

Clinical practice

Therapies to watch for in 2013



Patient comfort, compliance seen as benefits of new therapies

■ Patients with axillary hyperhidrosis who are averse to injections may find benefit in new microwave therapy

by LOUISE GAGNON,
Correspondent, The Chronicle

Some brand new therapeutic entries and some older therapies now available in a new delivery system are additions to the therapeutic armamentarium likely to be appreciated by dermatologists and patients in 2013.

In terms of the neuromodulating toxins available for cosmetic purposes, dermatologists will have options in 2013 in addition to botulinum toxin type A (Botox Cosmetic), to utilize in their patients including incobotulinum toxin type A (Xeomin Cosmetic) and abobotulinum toxin type A (Dysport).

"From my perspective, I find Dysport to be a very exciting addition to our clinical practice," says Dr. Andrei Metelitsa, medical co-director of the Institute for Skin Advancement in Calgary, and clinical assistant professor at the University of Calgary.

"It's a slightly different molecule. Dysport has a faster onset of action. It can act as early as 24 hours [after it has been administered]. Several studies have shown that it has a

longevity advantage over Botox."

Dr. Benjamin Barankin, a dermatologist and medical director of the Toronto Dermatology Centre in Toronto, agrees that Dysport will "kick in" more quickly than Botox, but notes that the reconstitution of the neurotoxin means dermatologists will have to invest time to evaluate how to optimally inject Dysport.

"It seems more complex, and it represents a new learning curve," says Dr. Barankin.

New minoxidil formulation available

A new formulation of minoxidil, used to help regrow hair in the treatment of male pattern baldness, is now available in a 5% topical aerosol foam.

"It does not contain propylene glycol, which is in the [minoxidil] lotion," explains Dr. Barankin. "Some people are allergic to [propylene glycol], and others find it irritating



Dr. Andrei Metelitsa



Dr. Benjamin Barankin



Dr. Marti Gidon



Dr. Marc Bourcier

because of the alcohol. It should be better tolerated than the lotion. It's a nice recent [treatment] addition."

The other advantage of the foam is that it avoids the need for compounding, observes Dr. Marti Gidon, a cosmetic dermatologist in Toronto, director of Gidon Aesthetics & Medispa, and a

lecturer in the division of dermatology in the faculty of medicine at the University of Toronto.

"The foam is easier to apply than the drops and is ready-made at five per cent, rather than relying on a pharmacy to formulate it," says Dr. Gidon.

Another cosmetic innovation is a new tip available with Thermage technology designed to treat the face. The Thermage Comfort Pulse Technology contains a vibrating handpiece to increase patient comfort.

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New therapies *expected to offer benefits to patients*

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“It is for tightening and lifting the skin,” explains Dr. Gidon. “It stimulates collagen as well. For some patients, it’s an alternative to surgery, and for some it can be used after surgery.”

An efinaconazole 10% solution is proving effective in the treatment of onychomycosis. Efinaconazole has shown a broad spectrum of anti-fungal activity (*Antimicrobial Agents and Chemotherapy* 2013; Jan 14).

Herpes therapy on horizon

Endermologie, a cosmetic innovation involving mechanical stimulation on the surface of the skin that elicits a physiological response like collagen activation and elastin production, was developed in France, but is gaining a foothold in North America, according to Dr. Barankin. “I think we are going to start seeing more Endermologie,” predicts Dr. Barankin. “It’s already quite popular in Quebec.”

Still another innovation is a topical product that combines 5% acyclovir and 1% hydrocortisone, combined in a cream to treat recurrent herpes simplex labialis. “By adding hydrocortisone, you get decreased inflammation, and [herpes] resolves more quickly,” explains Dr. Gidon.

Tattoo removal has been a challenge for clinicians, and there have not been a lot of major advances of late, despite a high demand for effective tattoo removal. Emerging technologies, such as the Picosecond Alexandrite Laser, are proving more effective, notes Dr. Metelitsa, who published a study in the fall of 2012 where 15 patients with darkly pigmented tattoos were enrolled, and 12 patients completed the study (*Archives of Dermatology* 2012; Sep 17:1-4).

“A total of 75 per cent of tattoos were cleared in four treatment sessions, and all patients were satisfied,” says Dr. Metelitsa, noting established technologies require close to 10 treatment sessions to remove tattoos. “It is a very exciting and effective technology, and the side effect profile was comparable to previous types of treat-

ment.”

Patients with axillary hyperhidrosis can look forward to alternative therapies aimed at eliminating the sweat glands under the arms.

The miraDry system uses microwave technology and involves the delivery of electromagnetic energy to the site where the sweat glands are located. Prior to the procedure, anesthetic is adminis-

tered to numb the underarms. Typical treatment consists of two procedures scheduled three months apart.

“It’s an exciting option,” notes Dr. Barankin. “It has a longer effect, and it’s good for people who are needle-phobic.”

One trend that some clinicians find disturbing is the use of smartphone apps for

melanoma detection. A recent study found three of four smartphone applications misclassified 30% or more of melanomas as un concerning. The study’s investigators noted dependence of these applications could delay melanoma diagnosis (*Journal of the American Medical Association* 2013; Jan. 16:1-4.

“I would caution patients who use these devices,” says

Dr. Metelitsa, commenting on the study’s findings. “It could lead to tremendous misdiagnosis. Patients may get a false measurement, and it could progress to a very aggressive or metastatic melanoma.

“No matter the technology, it is the dermatologist who makes the final assessment. We [dermatologists] use technologies as an adjunct to

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Therapeutic Report

Soriatane for Psoriasis: What’s New?

Soriatane (acitretin) is a retinoid indicated for the treatment and long-term management of patients with severe psoriasis. It inhibits the excessive cell growth and keratinization seen in psoriasis, and reduces skin thickening, plaque formation, and scaling. Soriatane is distributed in Canada by Tribute Pharmaceuticals.

This panel discussion, held during Dermatology Update in Vancouver, examined the clinical uses and new information about Soriatane. Chair of the session, Dr. Lyn Guenther, outlined its clinical uses, along with its mechanism of action, absorption/half life, and indications and contraindications.

In PPP (palmoplantar pustular psoriasis), Soriatane is the first systemic of choice, said Dr. Guenther. “Of the various types of psoriasis, Soriatane is most effective in localized and generalized pustular psoriasis.”

Soriatane is a relatively safe therapy for the appropriate patient, said Dr. Guenther. It is not cytotoxic, and is not immunosuppressive.

A typical starting dose is 25 mg/day, said Dr. Guenther. The dose can be titrated



Dr. Lyn Guenther

down or up to 75 mg/day depending on the effects observed after about four weeks of treatment, she added. It may take three to six months to obtain maxi-

mum effects. The daily dose should be delivered with a meal.

To optimize treatment, Soriatane can also be combined with other psoriasis therapies, including topicals such as calcipotriol, phototherapy, or biologics.

Soriatane plus phototherapy is a synergistic combination, Dr. Guenther said, noting there is a reduction in the mean cumulative dose of UVB and the overall number of treatments as well. “RePUVA produces greater efficacy, less total amount of therapy, and fewer treatments.”

Broadband UVB therapy produces therapeutic results comparable to Soriatane at 12 weeks, but improvement doubles when the combination is used, she said.

Soriatane is also chemopreventive, but

not immunosuppressive. “PUVA plus retinoids have shown a 30 per cent reduction of SCC [in psoriasis patients],” Dr. Guenther said.

She noted that Soriatane is the ideal systemic agent to consider in combination with biologic psoriasis therapies.

A slight change in acitretin dosage, as little as 5 mg, can make significant differences in response and tolerability of side effects, she said. Potential side effects of Soriatane include alopecia, hyperphototoxicity, hyperlipidemia, osteoporosis, hyperostosis, and decreased colour vision and/or night vision. Depression has also been reported, although persons with psoriasis may already be depressed.

“You want to document in the patient’s chart that you had a discussion regarding headache, depression, or mood changes at follow-up,” she said.

Retinoid dermatitis may occur in up to 25% of treated patients. Skin fragility and pyogenic granulomas may also occur.

“Monitoring is important,” said Dr. Guenther, adding that prior to prescribing Soriatane a minimum baseline should be established for LFT and fasting lipid levels, although she also obtains a baseline CBC and creatinine. For diabetic patients, particularly those on antidiabetic therapy, she also orders a fasting glucose level.

“Glucose levels are something you should be aware of [in diabetic patients],” said Dr. Guenther, who emphasized these levels should also be monitored in patients who might be pre-diabetic.

Lipid and LFT profiles should be taken every one to two weeks for several months following initiation of therapy, then every three months thereafter, she said. A transaminase increase is usually transient.

Growth parameters in children should be monitored closely.

Pregnancy must be avoided during Soriatane therapy and for three years following cessation of therapy. During treatment, pregnancy testing should be conducted every four weeks while on therapy then every one to three months for three years after drug cessation.

The patient must not donate blood for three years.

A consent form acknowledging these guidelines is required by Health Canada for all patients on retinoids. A form for Soriatane is being developed by Tribute Pharma.

HIGHLIGHTS OF GROUP DISCUSSION

Following Dr. Guenther’s presentation, attendees broke into groups to discuss the strengths and challenges related to the use of Soriatane in clinical practice. These are the main points:

STRENGTHS OF SORIATANE

- Soriatane is a relatively inexpensive therapy in an era of biologics
- Soriatane may prevent the development of skin cancer
- Soriatane is not immunosuppressive
- Soriatane has a unique mechanism of action
- Soriatane has a long track record of safety

CHALLENGES

- Teratogenicity: no pregnancy or blood

donation for three years

- Slow onset, can take up to three to six months
- Side effects such as alopecia
- Dryness and retinoid dermatitis depending on climate; may be more of an issue in winter

HOW DO WE OVERCOME CHALLENGES?

- Clinicians can address all of these issues with good counselling
- Use of consent form
- Thorough documentation in patient’s chart

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New therapies expected to offer benefits to patients

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our clinical diagnosis.”

A new form of oral isotretinoin called Absorica and taken twice daily, is expected to be of assistance to patients in terms of improved drug absorption, notes Dr. Marc Bourcier, a dermatologist in Moncton, N.B., and assistant professor, Faculty of Medicine, University of Sherbrooke, Sherbrooke, Que.

“It permits better absorption on an empty stomach,” explains Dr. Bourcier. “Currently, our patients need to take the therapy with a fatty meal. Sometimes, there is very little drug absorbed.”

Depression in psoriasis
Clinicians like Dr. Bourcier maintain on their radar the co-morbidities associated with psoriasis, such as obesity or depression when managing their psoriasis patients.

“If you have a patient who has significant depression and anxiety, you should treat this independently,” stresses Dr. Bourcier. “Don’t assume that the depression will improve if the skin improves.

“We also know that there is a window of opportunity for early intervention,” he says. “The anxiety or depression may become chronic without early intervention.”

An important development for dermatologists is that they can now safely prescribe biologic agents to treat psoriasis in patients who may be taking anti-depressant pharmacologic agents or anti-anxiety pharmacologic agents.

The advent of biologic psoriasis medications in oral form is expected to represent a clear advantage to a seg-

ment of patients with psoriasis who may have steered away from therapies available by injection.

“There is a perception among some patients and physicians that injections are aggressive,” says Dr. Barankin. “People are used to taking pills, so that will help people get over their mental block.”

But there is a risk that if compliance is sub-optimal, it may compromise patient out-

comes. “We do not want people missing their doses,” says Dr. Barankin. “There may be a therapeutic issue if you develop antibodies, and the patient stops responding to the drug. We would prefer if people take the drug the same time every day.”

One of the recent advances in pediatric dermatology is the use of topical propranolol for the treatment of infantile hemangiomas, says

Dr. Barankin, noting topical application can avoid the adverse events that may be associated with systemic use of the non-selective, beta-adrenergic receptor antagonist. “Topical propranolol can be safely used on hemangiomas in children,” explains Dr. Barankin.

Non-proprietary and brand names of therapies: botulinum toxin A (Botox

Cosmetic, Allergan); incobotulinum toxin A (Xeomin Cosmetic, Merz); abobotulinum toxin A (Dysport, Medicis Aesthetics); minoxidil foam (Rogaine 5%, Johnson & Johnson); topical 5% acyclovir and 1% hydrocortisone cream (Xerese. Coria Laboratories, a division of Valeant); oral isotretinoin (Absorica, Ranbaxy); topical propranolol (no branded products).



Prescribing Summary

Patient Selection Criteria

THERAPEUTIC CLASSIFICATION
Acne Vulgaris Therapy

INDICATIONS AND CLINICAL USE
BenzaClin™ Topical Gel (clindamycin, as phosphate, 1% and benzoyl peroxide 5%) is indicated for the topical treatment of moderate *acne vulgaris* characterized by comedones, inflammatory papules/pustules, with or without an occasional cyst or nodule (Grade II to III).
BenzaClin™ is not indicated for the treatment of cystic acne (Grade IV).

CONTRAINDICATIONS
Patients who have a history of hypersensitivity to preparations containing clindamycin, lincomycin, or any other component of the preparation (see **Dosage Forms, Composition** in the Product Monograph). Patients with a history of regional enteritis, ulcerative colitis, or a history of antibiotic-associated colitis (see **WARNINGS AND PRECAUTIONS**).

SPECIAL POPULATIONS
Pregnant Women: There are no well-controlled trials in pregnant women. It is not known whether BenzaClin™ can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. BenzaClin™ should not be given to a pregnant woman unless the benefits to the mother clearly outweigh the possible risks to the fetus.
Nursing Women: It is not known whether BenzaClin™ is excreted in human milk after topical application. 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 discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.
Pediatrics (<12 years of age) and geriatrics (>65 years of age): The safety and effectiveness have not been established.

Safety Information

WARNINGS AND PRECAUTIONS
General: For external (dermatological) use only. Not for ophthalmic use.
Concomitant topical acne therapy is not recommended because a possible cumulative irritancy effect may occur, especially with the use of peeling, desquamating, or abrasive agents.
Exposure to sunlight or unnecessary UV light should be minimized.
Gastrointestinal: Orally and parenterally administered clindamycin have been associated with severe colitis, which may result in patient death. Use of the topical formulation of clindamycin can result in absorption of the antibiotic from the skin surface. Diarrhea, bloody diarrhea, and colitis (including pseudomembranous colitis) have been reported with the use of topical and systemic clindamycin. Studies indicate that a toxin produced by clostridia is a 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. Endoscopic examination may reveal pseudomembranous colitis. Stool culture for *Clostridium difficile* and stool assay for *Clostridium difficile* toxin may be helpful diagnostically. **When significant diarrhea occurs, the drug should be discontinued. Large bowel endoscopy should be considered to establish a definitive diagnosis in cases of severe diarrhea.** Diarrhea, colitis, and pseudomembranous colitis have been observed to begin up to several weeks following cessation of oral and parenteral therapy with clindamycin.
Ophthalmologic/Mucosal/Skin: Avoid contact with eyes and mucous membranes. In the event of accidental contact with such sensitive surfaces (mucous membranes, eyes, abraded skin), rinse with large amounts of tepid tap water.

ADVERSE REACTIONS (also see Supplemental Product Information)
Adverse Drug Reaction Overview: The most frequent adverse reactions that may occur with BenzaClin™ Topical Gel are mild to moderate adverse reactions of the skin; most commonly, dry skin. To monitor drug safety, Health Canada collects information on serious and unexpected effects of drugs. To report a serious or unexpected reaction to BenzaClin™, you may notify Health Canada by toll-free telephone at 1-866-234-2345.

DRUG INTERACTIONS (also see Supplemental Product Information)
Drug-Drug Interactions: Clindamycin, erythromycin, lincomycin and chloramphenicol containing products should not be used concurrently. In vitro studies have shown antagonism among these antimicrobials. In vitro studies suggest that benzoyl peroxide contributes to the degradation of tretinoin especially when combined with exposure to UV light.

Administration

DOSAGE AND ADMINISTRATION (also see Supplemental Product Information)
Recommended Dose and Dosage Adjustment: BenzaClin™ should be applied twice daily, morning and evening, or as directed by a physician, to affected areas of the skin after it is gently washed with a mild non-medicated soap, rinsed with warm water and patted dry. Improvement has been seen as early as two weeks, although up to ten weeks of treatment may be required for best results.

Study Reference

1. BenzaClin™ Product Monograph. Valeant Canada LP. February 29, 2012.
SUPPLEMENTAL PRODUCT INFORMATION

ADVERSE REACTIONS
Clinical Trial Adverse Reactions: Table 1 presents a pooled summary of the most frequent (≥1%) adverse reactions reported during four randomized, double-blind, vehicle-controlled, multicentre trials conducted with BenzaClin™ Topical Gel in patients with moderate acne vulgaris. A total of 420 male and female patients with an average age of 19 years received BenzaClin™ Topical Gel in these studies; 168 patients received vehicle. The average duration of treatment with BenzaClin™ Topical Gel was 69 days.
Table 1: Most Frequent Adverse Events (≥1%) Reported in the BenzaClin™ Topical Gel or Vehicle Groups Considered to be Possibly, Probably or Definitely Related to Product Administration

Body System: Skin and Appendages	BenzaClin™ Topical Gel (n=420)	Vehicle (n=168)
Very Common Adverse Reaction:		
Dry Skin	12%	6%
Common Adverse Reactions:		
Application site reaction	3%	<1%
Peeling	2%	-
Pruritus	2%	<1%
Erythema	1%	<1%

Sunburn was observed in 1% of the BenzaClin™ Topical Gel group but considered related to the drug in less than 1% (2 patients). The use of a moisturizer in the studies may have reduced the incidence of dry skin.

DRUG INTERACTIONS
Drug-Food Interactions: Interactions with food have not been established.
Drug-Herb Interactions: Interactions with herbal products have not been established.
Drug-Laboratory Test Interactions: Interactions with laboratory tests have not been established.

DOSAGE AND ADMINISTRATION
Administration; Reconstitution: BenzaClin™ Topical Gel is supplied to the pharmacist as two components: 1) a jar of benzoyl peroxide gel; 2) a vial containing clindamycin phosphate powder, both of which are to be admixed by the pharmacist and dispensed to the patient in the jar as 1% clindamycin and 5% benzoyl peroxide.

Table 2: How Supplied and Mixing Instructions for the Pharmacist

Size (Net Weight)	Benzoyl Peroxide Gel	Total Active Clindamycin Phosphate Powder	Purified Water to be Added to Vial
50 g (pump)	41.4 g	0.6 g	10 mL

Prior to dispensing, tap the vial until powder flows freely. Add indicated amount of purified water to the vial (to the mark) and immediately shake to completely dissolve clindamycin. If needed, add additional purified water to bring level up to the mark. Add the solution in the vial to the gel and stir until homogenous in appearance (1 to 1^{1/2} minutes). Reassemble jar with pump dispenser. BenzaClin™ Topical Gel (as dispensed) can be stored between 15-25°C for 3 months. Place a 3-month expiration date on the label immediately following mixing.

OVERDOSAGE
Acute overdosage with the topical use of BenzaClin™ Topical Gel (clindamycin, as phosphate, 1% and benzoyl peroxide 5%) is unlikely. If BenzaClin™ is applied excessively, marked dryness, peeling and redness might occur. The literature indicates that clindamycin could be absorbed topically (see **WARNINGS AND PRECAUTIONS**). In the event of accidental ingestion, treatment should be symptomatic.

STORAGE AND STABILITY
Store BenzaClin™ Topical Gel and its individual components between 15°C and 25°C (before and after reconstitution). After reconstitution for dispensing to the patient, label BenzaClin™ Topical Gel with a 3-month expiration date. **Do not freeze. Keep tightly closed. Keep out of the reach of children.**

DOSAGE FORMS
BenzaClin™ Topical Gel is dispensed in a 50 g jar equipped with a hand-actuated pump.

Product Monograph available upon request.

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But, what do you think?

A question for our readers: We’d like to know which new therapy you might be most anticipating in 2013. Send us your selection (up to three, either from this article or additional choices) and we’ll publish them in an upcoming issue.
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