

The New Jersey
JOURNAL of Pharmacy

New Jersey Pharmacists Association

Summer 2015 • Volume LXXXIX • Number 3

**RETAIL • COMMUNITY • COMPOUNDING • HEALTH SYSTEM
DISASTER MANAGEMENT • CONSULTANT • INDUSTRY • ACADEMIA
PHARMACY TECHNICIANS**



Peer Reviewed

DON'T GET CUFFED BY PRIME VENDOR AGREEMENTS!



In a business that is as fast changing as Independent Pharmacy do you really think signing a multi-year Prime Vendor Agreement makes sense?

At RDC we understand your business and your need for a flexible partnership! And we never charge for deliveries.

BEFORE YOU SIGN, CALL US!



800.333.0538 | www.rdcdrug.com

The New Jersey Pharmacists Association

OFFICERS & TRUSTEES 2014-2015

President	Moriah Weissman, PharmD, CCP	
		<i>Region 2</i>
First Vice President	Ruth Marietta, RPh, CCP	
		<i>Region 4</i>
Second Vice President	Ronald Mannino, RPh	
		<i>Region 1</i>
Treasurer	John Colaizzi, Jr., PharmD, CCP	
		<i>Region 1</i>
Chair of the Board	Carrie Corboy, PharmD, CCP	
		<i>Region 3</i>
President Emeritus	Donald Wernik, RPh	
		<i>Region 3</i>

BOARD OF TRUSTEES

Region One	Salvatore Peritore, RPh	2015
	Louis Spinelli, RPh (A)	2015
Region Two	Sandy Fishman, RPh	2015
	Eileen Fishman, RPh (A)	2015
Region Three	Steven Gooen, RPh	2015
	Carmela Silvestri, RPh (A)	2015
Region Four	Tony Qi, PharmD	2017
	Sandra Moore, PharmD (A)	2016
Region Five	Mark Taylor, RPh	2015
	Vacant (A)	2015
Region Six	Azuka Obianwu, RPh	2015
	Vacant (A)	2015
Academy of Compounding Pharmacists	Shara Rudner, RPh	
Academy of Consultant Pharmacists	Steven Zlotnick, PharmD	
Student Trustee	Rutgers: FDU: Jaquan Williams (A)	2015

STAFF

Chief Exec. Officer	Elise M. Barry, MS, CFRE
Program, Meeting and Event Coordinator	Fiona Romaine
Communications and Content Management Associate	Lisa Sarachman
Publisher	Elise M. Barry
Co-Editors	Maria Leibfried, PharmD; Marcella R. Brown, PharmD

Legislative Counsel	Laurie Clark
---------------------	--------------

The New Jersey Journal of Pharmacy (ISSN0028-5773 USPS #380-360) is published seasonally by the NJ Pharmacists Association
782 Alexander Road, PO Box 1
Princeton, NJ 08543-0001
609-275-4246 Fax 609-275-4066
www.njpharmacists.org

Periodicals Postage Paid at Princeton, NJ and additional mailing offices. Subscriptions paid for through allocation of membership dues. US Subscription \$50 per year; Foreign Rate \$100 per year.

POSTMASTER: Send address changes to The New Jersey Journal of Pharmacy, 760 Alexander Rd., PO Box 1, Princeton, NJ 08543-0001. 609-275-4246. www.njpharma.org

Advertising Rates Upon Request. The acceptance of advertising in this publication does not constitute or imply endorsement by NJPhA or any advertised product or service.

Byline articles, features and columns express the views of the authors and do not necessarily reflect Association policy or opinion.

Table of Contents

- 4** President's Letter
- 4** Message from the Convention Chair
- 5** Message from the BOT Chairman
- 5** From The Editors' Desks
- 6** Cosentyx™: A Novel Approach to the Treatment of Psoriasis
- 8** New Drug Update: Prestalia® (amlodipine besylate/perindopril arginine)
- 10** The Role of Probiotic Supplements in the Prevention and Treatment of Atopic Dermatitis
- 14** Continuing Education:
Biologic Response Modifiers Used in the Treatment of Plaque Psoriasis
- 24** Continuing Education:
Vitamin D Deficiency and Treatment
- 32** Practice Spotlight: Senior Medical Writer at Maxcess Managed Markets

Mission Statement:

To advance the profession of pharmacy, enabling our members to provide optimal care to those they serve.

President's Letter

One Profession, One Voice.

Hi Everyone! Here we are again; another summer as passed and the Annual Meeting and Convention is upon us. We have made great strides for our profession this year and I am proud of each and every one of us for standing up and supporting pharmacists in New Jersey. Our educational programs and +TONIC Rx social events have been in full swing – including Shakespeare in the Park and a night out at Hopewell Vineyards. If you couldn't make any so far, don't worry there will be plenty of more in the future. Great things are happening and it takes YOU to make them amazing!

I'm looking forward to seeing everyone in Atlantic City for Convention in just a few weeks! We have a great line-up for

educational and social events, dinner programs, the third annual poster session, student programming and networking.

Remember, NJPhA is the only organization that lobbies on behalf of ALL pharmacists in the State of New Jersey – spread the word, tell your friends!

Let's continue making strides for our profession!

Moriah J. Weissman, PharmD, CCP
NJPhA President

Message from the Convention Chair

FINDING BALANCE...Past, Present, Future

It's getting close to the 145th year of our annual convention on October 16-18, 2015 at Harrah's in Atlantic City! This will be an exciting time as we will honor NJPhA past presidents, how they shaped our profession, where we stand today and how we move forward.

There's still time to register for convention. The committee and office have planned fun-filled activities and educational events for students, interns, and pharmacists who practice in all areas. Also, working with the folks at Harrah's, I am confident you will walk away with a positive experience. I am so honored to work with dedicated and talented professionals!

On-site registration will open late Friday morning, starting with certificate programs at Noon. Our regional presidents and committee round table meetings will be held in the afternoon. All members are welcome to get more involved by attending the roundtable sessions in their region or by getting more involved in a committee! This is an excellent way to learn more about behind the scenes in what we do. The day will finish off with a relaxing cocktail reception.

Informative continuing education, certificate programs and networking events await you on Saturday and Sunday. Our student track is held Saturday, too! Our exhibitors will be engaged in a fun-filled theme 'Under the Boardwalk' on Saturday night. This will include reception, games, prizes, historical exhibits as we dance the evening away.

On Sunday, exhibits, CE & certificate programming follow breakfast. Don't forget to check out Michael Cohen from ISMP who is our keynote speaker this year! After installation luncheon and awards presentation we will have an educational law program and wrap up.

On behalf of NJPhA leadership, I encourage you to come celebrate our past leaders, contribute in meetings, obtain credits and, have fun... as we find balance.

Professionally yours,
Ruth Marietta, RPH, CCP
2015 Convention Chair

Message from the BOT Chairman

Dear NJPhA Members,

Not only has the last year flown by, bringing an end to my time as NJPhA Board Chair, my election to NJPhA 2nd Vice President 5 years ago seems like yesterday.

It has been a privilege to serve with the amazing colleagues that make up the Board of Trustees, Regional Officers, Committee Chairs and my fellow Line Officers. I also continue to be impressed by what our CEO and small office staff achieve every day. Thank you for giving me this experience and the friendships that go with it.

I wish everyone tremendous success in the coming year, starting with our 2015 Convention at Harrah's Atlantic City and the newly updated Atlantic City Convention Center. Please join us for excellent programming and an exciting new venue. Then, considering joining us in a new way...becoming more active through committees, region or state roles is tremendously rewarding. Speaking from experience, you will be glad you did.

Kind regards,
Carrie Corboy, RPh, PharmD, CCP

From The Editors' Desk...

Dear Colleagues,

I hope the Labor Day weekend was great, as summer of 2015 becomes a memory! *The NJ Journal of Pharmacy* – the official peer-reviewed journal of the NJ Pharmacists Association is pleased to provide an issue dedicated to dermatological pharmacy. This issue will focus on two modalities for the treatment of psoriasis. One is a novel drug, secukinumab; the other is a discussion on biologic response modifiers. You can earn continuing education by completing and submitting the Ohio CE which focuses on Vitamin D and deficiencies or a free CE which reviews Newborn Skin Care. Our community pharmacy spotlight is on a pharmacist's daily involvement in medical writing.

While the theme of this issue is dermatology, we feel it's important to include a new combination cardiovascular medication, Pres-talia®, to ensure that everyone is empowered with information for effective patient consultation and care. As always, please con-

sider becoming active in the development of the *NJ Journal of Pharmacy*, through either submission of an article, or becoming a peer-reviewer. If interested please reach out to me, Maria Leibfried, Elise Barry, or one of the NJPhA officers. You may email ideas and submissions to leibfried2@hotmail.com or marcella.r.brown@gmail.com. We can help you with a topic consideration for the journal.

I look forward to meeting you at the Convention in October!

Happy reading!

Marcella R Brown, BS, MS, PharmD, MPH, CGP,BCACP
Maria Leibfried, BS, PharmD, BCNSP, CCP
Co-editors

Cosentyx™: A Novel Approach to the Treatment of Psoriasis

By: Ahmed Elabbasy, PharmD Candidate; William Maidhof, PharmD

Introduction

Psoriasis is a chronic inflammatory skin condition that affects approximately 3% of the United States population.^{1,2} It is an autoimmune disorder that results in an accelerated skin cell turnover rate. In healthy patients the process of skin cell turnover takes approximately one month, with cells forming far below the surface of the skin and gradually moving towards its surface. In patients with psoriasis the turnover process is quicker and may take only days, resulting in an accumulation of cells at the skin's surface. This accumulation of cells is what leads to red, irritated skin patches. Considering the undesirable appearance of the affected skin in addition to possible limitations on daily activities due to joint pain, psoriasis is a skin condition that can have a profoundly negative effect on an individual's quality of life.

Although no cure for psoriasis exists, a variety of medications are currently approved to treat the condition. Treatment is patient-specific and severity-dependent. Some of the most important goals of treatment are to minimize signs of the condition such as itching and scaling, reduce the frequency of flare-ups, decrease the potential for medication-related adverse effects, and provide patient education with an empathetic and supportive attitude. Existing treatment options include topical therapies (i.e.: corticosteroids), phototherapy, systemic therapies (i.e.: acitretin, methotrexate), and biologic response modifiers (i.e.: etanercept).³

On January 21st 2015, the United States Food and Drug Administration (FDA) approved Cosentyx, the marketed name for secukinumab, as a novel option for the treatment for psoriasis. It is indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy. Secukinumab is the first IL-17A inhibitor to be approved by the FDA.

Pharmacology and Pharmacokinetics

Because of its documented effect on keratinocytes and subsequent activation of various inflammatory processes, Interleukin 17 (IL-17) is an interesting target for drug therapy in treating plaque psoriasis. Secukinumab is a human IgG 1 monoclonal antibody that selectively binds to the interleukin-17A cytokine (IL-17A), inhibiting its interaction with the IL-17 receptor. IL-17A cytokine is a known cytokine that is involved in inflammation and immune responses. Elevated levels of IL-17A are found in psoriatic plaques. Thus, by inhibiting the IL-17 receptor, secukinumab inhibits the activation of proinflammatory processes and reduces the severity of the disorder.^{4,5}

Secukinumab is given via the subcutaneous route (*intravenous administration is not recommended*) and has a bioavailability ranging from 55% to 77% in healthy patients and those with the condition. Steady-state plasma levels are achieved at week 24 of treatment (using an "every 4 week" dosing schedule). The mean

volume of secukinumab distribution during the terminal phase following a single *intravenous* administration ranged from 7.1 to 8.6 L in plaque psoriasis patients. Secukinumab's mean systemic clearance ranged from 0.14 to 0.22 L/day and its half-life ranged between 22 and 31 days in plaque psoriasis patients following subcutaneous and *intravenous* administration during all drug trials. Patients aged 65 years of age or older demonstrated no significant difference in drug clearance compared to patients less than 65 years of age. A trial has yet to be conducted that examines the effect of hepatic or renal impairment on the pharmacokinetics of secukinumab.⁵

Clinical Trials

Secukinumab (Cosentyx) was approved by the FDA in January 2015 based on its documented safety and effectiveness in four phase III clinical trials. A total of 2403 participants with plaque psoriasis who were candidates for systemic therapy or phototherapy were enrolled in the studies. All trials were multi-centered, randomized, double-blind, and placebo-controlled. The first (ERASURE: Efficacy of Response and Safety of Two Fixed Secukinumab Regimens in Psoriasis) and second (FIXTURE: Full Year Investigative Examination of Secukinumab vs. Etanercept Using Two Dosing Regimens to Determine Efficacy in Psoriasis) trials were 52 weeks in duration. The third and fourth trials, both 12 weeks in duration, examined the safety, benefit, and usability of self-administered secukinumab versus placebo. Trial 3 utilized prefilled syringes and Trial 4 utilized autoinjectors. With the exception of the FIXTURE trial that had a fourth study arm (the fourth arm received etanercept), all four trials had the following groups: a 300mg per dose secukinumab group, a 150mg per dose secukinumab group, and a placebo group. Co-primary endpoints for all trials were a greater percentage of patients reaching a 75% or higher improvement from baseline in their Psoriasis Area and Severity Index score (PASI 75), as well as the percentage of patients reporting a score of "0" (clear) or "1" (almost clear) on a 5-point modified investigator's global assessment tool for psoriasis.^{5,6}

In both the ERASURE and FIXTURE trials, secukinumab at a dose of either 150mg or 300mg (compared to placebo in the ERASURE trial and both placebo and etanercept in the FIXTURE trial) yielded a higher percentage of patients reaching PASI 75. In both trials a higher percentage of patients also reported a score of "0" (clear) or "1" (almost clear) on a 5-point modified investigator's global assessment tool. Trials 3 and 4, although shorter in duration, produced similar co-primary endpoint results compared to ERASURE and FIXTURE. At week 12 of trials 3 and 4, secukinumab administered at a dose of 150mg or 300mg (compared to placebo) generated a higher percentage of patients reaching PASI 75 as well as a higher percentage of patients reporting a score of "0" (clear) or "1" (almost clear) on the 5-point modified investigator's global assessment tool.^{5,6}

In addition to the aforementioned studies, two trials have recently been published to further evaluate the effectiveness of secukinumab in treating moderate to severe plaque psoriasis. The SCULPTURE trial investigated a “fixed interval” versus “as-needed” secukinumab maintenance dosing schedule, while the CLEAR study sought to compare long-term efficacy, safety, and tolerability of secukinumab compared to ustekinumab.^{7,8}

Recommended Dosage and Administration and Product Availability

Secukinumab is available in injectable form. The standard dosing is 300mg (two 150mg injections) administered by the subcutaneous route at weeks 0, 1, 2, 3, 4, and then 300mg every 4 weeks thereafter. In certain patients, a dose of 150mg may be acceptable.⁵

Secukinumab is commercially available as a single-use Sensoready pen, a single-use prefilled syringe, and a lyophilized powder. Secukinumab is available as a 150mg/mL solution for both the Sensoready pen and the prefilled syringe, which can both be dispensed to patients for self-administration following education. Individuals requiring a 300mg dose would inject the contents of either two Sensoready pens or prefilled syringes. The recommended sites of administration for both the Sensoready pen and prefilled syringe are the front of the thighs (upper legs), abdomen (not the area two inches around the navel), and outer upper arm (by caregivers only). For both the Sensoready pen and the prefilled syringe the solution should be a clear to slightly yellow color. The difference between the Sensoready pen and the prefilled syringe is the mechanism by which the medication is administered. The Sensoready pen is designed so the patient can press the pen firmly against their skin and listen for a series of “clicks” to alert them the auto-injection process is complete, while the prefilled syringe is the traditional syringe where the patient pushes on a plunger. Available for healthcare professional use only, secukinumab is also available as a 150 mg lyophilized powder in a single-use vial for reconstitution.⁵

Patient access to secukinumab is limited, as it is available only through the manufacturer or a designated specialty pharmacy. Patients must receive training on injection technique prior to self-administering the drug at home. The manufacturer created a patient support and education program called the Cosentyx Connect Personal Support Program. The program offers many advantages such as a liaison that assists throughout the process, potential cost assistance, additional device training, and possibly a no-cost initial supply of the medication.⁹

Pharmacists dispensing Cosentyx must always dispense the drug with the product’s accompanying medication guide.

Adverse drug Reactions/Warnings

Adverse drug reactions reported during the clinical trials (greater than 1% of subjects with plaque psoriasis) were nasopharyngitis, diarrhea, upper respiratory tract infection, rhinitis, oral herpes, pharyngitis, urticaria, and rhinorrhea. Adverse reactions such as oral candidiasis, tonsillitis, sinusitis, otitis media and externa, and tinea pedis occurred in less than 1% of subjects with plaque psoriasis. As a result of secukinumab’s mechanism of action, warnings are documented for increased infection risk, exacerbation of Crohn’s Disease, and risk of hypersensitivity reactions. A

warning also exists for latex-allergic patients as the caps for both the Sensoready pen and prefilled syringe contain natural rubber latex (the safety of the both has not been studied in latex-allergic individuals).⁵

About the Authors

Ahmed Elabbasy, PharmD Candidate

William Maidhof, PharmD *corresponding author

St. John’s University College of Pharmacy & Health Sciences

Associate Professor-Industry Professional

Dept of Clinical Health Professions

St. Albert Hall 114

8000 Utopia Pkwy

Queens, NY 11456

718-990-5275 maidhofw@stjohns.edu

References:

¹Cather J, Crowley J. Use of Biologic Agents in Combination with Other Therapies for the Treatment of Psoriasis. Am J Clin Dermatol. 2014;15:467-478.

²Rachakonda TD, Schupp CW, Armstrong AW. Psoriasis prevalence among adults in the United States. J Am Acad Dermatol. 2014;70:512-516.

³Law R, Gulliver W. Psoriasis. In: DiPiro J, Talbert R, Yee G, Matzke G, Wells B, Posey LM, ed. *Pharmacotherapy: A Pathophysiological Approach*. 9th Edition. New York, NY: McGraw-Hill Education; 2014:1579-1594.

⁴Gooderham M, Posso-De Los Rios C, Rubio-Gomez G, Papp K. Interleukin-17 (IL-17) Inhibitors in the Treatment of Plaque Psoriasis: A Review. Skin Therapy Lett. 2015 Jan-Feb;20(1):1-5.

⁵Cosentyx Prescribing Information. Available at: <http://www.pharma.us.novartis.com/product/pi/pdf/cosentyx.pdf>

⁶Langley R, Boni E, Lebwohl M, et al. Secukinumab in Plaque Psoriasis – Results of Two Phase 3 Trials. N Eng J Med. 2014; 371:326-338.

⁷Mroweitz U, Leonardi CL, Girolomoni G, et al. Secukinumab retreatment-as-needed versus fixed-interval maintenance regimen for moderate to severe plaque psoriasis: A randomized, double-blind, noninferiority trial (SCULPTURE). J Am Acad Dermatol. 2015;73(1):27-36.

⁸Thaci D, Blauvelt A, Reich K, et.al. Secukinumab is superior to ustekinumab in clearing skin of subjects with moderate to severe plaque psoriasis: CLEAR, a randomized controlled trial. J Am Acad Dermatol. 2015;73(3):400-409.

⁹Cosentyx Connect Personal Support Program. Available at: <http://www.cosentyx.com/info/support-program.jsp>



New Drug Update: Prestalia® (amlodipine besylate/perindopril arginine)

By: Sara Hammad, Pharm.D.
PGY-2 Solid Organ Transplantation Pharmacy Resident

Hypertension (HTN) remains one of the leading causes of death, affecting approximately 78 million people in the United States¹⁻². Treating HTN can reduce the risk of stroke, coronary heart disease, and mortality³. Available antihypertensive agents include thiazide diuretics, calcium channel blockers (CCBs), angiotensin converting enzyme inhibitors (ACE-Is), angiotensin receptor blockers (ARBs), and beta blockers (BBs)⁴. Evidence has shown that, on average, at least 2 medications are needed to achieve blood pressure (BP) goals, although there remains a lack of randomized controlled trials comparing initiation of monotherapy versus combination therapy⁴⁻⁵. The Eighth National Joint Committee (JNC8) Guidelines outline different HTN management strategies, including initiating monotherapy and titrating to maximum dose before adding a second medication; initiating monotherapy and adding a second medication before achieving maximum dose of the first medication; or initiating 2 medications (as separate pills or single-pill combinations) (Grade E)⁴. One retrospective study of 106,621 hypertensive patients concluded that initial therapy with single-pill combinations provided better BP control in the first year than free combinations or monotherapy (HR 1.53, 95% CI 1.47-1.58 vs. 1.34, 95% CI 1.31-1.37, reference, respectively); however, patient adherence was not assessed⁶. Although there are single-pill combination antihypertensive medications available, such as Lotrel® (amlodipine/benazepril), which received FDA approval in 1995, new combination medications continue to receive FDA approval. This article will provide a review Prestalia® (amlodipine besylate/perindopril arginine), a new single-pill combination antihypertensive medication.

Amlodipine/perindopril received FDA approval on January 21, 2015 for the initial treatment of HTN in patients likely to need multiple medications, or for patients not controlled on monotherapy⁷. This medication consists of a dihydropyridine CCB (amlodipine) and an ACE-I (perindopril). Per JNC8, thiazide diuretics, CCBs, ACE-Is, or ARBs are recommended as initial therapy in the nonblack population (Grade B), while CCBs or thiazide diuretics are recommended as first line in the general black population (Grade B)⁴, providing a possible place in therapy for amlodipine/perindopril.

Amlodipine inhibits the influx of calcium ions in the vascular smooth muscle, which results in peripheral arterial vasodilation, decreasing peripheral vascular resistance and reducing BP. Perindopril is a pro-drug that is hydrolyzed to the active metabolite perindoprilat. Perindoprilat prevents the conversion from angiotensin I to angiotensin II (a potent vasoconstrictor) thereby decreasing BP, increasing plasma renin activity, and decreasing aldosterone secretion⁷.

Amlodipine/perindopril is an oral medication dosed once daily. Peak plasma concentrations for amlodipine and perindopril occur at about 6-12 hours and 1 hour, respectively, with a terminal elimination half-life of approximately 30-50 hours and 100

hours, respectively. Perindopril is hydrolyzed by hepatic esterases and has 6 metabolites. Amlodipine is extensively metabolized by the liver (about 90%) and is excreted as 10% unchanged drug in urine. This medication is not recommended in patients with a creatinine clearance of < 60 mL/min, as it has not been studied in this patient population⁷.

Perindopril can lead to an increased risk of hyperkalemia if given with other agents that affect the renin-angiotensin system and potassium-sparing diuretics. Additionally, perindopril can increase serum lithium levels. Co-administration of perindopril and non-steroidal anti-inflammatory agents (NSAIDs) may lead to acute renal failure, although these effects are usually reversible. Amlodipine is metabolized primarily hepatically and is a weak CYP3A4 inhibitor, causing interactions with other CYP3A4 substrates and inhibitors. An example of this interaction is seen with the co-administration of amlodipine and simvastatin (also metabolized through CYP3A4), which results in a 77% increase in exposure to simvastatin. Patients therefore should not take more than 20 mg of simvastatin while on amlodipine⁷.

Amlodipine/perindopril was compared to a BB and low dose thiazide diuretic in the ASCOT-BPLA trial. This randomized trial included over 19,000 adult hypertensive patients (untreated HTN defined as a SBP of \geq 160 mm Hg, a DBP of \geq 100 mm Hg, or both, and treated HTN defined as a SBP of \geq 140 mm Hg, a DBP of \geq 90 mm Hg, or both) with at least 3 other common cardiovascular risk factors. The trial was stopped early after a median follow-up period of 5.5 years because amlodipine/perindopril showed a significant all-cause mortality benefit compared to the BB/thiazide diuretic group (HR 0.89, 95% CI 0.81-0.99, p=0.025). Although the results for the primary endpoint of development of a nonfatal myocardial infarction were not significant (unadjusted HR 0.90, 95% CI 0.79-1.02, p=0.1052), there were significantly less fatal and non-fatal strokes (HR 0.77, 95% CI 0.66-0.89, p=0.0003), and total cardiovascular events and procedures (HR 0.84, 95% CI 0.78-0.90, p<0.0001)⁸.

In a more recent randomized trial including 837 hypertensive adults at 59 centers, amlodipine/perindopril was compared to amlodipine and perindopril individually, with a primary endpoint of the change in mean seated diastolic BP (DBP) from baseline to day 42. The combination resulted in a significantly larger change in seated BP (-23.7/-15.7 mmHg) vs. perindopril (-13.7/-9.5 mmHg) and amlodipine (-19.3/-13.2 mmHg) (p<0.0001), and a higher proportion of patients at goal BP (51% vs. 26% vs. 37%, respectively; p<0.0001). Patients in the combination group also experienced less pedal edema and adverse events compared to the amlodipine group. The study authors, however, had a large exclusion criteria, such as night shift workers, a baseline seated mean systolic BP (SBP) \geq 180 mm Hg, ischemic heart disease, heart failure, significant cardiac dysrhythmias, chronic kidney disease

stage ≥ 3, major surgery in the prior 3 months, cancer in the prior 5 months (excluding squamous skin cancers), or major psychiatric disorders⁹.

Amlodipine/perindopril is a newly approved antihypertensive combination medication that has proven to be superior in BP lowering when compared to the individual agents used as monotherapy⁹. This combination has also been proven superior in BP lowering and all-cause mortality when compared to a BB and a thiazide diuretic regimen⁸. Data shows that this medication has little side effects, and can even have a synergistic action on pedal edema. While amlodipine/perindopril is not recommended in patients with renal dysfunction, it can potentially be used first line in patients who can tolerate a CCB and an ACE-I and likely need more than one agent to control their BP.

About the Author

Sara Hammad, Pharm.D.

PGY-2 Solid Organ Transplantation Pharmacy Resident

NewYork-Presbyterian Hospital

622 West 168th Street, VC-B

New York, NY 10032

(646) 317-6347

sah9106@nyp.org

References

¹Ezzati M, Lopez AD, Rodgers A, et al. Selected major risk factors and global and regional burden of disease. *Lancet*. 2002;360(9343):1347-60.

²Go AS, Mozaffarian D, Roger VL, et al on behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2014 update: a report from the American Heart Association. *Circulation*. 2014;129(3):e28-e292.

³Wang TJ, Vasan RS. Epidemiology of uncontrolled hypertension in the United States. *Circulation*. 2005;112:1651-62.

⁴James PA, Oparil S, Carter BL, et al. 2014 Evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the eighth joint national committee (JNC 8). *JAMA*. 2014;311(5):507-520.

⁵Poulter NR. A new dimension in hypertension management with the amlodipine/perindopril combination. *Journal of Hypertension*. 2011;29(suppl 1):S15-21.

⁶Egan BM, Bandyopadhyay D, Shaftman SR, et al. Initial monotherapy and combination therapy and hypertension control the first year. *Hypertension*. 2012;59:1124-31.

⁷Prestalia [package insert]. Cincinnati OH: Symplmed LLC. January 2015.

⁸Dahlof B, Server PS, Poulter NR, et al. Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA): a multicentre randomised controlled trial. *Lancet*. 2005;366(9489):895-906.

⁹Elliott WJ, Whitmore J, Feldstein JD, et al. Efficacy and safety of perindopril arginine + amlodipine in hypertension. *Journal of the American Society of Hypertension*. 2015;9(4): 266-274.

Don't leave money on the table when you transition the ownership of your business.

Do you know the three most common mistakes that pharmacy owners make when contemplating the sale of their pharmacy?

To learn what they are, and to learn much more about the services we provide for independent pharmacy owners thinking about ownership transition and/or retirement, visit our web site, www.buy-sellapharmacy.com. Click on the button on the home page that says "Pharmacy Owner's Questions" or call your local Buy-Sell Associate directly at any time. By doing so, you will have the opportunity to earn a \$100.00 GIFT of valuable marketing materials for use in your pharmacy.



Your Local Specialist

Jim Beatty, R.Ph.

jimb@buy-sellapharmacy.com

Tel: 1-(732)-563-0295

Completely
confidential!

 **Buy-Sellapharmacy.com®**

1-(877)-360-0095

www.buy-sellapharmacy.com

"Our 15 year track record of successfully completing more than 400 independent pharmacy sales speaks for itself."

The Role of Probiotic Supplements in the Prevention and Treatment of Atopic Dermatitis

By: Celia Lu, Pharm.D, BCACP and Jacqueline Chirico, Candidate

Introduction

With the rising interest in probiotics from patients, pharmacists have the opportunity to serve as a resource to ensure safe and effective use of probiotics. Probiotics are available not only in food products, but also as dietary supplements containing species such as the *Lactobacillus* and *Bifidobacterium* species or the yeast *Saccharomyces cerevisiae*. According to the International Scientific Association for Probiotics and Prebiotics, probiotics are defined as “live microorganisms that confer a health benefit on the host when administered in adequate amounts”. Probiotics are believed to exert its positive effects on the immune system and gastrointestinal health by promoting the growth of beneficial bacteria that live endogenously in the intestine as well as competitively inhibiting bacteria that can harm the human host.¹ Due to these effects, probiotics may play a role in the management of inflammatory diseases associated with abnormalities in the intestinal flora. For instance, adhesion of the *Bifidobacterium* species to the intestinal mucosal have shown to be reduced among infants with allergic conditions compared to healthy infants.² Although probiotics have been shown to improve symptoms of gastrointestinal disorders such as inflammatory bowel disease,^{3,4} the role of probiotics in atopic dermatitis (AD) is uncertain. For example, a randomized controlled trial from Australia demonstrated an improvement in the severity of AD among infants with moderate to severe AD after administration of *Lactobacillus fermentum* for 8 weeks.⁵ However, another randomized controlled trial in Germany found no statistical difference in symptoms after administration of *Lactobacillus rhamnosus* for 8 weeks compared to placebo among infants with moderate to severe AD.⁶ This article describes current data that is available regarding the use of probiotics in the prevention and treatment of AD.

Overview of AD

Atopic dermatitis, also known as atopic eczema, is a chronic inflammatory skin disease that is characterized by pruritic, erythematous, and scaly skin lesion as well as xerosis (dry skin). It is part of the allergic triad, alongside asthma and allergic rhinitis. AD generally occurs before two years of age, but it can still develop in adolescents and adults.⁷ The pathophysiology of atopic dermatitis is complex and still not fully understood. It is believed that a combination of genetics, immunologic factors, and host environment abnormalities are involved in the development of the disease. In general, atopic dermatitis is a familial transmitted disease that is strongly influenced through the maternal side. Due to the complexity of the disease, genetics alone aren't sufficient to explain the pathology. Most patients with atopic dermatitis have an immunologic component involved, usually seen as increased blood eosinophils and increased serum IgE. Patients also have reduced levels of interferon γ , an immunoregulator that is involved in inhibiting the production of IgE and Th2-mediated inflammation.⁸ Skin barrier abnormality is another mechanism involved in the development of atopic dermatitis. The primary function of the

skin is to prevent the loss of excess water, while preventing the entry of irritants, allergens, and pathogens. Loss of function mutations in FLG, which encodes filaggrin, has been implicated in up to 50% of patients with moderate to severe atopic dermatitis. The protein filaggrin is important in the structure and formation of the outer layer of skin, known as the stratum corneum. Inadequate filaggrin production reduces the skin's ability to retain water and prevent water loss. Furthermore, inadequate skin barrier can result in the passage of allergens into the skin, causing an inflammatory response that is heightened in patients with atopic dermatitis. This leads to dry skin and itching, which results in a rash that is characteristic of the disease.⁹

The American Academy of Dermatology recommends some evidence-based non-pharmacologic and pharmacologic treatment options for patients that can help alleviate the symptoms of the disease as well as improve quality of life. Most non-pharmacologic treatments aim to treat xerosis. One of the most common ways is through the use of moisturizers. Moisturizers help the skin retain water, making them a main part of treatment for mild atopic dermatitis and an adjunctive treatment in moderate to severe cases. Patients should be encouraged to bathe frequently to keep the skin clean, though it is important for patients to use a moisturizer after they bathe to retain the moisture in their skin. Wet wraps are another option for patients who would like to use a non-pharmacologic treatment to control their atopic dermatitis.¹⁰ The mainstay of topical pharmacologic anti-inflammatory therapy for AD is the use of topical corticosteroids. Their efficacy has been demonstrated in many randomized controlled trials.¹¹ Another anti-inflammatory treatment that is available for atopic dermatitis is topical calcineurin inhibitors. These agents are used second line in therapy for short-term use in patients with atopic dermatitis who have failed other topical prescription options.¹⁰ They are used as a steroid-sparing option so they can help reduce the need for topical corticosteroids.¹² However, concerns with adverse effects may limit patients' use of these pharmacologic agents and prompt them to look for alternative therapies such as probiotics. Currently, the American Academy of Dermatology does not recommend the use of probiotics in the treatment of AD due to the lack of evidence supporting its use.¹³ This article reviews the evidence available evaluating the use of probiotics in the prevention and treatment of AD.

Probiotics & Primary Prevention of AD

A meta-analysis was conducted by Pandura, et al. to determine the role of probiotics in primary prevention of atopic dermatitis. The meta-analysis included 16 randomized controlled trials from 1995 to 2013 that evaluated the occurrence of atopic dermatitis among infants with or without family history of atopic diseases, a risk factor for developing atopic dermatitis. Those in the intervention group received probiotics during pregnancy (prenatal

period) and/or after birth (postnatal period) via breast feeding or direct supplementation. Probiotics were administered for at least one month in the studies before delivery and/or up to 6-12 months after delivery, which included follow-up for at least one year. The probiotics studied in the intervention group included monotherapy with a single *Lactobacillus* strain (e.g. GG) as well as combination with other strains of the *Lactobacillus* species and/or *Bifidobacterium* species. Doses of the probiotics used ranged widely from 1×10^8 CFU to 9×10^9 CFU. Diagnosis of atopic dermatitis was determined by a physician.

The use of probiotics was shown to decrease the risk of developing atopic dermatitis (OR =0.64, CI=0.56-0.74, P<0.001). An analysis of the subgroups indicated that this was shown regardless of the infant's risk for developing atopic dermatitis. The result also applied for monotherapy with *Lactobacillus* or combination therapy with *Bifidobacterium*. However, this protection was only found among infants who received probiotics during both the prenatal and postnatal period (OR=0.61, CI=0.52-0.71, P<0.001), and not those who received probiotics only in the postnatal period (OR=0.95, CI=0.63-1.45, P=0.82). The investigators concluded that probiotics may provide protection against the development of atopic dermatitis regardless of family history when the probiotics are given during the final weeks of pregnancy and during the first few months of infancy. However, a limitation to the meta-analysis was the significant heterogeneity that was found among the studies.¹⁴

Probiotics & Treatment of AD

Kim, et al. conducted a meta-analysis to determine the effects of probiotics in the treatment of atopic dermatitis. Their meta-analysis included 25 randomized controlled trials that evaluated the change in the total SCORAD (Scoring of Atopic Dermatitis) score from baseline to post-treatment with at least one probiotic. The SCORAD assessment was used to evaluate the severity of the disease. The age groups that were studied included infants (<1 year of age), children (1-18 years of age), and adults (>18 years of age). The probiotics used for the treatment group consisted of monotherapy with strains from the *Lactobacillus* or *Bifidobacterium* species, or a mixture of both. Doses of the probiotics used also ranged from 1×10^{10} to 5×10^9 CFU twice daily.

Overall, those treated with probiotics showed an improvement in SCORAD scores that was statistically significant compared to placebo (Weighted Mean Difference or WMD -4.51, 95% CI -6.78 to -2.24, P<0.001). When the results were stratified by age group, the beneficial effect of the probiotic intervention was still statistically significant for children (WMD -5.74, 95% CI -7.27 to -4.20, P<0.001) and adults (WMD -8.26, 95% CI -13.29 to -3.25, P=0.001), but not for infants (WMD 0.52, 95% CI -1.59 to 2.63, P=0.63). Subgroup analyses were performed for the type of probiotic strain, treatment duration, as well as disease severity at baseline. Treatment with either the *Lactobacillus* species (WMD -3.81, 95% CI -6.42 to -1.21, P=0.004) or the mixture of the *Lactobacillus* and *Bifidobacterium* species (WMD -6.60, 95% CI -10.42 to -2.79, P<0.001) achieved improvement in SCORAD scores that were statistically significant. However, use of the *Bifidobacterium* species was shown to worsen SCORAD scores (WMD 1.75, 95% CI 1.10 to 2.40). Treatment duration greater than 8 weeks with probiotics showed lowering in SCORAD scores

that were statistically significant (WMD -4.98, 95% CI -7.69 to -2.27, P<0.001), but statistical significance was not shown in the group who received treatment for less than 8 weeks (P=0.34). Patients with moderate disease (SCORAD score 25-50) to severe disease (SCORAD score >50) benefited from probiotic treatment over placebo (WMD -4.66, 95% CI -7.33 to -1.99, P<0.001), but those with mild disease (SCORAD score <25) did not (WMD -0.81, 95% CI -4.21 to 2.60, P=0.25). Adverse events that were reported for probiotics included gastrointestinal symptoms (diarrhea, vomiting) but these were not statistically significantly different from those reported in the placebo group.

According to the authors, the meta-analysis suggested that probiotics could be a beneficial option for the treatment of moderate to severe atopic dermatitis in children and adults, though the clinical significance of the amount of SCORAD score lowering is uncertain. The results should be interpreted cautiously for the overall population due to the significant heterogeneity found between studies. Factors that may have contributed to the heterogeneity included the varying doses of probiotics used, concurrent treatment with other therapies for atopic dermatitis, and compliance.¹⁵ Though this meta-analysis found that probiotics did not have a beneficial effect among infants, a newer study published by Lin, et al. after this meta-analysis suggests otherwise. A small randomized placebo-controlled trial by Rong-Jun, et.al. evaluated the use of *Bifidobacterium bifidum* supplementation to treat infants with AD. Infants who received the probiotic over 4 weeks showed a greater improvement in their SCORAD score compared to placebo (p<0.05).¹⁶

Conclusion

Probiotic supplements may be beneficial in the prevention of AD when given during the last month of pregnancy and for at least a few months after the birth of the newborn. They may also help reduce the severity of the disease among patients with moderate and severe AD. However, larger studies will need to be conducted to form more definite conclusions regarding the effects of probiotics, including effective dosing and duration. Pharmacists should keep in mind that effects may also differ depending on the patient population and the type of probiotic species and strains used. Generally, probiotics are well tolerated with some mild gastrointestinal adverse effects. If patients wish to take probiotic supplements, they should purchase from reputable manufacturers that follow good manufacturing practices and provide clear, accurate labeling.

About the Authors

Celia Lu, Pharm.D, BCACP *corresponding author

Assistant Clinical Professor-Industry Professional

St. John's University

College of Pharmacy and Health Sciences

8000 Utopia Parkway, Queens, NY 11439

E-mail: luc@stjohns.edu

Jacqueline Chirico

Pharm.D. Candidate, Class of 2016

St. John's University College of Pharmacy & Health Sciences

References:

- ¹Guarner F, Khan AG, Garisch J, et al. World Gastroenterology Organisation Global Guidelines: probiotics and prebiotics October 2011. *J Clin Gastroenterol* 2012;46:468-481.
- ²He F, Ouwehand AC, Isolauri E, et al. Comparison of mucosal adhesion and species identification of bifidobacteria isolated from healthy and allergic infants. *FEMS Immunol Med Microbiol* 2001;30(1):43-7.
- ³Saggioro A. Probiotics in the treatment of irritable bowel syndrome. *J Clin Gastroenterol* 2005;38(6):S104-6.
- ⁴Tursi A, Brandimarte G, Papa A, et al. Treatment of relapsing mild-to-moderate ulcerative colitis with the probiotic VSL#3 as adjunctive to a standard pharmaceutical treatment: a double blind, randomized, placebo-controlled study. *Am J Gastroenterol* 2010;105(10):2218-27.
- ⁵Weston S, Halbert A, Richmond P, Prescott SL. Effects of probiotics on atopic dermatitis: a randomised controlled trial. *Arch Dis Child* 2005;90(9):892-897.
- ⁶Folster-Holst R, Muller F, Schnopp N, et al. Prospective, randomized controlled trial on Lactobacillus rhamnosus in infants with moderate to severe atopic dermatitis. *Br J Dermatol* 2006;155:1256-1261.
- ⁷Berke R, Arshdeep S, Guralnick M. Atopic dermatitis: an overview. *Am Fam Physician*. 2012;86(1):35-42.
- ⁸Leung DYM, Bieber T. Atopic dermatitis. *The Lancet* 2003; 361(9352):151-160.
- ⁹Tollefson MM, Bruckner AL. Atopic dermatitis: skin-directed management. *Pediatrics* 2014;134(6):e1735-44.
- ¹⁰Eichenfield LF, Tom WL, Berger TG, et al. Guidelines of care for the management of atopic dermatitis: section 2. Management and treatment of atopic dermatitis with topical therapies. *J Am Acad Dermatol* 2014;71(1):116-32.
- ¹¹Schmitt J, von Kobyletzki L, Svensson A, Apfelbacher C. Efficacy and tolerability of proactive treatment with topical corticosteroids and calcineurin inhibitors for atopic eczema: a systematic review and meta-analysis of randomized controlled trials. *Br J Dermatol* 2011;164(2):415-428.
- ¹²Sigurgeirsson B, Boznanski A, Todd G, et al. Safety and efficacy of pimecrolimus in atopic dermatitis: a 5-year randomized trial. *Pediatrics* 2015; 135(4):597-606.
- ¹³Sidbury R, Tom WL, Bergman JN, et al. Guidelines of care for the management of atopic dermatitis: section 4. Prevention of disease flares and the use of adjunctive therapies and approaches. *J Am Acad Dermatol* 2014;71(6):1218-33.
- ¹⁴Pandura M, Panduru NM, Salavastru CM, Tiplica GS. Probiotics and primary prevention of atopic dermatitis: a meta-analysis of randomized controlled studies. *J Eur Acad Dermatol Venereol* 2015; 29(2):232-42.
- ¹⁵Kim SO, Ah YM, Yu YM, Choi KH, Shin WG, Lee JY. Effects of probiotics for the treatment of atopic dermatitis: a meta-analysis of randomized controlled trials. *Ann Allergy Asthma Immunol* 2014;113(2):217-26.
- ¹⁶Lin RJ, Qiu LH, Guan RZ, Hu SJ, Liu YY, Wang GJ. Protective effect of probiotics in the treatment of infantile eczema. *Exp Ther Med* 2015;9(5):1593-1596.

PHARMACY ATTORNEYS HELPING PHARMACISTS

In a time in which the profession of pharmacy is under heightened scrutiny, it is *essential* to make sure your rights are being protected.

Wilentz, Goldman & Spitzer represents pharmacists and pharmacies in the following areas:

- ◆ Board of Pharmacy Administrative Matters
- ◆ Pharmacy Sales and Purchases
- ◆ Third-Party Reimbursement Issues
- ◆ Pharmaceutical Malpractice Matters
- ◆ Pharmaceutical Criminal Matters

Our firm has been practicing in the Pharmacy Law area for over 15 years, and we understand your problems. For a free *initial consultation*, please call:

Angelo J. Cifaldi, RPh JD
Adjunct Professor of Pharmacy Law,
Rutgers School of Pharmacy
(732) 855-6096





We've built something completely new. On top of a 200-year old foundation.

The Jefferson College of Pharmacy is not the same old, same old. We empower students to work in real pharmacy environments from their very first weeks of school. They'll work alongside students from other healthcare disciplines in our unique Health Mentors Program. And they'll have the opportunity to learn from some of the most prominent clinical and administrative pharmacists in the nation – all at an institution with one of the most advanced health-system pharmacy practices in the world. Jefferson College of Pharmacy. The best of the old. And the new.



Thomas Jefferson University®
Jefferson College of Pharmacy

Learn more at Jefferson.edu/Pharmacy

Provided courtesy of NJPhA

NJPhA Continuing Education Activity

Audience: Pharmacists & Pharmacy Technicians



Biologic Response Modifiers Used in the Treatment of Plaque Psoriasis

Faculty:

Julie Kalabalik, PharmD, BCPS
Assistant Professor of Pharmacy Practice
230 Park Avenue, M-SP1-01
Florham Park, NJ 07932
Tel.: 973-443-8418
Fax: 973-443-8431
E-mail: juliek@fdu.edu

*Corresponding Author - Ligia Westrich, PhD, RPh
Assistant Professor of Pharmaceutical Sciences
Fairleigh Dickinson University
School of Pharmacy
230 Park Avenue, M-SP1-01
Florham Park, NJ 07932
Tel.: 973-443-8418
Fax: 973-443-8431
E-mail: westrich@fdu.edu

Janna Denisenko, BS
PharmD Candidate
Fairleigh Dickinson University
School of Pharmacy
230 Park Avenue, M-SP1-01
Florham Park, NJ 07932
Tel.: 973-443-8418
Fax: 973-443-8431
E-mail: jidenis@student.fdu.edu

Learning Objectives:

After participating in this activity, the participant shall be able to:

Pharmacist:

1. Describe the incidence of psoriasis
2. Identify the symptoms of psoriasis
3. Discuss new treatment options for psoriasis

Pharmacy Technician:

1. Describe the incidence of psoriasis
2. Identify the symptoms of psoriasis
3. List new treatment options for psoriasis

Author disclosures: none

UAN: 0136-0000-15-021-H01-P; 0136-0000-15-021-H01-T

Expiration: 9/15/2018

CEU Hours 0.1 CEUs, 1 Contact Hour

INTRODUCTION

Psoriasis is a chronic, immune-mediated disorder. Psoriasis is the most prevalent autoimmune disease in the United States and approximately 2-3 percent of the worldwide population is afflicted with the disorder. The onset is usually between the ages of 15 and 35, but can emerge at any age.¹ Genetics and environmental triggers are important components in the development of psoriasis, but the exact cause is unknown.² Clinical presentation includes raised, red, scaly patches that appear on the skin. Five types of psoriasis exist: plaque, guttate, inverse, pustular and erythrodermic. Severity ranges from mild to severe. Diagnosis is based on a visual examination of the patient's skin and at times a skin biopsy may be performed.³ Symptoms include burning, stinging and itching. Complications of psoriasis include psoriatic arthritis and infections. Although no cure for psoriasis exists, treatments aimed at reducing the severity of symptoms and improving the physical appearance of the skin are available. Several treatment options are available, including biologic response modifiers (BRMs). BRMs for the treatment of plaque psoriasis include infliximab, adalimumab, etanercept, ustekinumab and secukinumab. BRMs are also approved for the treatment of several other diseases, such as rheumatoid arthritis and Crohn's disease. BRMs are safe and effective treatments for moderate to severe, recalcitrant psoriasis. BRMs are emerging as an essential treatment option for patients who have debilitating severe plaque psoriasis or inadequate response to other systemic agents. The purpose of this review is to describe and compare the use of BRMs in the treatment of plaque psoriasis.

EPIDEMIOLOGY

As of 2013, 7.5 million people in the United States are affected by psoriasis and 125 million people worldwide. Rates of psoriasis in men and women are similar⁴ and the disease is more prevalent in Caucasians compared to African Americans (2.5% vs. 1.3%).¹ Psoriasis in children occurs at lower rates.⁵ The majority of the cases (80%) are reported as mild to moderate with the remaining (20%) being moderate to severe, affecting more than 5% of the body surface area.³ Severe psoriasis is associated with comorbidities such as metabolic syndrome and liver disease.² Plaque psoriasis is the most common form, with 80-90% of patients experiencing patches with silvery buildup of dead skin cells on the elbows, lower back and knees.³ Up to 40% of people with psoriasis will develop joint inflammation and psoriatic arthritis.²

PATHOPHYSIOLOGY

Plaque psoriasis is a papulosquamous skin disorder characterized by development of confined inflamed, raised plaques. Initially, it was described as a chronic disorder involving the continuous shedding of scales composed of partially differentiated skin epithelial cells (keratinocytes), but recently the involvement of the immune system came under scrutiny.⁶ The disease involves a multitude of genetic and environmental factors, immune-mediated inflammation and various modifying factors, such as drugs, trauma, stress, obesity and infection. The activated immune response, affecting a number of organs including the gastrointestinal tract, the joint and the nervous system parallels related immune-mediated disorders, such as Crohn's disease, rheumatoid arthritis and multiple sclerosis.^{6,7} The underlying cellular changes include rapid proliferation of keratinocytes, but incomplete maturation, alongside infiltration of white blood cells (leukocytes). The key immune components are activated T-lymphocytes, neutrophils, natural killer-T cells, dendritic cells, and various chemoattractants, such as chemokines and cytokines. The cytokines further contribute to proliferation of keratinocytes and activation of dermal macrophages (Langerhans cells) and dendritic cells in the skin layers. The increase in the number of keratinocytes results in epidermal hyperplasia, while the cytokines induce vasodilation, formation of new blood vessels and promote the migration of inflammatory leukocytes into the dermis, resulting in the erythematous, thick, scaly plaques.^{7,8} Specifically, in psoriasis, the pro-inflammatory cytokine tumor necrosis factor- α (TNF α) augments the actions of activated immune cells by inducing the expression of adhesion molecules on endothelial cells, thereby facilitating the entry and accumulation of inflammatory cells in the skin layers. Furthermore, TNF α induces several other pro-inflammatory cytokines (e.g., interleukin (IL)-1, IL-6, IL-8) and prevents apoptosis of keratinocytes.^{9,10} In fact, validation of this proposed pathogenesis of psoriasis comes from the observed clinical improvement following initiation of therapies with infliximab, ustekinumab, and alefacept, to name a few, which block the actions of overexpressed cytokines TNF α , IL-12 and IL-23, and activation of T-lymphocytes, respectively.¹¹

TREATMENT APPROACH

Treatment of plaque psoriasis consists of topical medications, such as corticosteroids, retinoids, and calcineurin inhibitors, phototherapy, and systemic therapies, such as methotrexate, cyclosporine, acitretin, and BRMs.^{1,2} Treatment goals

include minimizing plaques, reducing flare-up frequency, minimizing adverse effects, and improving patient's quality of life.¹² Treatment selection should be individualized for each patient based on disease severity, patient response, preference, and tolerability, in order to optimize outcomes.¹² Mild cases may be managed with topical agents such as anthralin, coal tar, emollients, salicylic acid, corticosteroids and vitamin D analogues. In moderate to severe psoriasis, options include systemic agents, phototherapy, and biologics. Traditional systemic agents such as methotrexate, cyclosporine, and acitretin are associated with safety concerns, end-organ toxicity, teratogenicity, adverse effects, and significant drug interactions. BRMs represent a safe and effective treatment option for patients with moderate-to-severe psoriasis. Combining agents is common in extensive psoriasis.^{1,2,13} A European Consensus on treatment goals for patients with plaque psoriasis receiving systemic therapy defined treatment success as a reduction in Psoriasis Area and Severity Index (PASI) by $\geq 75\%$. If improvement in PASI is $< 50\%$, modification in treatment regimen is recommended. Establishing treatment goals and assessing patient response to treatment regularly is recommended.^{14,15}

TNF ANTAGONISTS

TNF α is a soluble pro-inflammatory cytokine secreted by T-lymphocytes and dendritic cells and it exerts its action via binding to soluble TNF receptors or cell surface receptors. Some studies suggest that patients with psoriasis have higher serum TNF α levels than controls and this correlates with disease severity.^{16,17,18} Drugs that interfere with the binding of TNF α with its receptors prevent the aforementioned biological actions of TNF α and improve the symptoms observed in psoriasis.

Adalimumab received FDA approval for treatment of adult patients with moderate-to-severe chronic plaque psoriasis in 2008. Adalimumab is a recombinant human IgG1 monoclonal antibody that binds and inactivates the soluble and membrane-bound forms of TNF α , similar to infliximab. Additionally, *in vitro* studies suggest that binding of adalimumab to TNF expressed on the cell surface, induces lysis of these cells via activation of the complement system. Therefore, the biological processes induced or regulated by TNF α , including changes in the levels of adhesion molecules responsible for leukocyte migration (ELAM-1, VCAM-1, and ICAM-1) are inhibited during treatment with adalimumab.^{19,20} The safety and efficacy of this drug was demonstrated in two Phase III trials: REVEAL (Randomized Controlled Evaluation of Adalimumab Every Other Week Dosing in Moderate to Severe Psoriasis Trial) and CHAMPION (Comparative Study of Humira versus Methotrexate versus Placebo in Psoriasis Patients). The REVEAL trial was a 52-week, double blind, multicenter study of 1,212 patients randomized to receive adalimumab or placebo every other week. A significantly greater percentage of patients in the adalimumab group achieved a clinical response (defined as at least 75% improvement in PASI score [PASI-75]) compared to placebo (71% vs. 7%, $p<0.001$).⁷ The CHAMPION trial was a 16-week study where 271 patients were randomized to adalimumab, methotrexate, or placebo for 16 weeks. Adalimumab was significantly superior to methotrexate (79.6% vs. 35.5%, $p<0.001$) and placebo (79.6% vs. placebo 18.9%, $p<0.001$) in achieving PASI-75. Most common adverse effects included non-serious infections, headache, and nasopharyngitis for all treatment groups.²¹

Etanercept received FDA approval for treatment of adult patients with moderate to severe psoriasis in 2004. It is a dimeric fusion protein composed of the extracellular ligand-binding portion of the human 75 kDa (p75) TNF receptor linked to the Fc portion of human IgG1. It acts as a decoy receptor that binds soluble TNF thereby inhibiting its actions at the endogenous receptors. Etanercept blocks the positive feedback loop induced by TNF α , downregulating several inflammatory effects and diminishing disease progression.^{22,23} The safety and efficacy of this drug was demonstrated in two Phase III trials. Leonardi and colleagues evaluated etanercept, low, medium, or high dose, versus placebo in a 24-week, double blind, randomized study. At 12 weeks, patients in all 3 etanercept groups experienced significantly greater improvement from baseline based on PASI-75 (etanercept low dose 14%, etanercept medium dose 34%, etanercept high dose 49% vs. placebo 4%, $p<0.001$).²⁴ Papp and colleagues randomized 583 patients to receive etanercept or placebo. At 12 weeks, significantly greater percentages of patients in both etanercept groups achieved PASI-75 compared to placebo (etanercept 50mg group 49%, etanercept 25mg 34%, placebo 3%, $p<0.0001$).²⁵ Etanercept was well-tolerated in these two clinical trials with most common adverse effects being injection-site reactions, headache, and upper respiratory tract infection.^{24,25}

In 2006, infliximab received FDA approval for treatment of adult patients with chronic severe (i.e., extensive and/or disabling) plaque psoriasis who are candidates for systemic therapy and when other systemic therapies are medically less

appropriate. Infliximab is a chimeric IgG1κ monoclonal antibody (composed of human constant and murine variable regions) that binds with high affinity to the soluble and transmembrane forms of TNFα. By neutralizing this cytokine, infliximab prevents further infiltration and activation of leukocytes and further cytokine production. Consequently, decreased skin inflammation, appropriate keratinocyte differentiation and apoptosis of damaged keratinocytes are observed.^{5,26} The safety and efficacy of this drug was demonstrated in two Phase III trials: EXPRESS (European Infliximab Psoriasis [Remicade] Efficacy and Safety Study) and EXPRESS II. EXPRESS was a multicenter, double-blind trial comparing infliximab to placebo. At Week 10, 80% of patients in the infliximab group achieved PASI-75 compared to 3% in the placebo group ($p<0.0001$). Fifty-seven percent of patients in the infliximab group achieved PASI-90 compared to 1% in the placebo group ($p<0.0001$). At Week 24, 82% achieved PASI-75 and 45% achieved PASI-90 in the infliximab group, significantly greater than placebo.²⁷ In EXPRESS II, continuous (every 8 weeks) and intermittent (as-needed) infliximab maintenance regimens were investigated. PASI responses were best maintained with continuous infliximab versus intermittent regimens.²⁸ Infliximab was generally well-tolerated in both studies.^{27,28}

Infliximab is the only TNF antagonist administered by intravenous infusion. Since it is associated with infusion-related reactions, patients should be closely monitored. Patients with infusion-related reactions present with flu-like symptoms, headache, dyspnea, hypotension, chills, transient fever, gastrointestinal symptoms, and skin rashes. Anaphylaxis may occur at any time during the infusion. The infusion should be suspended and upon resolution, reinitiated at a lower rate.²⁹ The patient may be premedicated with antihistamines, acetaminophen, and/or corticosteroids. Infliximab should be avoided in patients that develop severe infusion-related hypersensitivity reactions.

TNF antagonists administered subcutaneously are associated with pain and reactions at the injection site.^{13,30} TNF antagonists should not be started during an active infection due to the immunomodulating effects of biologics. Prior to initiating BRMs, and periodically during therapy, patients should be evaluated for active tuberculosis (TB) and tested for latent infections.⁶ TNF antagonists can reactivate latent infections such as HBV.^{3,13,30,32} If an infection develops, the patient should be monitored carefully, and the drug should be discontinued if the infection becomes serious.³ Live vaccines should not be given to patients receiving BRMs. Prior to therapy, baseline measurements of liver function, complete blood cell counts and platelet counts should be taken and periodically monitored throughout therapy to identify underlying risk factors such as skin cancer, infection susceptibility and acute liver failure.^{3,31} Adverse effects include rash, headache, risk of infections, greater incidence of malignancies in patients treated with BRMs, hypersensitivity reactions, exacerbations or new onset of heart failure and demyelinating diseases, cytopenias, invasive fungal infections and Lupus-like syndrome. Concomitant use of anakinra or abatacept with infliximab, adalimumab, or etanercept increases the risk of infection.^{5,20,24} TNF antagonists are pregnancy category B.³ A comparison of drug characteristics is provided in Table 1.

INTERLEUKIN ANTAGONISTS

Ustekinumab was FDA-approved in 2009 for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for phototherapy or systemic therapy. Ustekinumab is a humanized monoclonal antibody that targets the p40 subunit of both interleukin (IL)-12 and -23. These cytokines activate T-lymphocytes and contribute to pathogenesis of psoriasis. In binding and neutralizing these interleukins, ustekinumab can prevent activation of targeted T-lymphocytes and reduce further inflammation.^{32,33} Three Phase III trials support the efficacy and safety of ustekinumab in psoriasis: PHOENIX 1, PHOENIX 2, and ACCEPT (Active Comparator [CNTO 1275/Enbrel] Psoriasis Trial). PHOENIX 1, a parallel, double-blind, placebo-controlled study, included 766 patients randomly assigned to ustekinumab or placebo. At Week 12, significantly greater patients in the ustekinumab groups achieved PASI 75 compared to placebo (ustekinumab 45mg 67.1%, ustekinumab 90mg 66.4%, placebo 3.1%, $p<0.0001$ for both).³⁴ PHOENIX 2 showed similar results at Week 12. At Week 28, partial responders (patients achieving $\geq 50\%$ but $< 75\%$ improvement from baseline PASI) were randomized against either continued dosing every 12 weeks or changed to dosing every 8 weeks. Partial responders switched to ustekinumab 90mg every 8 weeks were more likely to achieve PASI 75 at Week 52 compared to those maintained on the same dose every 12 weeks (68.8% vs. 33.3%; difference in response rate 35.4%, 95% CI 12.7 – 58.1, $p=0.004$).³⁵ ACCEPT compared ustekinumab to etanercept. Patients who received ustekinumab were more likely to achieve PASI 75 compared to etanercept at Week 12 (ustekinumab 45mg 67.5%, ustekinumab 90mg 73.8%, etanercept 56.8% ($p=0.01$ and $p<0.001$, respectively)). Ustekinumab was generally well-tolerated in clinical trials.

Table 1. Comparison of BRM Drug Characteristics

Generic Name (Brand)	Dosing and Administration (Route)	Dosage Form	Common Adverse Reactions	Warnings	Monitoring
TNF antagonists					
Adalimumab (Humira®) ²⁰	80mg initial dose, then 40mg every other week starting one week after initial dose. (Subcutaneous)	40mg/0.8mL single-use prefilled pen	Injection site reactions, headache, rash, infections (upper respiratory, sinusitis) (>10%)	Do not give during active infection. CBC, LFT, PPD, physical exam	Infections, malignancy,
Etanercept (Enbrel®) ²⁴	Initial dose: 50 mg 2x weekly for 3 months. Maintenance dose: 50 mg weekly. (Subcutaneous)	0.98mL of a 50mg/mL solution, single-use syringe or autoinjector	Injection site reactions, infections (>5%)	Contraindicated in sepsis. Do not give during active infection or with cyclophosphamide	Infections, CBC, LFT, PPD, physical exam
Infliximab (Remicade®) ⁵	IV infusion ≥2 hours. 5mg/kg at 0, 2, 6 weeks, then every 8 weeks. (Intravenous)	Lyophilized powder: 100mg/vial reconstituted with Sterile Water for Injection, USP. Dilute to 250mL with 0.9% NaCl, USP	Infections (upper respiratory, sinusitis, pharyngitis), infusion-related reactions, headache, abdominal pain (>10%)	Contraindications: Doses >5mg/kg in severe heart failure, hypersensitivity to active/inactive components or to any murine proteins. Do not give during active infection.	Infections (HBV), CBC, LFT, PPD, physical exam
Interleukin antagonists					
Ustekinumab (Stelara®) ³²	<100 kg: 45mg at 0- and 4 weeks, then every 12 weeks. >100 kg: 90mg at 0- and 4 weeks, then every 12 weeks. (Subcutaneous)	45mg/0.5mL or 90mg/mL single-use prefilled syringe or single-use vial	Nasopharyngitis, upper respiratory tract infections, headache, fatigue (≥3%)	Contraindicated in clinically significant hypersensitivity.	RPLS, CBC, non-melanoma skin cancer, infection
Secukinumab (Cosentyx®) ³⁶	300mg at Weeks 0, 1, 2, 3, 4 followed by 300mg every 4 weeks (150mg may be acceptable for some patients) (Subcutaneous)	150mg/mL Sensoready pens or single-use prefilled syringe single-use vial	Nasopharyngitis, upper respiratory tract infections, diarrhea (>1%)	Contraindicated in serious hypersensitivity reaction to active/inactive components	Infections, active tuberculosis, exacerbation of Crohn's disease

Ustekinumab is efficacious for treating psoriasis and has been demonstrated to be well tolerated, however long term safety data does not yet exist. Based on recent trials, there is no substantial risk of malignant neoplasm or infections. Ustekinumab is contraindicated in clinically significant hypersensitivity to the active ingredient or any inactive excipients.³² Common adverse reactions are nasopharyngitis, upper respiratory tract infections, headache and fatigue. Baseline measurements include TB test, liver function test, complete blood cell counts and platelet counts and should be periodically monitored throughout therapy. Other precautions include the possible development of infections, malignancies, anaphylaxis, and a single case of Reversible Posterior Leukoencephalopathy Syndrome has been reported.³² Ustekinumab is a Pregnancy Category B.

The newest interleukin antagonist is secukinumab and it was approved by the FDA in January 2015. Secukinumab is indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.³⁶ This drug represents the first human monoclonal antibody against the IL-17A cytokine, approved by the FDA for this indication. By neutralizing the IL-17A cytokine, secukinumab prevents the interaction of this cytokine with its IL-17 receptor. In this way, secukinumab inhibits the release of proinflammatory cytokines and chemokines and diminishes inflammation.^{36,37} Secukinumab was approved based on 4 multicenter, randomized, double blind, placebo-controlled phase III trials: ERASURE, FIXTURE, FEATURE, and JUNCTURE.^{38,39,40} Trials demonstrated that

secukinumab is more effective than placebo, etanercept, and ustekinumab in improving psoriasis symptoms and quality of life in patients with moderate to severe plaque psoriasis. Significantly greater proportion of patients in the secukinumab 150 and 300 mg groups achieved a PASI 75 response and a modified (2011) investigator's global assessment (IGAmid2011) of 0 or 1 after 12 weeks of treatment compared to placebo and etanercept (all p<0.0001).^{38,39,40} A significantly greater number of secukinumab patients achieved PASI 90 at 12 weeks compared to placebo and etanercept patients.^{38,39,40} Maintenance of PASI 75 response at week 52 was significantly greater in secukinumab groups compared to placebo and etanercept.³⁸ Secukinumab was associated with faster response than etanercept in the FIXTURE trial with a median time to 50% reduction from baseline mean PASI score of 3.9 weeks for secukinumab 150mg, 3 weeks for secukinumab 300 mg, and 7 weeks for etanercept (p<0.001).³⁸ In the CLEAR trial, secukinumab was compared to ustekinumab in patients with moderate to severe plaque psoriasis poorly controlled with other treatments. A significantly greater number of patients who received secukinumab 300mg achieved a PASI 90 and PASI 100 response at 16 weeks compared to patients in the ustekinumab group (p<0.0001).⁴¹

Secukinumab is contraindicated in patients with serious hypersensitivity reaction to secukinumab or any of the excipients. Generally well-tolerated, common adverse reactions are nasopharyngitis, upper respiratory tract infections, and diarrhea. Precautions include the possible development of infections. Secukinumab should be discontinued if a serious infection develops. Patients should be evaluated for TB prior to initiating treatment with secukinumab and monitored for active TB during and after treatment. Exacerbation of Crohn's disease has been reported in clinical trials and patients with active Crohn's disease should be monitored closely. Secukinumab is Pregnancy Category B.³⁶

GUIDELINE RECOMMENDATIONS

According to the American Academy of Dermatology (AAD) treatment guidelines for BRMs, it is recommended to obtain an appropriate history, laboratory values, medication list and physical examination prior to initiating therapy due to the side effect profile.⁴² BRMs are started in active, moderate to severe psoriasis. General recommendations, as stated by the AAD, include: avoid/limit the use of BRMs in patients with active infections, perform a PPD test prior to initiation, and live vaccines should be avoided (inactive or recombinant may be considered). Patients with MS or demyelinating disease or with congestive heart failure (CHF) class III or IV should not receive TNF antagonists due to worsening of these conditions. Infliximab, adalimumab and etanercept are classified as having a level A-1 strength of recommendation and level of evidence for treatment of psoriasis. Ustekinumab has yet to be classified by the AAD because it was approved in 2009 following the publication of the AAD guidelines.

DEVELOPMENT OF ANTIDRUG ANTIBODIES

The development of antidrug antibodies to BRMs has been reported and may be associated with a decreased clinical response to therapy and potential loss of efficacy.⁴ Patients treated with adalimumab who developed antibodies had an increased risk of failure to re-achieve efficacy following treatment discontinuation and relapse.⁴³ Antidrug antibody development to etanercept, infliximab, and ustekinumab have also been reported.⁴⁴⁻⁴⁷ In rheumatology literature, the addition of methotrexate to BRM therapy shows promise in reducing antidrug antibody formation.¹⁷ Additional research is needed to explore the role of combination therapy with methotrexate. The use of assays to detect the presence of antidrug antibodies may assist the clinician in individualizing therapy for patients, yet more research is needed in this area.⁴⁸

CONCLUSION

The use of anti-TNF α and anti-cytokine agents, which possess a myriad of anti-inflammatory properties, results in the improvement of psoriasis. BRMs represent a safe and effective treatment option for patients with moderate-to-severe plaque psoriasis. Drug selection should be based on disease severity, patient response, preference, and tolerability in order to minimize plaque formation, reduce flare-up frequency, minimize adverse effects, and improve patient quality of life. Pharmacists play a crucial role in optimizing pharmacological management and monitoring of patients with plaque psoriasis receiving individualized treatment.

References:

- ¹Papoutsaki, M., & Costanzo, A. Treatment of Psoriasis and Psoriatic Arthritis. *BioDrugs*, 2013;27(1), 3-12.
- ²Menter A, Gottlieb A, Feldman SR, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 1. Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2008;58(5):826-50.
- ³American Academy of Dermatology. Aad.org. Psoriasis Section 1 General Principles | Aad.org. 2015. Available at: <https://www.aad.org/education/clinical-guidelines/psoriasis-guideline/biologics/psoriasis-section-1-general-principles>. Accessed April 8, 2015.
- ⁴Menter A, Tyring SK, Gordon K, et al. Adalimumab therapy for moderate to severe psoriasis: A randomized, controlled phase III trial. *J Am Acad Dermatol*. 2008;58(1):106-15.
- ⁵Remicade (infliximab) [package insert]. Horsham, PA: Janssen Biotech, Inc; 2015.
- ⁶Al-Shobaili HA, Qureshi MG. Chapter 4: Pathophysiology of Psoriasis: Current Concepts. In: Lima H, ed. Psoriasis - Types, Causes and Medication. Rijeka, Croatia: Intech; 2013. (<http://dx.doi.org/10.5772/54113>)
- ⁷Griffiths CE, Barker JN. Pathogenesis and clinical features of psoriasis. *Lancet*. 2007; 370(9583):263-71.
- ⁸Chong HT, Kopecki Z, Cowin AJ. Lifting the Silver Flakes: The Pathogenesis and Management of Chronic Plaque Psoriasis. *Biomed Res Int*. 2013; 2013: 168321. (doi: 10.1155/2013/168321)
- ⁹Gall JS, Kalb RE. Infliximab for the treatment of plaque psoriasis. *Biologics*. 2008; 2(1):115-24.
- ¹⁰Tan JK, Aphale A, Malaviya R, et al. Mechanisms of action of etanercept in psoriasis. *J Invest Dermatol Symp Proc*. 2007; 12:38-45.
- ¹¹Krueger JG, Bowcock A. Psoriasis pathophysiology: current concepts of pathogenesis. *Ann Rheum Dis*. 2005; 64 Suppl 2:i30-6.
- ¹²Law RM. Chapter 64: Psoriasis. In: Chisholm-Burns M, ed. *Pharmacotherapy Principles and Practice*, 3rd ed. New York: McGraw-Hill; 2013:1127-1141.
- ¹³Hsu S, Papp KA, Lebwohl MG, et al. Consensus guidelines for the management of plaque psoriasis. *Arch Dermatol*. 2012;148(1):95-102.
- ¹⁴Mrowietz U, Kragballe K, Reich K et al. Definition of treatment goals for moderate to severe psoriasis: a European consensus. *Arch Dermatol Res*. 2011;303(1):1-10.
- ¹⁵Brezinski EA, Armstrong AW. Strategies to maximize treatment success in moderate to severe psoriasis: establishing treatment goals and tailoring of biologic therapies. *Semin Cutan Med Surg*. 2014;33(2):91-7.
- ¹⁶Kyriakou A, Patsatsi A, Vyzantiadis T-A, Sotiriadis D. Serum Levels of TNF-, IL-12/23p40, and IL-17 in Plaque Psoriasis and Their Correlation with Disease Severity. *J Immunol Res*. 2014; 2014: 467541. (doi: 10.1155/2014/467541)
- ¹⁷Mussi A, Bonifati C, Carducci M, et al. Serum TNF-alpha levels correlate with disease severity and are reduced by effective therapy in plaque-type psoriasis. *J Biol Regul Homeost Agents*. 1997; 11(3):115-8.
- ¹⁸Zaba LC, Cardinale I, Gilleaudeau P, et al. Amelioration of epidermal hyperplasia by TNF inhibition is associated with reduced Th17 responses. *J Exp Med*. 2008; 205(8):3183-94.
- ¹⁹Alwawi EA, Mehlis SL, Gordon KB. Pathogenesis and clinical features of psoriasis. *Ther Clin Risk Manag* 2008; 4(2):345-351.
- ²⁰Humira (adalimumab) [package insert]. North Chicago, IL: AbbVie, Inc; 2014
- ²¹Saurat JH, Stingl G, Dubertret L et al. Efficacy and safety results from the randomized controlled comparative study of adalimumab vs. methotrexate vs. placebo in patients with psoriasis (CHAMPION). *Br J Dermatol*. 2008;158(3):558-66.
- ²²Tan JK, Aphale A, Malaviya R, et al. Mechanisms of action of etanercept in psoriasis. *J Invest Dermatol Symp Proc*. 2007; 12:38-45.
- ²³Enbrel (etanercept) [package insert]. Thousand Oaks, CA: Amgen, Inc; 2015
- ²⁴Leonardi CL, Powers JL, Matheson RT et al. Etanercept as monotherapy in patients with psoriasis. *N Engl J Med* 2003;349:2014-22.
- ²⁵Papp KA, Tyring S, Lahfa M et al. A global phase III randomized controlled trial of etanercept in psoriasis: safety, efficacy, and effect of dose reduction. *Br J Dermatol* 2005;152(6):1304-12.
- ²⁶Gall JS, Kalb RE. Infliximab for the treatment of plaque psoriasis. *Biologics*. 2008; 2(1):115-24.
- ²⁷Reich K, Nestle FO, Papp K, et al. Infliximab induction and maintenance therapy for moderate-to-severe psoriasis: a phase III, multicentre, double-blind trial. *Lancet* 2005;366(9494):1367-74.
- ²⁸Menter A, Feldman SR, Weinstein GD, et al. A randomized comparison of continuous vs. intermittent infliximab maintenance regimens over 1 year in the treatment of moderate-to-severe plaque psoriasis. *J Am Acad Dermatol* 2007; 56 (1): 31 e1-15.
- ²⁹Sandoval LF, Pierce A, Feldman SR. Systemic therapies for psoriasis: an evidence-based update. *Am J Clin Dermatol*. 2014;15(3):165-80.
- ³⁰International Federation of Psoriasis Organizations. Ifpa-pso.org. About Psoriasis. 2015. Available at: <http://www.ifpa-pso.org/web/page.aspx?refid=42>. Accessed April 10, 2015.
- ³¹Parisi R, Symmons DP, Griffiths CE, Ashcroft DM. Global epidemiology of psoriasis: a systematic review of incidence and prevalence. *J Invest Dermatol*. 2013;133(2):377-85.
- ³²Stelara (ustekinumab) [package insert]. Horsham, PA: Janssen Biotech, Inc; 2014.
- ³³Benson JM, Sachs CW, Treacy G et al. Therapeutic targeting of the IL-12/23 pathways: generation and characterization of ustekinumab. *Nature Biotechnol* 2011; 29:615-624.
- ³⁴Leonardi CL, Kimball AB, Papp KA, et al. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 76-week results from a randomised, double-blind, placebo-controlled trial (PHOENIX 1). *Lancet* 2008; 371 (9625): 1665-74.
- ³⁵Papp KA, Langley RG, Lebwohl M, et al. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 52-week results from a randomised, double-blind, placebo-controlled trial (PHOENIX 2). *Lancet* 2008; 371 (9625): 1675-84.
- ³⁶Cosentyx (secukinumab) [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; 2015
- ³⁷Patel DD, Lee DM, Kolbinger F, et al. Effect of IL-17A blockade with secukinumab in autoimmune diseases. *Ann Rheum Dis*. 2013;72:ii106-ii123. (doi:10.1136/annrheumdis-2012-202371)
- ³⁸Langley RG, Elewski BE, Lebwohl M, et al. Secukinumab in plaque psoriasis—results of two phase 3 trials. *N Engl J Med*. 2014;371(4):326-38.
- ³⁹Blauvelt A, Prinz JC, Gottlieb AB, et al. Secukinumab administration by pre-filled syringe: efficacy, safety and usability results from a randomized controlled trial in psoriasis (FEATURE). *Br J Dermatol*. 2014;172(2):484-93.
- ⁴⁰Paul C, Lacour JP, Tedremets L, et al. Efficacy, safety and usability of secukinumab administration by autoinjector/pen in psoriasis: a randomized, controlled trial (JUNCTURE). *J Eur Acad Dermatol Venereol*. 2014;29(6):1082-90.
- ⁴¹Thaci D, Blauvelt A, Reich K, et al. Secukinumab is superior to ustekinumab in clearing skin of subjects with moderate to severe plaque psoriasis: CLEAR, a randomized controlled trial. *J Am Acad Dermatol*. 2015;73(3):400-9. (doi:10.1016/j.jaad.2015.05.013)
- ⁴²National Psoriasis Organization. Psoriasis.org. Symptoms | Types | Treatments | Research | Finding a Cure | Psoriasis and Psoriatic Arthritis - National Psoriasis Foundation. 2015. Available at: <https://www.psoriasis.org>. Accessed April 8, 2015.
- ⁴³Papp K, Crowley J, Ortonne JP, et al. Adalimumab for moderate to severe chronic plaque psoriasis: efficacy and safety of retreatment and disease recurrence following withdrawal from therapy. *Br J Dermatol*. 2011;164(2):434-41.
- ⁴⁴Brezinski EA, Armstrong AW. Off-label biologic regimens in psoriasis: a systematic review of efficacy and safety of dose escalation, reduction, and interrupted biologic therapy. *PLoS ONE*. 2012;7(4):e33486.
- ⁴⁵Leonardi CL, Powers JL, Matheson RT et al. Etanercept as monotherapy in patients with psoriasis. *N Engl J Med*. 2003;349(21):2014-22.
- ⁴⁶Reich K, Nestle FO, Papp K et al. Infliximab induction and maintenance therapy for moderate to severe psoriasis: a phase III, multicenter, double-blind trial. *Lancet*. 2005;366(9494):1367-74.
- ⁴⁷Leonardi CL, Kimball AB, Papp KA et al. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 76-week results from a randomized, double-blind, placebo-controlled trial (PHOENIX 1). *Lancet* 2008;371(9625):1665-74.
- ⁴⁸Hsu L, Snodgrass BT, Armstrong AW. Antidrug antibodies in psoriasis: a systematic review. *Br J Dermatol* 2014;170(2):261-73.

The New Jersey Pharmacists Association is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

Pharmacist post-test

1. Which statement is true regarding psoriasis?
 - a. it is an acute condition that affects neonates
 - b. the onset is usually between the ages of 50 to 65 years
 - c. the exact cause is unknown but it is thought to have environmental and genetic components
 - d. it affects approximately 25 to 35 % of the worldwide population

2. Psoriasis is an autoimmune
 - a. chronic skin disorder
 - b. chronic eye disorder
 - c. acute respiratory disorder
 - d. acute renal disorder

3. Symptoms of psoriasis include
 - a. burning, itching, stinging with raised red scaly patches on the skin
 - b. fever, itching, burning with oozing blisters on the skin
 - c. impaired renal function with electrolyte abnormalities
 - d. upper and lower extremity edema with decreased cardiac output

4. The immune response in psoriasis parallels the immune response in multiple sclerosis and rheumatoid arthritis because they all
 - a. affect the elderly most often
 - b. respond to diet modification
 - c. are treated with phototherapy
 - d. affect a number of organs

5. Psoriasis can be treated with
 - a. systemic medications only
 - b. topical medications and treatments only
 - c. both systemic and topical medications and treatments

6. Goals of treating psoriasis include
 - a. maintaining adequate vision, respiratory function, and range of motion
 - b. minimizing plaques, reduce frequency of flare-ups and adverse drug reactions, and improving quality of life
 - c. delaying time to hemodialysis, minimizing edema, and improving gait
 - d. maximizing oral treatment regimens, identifying drug interactions, and facilitating end-organ toxicity

Pharmacy technician post-test

1. Which statement is true regarding psoriasis?
 - a. it is an acute condition that affects neonates
 - b. the onset is usually between the ages of 50 to 65 years
 - c. the exact cause is unknown but it is thought to have environmental and genetic components
 - d. it affects approximately 25 to 35 % of the worldwide population

2. Psoriasis is an autoimmune
 - a. chronic skin disorder
 - b. chronic eye disorder
 - c. acute respiratory disorder
 - d. acute renal disorder

3. Symptoms of psoriasis include
 - a. burning, itching, stinging with raised red scaly patches on the skin
 - b. fever, itching, burning with oozing blisters on the skin
 - c. low kidney function and electrolyte abnormalities
 - d. upper and lower extremity edema with decreased heart function

4. The immune response in psoriasis parallels the immune response in multiple sclerosis, rheumatoid arthritis, and
 - a. renal failure
 - b. asthma
 - c. pancreatitis
 - d. Crohn's disease

5. Psoriasis can be treated with
 - a. systemic medications only
 - b. topical medications and treatments only
 - c. both systemic and topical medications and treatments

6. Goals of treating psoriasis include
 - a. maintaining adequate vision, respiratory function, and range of motion
 - b. minimizing plaques, reduce frequency of flare-ups and adverse drug reactions, and improving quality of life
 - c. delaying time to hemodialysis, minimizing edema, and improving gait
 - d. maximizing oral treatment regimens, identifying drug interactions, and facilitating end-organ toxicity

Pharmacist post-test

7. Medications that bind to TNF α receptors to treat psoriasis include
a. ustekinumab and secukinumab
b. methotrexate and methylprednisolone
c. retinoids and cyclosporine
d. adalimumab and infliximab
8. Medications that are interleukin antagonists to treat psoriasis include
a. ustekinumab and secukinumab
b. methotrexate and methylprednisolone
c. retinoids and cyclosporine
d. adalimumab and infliximab
9. Which would be an appropriate prescription or order for a 32 yo male with psoriasis?
a. secukinumab 300 mg SQ daily x 7 days, then 300 mg SQ weekly
b. entanercept 50 mg PO twice weekly for 3 months then reevaluate
c. adalimumab 80 mg SQ x 1, then in one week start 40 mg SQ every other week
d. infliximab 300 mcg IM at week 0, 2, 6; then every 8 weeks
10. Which statement is true regarding medications used to treat psoriasis?
a. ustekinumab and infliximab are in the same drug class
b. etanercept and adalimumab are in the same drug class
c. secukinumab and adalimumab are in the same drug class
d. ustekinumab and etanercept are in the same drug class

Passing Score is 70% or above - Please circle your answers (one answer per question)

- | | |
|---------------------------|----------------------------|
| 1. A B C D | 6. A B C D |
| 2. A B C D | 7. A B C D |
| 3. A B C D | 8. A B C D |
| 4. A B C D | 9. A B C D |
| 5. A B C | 10. A B C D |

Program Evaluation – Must be completed for credit

Please rate the following items on a scale from 1 (poor) to 4 (excellent).

- | | | | | |
|-----------------------------------|---|---|---|---|
| 1. Overall quality of the article | 1 | 2 | 3 | 4 |
| 2. Relevance to pharmacy practice | 1 | 2 | 3 | 4 |
| 3. Value of the content | 1 | 2 | 3 | 4 |

Please answer each question, marking whether you agree or disagree

4. The program met the stated learning objectives:
 Agree Disagree

Impact of the Activity

5. The information presented (check all that applies):
 Reinforced my current practice/treatment habits
 Provided new ideas or information I expect to use
 Will improve my practice/patient outcomes
 Adds to my knowledge

Pharmacy technician post-test

7. Medications that bind to TNF α receptors to treat psoriasis include
a. ustekinumab and secukinumab
b. methotrexate and methylprednisolone
c. retinoids and cyclosporine
d. adalimumab and infliximab
8. Medications that are interleukin antagonists to treat psoriasis include
a. ustekinumab and secukinumab
b. methotrexate and methylprednisolone
c. retinoids and cyclosporine
d. adalimumab and infliximab
9. Which would be an appropriate prescription or order to treat psoriasis?
a. secukinumab 300 mg SQ daily x 7 days, then 300 mg SQ weekly
b. entanercept 50 mg PO twice weekly for 3 months then reevaluate
c. adalimumab 80 mg SQ x 1, then in one week start 40 mg SQ every other week
d. infliximab 300 mcg IM at week 0, 2, 6; then every 8 weeks
10. Which statement is true regarding medications used to treat psoriasis?
a. ustekinumab and infliximab are in the same drug class
b. etanercept and adalimumab are in the same drug class
c. secukinumab and adalimumab are in the same drug class
d. ustekinumab and etanercept are in the same drug class

Passing Score is 70% or above - Please circle your answers (one answer per question)

- | | |
|----------------------------|----------------------------|
| 6. A B C D | 11. A B C D |
| 7. A B C D | 12. A B C D |
| 8. A B C D | 13. A B C D |
| 9. A B C D | 14. A B C D |
| 10. A B C D | 15. A B C D |

6. Will the information presented cause you to make any changes in how you do your job? Yes No

7. How committed are you to making these changes?
(Not - Very) 1 2 3 4

8. Do you feel future activities on this subject matter are necessary and/or important? Yes No

Follow-Up

As part of our ongoing quality-improvement effort, we would like to be able to contact you in the event we conduct a follow-up survey to assess the impact of our educational interventions on professional practice. Are you willing to participate in such a survey?

Yes No

This lesson is a knowledge-based CE activity and is targeted to pharmacists and pharmacy technicians. This program has been approved for 1 contact hour of continuing education credit (0.1 CEU). UAN:0136-0000-15-021-H01-P; 0136-0000-15-021-H01-T. Expiration: 9/15/2018

To receive continuing education credit, please provide the following information:

CPE credit for successfully completed quizzes will be uploaded to CPE Monitor. CE statement of credits will not be mailed but can be printed from CPE Monitor website within 60 days of receipt of the mailed materials.

Circle correct test answers and return to:

NEW JERSEY PHARMACISTS ASSOCIATION

Attention: **Journal C.E. Department, 760 Alexander Rd., PO Box 1, Princeton, NJ 08543-0001**

Please enroll me in the New Jersey Pharmacy Continuing Education Program. I will submit examinations for each issue and I understand that the passing grade is 70% for each examination.

Name (First, Last): _____

Phone Number: _____

Email: _____

Address: _____

City: _____ State: _____ Zip: _____

License No: _____ E-PID#: _____ DOB (MM/DD): _____

Payment Information:

Enclosed is: NJPhA Member (FREE) \$15.00 Non-member

VISA Master Card American Express Discover

Card Number: _____

Security Code: _____ Expire date: _____

Amount of charge: _____ Signature: _____

Check enclosed: Payable to NJPhA

Check # _____ Amount: _____

N/A, my NJPhA membership is currently up-to-date

OFFICE USE ONLY DATE: _____ GRADE: _____

Membership: _____

continuing education for pharmacists

Volume XXXII, No. 2

Vitamin D Deficiency and Treatment

Melody L. Hartzler, R.Ph., PharmD, AE-C, BCACP, Assistant Professor of Pharmacy Practice and
Tracy R. Frame, R.Ph., PharmD, BCACP, Assistant Professor of Pharmacy Practice, Cedarville University
School of Pharmacy

Drs. Melody Hartzler and Tracy Frame have no relevant financial relationships to disclose.

Goal. The goal of this lesson is to provide information on vitamin D deficiency and insufficiency including prevalence, epidemiology, screening, prevention, treatment recommendations, and the relationship to various diseases; as well as vitamin D supplements, dietary sources, and symptoms of toxicity.

Objectives. At the completion of this activity, the participant will be able to:

1. identify clinical manifestations of vitamin D deficiency and insufficiency;
2. recognize the relationship of vitamin D deficiency to common disease states;
3. demonstrate an understanding of screening, prevention and treatment of vitamin D deficiencies, including vitamin D supplements and dietary sources; and
4. list signs and symptoms of vitamin D toxicity.

Despite the lack of consensus on optimal levels of serum 25-hydroxyvitamin D [25(OH)D], vitamin D deficiency is most often defined as a level of less than 20 ng/mL, and insufficiency is defined as a serum 25(OH)D level of 20 to 29 ng/mL. The major source of vitamin D in the human body is produced in the skin by a UVB-mediated, photolytic, non-enzymatic reaction that converts 7-dehydrocholesterol to previtamin

D₃. Previtamin D₃ then undergoes another conversion to vitamin D₃ (cholecalciferol), which also occurs in the skin. Vitamin D₃ can also be obtained from the diet via animal sources and supplements. Another form of vitamin D, vitamin D₂ (ergocalciferol), is found in some plants and is commonly produced commercially by irradiation of yeast for supplementation and fortification in the food supply. Both of these forms of vitamin D undergo the same metabolism and are converted to 25(OH)D in the liver. Finally in the kidney, 25(OH)D is hydroxylated to 1,25 dihydroxyvitamin D [1,25(OH)₂D], the biologically active form of vitamin D, which increases calcium absorption, and acts on the osteoblasts and osteoclasts in bone to mobilize calcium. This last step in the process is regulated primarily by serum parathyroid hormone (PTH), as well as low serum calcium or phosphorus levels.

Research suggests vitamin D₃ is a prohormone rather than a vitamin. In addition to increasing calcium absorption and mobilization, new information suggests the activated hormone 1,25(OH)₂D plays other non-calcemic roles in intracellular biological reactions. The vitamin D receptor (VDR) is a phosphoprotein member of the nuclear receptor superfamily that can be affected by glucocorticoids, estrogens, retinoids, and cell proliferation rates. Vitamin D and VDR have shown important roles in immune, cardiovascular, reproductive systems and in hair growth. Serum 1,25(OH)₂D has been found to

control more than 200 genes in the body that regulate cellular proliferation, differentiation, apoptosis, and angiogenesis.

Some reports have estimated over a billion people worldwide have vitamin D deficiency or insufficiency. Data from National Health and Nutrition Examination Surveys (NHANES) report that from 2001 to 2006 an estimated one-quarter of Americans were at risk of vitamin D inadequacy [serum 25(OH)D of 30 to 49 nmol/L or 11 to 20 ng/mL], and 8 percent were at risk of vitamin D deficiency [serum 25(OH)D less than 30 nmol/L or less than 10 ng/mL]. The prevalence was lower in younger, male, or non-Hispanic white individuals. Among women, the prevalence was also lower in pregnant or lactating females. Risk factors for vitamin D deficiency include age greater than 65 years, babies breastfed exclusively without vitamin D supplementation, dark skin, insufficient sunlight exposure, medication use that alters vitamin D metabolism (such as anticonvulsants or glucocorticoids), obesity (BMI greater than 30 kg/m²), and a sedentary lifestyle.

In light of this information, researchers have begun to ask the question, "Is vitamin D the reason for the racial disparities seen across a variety of disease states?" For example, the NHANES data from 2001 to 2006 suggest suboptimal vitamin D status may contribute to racial disparity in albuminuria due to an inverse relationship between 25(OH)D levels and albuminuria. Other observational stud-

ies have shown vitamin D levels to be lower in African Americans than White Americans with worse disease outcomes for those with cancer, cardiovascular disease, diabetes, end-stage renal disease, and all-cause mortality. It has been shown that African Americans have a mean serum 25(OH)D level of 16 ng/mL, while White Americans have a level of 26 ng/mL. The African American population has a higher rate of obesity. Because vitamin D is a fat-soluble vitamin, heavier individuals may require more, which could be a confounding explanation of the lower serum 25(OH)D levels.

Additional data from NHANES III, as well as the mortality data from the National Death Index, has also been consistent with the hypothesis that vitamin D deficiency contributes to increased African American mortality from colorectal cancer. Although there is limited evidence, vitamin D may play a role in higher rates of preterm birth in the African American population due to the active form serving as a key modulator of immune response, and as a potent regulator of placental immunity.

Lastly, there is a higher prevalence of hypertension among African American individuals versus Caucasians, and in a recent cross-sectional analysis serum 25(OH)D levels explained one-quarter of the disparity in systolic blood pressure. It is important to recognize these racial disparities, especially among the African American population, in order to properly screen patients for deficiency.

Vitamin D Deficiency and Non-Skeletal Disease

Diabetes

Due to vitamin D's effect on more than 200 genes in the body, vitamin D has been linked to various non-skeletal diseases in multiple epidemiological studies. Data has established a link between vitamin D deficiency and an increased incidence of both type 1 and type 2 diabetes. Calcium intake has

evidence demonstrating an inverse relationship to incidence of metabolic syndrome and diabetes.

There is evidence that suggests vitamin D influences beta cell function directly, and may make beta cells more resistant to types of cellular stress due to vitamin D receptors present on beta cells in the pancreas. A significant increased risk of type 2 diabetes has been reported among persons with serum 25(OH)D levels below 30 ng/mL (after adjustments for BMI and percent body fat.) A European study also showed evidence of vitamin D supplementation decreasing the risk of type 1 diabetes. Other small population studies in type 1 diabetic patients have shown supplementation improved glycemic control, although there is mixed evidence regarding improvement in type 2 diabetic patients. Other small trials have shown evidence for increased insulin secretion and decreased hemoglobin A1c (HbA1c) in patients supplemented with vitamin D. There are currently multiple on-going trials regarding this topic.

In addition to glycemic control in diabetes, vitamin D has also been linked in one study to complications such as diabetic peripheral neuropathy. In this small study of 210 type 2 diabetic patients with or without diabetic peripheral neuropathy, vitamin D was assessed. Eighty-seven patients had diabetic peripheral neuropathy with a significantly longer duration of diabetes and higher HbA1c than those without. The mean serum 25(OH)D level was significantly lower in individuals with neuropathy, and there were significant correlations between serum 25(OH)D levels and total cholesterol, LDL-cholesterol and urine microalbumin:creatinine ratio. This data suggests vitamin D deficiency may be an independent risk factor for diabetic peripheral neuropathy.

Cardiovascular Disease

Adding to the increased risk of metabolic syndrome and diabetes, cardiovascular disease (CVD) has

been linked in epidemiological studies to vitamin D deficiency. A few studies in relation to endothelial dysfunction have shown statistically significant improvement in arterial stiffness compared to placebo when supplemented with vitamin D. Vitamin D supplementation has also been shown to have a beneficial effect on elastic properties of the arterial wall in a randomized placebo-controlled intervention study in post-menopausal women.

Epidemiological studies also suggest that low levels of serum 25(OH)D are associated with an increased risk of CVD and mortality. There is expression of VDR in the heart and blood vessels, which suggests a role of vitamin D in the cardiovascular system. VDR-knockout mice suffer from CVD, and various experimental studies suggest cardiovascular protection by vitamin D. A retrospective, cross-sectional analysis report displayed increased rates of hypertension in individuals who tested for lower levels of 25(OH)D, which started at 40 ng/mL. The odds ratio was 2.7 for vitamin D levels less than 15 ng/mL, 2.0 from 15 to 30 ng/mL, and 1.3 for 30 to 39 ng/mL.

A few randomized controlled trials (RCTs) looking at CVD events as a secondary outcome have found a moderate reduction in CVD risk (not shown to be statistically significant) using exclusive vitamin D supplementation. Further studies are being explored, such as the VITAL Study, in which researchers have enrolled 20,000 men and women across the U.S. to investigate whether taking daily dietary supplements of vitamin D₃ (2,000 IU or placebo) or omega-3 fatty acids (Omacor® fish oil/EPA+DHA [1 gm/840 mg] or placebo) reduces the risk for developing cancer, heart disease, and stroke in persons who do not have a prior history of these illnesses.

Depression

Psychological conditions, such as depression and seasonal affective disorder (SAD), have also been

linked to vitamin D deficiency. An RCT of overweight and obese patients with depression compared 20,000 IU or 40,000 IU of vitamin D supplementation with placebo weekly for one year. Both groups with vitamin D supplementation had improved BECK depression scores from baseline, but the placebo groups did not. This trial did exclude patients on antidepressant medications. Gloth *et al.* studied vitamin D deficiency in SAD, and in this small trial of 15 patients, eight received vitamin D therapy and seven received ultraviolet light therapy. All had improved vitamin D status (74 percent in the vitamin D group; 36 percent in the ultraviolet light therapy group). Vitamin D level improvements in this study were also significantly associated with improvements in depression scores. Available evidence does not definitively demonstrate that vitamin D deficiency is a cause of or risk for developing depression, or that vitamin D is an effective therapy for depression.

Infectious Disease

There is additional evidence that vitamin D is required for the expression of cathelicidin by macrophages, which is involved in killing bacteria. Most data about vitamin D and infectious disease surrounds tuberculosis (TB). A meta-analysis of seven observational studies found a higher risk of tuberculosis in those with the lowest vitamin D levels, although supplementation with vitamin D in one trial did not improve TB treatment outcomes. However, in this particular trial, the dose of 100,000 IU of vitamin D at zero, three and eight months may have been subtherapeutic in regard to treatment, since serum 25(OH)D levels did not differ from placebo. Ginde *et al.* also demonstrated that the prevalence of upper respiratory tract infections in the NHANES III population increased significantly as the serum 25(OH)D levels dropped, regardless of the season of the year, and was greatest during the winter when 25(OH)D levels were lowest.

Asthma

Evidence continues to reveal that vitamin D may also play a role in asthma. Vitamin D receptors are also located on lung bronchial smooth muscle cells, mast cells, dendritic cells and regulatory T-cells. Vitamin D then inhibits cytokine synthesis and release, decreases inflammation, and inhibits bronchial smooth muscle cell proliferation and remodeling. Vitamin D can also enhance interleukin-10 synthesis, which is a potent anti-inflammatory cytokine.

In addition, evidence demonstrated that men and women with serum 25(OH)D levels above 35 ng/mL had a 176 mL increase in forced-expiratory volume in one second (FEV₁). Children of women who had vitamin D deficiency during pregnancy were shown to be at an increased risk of wheezing illnesses. A small study of 86 children also revealed there were lower serum 25(OH)D levels in children with severe, therapy-resistant asthma, which were associated with increased airway smooth muscle masses, and worsened asthma control and lung function ($p<0.001$). Data on asthma in the literature is growing, and researchers have hypothesized that vitamin D supplementation may improve asthma control, but there are limited prospective studies to confirm this hypothesis.

Cancer

Carcinomas have also been linked to vitamin D deficiency and insufficiency in recent literature. A meta-analysis of case-control studies assessing serum 25(OH)D levels has shown for each 20 ng/mL increase in serum 25(OH)D levels, odds of colon cancer were reduced by more than 40 percent. One large RCT sought to determine if supplementation of 400 IU per day plus calcium had an effect on the incidence of colon cancer. There was no significant effect seen, as concentrations of serum 25(OH)D were measured at baseline but not during follow-up. Thus, it was difficult to determine if the dose even increased deficient levels.

Due to colon cancer's long latency period, a trial length of only eight years could have been a significant limitation to the study.

Other forms of cancer, such as breast cancer, have also been linked to vitamin D deficiency. A meta-analysis of vitamin D and the prevention of breast cancer found a 45 percent decrease in breast cancer for those in the highest quartile of circulating 25(OH)D of 60 nmol/L (about 24 ng/mL) compared with the lowest. A limitation with breast cancer and vitamin D research is that obesity can be a confounding factor that is difficult to separate.

Other cancers, such as prostate cancer and pancreatic cancer, have been reviewed as well. The most recent meta-analysis for the U.S. Preventative Services Task Force suggests evidence is not sufficiently robust to draw conclusions regarding the benefit or harm of vitamin D supplementation for the prevention of cancer.

Chronic Kidney Disease (CKD)

Supplementation and treatment deficiency guidelines in CKD vary depending upon serum 25(OH)D levels and stage of CKD, and are discussed in the Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guidelines for Bone Metabolism and Disease in Chronic Kidney Disease. There have been recent reports demonstrating these guidelines may be outdated and not adequate. A recent review by Melamed *et al.* in the *Clinical Journal of the American Society of Nephrology* provides detailed information on recent studies done in CKD and ongoing studies in vitamin D therapy for CKD.

Overall Mortality

In addition to individual disease processes, the role of vitamin D deficiency in overall mortality has been studied and prospective observational data in older adults suggest a 45 percent lower risk of overall mortality in those with serum 25(OH)D levels greater than

Table 1
Recommendations for vitamin D intake to prevent deficiency

Age/ Condition	Institute of Medicine		Endocrinology Society	
	Recommended Intake (IU/day)	Upper Limit (IU/day)	Recommended Intake (IU/day)	Upper Limit (IU/day)
0-6 months	400	1,000	400	2,000
6-12 months	400	1,500	400	2,000
1-3 years	600	2,500	600	4,000
4-8 years	600	3,000	600	4,000
9-18 years	600	4,000	600	4,000
19-50 years	600	4,000	600	10,000
51-70 years	600	4,000	600	10,000
>70 years	800	4,000	800	10,000
Pregnancy	600	4,000	600	10,000
Lactation	600	4,000	600	10,000

40 ng/mL compared with those less than 10 ng/mL (HR 0.55; 95 percent CI, 0.34-0.88). The NHANES III Database also shows an increase in adjusted all-cause mortality as serum 25(OH)D levels fall to less than 30 ng/mL, especially in women, as well as peak protection from death with a 25(OH)D level in the 35 to 40 ng/mL range.

Most of the increase in all-cause mortality from this evidence can be accredited to cardiovascular deaths. Although epidemiological studies have shown links to vitamin D deficiency and insufficiency, this information must be taken lightly due to the fact there is no cause and effect relationship. It is not known whether the vitamin D deficiency happened first or second. Vitamin D may also be a surrogate marker for poor health status because it reflects an inability to get outdoors for ultraviolet B exposure due to comorbid conditions or poor exercise tolerance. A recent study by Dror *et al.* has suggested there might actually be a nonlinear association between vitamin D levels and cardiovascular mortality. They found that vitamin D levels in the 20 to 36 ng/mL range were associated with the lowest risk for mortality and morbidity, and the hazard ratio below and above this range increased significantly. This is controversial due to the popular belief that the more vitamin D, the better. Limitations to this study were the small sample size and a

primarily Israeli population.

Continued interest in vitamin D and the non-calcemic mechanisms have led to trials such as the VITAL Study mentioned earlier. More information from both this study and other large scale studies will be needed to determine if supplementation can improve chronic disease states.

Screening for Vitamin D Deficiency

At the time of writing this lesson, screening for vitamin D deficiency is not recommended for everyone. Screening should only be performed in individuals thought to be at risk. Individuals at risk for vitamin D deficiency typically include those at risk for (1) bone disorders (rickets, osteomalacia, osteoporosis), (2) chronic kidney disease, (3) hepatic failure, (4) malabsorption syndromes, (5) hyperparathyroidism, (6) granuloma-forming disorders and (7) some lymphomas; (8) patients on certain medications (antiseizure medications, glucocorticoids, AIDS medications, antifungals, and cholestyramine), (9) African American and Hispanic children and adults, (10) pregnant and lactating women, (11) older adults with history of falls or non-traumatic fractures, (12) obese children and adults.

Recommended Dosing for Prevention and Treatment

Proper prevention and treatment recommendations for patient populations are dependent upon age, disease states and conditions. To monitor vitamin D levels, most organizations recommend using the serum 25(OH)D. A serum 1,25(OH)₂D level is not recommended unless there are certain conditions present, such as acquired and inherited disorders of vitamin D and phosphate metabolism. Serum 25(OH)D is considered the best measure of vitamin D status in patients at the time of writing this lesson due to serum 25(OH)D's half-life of approximately three weeks, and its ability to assess both nutritional intake and skin synthesis of vitamin D.

Differing recommendations exist for the definition of serum 25(OH)D deficiency and insufficiency. The most recent clinical practice guidelines from the Endocrine Society in July 2011 state adequate serum 25(OH)D levels should be at or above 30 ng/mL. A serum 25(OH)D level below 20 ng/mL and between 21 and 29 ng/mL is defined as deficiency and insufficiency, respectively. The National Osteoporosis Foundation also recommends serum 25(OH)D levels be at the desired level of at least 30 ng/mL. On the other hand, the Institute of Medicine has recommended a serum 25(OH)D level above 20 ng/mL for good bone health, but has defined deficiency as serum 25(OH)D levels below 12 ng/mL and inadequate levels with serum 25(OH)D of 12 to 20 ng/mL. Table 1 includes recommendations of the Institute of Medicine and the Endocrinology Society for vitamin D dosing to prevent deficiency.

Due to changes in society and occupational transformations over the past few decades, vitamin D deficiency today often results from lack of exposure to sunlight or decreased consumption of vitamin D-fortified milk. The dosage range for vitamin D supplementation recommendations differ among organizations and experts. Vitamin D deficiency and supplementation is a very expansive topic at this time with numerous

studies and controversies. Therefore, in this lesson, the ranges discussed below are from recent guideline recommendations for prevention and treatment of vitamin D deficiency for pediatrics, adults, pregnant and lactating females, and obese adults.

Infants and Children

For prevention of deficiency, infants up to one year of age require at least 400 IU/day of vitamin D. Colostrum and human breast milk contain low amounts of vitamin D. Breastfed infants, even if being supplemented with formula, should be supplemented with 400 IU/day of vitamin D beginning in the first few days of life; this should continue until the infant is weaned to at least 1,000 mL/day of formula. Infants receiving \geq 1,000 mL of formula per day should be receiving the recommended 400 IU/day of vitamin D in the formula; therefore, they do not need to be supplemented until formula intake falls below this threshold. As infants are weaned from breastfeeding or formula, vitamin D-fortified milk (after one year of age) or vitamin supplements should be encouraged to provide 400 IU/day of vitamin D.

The recommendation for children one to 18 years of age is 600 IU/day of vitamin D. For treatment of deficiency in infants up to one year of age and children one to 18 years, the suggested dose is 2,000 IU/day of vitamin D for six weeks, or 50,000 IU once weekly for six weeks to achieve a serum 25(OH)D level above 30 ng/mL. After this level is achieved, maintenance therapy of 400 to 1,000 IU/day of vitamin D to promote optimal bone health is recommended for infants up to one year of age, and 600 to 1,000 IU/day for children one to 18 years of age.

Adults

In adults, the recommended vitamin D intake to maximize bone health and muscle function is at least 600 IU/day and 800 IU/day for adults aged 19 to 70 and 70 or more years, respectively. The

National Osteoporosis Foundation recommends a higher dosage of 800 to 1,000 IU/day for all adults aged 50 or older. Treatment recommendations for vitamin D deficiency in adults are 6,000 IU/day of vitamin D or 50,000 IU once a week for eight weeks, to achieve a serum 25(OH)D level above 30 ng/mL. Once achieved, this should be maintained by using 1,500 to 2,000 IU/day of vitamin D. It has also been shown that 50,000 IU of vitamin D₂ once every other week allowed serum 25(OH)D levels to be maintained at 35 to 50 ng/mL without toxicity. Nursing home residents have also used 50,000 IU of vitamin D₂ three times per week for one month, or 100,000 IU every four months.

Obese Individuals

Due to the body's ability to store the fat-soluble vitamin D in adipose tissue, the recommended dose of vitamin D for obese adults (BMI $>30 \text{ kg/m}^2$) should be at least two to three times the amount that is typically recommended for the individual's age group. Previously, to prevent vitamin D deficiency in obese individuals, recommendations have been to provide 1,000 to 2,000 IU/day or 50,000 IU vitamin D every one, two or four weeks to achieve serum 25(OH)D levels of at least 30 ng/mL. Treatment of vitamin D deficiency could require at least 6,000 to 10,000 IU/day to maintain a serum 25(OH)D level above 30 ng/mL. Another treatment recommendation would be to provide 50,000 IU of vitamin D every week for eight to 12 weeks, and then repeat for another eight to 12 weeks if serum 25(OH)D is found to be less than 30 ng/mL.

Pregnant and Lactating Women
For pregnant and lactating females, vitamin D deficiency can be common, notably in high-risk women, including vegetarians, women with limited sun exposure, and ethnic minorities (especially with darker skin). Deficiency has also been shown to be linked to developing preeclampsia, gesta-

tional diabetes, and cesarean section delivery.

Also, vitamin D deficiency in pregnant women has shown an increased risk of babies with lower birth weight for their gestational age and for development of disease in the future. Vitamin D supplementation is also very important to help prevent childhood rickets and osteomalacia in pregnant women. Recommendations for both pregnant and lactating females for vitamin D supplementation are at least 600 IU/day. Supplementing above the recommended 400 IU/day in most prenatal vitamins has not been studied extensively. There is insufficient evidence at this time to screen all pregnant women for vitamin D deficiency, unless there is concern.

The Endocrine Society recommends that serum 25(OH)D levels should be maintained at 30 ng/mL or above, and that the 1,000 to 2,000 IU/day of vitamin D needed to reach this level is considered safe by most experts. A recent study by Hollis *et al.* concluded that for all women, regardless of race, 4,000 IU/day of vitamin D is a safe and effective way to raise 25(OH)D levels to achieve sufficiency. In this study, pregnant women were randomized to receive either placebo, 400 IU/day, 2,000 IU/day, or 4,000 IU/day depending on baseline 25(OH)D levels. The primary outcome one month prior and at delivery was statistically different between each group, with the patients receiving 4,000 IU/day at the highest mean 25(OH)D level. Half of the mothers who received 400 IU/day met a secondary outcome with serum 25(OH)D levels $>32 \text{ ng/mL}$ prior to delivery. In all groups, improvement of vitamin D status came without toxicity or adverse events. Women with serum 25(OH)D levels greater than 40 ng/mL at the initial visit were not included in the 4,000 IU/day group. Thus, it is difficult to extrapolate this data to all females without testing baseline serum 25(OH)D levels. Supplementation with vitamin D was not used during the first 12 weeks of gestation; thus data cannot speak to the safety of these regimens during the first tri-

mester. Overall, vitamin D supplementation above the recommended dosage during pregnancy should be individualized until further studies are done, especially during the first 12 weeks of pregnancy.

Vitamin D Supplements and Dietary Sources

The two forms of vitamin D supplements available are vitamin D₂ (ergocalciferol, plant-derived) and vitamin D₃ (cholecalciferol, fish-derived). Vitamin D₃ is the natural form of vitamin D and is chemically similar to what is produced by the skin during sun exposure. Some evidence has shown vitamin D₃ to be superior in raising vitamin D levels to sufficient concentrations due to slower metabolism.

Another study reports vitamin D₂ and D₃ to be equally effective in maintaining vitamin D levels. Dosage forms of vitamin D₂ and D₃ supplements are available in strengths of 400 IU, 800 IU, 1,000 IU, 2,000 IU, 5,000 IU, 8,000 IU, 10,000 IU, and 50,000 IU as capsules, solutions, drops, gummies, and tablets. Few foods provide the needed source of vitamin D, with most averaging vitamin D content between 100 to 200 IU. Dietary sources that are vitamin D-fortified include milk, orange juice, yogurt, margarine, cheeses, some bread products and cereal. Other dietary sources of vitamin D include swordfish, salmon, tuna, sardines, liver, and egg yolk.

Vitamin D Toxicity

Toxicity is always a concern with any supplement or medication. Vitamin D toxicity can cause hypercalcemia, hypercalciuria, vascular and soft tissue calcification, nephrolithiasis, and retarded growth and hypercalcemia in infants. There is also emerging evidence that toxicity can contribute to all-cause mortality, selected cancers, cardiovascular risks, falls and fractures. Hypercalcemia is usually the sign of acute toxicity with vitamin D, and has been seen with doses that exceed 10,000 IU/day and 25(OH)D levels above 150

calcemic mechanisms, once thought to be vitamin D's only role in the human body.

The authors, the Ohio Pharmacists Foundation and the Ohio Pharmacists Association disclaim any liability to you or your patients resulting from reliance solely upon the information contained herein. Bibliography for additional reading and inquiry is available upon request.

This lesson is a knowledge-based CE activity and is targeted to pharmacists in all practice settings.

Program 0129-0000-14-002-H01-P

Release date: 2-15-14

Expiration date: 2-15-17

CE Hours: 1.5 (0.15 CEU)

The Ohio Pharmacists Foundation Inc. is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.



Please see Continuing Education quiz on next page.

Endorsed[®] by:

NJPhA
New Jersey Pharmacists Association | est. 1870

*Our commitment to quality
means you can rest easy.*

Pharmacists Mutual has been committed to the pharmacy profession for over a century. Since 1909, we've been insuring pharmacies and giving back to the profession through sponsorships and scholarships.

Rated A (Excellent) by A.M. Best. Pharmacists Mutual is a trusted, knowledgeable company that understands your insurance needs. Our coverage is designed by pharmacists for pharmacists. So you can rest assured you have the most complete protection for your business, personal and professional insurance needs.

Learn more about Pharmacists Mutual's solutions for you – contact your local field representative or call 800.247.5930.

Jack Babnew or Joe Pace
Colonial Insurance Management Inc. | 732.203.1200



COLONIAL INSURANCE MANAGEMENT

**Pharmacists
Mutual Companies**

PO Box 370 • Algona Iowa 50511

*Compensated endorsement.
Not licensed to sell all products in all states.

continuing education quiz

Vitamin D Deficiency and Treatment

1. Which of the following is the biologically active form of vitamin D?
 - a. Ergocalciferol
 - b. Cholecalciferol
 - c. 25(OH)D
 - d. 1,25(OH)₂D
2. Data from National Health and Nutrition Examination Surveys (NHANES) from 2001 to 2006 report what percentage of Americans were at risk for vitamin D deficiency with a 25(OH)D level less than 10 ng/mL?
 - a. 5 percent
 - b. 8 percent
 - c. 15 percent
 - d. 30 percent
3. Risk factors for vitamin D deficiency include all of the following EXCEPT:
 - a. obesity.
 - b. age >65 years.
 - c. insufficient sunlight exposure.
 - d. light skin.
4. Which of the following statements is true regarding racial disparities and vitamin D?
 - a. African Americans have a higher serum 25(OH)D level than White Americans.
 - b. Suboptimal vitamin D status may contribute to racial disparity in albuminuria.
 - c. Preterm birth rates have never been associated with decreased vitamin D levels.
 - d. White Americans have a higher rate of hypertension vs. African Americans which could be related to 25(OH)D levels.
5. Which of the following is true regarding vitamin D and diabetes?
 - a. Vitamin D deficiency has only been linked to type 2 diabetes.
 - b. In a small study, mean vitamin D levels were found to be significantly higher in those with extensive peripheral neuropathy.
 - c. Evidence suggests vitamin D influences beta cell function directly and may make beta cells more resistant to types of cellular stress.
 - d. There is no established relationship between vitamin D and diabetes.
6. Ginde *et al.* demonstrated that the prevalence of upper respiratory tract infections increased significantly as the serum 25(OH)D levels dropped, regardless of the season of the year.
 - a. True
 - b. False

• • • • • • • • • • • • • • • • • • • • •
Completely fill in the lettered box corresponding to your answer.

1. [a] [b] [c] [d]
2. [a] [b] [c] [d]
3. [a] [b] [c] [d]
4. [a] [b] [c] [d]
5. [a] [b] [c] [d]
6. [a] [b]
7. [a] [b] [c]
8. [a] [b] [c] [d]
9. [a] [b] [c] [d]
10. [a] [b] [c] [d]
11. [a] [b] [c] [d]
12. [a] [b] [c] [d]
13. [a] [b]
14. [a] [b] [c] [d]
15. [a] [b] [c] [d]

I am enclosing \$5 for this month's quiz made payable to: Ohio Pharmacists Association.

1. Rate this lesson: (Excellent) 5 4 3 2 1 (Poor)
2. Did it meet each of its objectives? yes no
If no, list any unmet _____
3. Was the content balanced and without commercial bias?
 yes no
4. Did the program meet your educational/practice needs?
 yes no
5. How long did it take you to read this lesson and complete the quiz? _____
6. Comments/future topics welcome.

Please print.

Program 0129-0000-14-002-H01-P
0.15 CEU

Name _____

Address _____

City, State, Zip _____

Email _____

NABP e-Profile ID _____ Birthdate _____ (MMDD)

**Return quiz and payment (check or money order) to
Correspondence Course, OPA,
2674 Federated Blvd, Columbus, OH 43235-4990**

7. Cancers with potential links to vitamin D deficiency include all of the following EXCEPT:

- a. breast cancer.
- b. colon cancer.
- c. thyroid cancer.

8. What is the recommended daily intake of vitamin D for a 6-year-old?

- a. 200 IU
- b. 400 IU
- c. 600 IU
- d. 800 IU

9. Most of the data regarding all-cause mortality and vitamin D can be accredited to which of the following?

- a. Cardiovascular deaths
- b. Diabetes complication deaths
- c. End-stage renal disease
- d. Asthma deaths

10. All of the following individuals could be at risk for vitamin D deficiency and should be screened EXCEPT those:

- a. with chronic kidney disease.
- b. on glucocorticoids.
- c. who are obese.
- d. with hypoparathyroidism.

11. How much vitamin D supplementation is required per day for a three-month-old receiving both breast milk and approximately 600 mL of formula?

- a. 200 IU
- b. 400 IU
- c. 600 IU
- d. 800 IU

12. Because vitamin D is fat soluble and stored in adipose tissue, the recommended dose for individuals with BMIs >30 kg/m² is how much greater than typically required for that individual's age group?

- a. Should be the same
- b. Four to five times
- c. Three to four times
- d. Two to three times

13. All pregnant women should be screened for vitamin D deficiency.

- a. True
- b. False

14. Which of the following is NOT a dietary source of vitamin D?

- a. Swordfish
- b. Egg yolk
- c. Chicken
- d. Liver

15. Which of the following is NOT a sign of vitamin D toxicity?

- a. Tachycardia
- b. Metallic taste
- c. Vascular calcinosis
- d. Pancreatitis

• • • • • • • • • • • • • • • • • • • • •

To receive CE credit, your quiz must be received no later than February 15, 2017. A passing grade of 80% must be attained. CE credit for successfully completed quizzes will be uploaded to the CPE Monitor. CE statements of credit will not be mailed, but can be printed from the CPE Monitor website. Send inquiries to opa@ohiopharmacists.org.

february 2014



WILL YOU SURVIVE YOUR PHARMACY?

Will your pharmacy survive you?

At RDC, we believe the answer to these questions is a resounding... “Yes!” That’s why we’re proud to present a unique and powerful program for taking you far beyond mere survival.

The Inspired Independence Program delivers the strategies, tools and support you need to thrive as a pharmacy owner.

Created and delivered by Waypoint Pharmacist Advisors, the program is good news for:

- Exiting your pharmacy when and how you wish
- Enjoying greater independence during and after pharmacy ownership
- Making exceptional personal financial decisions
- Implementing a highly effective personal investment plan
- Leaving a meaningful and enduring family and business legacy

**Getting started is simple,
free and takes only
30 minutes**

Call: 843.873.4420
Email: Rick@waypointus.com
For more information visit
www.waypointus.com/RDC

Yes! It is your time to thrive!



INDEPENDENT PHARMACY IS OUR BUSINESS



*The Inspired
Independence
Program™*

WAYPOINT
PHARMACIST ADVISORS
WE TAKE CARE OF YOU!

Practice Spotlight:

How Did I Get Here?

If you ask me what I am, I will tell you I am a pharmacist; but if you ask me what I do, I will answer “medical writing.” My current position is Senior Medical Writer at Maxcess Managed Markets, the market access agency and fastest growing business unit within Publicis Healthcare Communications Group (PHCG). “How did I get here?” you ask. As a pharmacy student, I aspired to be a medical writer, but much like it still is today, the options available to me were elusive. I had already worked in a pharmacy since high school and I started working part-time as a retail community pharmacist immediately upon getting my pharmacist license while finishing 6th year clinical rotations at Ernest Mario School of Pharmacy at Rutgers University. Thanks to a Rutgers career fair, upon graduation I started my career as a medical writer in a small, privately-owned medical communications agency, focusing on publications planning and development, branded promotion for healthcare professionals, and later continuing medical education. I then went back to full-time retail community pharmacy for one of the large chains for the last seven years. During that time, I was also a freelance medical writer and worked on slide decks, curriculum development, and meeting reports to name a few types of projects. But my itch was always to go back to writing full-time.

Last year, an amazing opportunity came up not only to write again, but to specialize in managed markets. This is an up-and-coming niche, as many medical communications agencies are instituting specialized managed markets divisions in light of the ever-evolving and increasingly complicated health care landscape. What better activity for a pharmacist than to help create strategies to maximize market access? Do I miss patient care? Yes I do, but I am still helping patients by creating ways to overcome the barriers to access, whether they be health literacy issues, financial hurdles, or policy-related obstacles. Every day in practice, we as pharmacists see the myriad of reasons why patients often cannot and do not ultimately get the medications prescribed for them. And we intimately know the ins and outs of cost-containing measures, such as step edits and prior authorizations, how they actually occur in the real world, and how they affect our patients. How many of us have 10, 50, 100 pending prescriptions on which we are waiting a prior authorization form to be submitted to the payer, waiting for it to be reviewed, waiting for an approval, all while the patient should have started their treatment already? Well, now my job is to help expedite that process from the outside – by providing key stakeholders (formulary decision makers, providers, office staff, and pharmacists) with resources to ultimately get the prescription to the patient. In developing strategies and tactics, I can address the obstacles that are preventing patient access to prescriptions. While a brand teams’ goal is to encourage prescribers to write for their product, once the prescription makes it to the pharmacy, it is another challenge to ensure the patient purchases that prescription and keeps taking it.

As a strategic partner with pharmaceutical companies, Maxcess Managed Markets provides insights and expertise to design innovative strategic and tactical solutions across multiple channels

maxcess managed markets

to optimize access and strengthen brand plans. As a full-service agency with strategic and creative know-how, we help develop effective managed markets plans that solve communication challenges and create meaningful connections. We develop clear and concise strategic messaging and carry it through the payer-patient-provider continuum. Our in-house experts and industry advisors have a deep understanding of the dynamic health care landscape.

Select Examples of What We Do:

- Researching channel market opportunities
- Creating market access strategies to secure market readiness and product resonance
- Developing value proposition messaging and tactics
- Translating economic research data to support brand goals
- Designing pull-through strategies using nonpersonal and personal approaches
- Formulating training materials for account management and field sales teams
- Evaluating effectiveness of tactics and messages

Our staff consists of strategic thinkers, copy experts, creative minds, graphic artists, and account professionals. Some individuals are health care professionals, some have advanced degrees in the health sciences, and some have business and/or managed care experience. Our target audiences span the gamut of the health care landscape and include business decision makers as well as health care providers and patients. See Figure 1 on next page.

The Role of a Medical Writer

COLLABORATION IS KEY! The approach to any project from creative brief to execution is collaborative. In any given day, I have numerous interactions with account professionals, editors, the creative team (graphic designers and Art Directors), sister agencies (who offer expertise in web design, iPad programming, and app development) and of course, clients. I and my fellow medical writing colleagues are responsible for creating bold, on-strategy, medically accurate, persuasive, and relevant copy for our clients, with deliverables such as monographs, slide decks, visual aids, brochures, flashcards, and educational tools tailored to various specific audiences.

Our job responsibilities include:

- Researching and developing copy concepts that are relevant, strategically focused, evidence-based, and thought provoking
- Developing programs, incorporating external expert/client input, and being responsible for the quality, medical accuracy,

- and integrity of the content while adhering to budget and project specifications
- Becoming acquainted with clients and understanding a product's challenges in relation to the overall market
 - Researching the current medical/managed care landscape for up-to-date references and new strategies
 - Assuring that written materials and slides meet strategic goals and project objectives and contain appropriate scientific and marketing messages, through the development and implementation of an approved project brief
 - Initiating discussions with Account Leads regarding any potential barriers to successful project completion that may arise (deadline, hours, budget, etc) and suggesting solutions that address client and internal agency needs
 - Adhering to project parameters including deadlines, budget, and content limitations
 - Accurately referencing and annotating of all material following the style established by/for client (usually AMA)
 - Preparing materials for medical/legal review, and as required, participating in client's medical/legal review process and providing solutions to ensure/accelerate approval
 - Managing on-site coverage for medical conferences and symposia and developing associated slide decks, executive summaries, and meeting reports
 - Traveling on-site to provide input and expertise

In addition, a medical writer must be able to analyze and interpret scientific data, demonstrate strong organizational, analytical, and interpersonal communication skills, manage projects with limited direction and work within tight deadlines, possess strong verbal and written communication skills, have the ability to interface directly with client and external experts, be familiar with internet research (PubMed and other document delivery systems), and be able to determine appropriate references and resources.

Opportunities

If you are wondering about the career opportunities for pharmacists beyond direct patient care, or perhaps your students or interns want to know what types of post-graduate careers they can pursue, know that there are practice sites for pharmacists beyond inpatient and outpatient facilities where they can apply their clinical knowledge and communication skills in a unique way.

For more information and resources on medical writing, please visit the American Medical Writers Association (AMWA) at www.amwa.org.

For more information on managed care pharmacy, please visit the Academy of Managed Care Pharmacy (AMCP) at www.amcp.org.

For more information or careers within PHCG, please see our website: <http://www.maxcessmm.com> or contact me at: nicole.lovullo@maxcessmm.com

About the Author

Nicole M. Lovullo, PharmD, RPh
Senior Medical Writer

Maxcess Managed Markets

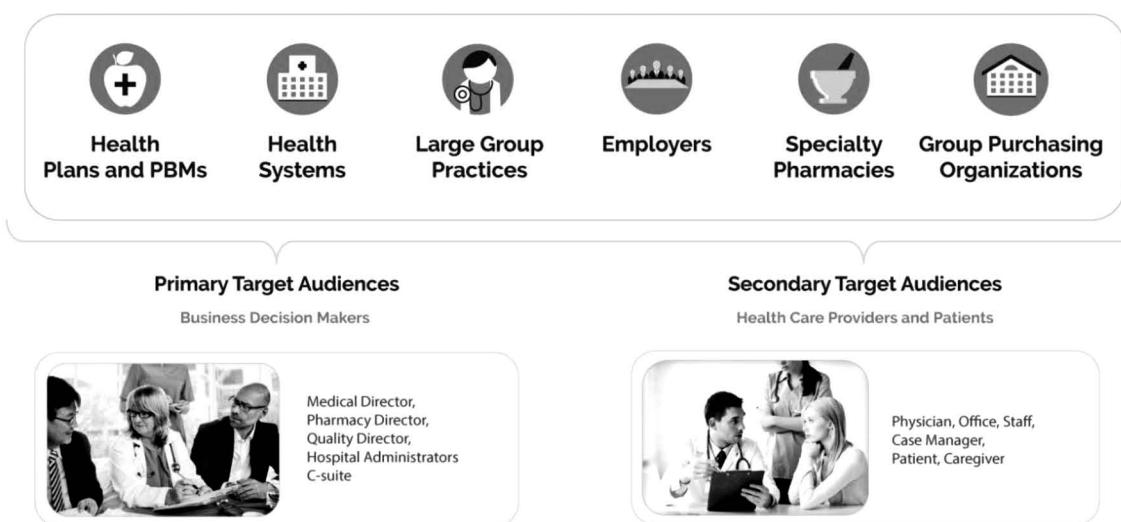
1200 Route 22 East
Bridgewater, NJ 08807

908-203-3462 (phone)

908-203-4588 (fax)

nicole.lovullo@maxcessmm.com

Figure 1. Primary and secondary target audiences



Don't miss these certificate training programs...

Presented at NJPhA's 145th Annual Convention

Harrah's Atlantic City, October 16 – 18

Register today at [www.njpharmacists.org!](http://www.njpharmacists.org)

- Preparing for a Consultant Pharmacist Career**

Total contact hours: 15 hours, 1.5 CEU

Accredited for pharmacists

- Delivering Medication Therapy Management Services**

Total contact hours: 21 hours, 2.1 CEU

Accredited for pharmacists

- Compounding Essentials**

Total contact hours: 15 hours, 1.5 CE

Accredited for pharmacists and pharmacy technicians



**PREPARING
for
A CONSULTANT
PHARMACIST CAREER**



COMPOUNDING ESSENTIALS

Walgreens
AT THE CORNER OF **HAPPY & HEALTHY™**



145th Annual Meeting and Convention

October 16-18, 2015

Harrah's Hotel and Casino Atlantic City, New Jersey

Registration is OPEN at www.njpharmacists.org.
Sign up today!

Call 1.800.553.2730

Email: bmotley@hlcoshatt.com



H. L. COSHATT COMPANY, INC.

www.hlcoshatt.com



ONE OF THE
LARGEST
DISTRIBUTORS
OF

Lozier®
SHELVING
IN THE NATION

Pharmacy Shelving

- Flex RX & Classic Shelving
- Under-Counter Units
- Pick-up/Drop-off Area
- Check-out & Consultation Area

Retail Shelving

- Merchandise Shelving
- Display Showcasing
- Shelving Accessories
- DME
- Décor & Signage



INDEPENDENT PHARMACY
IS
OUR BUSINESS

NOW PARTNERING WITH RDC

Jay Shearer
jjshearer@rdcdrug.com
(C) 607.759.2570



Lanny Doud
lanny@qcpharmacies.com
(C) 585.739.4268