tretinoin and because they were within the background natural occurrence rate for these tumors in this strain of mice.

There was no evidence of carcinogenic potential when 0.025 mg/kg/day of tretinoin was administered topically to mice (0.1 times the MRHD based on BSA comparison). Studies in hairless albino mice suggest that concurrent exposure to tretinoin may enhance the tumorigenic potential of carcinogenic doses of UVB and UVA light from a solar simulator. This effect has been confirmed in a later study in pigmented mice, and dark pigmentation did not overcome the enhancement of photocarcinogenesis by 0.05% tretinoin. Although the significance of these studies to humans is not clear, patients should minimize exposure to sunlight or artificial ultraviolet irradiation sources *[see Warnings and Precautions]*.

The genotoxic potential of tretinoin was evaluated in the Ames assay and in the in vivo mouse micronucleus assay, both of which were negative.

The components of the microspheres have shown potential for genetic toxicity and fetal malformation. EGDMA, a component of the excipient acrylates copolymer, was positive for induction of structural chromosomal aberrations in the in vitro chromosomal aberration assay in mammalian cells in the absence of metabolic activation, and negative for genetic toxicity in the Ames assay, and the in vivo mouse micronucleus assay.

In oral fertility studies in rats with tretinoin, the no-observable effect level was 2 mg/kg/day (19 times the MRHD based on BSA comparison).

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

Manufactured for:
Valeant Pharmaceuticals North America LLC
Bridgewater, NJ 08807 USA

By:
Valeant Pharmaceuticals International, Inc.
Laval, Quebec H7L 4A8, Canada

Based on 9612500 October 2017 RAM.0025.USA.17

RETIN-A MICRO 0.06%

HOW MANY MORE FACES ***CAN YOU REACH?***

MORE PATIENTS THAN EVER. RETIN-A MICRO 0.06% gives you more treatment options for your patients, with microsphere technology and pump-controlled dosing.[1]

SEE TOLERABILITY AND EFFICACY RESULTS AT **RETINAMICRO.COM**

INDICATION

RETIN-A MICRO (tretinoin gel) microsphere is indicated for topical application in the treatment of acne vulgaris.

IMPORTANT SAFETY INFORMATION

- The skin of certain individuals may become excessively dry, red, swollen or blistered during the use of RETIN-A MICRO.
- Tretinoin has been reported to cause severe irritation on eczematous skin and should be used with utmost caution in patients with this condition.
- If warranted, patients should temporarily reduce the amount or frequency of application, or discontinue use temporarily or altogether. If a reaction suggesting sensitivity occurs, use should be discontinued.
- Unprotected exposure to sunlight, including sunlamps, should be minimized during the use of RETIN-A MICRO, and patients with sunburn should be advised not to use the product until fully recovered because of heightened susceptibility to sunlight with the use of tretinoin.
- Patients should be encouraged to use a sunscreen with a SPF of 15 or higher and protective clothing over treated areas when exposure cannot be avoided.
- Weather extremes, such as wind or cold, also may be irritating to patients under treatment with tretinoin.
- The most common adverse events are mild to moderate irritation (erythema, peeling, dryness, burning/stinging, or itching of the skin).
- RETIN-A MICRO should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus, and caution should be exercised in prescribing for nursing mothers. Safety and efficacy in patients under 12 have not been established.

To report SUSPECTED ADVERSE REACTIONS, contact Ortho Dermatologics at 1-800-321-4576 or FDA at 1-800-FDA-1088 or visit www.fda.gov/medwatch.

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

Reference: 1. Retin-A Micro Gel Package Insert. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC.

Ortho | Dermatologics

RETIN-A MICRO®
(tretinoin) Gel microsphere
0.06% / 0.08%