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DERM Perspectives

Practical Advice for the Dermatology Physician Assistant

How Vehicles Affect Patient Adherence in Acne Therapy

Advancements in vehicle formulation can improve patient comfort.

By Coyle S. Connolly, DO

Concentration and dose-dependent irritation associated with benzoyl peroxide (BPO) and tretinoin are well known to clinicians and to many patients. Yet benzoyl peroxide—often used as a component of a fixed combination formulations that also contain clindamycin—and tretinoin are among the most commonly prescribed topical treatments for acne.¹⁻⁴ Patients who experience irritation and dryness associated with these agents are not likely to adhere to the treatment regimen as prescribed.⁵⁻⁹ Patients may discontinue therapy altogether, reduce the frequency



► 6

Patient Management: Frequent Urination and Increased Hunger in a 55-year-old Man

To help PAs stay sharp for the certification exam, this new feature of DermPerspectives tests your knowledge of medical and/or surgical subjects.

A 55-year-old African-American male with a history of moderate high blood pressure for four years presents to his general practice PA for an annual check-up. The patient has gained 12 lbs. over the past year, stating that much of the weight gain was in the past three to four months. He reports that he works out for about 30 minutes three times a week, but he “always feels hungry.”

He asks his PA about prostate health, noting that he finds himself urinating frequently.

He also notes that he is scheduled to see an ophthalmologist because his “reading glasses” are no longer sufficient; he occasionally experiences blurred vision. Upon further questioning, he indicates that blurriness is intermittent and not just evident when he tries to read small print or look at the computer screen.


The PA questions the patient and determines that his mother, now deceased, always said she was “pre-diabetic.” The PA orders a glucose tolerance test and blood glucose test.



Why? What other steps are indicated?

[Turn to Page 7 ►](#)

Exam Prep



Proven effective in the treatment of both inflammatory and noninflammatory lesions in moderate to severe acne

The clindamycin phosphate 1.2%/BPO 2.5% combination therapy with

Power to Please

Acanya® Gel – the once-daily combination optimized for both power *and* tolerability

Power to treat

In 2 double-blind, randomized, controlled studies of 2813 patients with moderate to severe acne, Acanya Gel demonstrated:

- 55% mean reduction in inflammatory lesion counts at 12 weeks (29% for vehicle)¹⁻³
- 43% mean reduction in noninflammatory lesion counts at 12 weeks (24% for vehicle)¹⁻³
- Patients reported significant improvement as soon as 2 weeks^{1,2}

Formulated to be one they'll love to use

- Favorable tolerability profile: in pivotal trials, no patient treated with Acanya Gel discontinued treatment due to erythema, scaling, burning, stinging, or itching¹
- Low potential for cutaneous irritation may lead to increased adherence to treatment
- Fragrance-free aqueous gel contains no alcohol, surfactants, parabens, or preservatives

Acanya Gel 
(Clindamycin Phosphate 1.2%
and Benzoyl Peroxide 2.5%)

To learn more, please visit www.AcanyaGel.com

Indication and Important Safety Information For the treatment of acne vulgaris in patients 12 years of age or older. In controlled clinical trials, the following application-site adverse reactions occurred in less than 0.2% of patients treated with Acanya Gel: application-site pain (0.1%), application-site exfoliation (0.1%), and application-site irritation (0.1%). Of the patients who experienced cutaneous symptoms of erythema, scaling, itching, burning, and/or stinging, regardless of the relationship to therapy, the majority of cases were mild to moderate in severity, occurred early in treatment, and decreased thereafter.

Acanya Gel is contraindicated in patients with a history of regional enteritis, ulcerative colitis, or antibiotic-associated colitis. Diarrhea, bloody diarrhea, and colitis have been reported with the use of topical clindamycin. Discontinuation is recommended if significant diarrhea develops.

Patients are advised to avoid applying in mouth, eyes, or nose, or on lips, and to minimize sun exposure following the application of Acanya Gel.

Please see reverse for brief summary of full prescribing information.

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Acanya Gel[®]

(Clindamycin Phosphate 1.2% and Benzoyl Peroxide 2.5%)

ACANYA[®] Gel

(clindamycin phosphate 1.2% and benzoyl peroxide 2.5%)

Brief summary. Please see full prescribing information for complete product information.

INDICATIONS AND USAGE

ACANYA Gel is indicated for the topical treatment of acne vulgaris in patients 12 years of older. The safety and efficacy of this product in the treatment of any other disorders have not been evaluated.

DOSE AND ADMINISTRATION

Apply a pea-sized amount of ACANYA Gel to the face once daily. Use of ACANYA Gel beyond 12 weeks has not been evaluated.

ACANYA Gel is not for oral, ophthalmic, or intravaginal use.

CONTRAINDICATIONS

ACANYA Gel is contraindicated in patients with a history of regional enteritis, ulcerative colitis, or antibiotic-associated colitis.

WARNINGS AND PRECAUTIONS

Colitis

Systemic absorption of clindamycin has been demonstrated following topical use of clindamycin. Diarrhea, bloody diarrhea, and colitis (including pseudomembranous colitis) have been reported with the use of topical and systemic clindamycin. When significant diarrhea occurs, ACANYA Gel should be discontinued.

Severe colitis has occurred following oral and parenteral administration of clindamycin with an onset of up to several weeks following cessation of therapy. Antiperistaltic agents such as the opiates and diphenoxylate with atropine may prolong and/or worsen severe colitis. Severe colitis may result in death.

Studies indicate toxin(s) produced by Clostridia is one primary cause of antibiotic-associated colitis. The colitis is usually characterized by severe persistent diarrhea and severe abdominal cramps and may be associated with the passage of blood and mucus. Stool cultures for Clostridium difficile and stool assay for C. difficile toxin may be helpful diagnostically.

Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation and treatment with an antibacterial drug clinically effective against C. difficile colitis.

Ultraviolet Light and Environmental Exposure

Minimize sun exposure following drug application. (See NONCLINICAL TOXICOLOGY)

ADVERSE REACTIONS

Clinical Studies Experience

Because clinical trials are conducted under prescribed conditions, adverse reaction rates observed in the clinical trial may not reflect the rates observed in practice. Because clinical trials are also conducted under widely varying conditions, adverse reactions observed in the clinical trials of a drug cannot always be directly compared to rates in the clinical trials of another drug. The adverse reaction information from clinical trials does, however, provide a basis for identifying the adverse reactions that appear to be related to drug use and for approximating rates.

The following selected adverse reactions occurred in less than 0.2% of patients treated with ACANYA Gel: application site pain (0.1%); application site exfoliation (0.1%); and application site irritation (0.1%).

During clinical trials, patients were assessed for local cutaneous signs and symptoms of erythema, scaling, itching, burning and stinging. Most local skin reactions increased and peaked around week 4 and continuously decreased over time reaching near baseline levels by week 12. The percentage of patients that had symptoms present before treatment, the maximum value recorded during treatment, and the percent with symptoms present at week 12 are shown below.

Local Skin Reactions—Percent Patients with Symptoms Present. Combined Results from the Two Phase 3 Trials (N = 773)

	Before Treatment (Baseline)			Maximum During Treatment ¹			End of Treatment (Week 12)		
	Mild	Mod*	Severe	Mild	Mod*	Severe	Mild	Mod*	Severe
Erythema	22	4	0	25	5	<1	15	2	0
Scaling	8	<1	0	18	3	0	8	1	0
Itching	10	2	0	15	2	0	6	<1	0
Burning	3	<1	0	8	2	0	2	<1	0
Stinging	2	<1	0	6	1	0	1	<1	0

*Mild-Moderate

DRUG INTERACTIONS

Erythromycin

ACANYA Gel should not be used in combination with topical or oral erythromycin-containing products due to its clindamycin component. In vitro studies have shown antagonism between erythromycin and clindamycin. The clinical significance of this in vitro antagonism is not known.

Concomitant Topical Medications

Concomitant topical acne therapy should be used with caution because a possible cumulative irritancy effect may occur, especially with the use of peeling, desquamating, or abrasive agents.

Neuromuscular Blocking Agents

Clindamycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. Therefore, ACANYA Gel should be used with caution in patients receiving such agents.

USE IN SPECIFIC POPULATIONS

Pregnancy Category C

There are no well-controlled trials in pregnant women treated with ACANYA Gel. It also is not known whether ACANYA Gel can cause fetal harm when administered to a pregnant woman. ACANYA Gel should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Animal reproductive/developmental toxicity studies have not been conducted with ACANYA Gel or benzoyl peroxide. Developmental toxicity studies of clindamycin performed in rats and mice using oral doses of up to 600 mg/kg/day (240 and 120 times amount of clindamycin in the highest recommended adult human dose based on mg/m², respectively) or subcutaneous doses of up to 200 mg/kg/day (80 and 40 times the amount of clindamycin in the highest recommended adult human dose based on mg/m², respectively) revealed no evidence of teratogenicity.

Nursing Mothers: It is not known whether clindamycin is excreted in human milk after topical application of ACANYA Gel. However, orally and parenterally administered clindamycin has been reported to appear in breast milk. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to use ACANYA Gel while nursing, taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness of ACANYA Gel in pediatric patients under the age of 12 have not been evaluated. Clinical trials of ACANYA Gel included patients 12-17 years of age.

Geriatric Use

Clinical studies of ACANYA Gel did not include sufficient numbers of patients aged 65 and older to determine whether they respond differently from younger patients.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility
Carcinogenicity, mutagenicity and impairment of fertility testing of ACANYA Gel have not been performed.

Benzoyl peroxide has been shown to be a tumor promoter and progression agent in a number of animal studies. Benzoyl peroxide in acetone at doses of 5 and 10 mg administered topically twice daily for 20 weeks induced skin tumors in transgenic Tg.AC mice. The clinical significance of this is unknown.

Carcinogenicity studies have been conducted with a gel formulation containing 1% clindamycin and 5% benzoyl peroxide. In a 2-year dermal carcinogenicity study in mice, treatment with the gel formulation at doses of 900, 2700, and 15000 mg/kg/day (1.5, 4.5, and 15 times amount of clindamycin and 3.6, 10.8, and 60 times amount of benzoyl peroxide in the highest recommended adult human dose of 2.5 g ACANYA Gel based on mg/m², respectively) did not cause any increase in tumors. However, topical treatment with a different gel formulation containing 1% clindamycin and 5% benzoyl peroxide at doses of 100, 500, and 2000 mg/kg/day caused a dose-dependent increase in the incidence of keratoacanthomas at the treated skin site of male rats in a 2-year dermal carcinogenicity study in rats. In an oral (gavage) carcinogenicity study in rats, treatment with the gel formulation at doses of 300, 900 and 3000 mg/kg/day (1.2, 3.6, and 12 times amount of clindamycin and 2.4, 7.2, and 24 times amount of benzoyl peroxide in the highest recommended adult human dose of 2.5 g ACANYA Gel based on mg/m², respectively) for up to 97 weeks did not cause any increase in tumors. In a 52-week dermal phototoxicity study in hairless mice, 140 weeks of treatment followed by 12 weeks of observation, the median time to onset of skin tumor formation decreased and the number of tumors per mouse increased relative to controls following chronic concurrent topical administration of the higher concentration benzoyl peroxide formulation (5000 and 10000 mg/kg/day, 5 days/week) and exposure to ultraviolet radiation.

Clindamycin phosphate was not genotoxic in the human lymphocyte chromosome aberration assay. Benzoyl peroxide has been found to cause DNA strand breaks in a variety of mammalian cell types. To be mutagenic in S. typhimurium tests by some but not all investigators, and to cause sister chromatid exchanges in Chinese hamster ovary cells.

Fertility studies have not been performed with ACANYA Gel or benzoyl peroxide, but fertility and mating ability have been studied with clindamycin. Fertility studies in rats treated orally with up to 300 mg/kg/day of clindamycin (approximately 120 times the amount of clindamycin in the highest recommended adult human dose of 2.5 g ACANYA Gel, based on mg/m²) revealed no effects on fertility or mating.

HOW SUPPLIED

ACANYA Gel (clindamycin phosphate 1.2% and benzoyl peroxide 2.5%) is supplied as a kit containing the following components:

Components	NDC#	Net Weight
Benzoyl Peroxide Gel	NDC 59987-101-25	40g
Clindamycin Phosphate Solution	NDC 59987-101-24	10g

Administering Instructions

Prior to dispensing, add the clindamycin phosphate solution in the bottle to the benzoyl peroxide gel and stir with the provided spatula until homogenous (at least 1 ½ minutes).

ACANYA Gel (admixed) can be stored at room temperature up to 25°C (77°F) for 2 months. Place a 2-month expiration date on the label immediately following admixing.

Storage and Handling

Store at 25°C (77°F). Protect from freezing. Keep out of the reach of children. Keep jar tightly closed.

RX Only

Marketed by CORIA Laboratories, a division of Valeant Pharmaceuticals North America, Aliso Viejo, CA 92656

Manufactured by Contract Pharmaceuticals Limited Niagara, Buffalo, NY 14213

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J Am Acad Dermatol. 2008;59:792-800. 2. Data on file, CORIA Laboratories.

3. Acanya Gel package insert, CORIA Laboratories.



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Professional
Opinions

Dear Physician Assistant:

This is certainly an exciting time to be caring for dermatology patients, as the specialty is enjoying an era of significant innovation. From a host of new topical drug formulations, a series of novel developments in the world of cosmetic dermatology, and the continued growth of the biologics field, therapeutic developments are extraordinary.

The beauty of our specialty is that it is so deceptively elegant. Consider the latest generation of optimized topical formulations optimized for many patients currently use. Their apparent simplicity belies the numerous technological considerations that go into ensuring their efficacy, efficiency, and tolerability. As discussed in this edition of **DermPerspectives**, the critical decisions made during the product formulation phase have important implications for the efficacy of a product as well as the likelihood that patients will adhere to therapeutic regimens—the ultimate ingredient for therapeutic success.

This edition of **DermPerspectives** will hopefully help you more critically consider therapeutic decisions and support your continued clinical success as you help to improve the cutaneous health of patients.

Best wishes,
Coyle S. Connolly, DO
Medical Editor

Letter From
The Editor

SDPA Student Website Benefits PAs in Training...and Established Derm PAs

A new website dedicated to meeting the information needs of PA students interested in dermatology has benefits for those in training and for the overall dermatology PA profession.

By Lauren R. Zajac MHS, PA-C
Director at Large, SDPA

When I was a student member of SDPA and paying \$100 membership fees, I didn't feel it was a valuable investment, nor that the derm fellow member population knew I existed for mentoring. As a student, money is much harder to come by, so it was important to me to decrease the student membership fee from \$100 to \$25, and then to provide a cohesive site (www.dermopa.org/students/) for students to obtain information they desire without hav-

ing to email PAs in the field for all the information they are seeking. Some students would take the initiative, but many would be lost in the process. Therefore, the goals of the new Derm PA Student Site are to provide the necessary information to students and make their transition to dermatology as smooth as possible, cutting down on their stress of starting a new job, in a new specialty, in a new career.

The site is now live, with a great deal of content available to dermatology PA students, including articles on practice/profes-

sional development topics, links to PDA/mobile technology tools, a student forum, resume guidance, and more.

How will Dermatology PAs overall and the dermatology specialty benefit from this new outreach?

Dermatology PAs and the specialty alike will benefit from this new outreach in maintaining the wonderful reputation we have built in the dermatology community. We are at the point where doctors appreciate and respect us, and call us colleagues. We want to continue to

AAPA Advocates for Six Elements of A Modern PA Practice Act

The American Academy of Physician Assistants has outlined six elements it says should be part of a modern PA practice act, but currently only two states have implemented all six elements. The majority of states have implemented three or fewer.

The six elements of a modern act are:

- "Licensure" as the Regulatory Term.
- Full Prescriptive Authority.
- Scope of Practice Determined at Practice Site.
- Adaptable Supervision Requirements.
- Chart Co-Signature Requirements Determined at the Practice.
- Number of PAs a Physician May Supervise Determined at Practice Level.

In a series of policy statements, AAPA explains the necessity of each element. Among the support given for its

elements, AAPA argues that *licensure* is a term that can "accurately describe the professional regulatory process, ensure compliance with applicable laws and be readily understandable by employers." It is more appropriate than "registering" or "certifying" PAs, according to the Academy.

When it comes to supervision, allowing each practice to determine appropriate supervision rather than implementing statewide standards can, "maximize team effectiveness," AAPA notes.

Physician supervision of PAs is an integral element of PA practice, but AAPA maintains that physicians should have the discretion to determine how to implement and document supervision. Therefore, chart co-signature (or "countersignature") on all PA chart entries is no longer necessary, the AAPA says.

More information on the six elements of a modern PA practice act, and a map of state adoption of the six points can be accessed at: <http://www.aapa.org/advocacy-and-practice-resources/state-advocacy/six-key-elements>. ■

provide our specialty and the patients we serve with qualified and professional new derm PA. With information obtained on the website (such as, "How to Research and Obtain New Derm Rotations," "How to Evaluate Medical Content on the Internet," or "How to Write a Derm Specific Resume"), we can continue to be proud to welcome these new members into our family.

What are the most important things that PA students should know if considering dermatology?

Dermatology PAs make up approximately three percent of the clinically practicing physician assistant population, with about 2,200 of us working for board-certified/board-eligible dermatologists. I see dermatology increasing in popularity, due to its attractive lifestyle of less hours for more lucrative pay due to better reimbursement, as well as the increased popularity of anti-aging campaigns worldwide.

It is most important that PA students build a strong medical base in dermatology; the most common conditions are just as if not more important than the cosmetic ones. Acne, rosacea, evaluating melanocytic and non-melanocytic lesions for benign or malignant status, verrucous lesions, and rashes are still the bread and butter of practicing dermatology and need to be respected as such.

How were the target topics for the site identified?

When deciding what material should be placed on the website, we brainstormed as a board to determine what subjects we were



most asked about by PA students or PAs interested in moving to dermatology. As the website continues to grow, the increasing student member population will most definitely be targeted for ideas in information that they feel is lacking.

How can established Derm PAs get involved in mentoring and guiding students through the SDPA?

In the leadership role, one of the Director at Large positions has become student-focused, and in charge of the new student coordinator, an applied-for position by PA students planning on entering dermatology. The student coordinator is charged with helping facilitate increased exposure of our specialty and its membership benefits to current PA students, as well upkeep of the website and addressing any new student issues that arise. On the fel-

low member level, PAs can certainly mentor students on elective rotations (a feature on the site) and continue that bond through the end of their PA education and help them land their first dermatology job.

Are there any lessons established PAs can learn from students?

I think that as PAs become more removed from the classroom and maybe some of the excitement of creating those first few patient bonds dwindles, students can help us to learn to listen wholeheartedly to our patients and not pigeonhole ourselves into preconceived diagnoses. Students also can remind seasoned PAs that while our schedules seem to be getting more packed each day, taking that extra minute with a patient can make all the difference to them and how the PA profession is perceived as a whole. ■

Rethink "Standard" Advice to Patients with Allergies

Treatment
Tips

Patients with allergic contact dermatitis often leave the dermatology clinic with a list of instructions and sometimes complicated strategies to avoid contact with known or suspected allergens. One piece of advice may be obsolete: Patients with fragrance allergies may not have to avoid scented laundry detergents after all.

New evidence confirms the growing suspicion that fragrance chemical residues left on fabrics do not elicit immediate or delayed allergic reactions in previously sensitized patients.

The newest data, which appear in the June issue of *Contact Dermatitis*, involve dose-response and fabric patch tests in 36 patients with previous positive patch reactions to two popular chemical fragrances. At a dose of 20 times the estimated exposure levels anticipated from washed fabrics, two of 36 patients reacted to fragrance. No patient reacted to lower levels. Results of the patch tests showed that 18

subjects reacted to vehicle alone, while 20 reacted to vehicle in combination with fragrance. Reactions were minor, non-specific skin reactions.

One source of allergens that still warrants concern is shampoo. When presented with an unusual outbreak on the face, keep possible contact allergy to shampoos in mind. Shampoos are a frequent source of contact allergy, which often manifests on the face, due to chemicals washing down the face during the rinse phase.

According to a recent review (*Dermatitis*; 20(2):106-10), the allergens most commonly present in shampoos, in order of prevalence, are: fragrance, cocamidopropyl betaine, methylchloroisothiazolinone/methylisothiazolinone, formaldehyde releasers, propylene glycol, vitamin E, parabens, benzophenones, iodopropynyl butylcarbamate, and methyl dibromoglutaronitrile/phenoxethanol. Patch testing can identify a sensitizing chemical. ■

Vehicles and Adherence

Continued from p. 1

of application, or attempt to spot-treat lesions rather than apply to the full face or full affected anatomic site.¹¹⁻¹³ Given that acne is a chronic disease mediated by faulty keratinization, *P. acnes* colonization, inflammation, and excess sebum production, long-term treatment is aimed not only at treating currently visible lesions but preventing formation of new lesions. As such, spot treatment undermines this therapeutic goal. Infrequent or inconsistent application of topical treatments will not achieve regulation of keratinization or sustained reduction of *P. acnes*.

Dermatologists have developed numerous strategies for the introduction of topical therapy to enhance patient comfort and encourage adherence to the regimen (Table 1). Recent advancements in drug development and vehicle formulation have improved retinoid tolerability, however, these strategies to optimize patient comfort remain important. By recommending these strategies in conjunction with optimized vehicles, clinicians can promote adherence.

Concentration Considerations

Certain drugs are inherently irritating, although irritation is often dose- or concentration-dependent. For example, when used at concentrations above 5%, BPO is well known to result in skin irritation, and it is a clinical reality and documented phenomenon that irritation interferes with patient adherence.¹⁴ A 21-day cumulative irritation study showed that reducing the BPO concentration from 5% to 2.5% in clindamycin-BPO fixed-combinations with common vehicle reduced irritation by 33 percent.¹⁵ Compared to two commonly-used fixed-combination products containing 5% BPO with clindamycin, the lower 2.5% concentration BPO/clindamycin-phosphate 1.2% (Acanya, Coria Laboratories) formulation has been shown to provide a meaningful reduction in irritation scores.^{15,16}

Data confirm that there is no need to use BPO concentrations in the irritation-producing range above 5%. BPO has been shown to have equal efficacy in the treatment of inflammatory acne lesions at 2.5%, 5%, and 10% concentrations.¹⁷ Acanya Gel was shown in an *in vitro* percutaneous absorption study to have comparable bioavailability to other marketed fixed-combination formulations that had a higher concentration of BPO (5%).¹⁵

Similar to benzoyl peroxide, topical tretinoin can cause irritation, especially in the initial days and weeks of treatment.^{18,19} This irritation may interfere with patient adherence^{18,20} and has been blamed for abandonment of therapy. Irritation appears to be related to characteristics of the vehicle formulation and to concentration, thus tretinoin has been made available in a range of concentrations and has been formulated into numerous vehicles since it first came to market in the 1970s.¹⁹ A microsphere release formulation of tretinoin

Strategies to Minimize Irritation Historically Associated with Topical Retinoids

- Apply a facial moisturizer with SPF 15 or higher each morning; apply a facial moisturizer, if desired, throughout the day and each evening before bed.
- Cleanse the face with a gentle, soap-free moisturizing wash.
- Avoid abrasive cleansing implements (loofas or pads) or cleansers. Avoid toners and other unnecessary cleansing items.
- Avoid over-application. Generally, a pea-sized amount of topical retinoid formulation is sufficient to treat the full face.
- Avoid applications of other topical medications along with a retinoid (besides increasing irritancy, this may degrade the retinoid).
- If needed, initiate therapy with nighttime application every other night and titrate to application every night.

0.04% (Retin-A Micro, Ortho Dermatologics) appears to provide better tolerability than the original 0.1% cream. A newer low-concentration formulation of tretinoin 0.05% (Atralin Gel 0.05%, Coria Laboratories) in a hydrogel vehicle (See sidebar) features a microsuspension that permits slow release of tretinoin and appears to provide better tolerability than other topical tretinoin formulations.

Formulation Considerations

While drugs may themselves be irritating, components of the vehicle can also contribute to therapy-induced irritation. In fact, in some sub-optimal formulations, high concentrations of chemical penetration enhancers, which can actually disrupt the epidermal barrier, are used. Certain excipients (preservatives, surfactants, alcohol) are known to cause cutaneous irritation and dryness.²¹ However, recently, formulators have emphasized the importance of vehicle formulations that efficiently deliver active drug while also minimizing or even reversing possible damaging effects of some drugs by helping to preserve transepidermal water loss (TEWL) and skin hydration.

Characteristics of the formulation can significantly affect irritation and dryness, as well as efficacy, of benzoyl peroxide and tretinoin.¹⁸ Novel hydrogel formulations of acne therapies—Acanya Gel and Atralin—have been shown to provide better patient comfort and tolerability compared to older formulations.

The aqueous gel formulation used in Acanya Gel ensures the stability of otherwise incompatible active ingredients: solubilized clindamycin phosphate and a microsuspension of BPO. The formulation contains low amounts of propylene glycol (PG) that act as a delivery solvent for the BPO microcrystals after application to the skin. However PG is also a humectant-type moisturizer, providing cosmetic elegance to the formulation. A benefit of micronized particles of BPO in suspension is that they can be uniformly distributed within the formulation, and thus evenly applied to the skin, compared to solubilized BPO. This even distribution appears to be associated with decreased drug-induced irritation.

One study compared the effects on TEWL and stratum corneum hydration of fixed-com-

bination of clindamycin phosphate 1.2% and BPO 5% (BenzaClin, Dermik/Sanofi-Aventis) to Acanya Gel. The investigators found that once-daily use of Acanya gel produced no relevant irritant effect or negative influence on stratum corneum hydration. However, clindamycin phosphate 1.2%/BPO 5% produced a significant decrease in skin hydration and had a clinically apparent drying effect.²²

First generation tretinoin formulations (and their generic equivalents) contained solubilized tretinoin and high levels of potentially irritating penetration enhancing excipients, such as isopropyl myristate or alcohol. When these formulations are applied to the skin, the penetration enhancers drive the active drug quickly into the epidermis, creating a “burst” of drug delivery. The burst delivery is associated with significant drying and peeling and in some cases scaling and redness.

By suspending micronized tretinoin in a moisturizing vehicle, Atralin Gel 0.05% minimizes the burst effect. The tretinoin micro-particles (85 percent of which are less than 10 microns in size) can easily enter the pilosebaceous unit and concentrate in the infundibulum, and slowly dissolve directly in the sebum.

In addition to this controlled release, Atralin Gel further minimizes irritation through the incorporation of excipients commonly found in skin hydration and moisturizer products: soluble collagen, sodium hyaluronate, and glycerin.

Optimized Formulations, Enhanced Adherence

Long-term patient adherence with topical therapeutic regimens for chronic skin diseases can be a clinical challenge. This is especially true in the case of acne, when adolescents may desire rapid response to therapy and have little tolerance for therapy-induced irritation or discomfort. Fortunately, modern formulation technologies continue to produce new, optimized topical formulations for a range of skin diseases, including acne.

Acanya Gel and Atralin Gel—each in moisturizing hydrogel vehicles—are both shown to reduce irritation and dryness in acne vulgaris. Prescribers should consider the patient’s likely therapeutic experience and comfort when

What Are Hydrogels?

Novel aqueous gel formulations called hydrogels offer advances over other dosage forms, like lotions and creams. Hydrogels do not contain potentially irritating alcohols, but they do contain moisturizers and humectants to support epidermal barrier function and barrier repair.

In order to deliver hydrophobic active drugs such as BPO and tretinoin via a hydrogel, the active drugs must be in a solid state, dispersed and suspended by a polymeric gelling agent, allowing for controlled release of the suspended active drug. The particles are micronized (85 percent are less than 10 microns in diameter) and can more easily enter the follicular openings (typically 11-66 microns), which is beneficial when targeting acne, a follicular disease.

selecting topical therapies. Optimized formulations associated with decreased irritation and enhanced patient comfort may be preferred to other formulations. ■

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Patient Management

Answer

This patient presents with two of the three classic symptoms (“Three Ps”) of diabetes:

Polyuria (frequent urination). This patient mistakenly attributes frequent urination to possibly enlarged prostate.

Polydipsia (increased thirst).

Polyphagia (increased hunger). The patient mentions feeling hungry and has recently gained weight.

He also complains of blurred vision, which is a common presenting symptom of diabetes. People with diabetes are at risk for retinopathy. They are 40 percent more likely to suffer from glaucoma than people without diabetes and are 60 percent more likely to develop cataracts. Risk for retinopathy increases as the duration of disease increases; Nonproliferative retinopathy is more common than proliferative. ■

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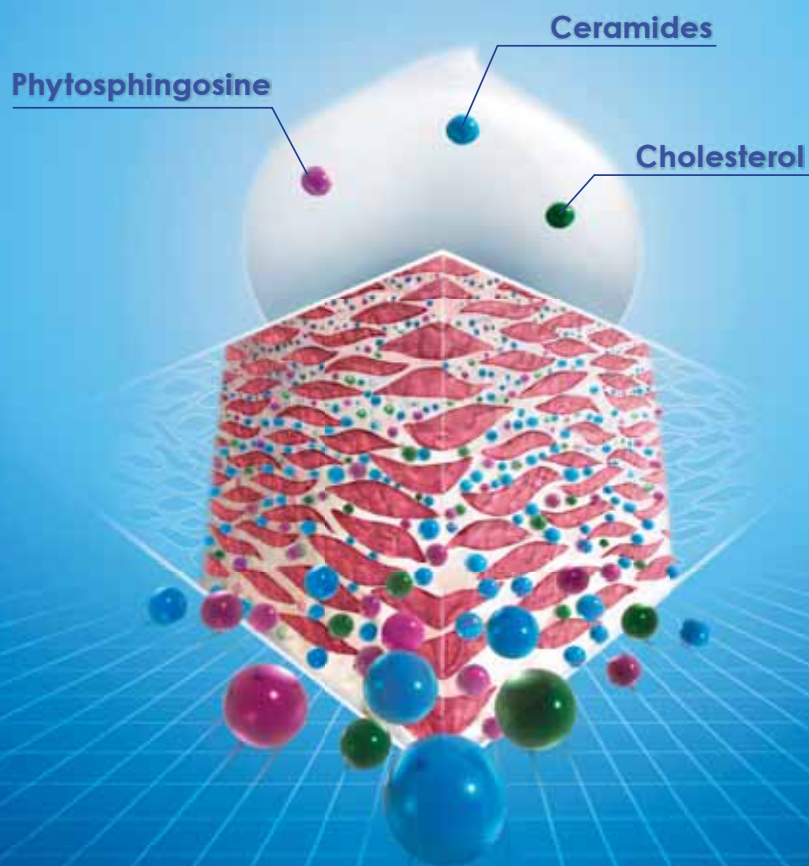


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