DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

TRANSMITTED BY FACSIMILE

Linda Fenney, M.D.
Senior Vice President
Research, Product Development and Regulatory Affairs
Connetics Corporation
3400 West Bayshore Road
Palo Alto, CA 94303

RE: Luxiq™ (betamethasone valerate) Foam, 0.12%
NDA 20-934
MACMIS ID#10501

Dear Dr. Fenney:

This letter objects to Connetics Corporation's (Connetics) dissemination of violative promotional materials for Luxiq (betamethasone valerate) Foam. As part of its monitoring program, the Division of Drug Marketing, Advertising and Communications (DDMAC) has become aware of professional promotional materials for Luxiq that are false or misleading, in violation of the Federal Food, Drug, and Cosmetic Act (Act) and its implementing regulations. Specifically, DDMAC objects to Connetics dissemination of the following promotional labeling pieces, described as Luxiq "Case Studies" (PRM-LUX1-082R, PRM-LUX1-089R, PRM-LUX1-090R, PRM-LUX-091R, PRM-LUX1-092R, and PRM-LUX1-101) for the reasons described below.

Promotion of Unapproved New Use

Promotional materials are misleading if they suggest that a drug is useful in a broader range of patients or conditions than has been demonstrated by substantial evidence. Luxiq's approved product labeling (PI) states that "Luxiq is a medium potency topical corticosteroid indicated for relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses of the scalp." In your promotional materials (PRM-LUX1-082R and PRM-LUX1-092R), you present that treatment with Luxiq is appropriate for patients such as a "58-year-old Caucasian male with 50-year history of erythematous, scaly, and pruritic eruption involving the scalp, elbows, and sacrum" and "45-year-old Caucasian female with an 8-year history of pruritic scaling and eruptions involving the elbows, knees, and scalp." These claims are misleading because Luxiq is only indicated for dermatoses of the scalp. Similarly, you present four of the case studies (PRM-LUX1-082R, PRM-LUX1-089R, PRM-LUX1-090R, and PRM-LUX1-092R) with the header "Case Study: Psoriasis." This implies that Luxiq is useful in patients with psoriasis on any part of the body when such has not been demonstrated by substantial evidence.

Overstatement of Efficacy

Luxiq's PI includes results from a clinical trial in 159 patients with moderate to severe scalp psoriasis demonstrating that Luxiq decreased scaling, erythema, and plaque thickness by 47%, 41% and 66%, respectively. In addition, according to the Investigator's Global assessment, 67% of patients treated with Luxiq were rated as completely clear or almost clear at endpoint. In your promotional materials (PRM-LUX1-082R, PRM-LUX1-089R, PRM-LUX1-090R, PRM-LUX-091R, PRM-LUX1-092R, and PRM-LUX1-101), you present the following claims from each of the case studies:

- "Following 1 month of treatment, patient no longer exhibited scaling, plaque thickness, erythema, and pruritus"
- "Scalp and retroauricular areas were completely clear after 1 month of use"
- "Scalp psoriasis completely cleared in 6 weeks"
- "Complete clearance in 6 weeks"
- "After initial 2 weeks of treatment, patient's scalp psoriasis markedly improved to 10% involvement of the scalp, with minimal erythema, scale, and induration"
- "After 4 weeks, patient's scalp was significantly improved, with >90% clearance, no erythema, and minimal scaling"

The totality of these claims implies that all patients (as represented by 6 out of 6 patients described in each of the case studies) using Luxiq will have 90-100% clearance. Therefore, these claims are misleading because they are inconsistent with your PI and are an overstatement of the efficacy of Luxiq.

In addition, the trial described in the PI required that patients be treated twice daily for four weeks. According to the PI, "At four weeks of treatment, study results of 159 patients demonstrated that the efficacy of Luxiq Foam in treating scalp psoriasis is superior to that of Placebo foam, and is comparable to that of a currently marketed BMV lotion." However, your materials (PRM-LUX1-090R and PRM-LUX1-089R) include statements such as:

- "I could see improvement within 2 days of using the foam."
- "Immediate relief from itching."
- "I could see lots of improvement in the first 2 weeks."

These statements are misleading because they are inconsistent with the PI and overstate the efficacy of Luxiq with respect to how long it takes to see results.

Superiority Claims

In describing the psoriasis case study of the 58-year-old male, your promotional material (PRM-LUX1-082R) contains the statements under the header (prior treatments) that "Various topical corticosteroids that ranged from moderate to ultra-high potency have been used in the past" and "He has achieved variable and temporary relief from these prior therapies." Furthermore, the case study states that the patient was treated with Luxiq twice daily for 2 weeks with the following outcome: "As of 1 year after therapy, patient has not returned for additional treatment." This presentation is misleading because it implies that Luxiq is superior to moderate and ultra-high potency corticosteroids

when such has not been demonstrated by substantial evidence. In addition, this presentation is misleading because it implies that Luxiq is a cure for psoriasis when such has not been demonstrated.

Requested Action

Connetics should immediately discontinue these and all other promotional materials and activities for Luxiq that contain the same or similar claims or presentations. We request that Connetics respond, in writing, with its intent to comply with the above. DDMAC should receive your written response no later than November 30, 2001. This response should list similarly violative materials with a description of the method for discontinuation and the discontinuation date.

If you have any questions or comments, please contact me by facsimile at (301) 594-6771, or at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, HFD-42, Rm. 17B-20, 5600 Fishers Lane, Rockville, MD 20857. DDMAC reminds you that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID #10501 in addition to the NDA number.

Sincerely,

{See appended electronic signature page}

Barbara S. Chong, Pharm.D., BCPS
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Barbara Chong
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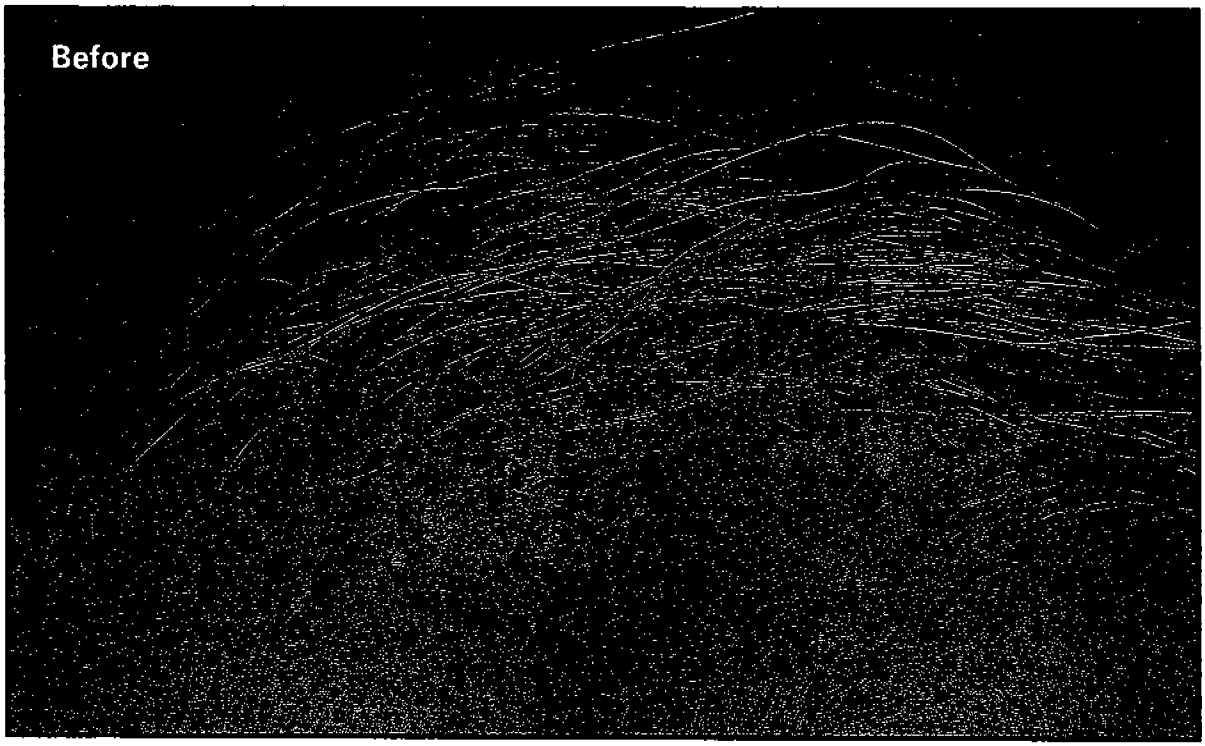
Body of Evidence:
The clinical effects of Luxiq

Case Study: Psoriasis



Physical Evidence

- 58-year-old Caucasian male with 50-year history of erythematous, scaly, and pruritic eruption involving the scalp, elbows, and sacrum.
- On presentation, approximately 35% of the scalp was involved, with moderate erythema, scale, and induration.

Diagnosis

- Psoriasis

Prior Treatments

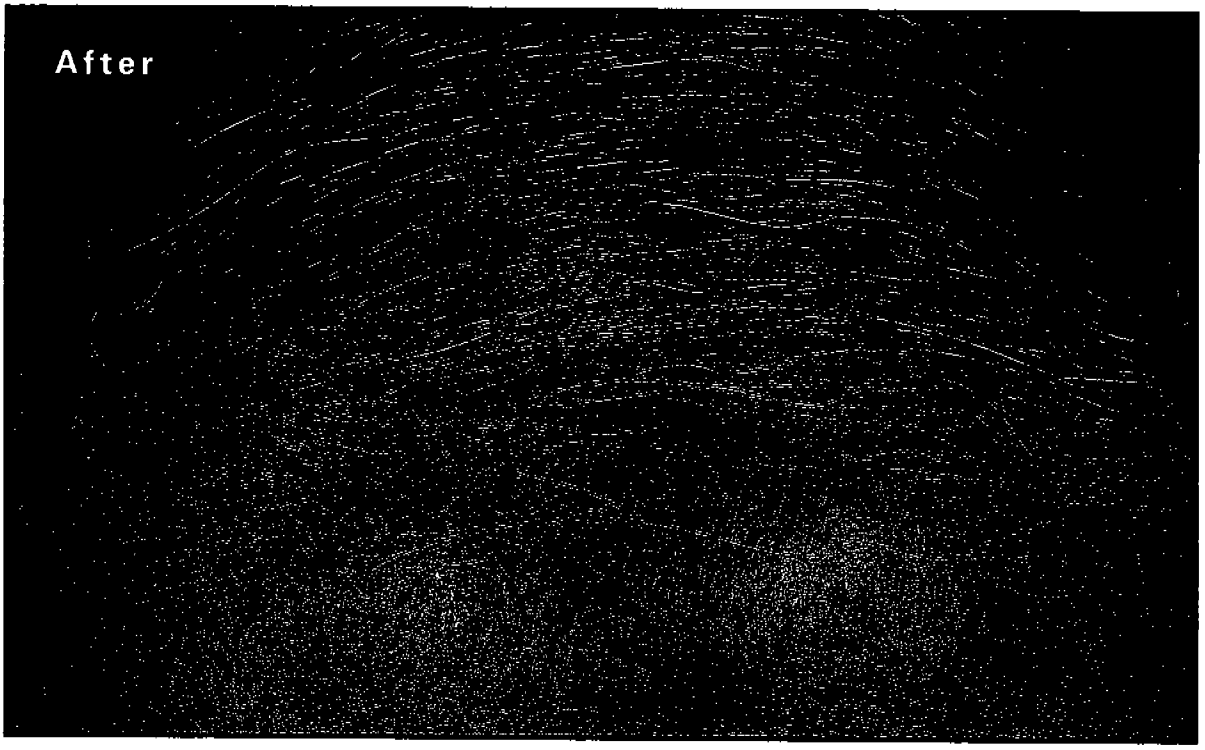
- Various topical corticosteroids that ranged from moderate to ultra-high potency have been used in the past.
- He has achieved variable and temporary relief from these prior therapies.

Treatment Plan

- Luxíq, BID application for 2 weeks

Physician authors: Ken Washenik, MD, PhD, Lesley Clark-Loeser, MD
Clinic/hospital affiliation: New York University
New York, NY

In just 2 weeks, recalcitrant scalp psoriasis is markedly improved



Outcome and Discussion

- After initial 2 weeks of treatment, patient's scalp psoriasis markedly improved to 10% involvement of the scalp, with minimal erythema, scale, and induration.
- As of 1 year after therapy, patient has not returned for additional treatment.

Patient Quote

"This stuff is great. I don't want to stop using it."

connetics®
Delivering Innovation to Dermatology

The most common side effects associated with the use of Luxiq in clinical trials were mild and transient burning, stinging, or itching at the application site.

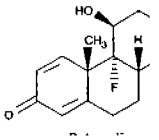
For more information, please see full prescribing information.

Luxiq™
(betamethasone val

For Dermatologic Use Only
Not for Ophthalmic Use

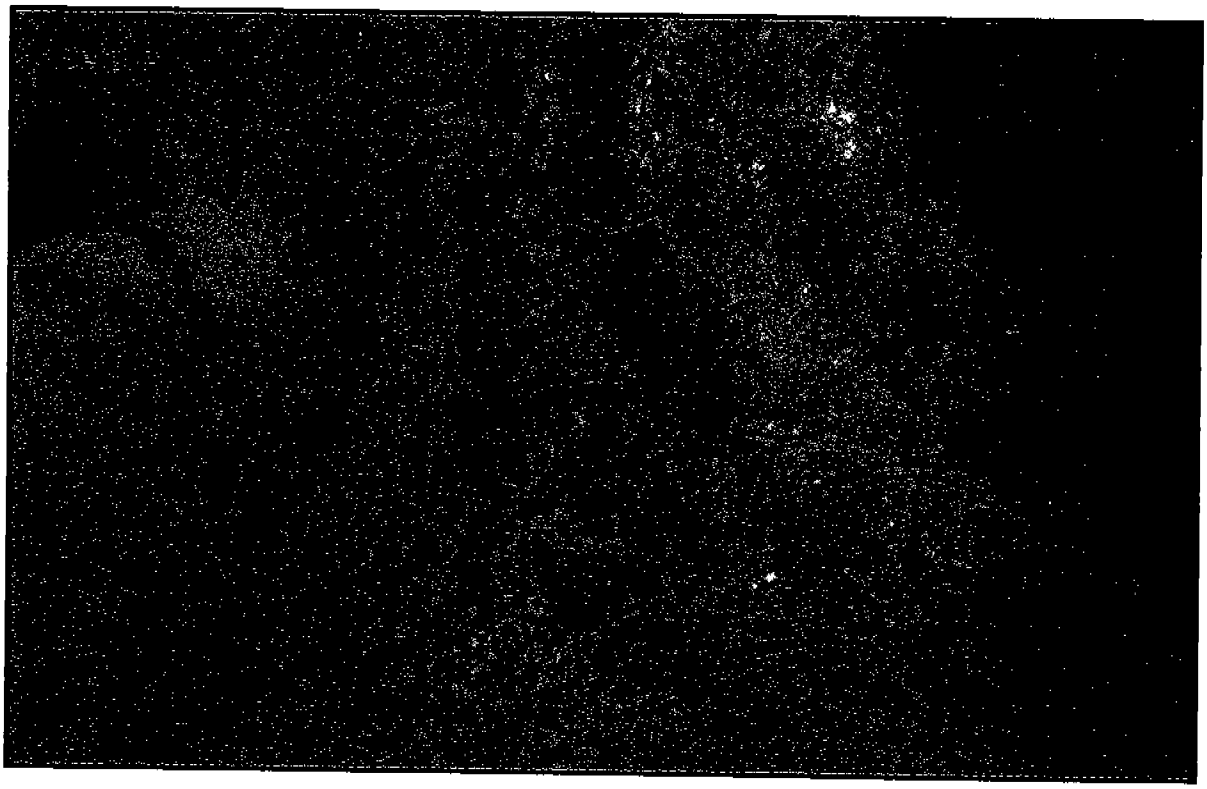
DESCRIPTION
Luxiq contains betamethasone valerate, USP, logic use. The corticosteroids constitute a cla as anti-inflammatory agents.

Chemically, betamethasone valerate is 9-flu 4-diene-3, 20-dione 17-valerate, with the emp 476.58 (CAS Registry Number 2152-44-5) an



Body of Evidence:
The clinical effects of Luxíq

Case Study: Psoriasis



Physical Evidence

- 24-year-old woman with an 8-year history of intermittent psoriasis
- On presentation, approximately 2% of her body surface area was involved (as focal plaques).
- The psoriasis primarily involved her scalp and was very itchy.

Diagnosis

- Psoriasis

Prior Treatments

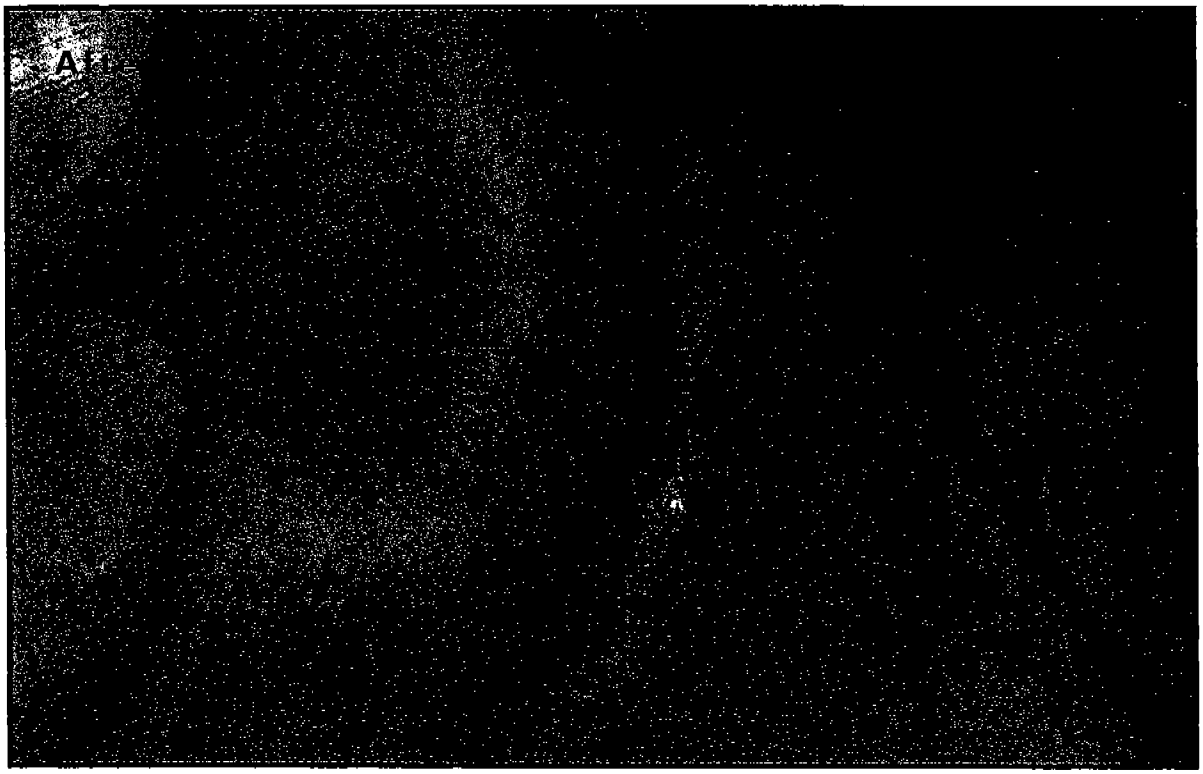
- No previous history of prescription treatment for psoriasis
- Multiple over-the-counter (OTC) antidandruff shampoos were tried in the past—many were irritating to the scalp.

Treatment Plan

- Luxíq, BID application for 6 weeks
- Use of OTC antidandruff shampoos (e.g., Nizoral) was permitted, if needed.

Physician author: Steven Feldman, MD, PhD
Clinic/hospital affiliation: Wake Forest University School of Medicine
Winston-Salem, NC

Immediate relief from itching; psoriasis completely cleared in 6 weeks



Outcome and Discussion

- Complete clearance in 6 weeks
- Patient has reported using the same canister of Luxíq for the past 2 years whenever symptoms recurred.

Patient Quote

"I could see lots of improvement in the first 2 weeks. The itching went away almost immediately."

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(betamethasone val

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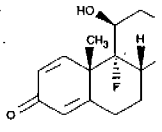

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Delivering Innovation to Dermatology

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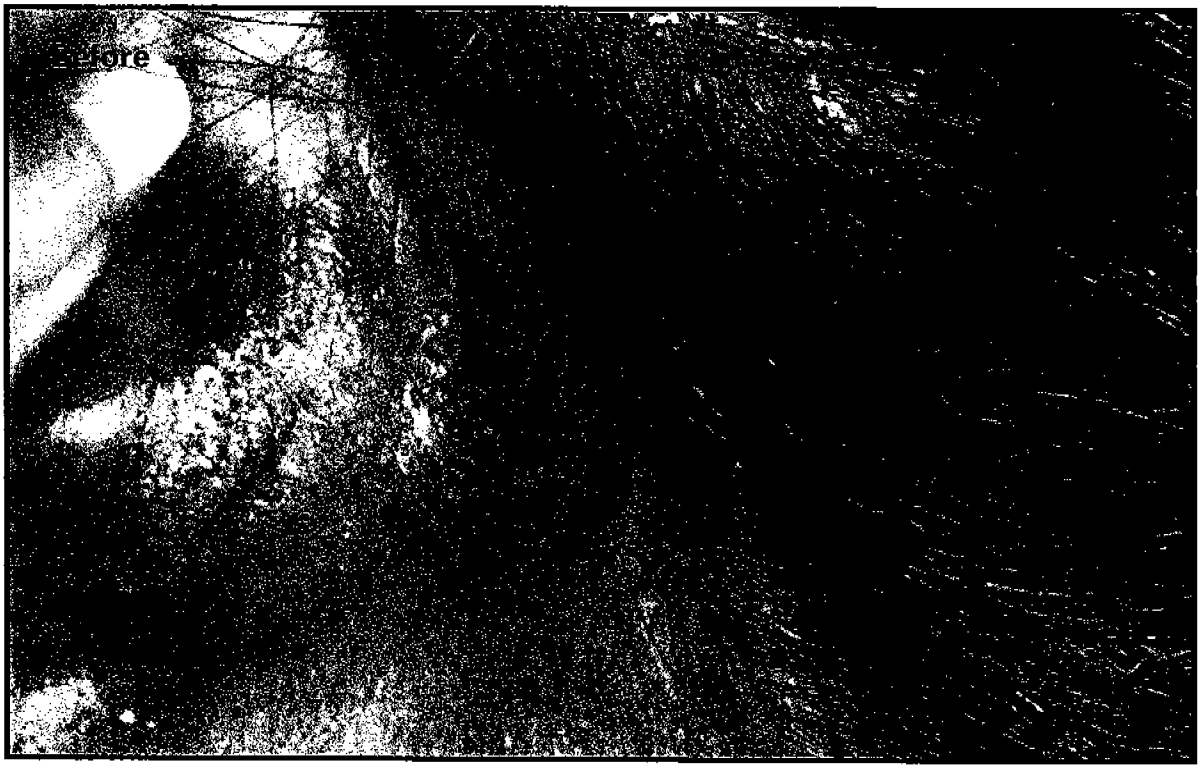
For more information, please see full prescribing information.

Body of Evidence:
The clinical effects of Luxiq

Case Study: Psoriasis



Physical Evidence
- 57-year-old woman with an 11-year history of chronic, intermittent psoriasis.
- On presentation, approximately 3% of her body surface area was involved as focal plaques of the scalp and elbows.

Diagnosis
- Psoriasis

Prior Treatments
- Various over-the-counter medications
- Phototherapy (psoralen and UVA—PUVA)
- Topical corticosteroids included fluocinolone acetonide topical oil and fluocinonide topical solution
- Calcipotriene solution and anthralin

Treatment Plan
- Luxiq, BID application for 6 weeks

Physician author: Steven Feldman, MD, PhD
Clinic/hospital affiliation: Wake Forest University School of Medicine
Winston-Salem, NC

Psoriasis completely cleared in 6 weeks

Outcome and Discussion

- Scalp psoriasis completely cleared in 6 weeks.
- Patient remained clear for 6 months post-treatment before symptoms returned.

Patient Quote

"I could see improvement within 2 days of using the foam."

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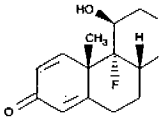
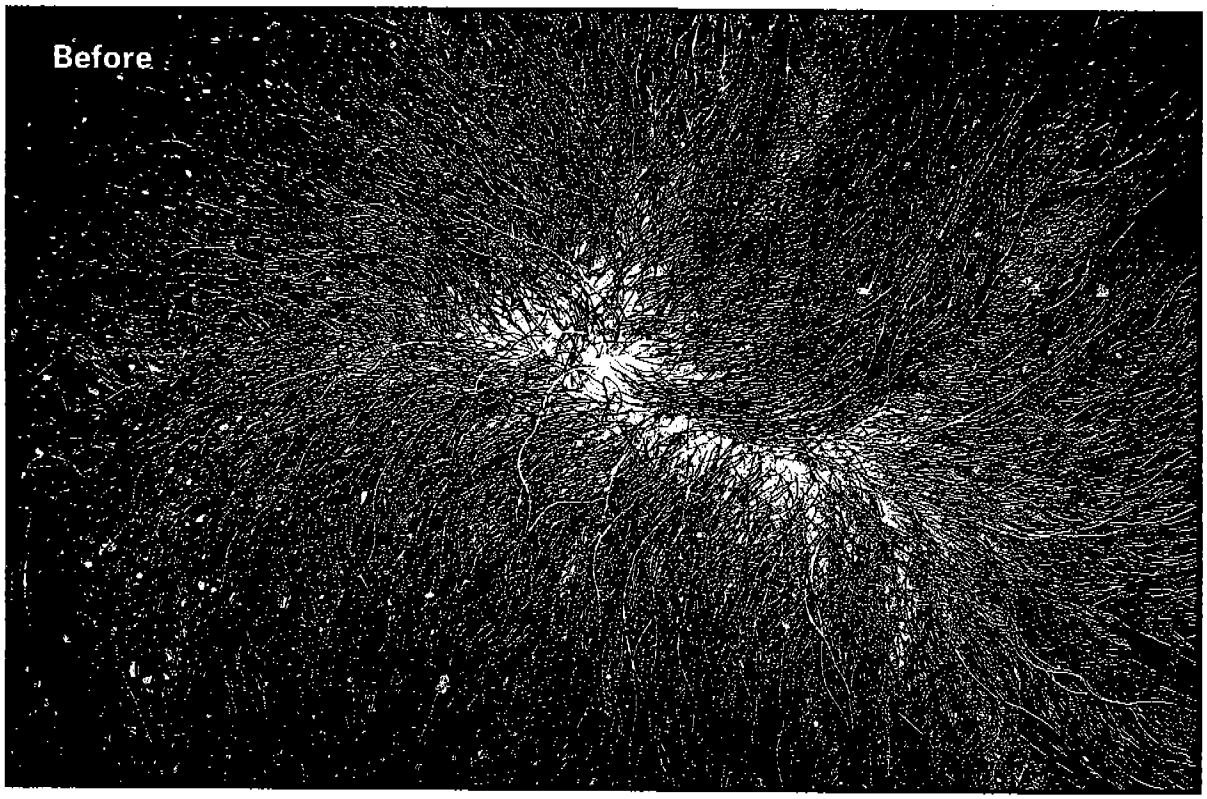


Body of Evidence:
The clinical effects of Luxiq

Case Study: Seborrheic Dermatitis



Physical Evidence

- 49-year-old African American female with a 5-year history of chronic scaling on the scalp
- Scales were associated with pruritus lasting for several months.
- The scales rapidly returned each time following over-the-counter (OTC) medicated shampoo use.

Diagnosis

- Seborrheic dermatitis

Prior Treatments

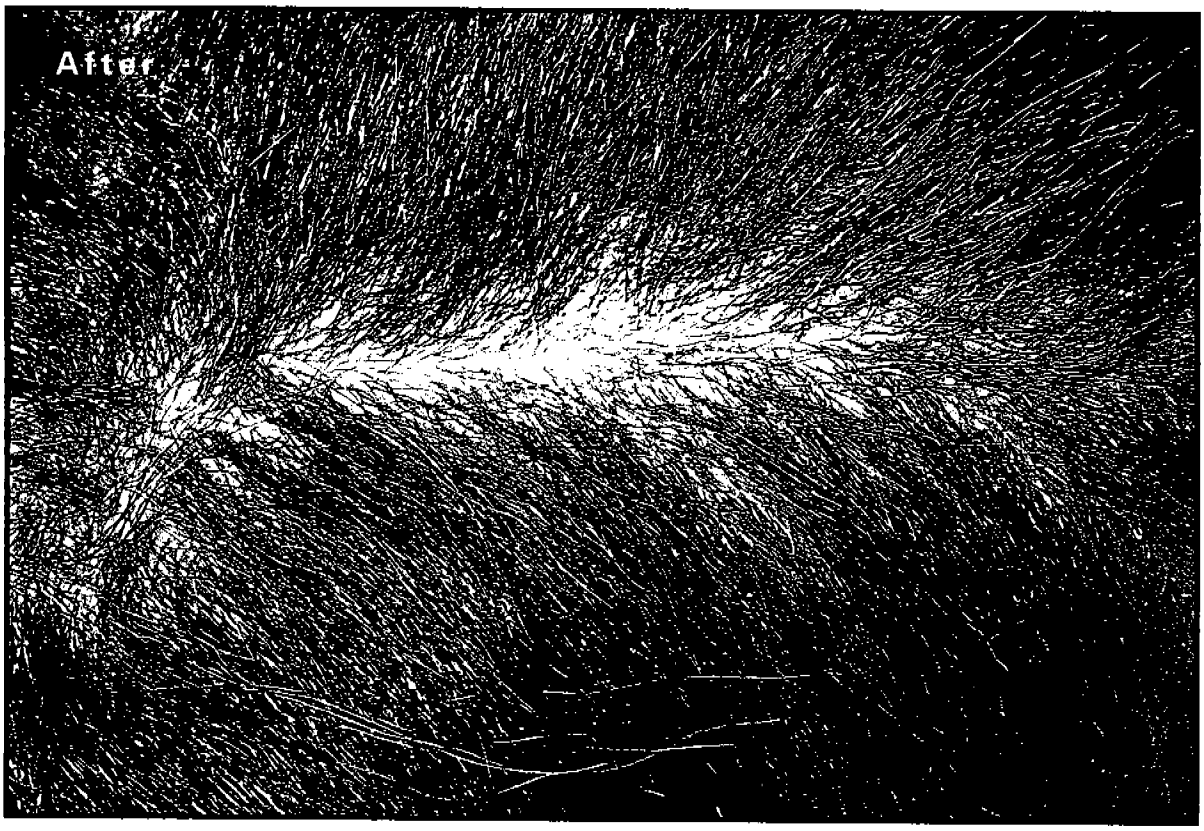
- Various OTC medicated shampoos were primarily used.
- Prescription medications were used intermittently in the past, with unsatisfactory results.

Treatment Plan

- Luxíq, BID for 4 weeks
- Approval to use nontar OTC medicated shampoos as needed.

Physician author: Wayne G. Woods, MD
Clinic/hospital affiliation: Central Piedmont Dermatology Center
Greensboro, NC

In just 4 weeks, long-standing seborrheic dermatitis is improved significantly



Outcome and Discussion

- After 4 weeks, patient's scalp was significantly improved, with >90% clearance, no erythema, and minimal scaling.

Patient Quote

"My scalp hasn't looked and felt so good in years!"

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(betamethasone val

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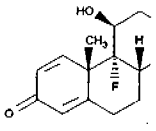

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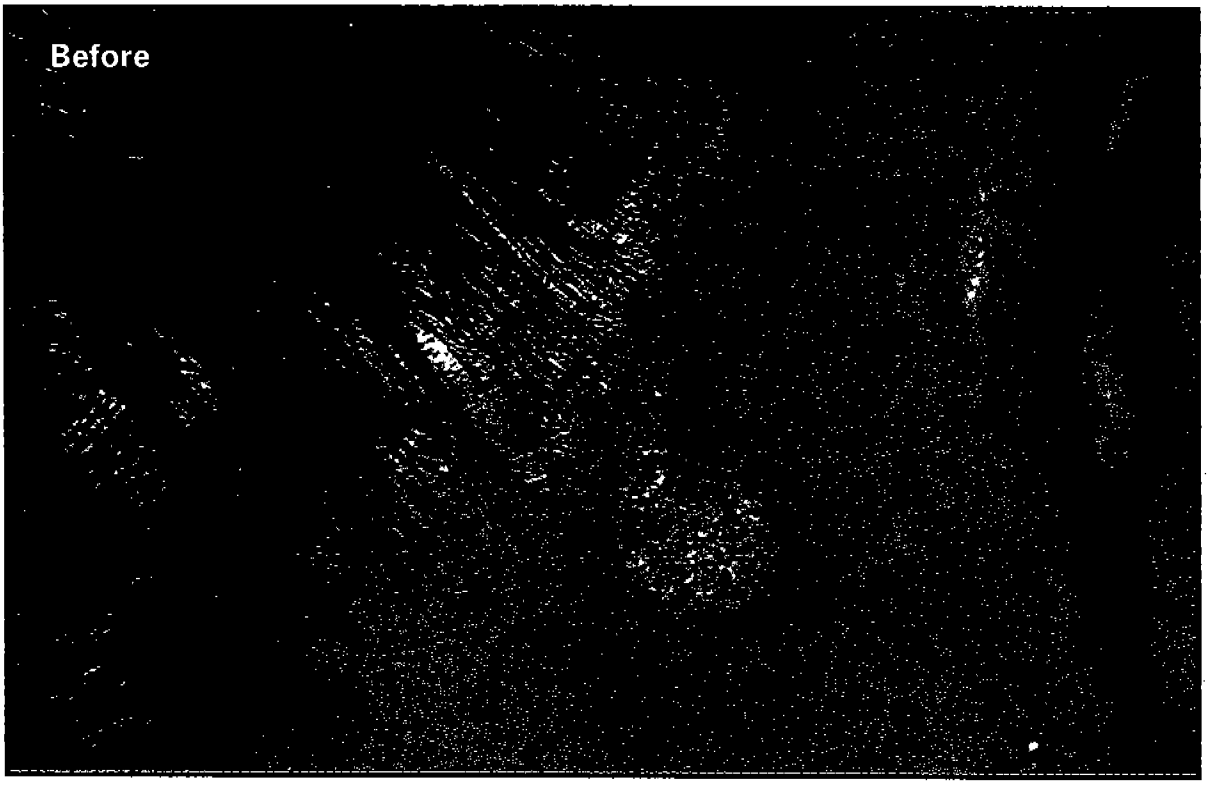
For more information, please see full prescribing information.

Body of Evidence:
The clinical effects of Luxiq

Case Study: Psoriasis



Physical Evidence
- 45-year-old Caucasian female with an 8-year history of pruritic scaling and eruptions involving the elbows, knees, and scalp.
- The retroauricular areas were significantly affected and bothersome to the patient.

Diagnosis
- Psoriasis

Prior Treatments
- Prescribed fluocinolone acetonide topical oil; however, the patient only used this when her husband "was out of town on a business trip."

Treatment Plan
- Luxiq, BID for 4 weeks to affected areas of damp scalp

Physician author: Val Pierre Vallat, MD
Clinic/hospital affiliation: University Dermatology, PLLC
Charlotte, NC

Recurring pruritic scaling on the scalp and retroauricular areas completely cleared in 1 month

Outcome and Discussion

- Scalp and retroauricular areas were completely clear after 1 month of use.

Patient Quote

"It's easy to use and not greasy!"

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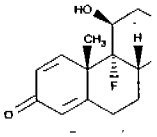

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For more information, please see full prescribing information.

Body of Evidence:
The clinical effects of Luxíq

Case Study: Scalp Psoriasis

Physical Evidence
- Caucasian male patient; 59 years of age.
- Presented with moderate scaling, plaque thickness, erythema, and pruritus.

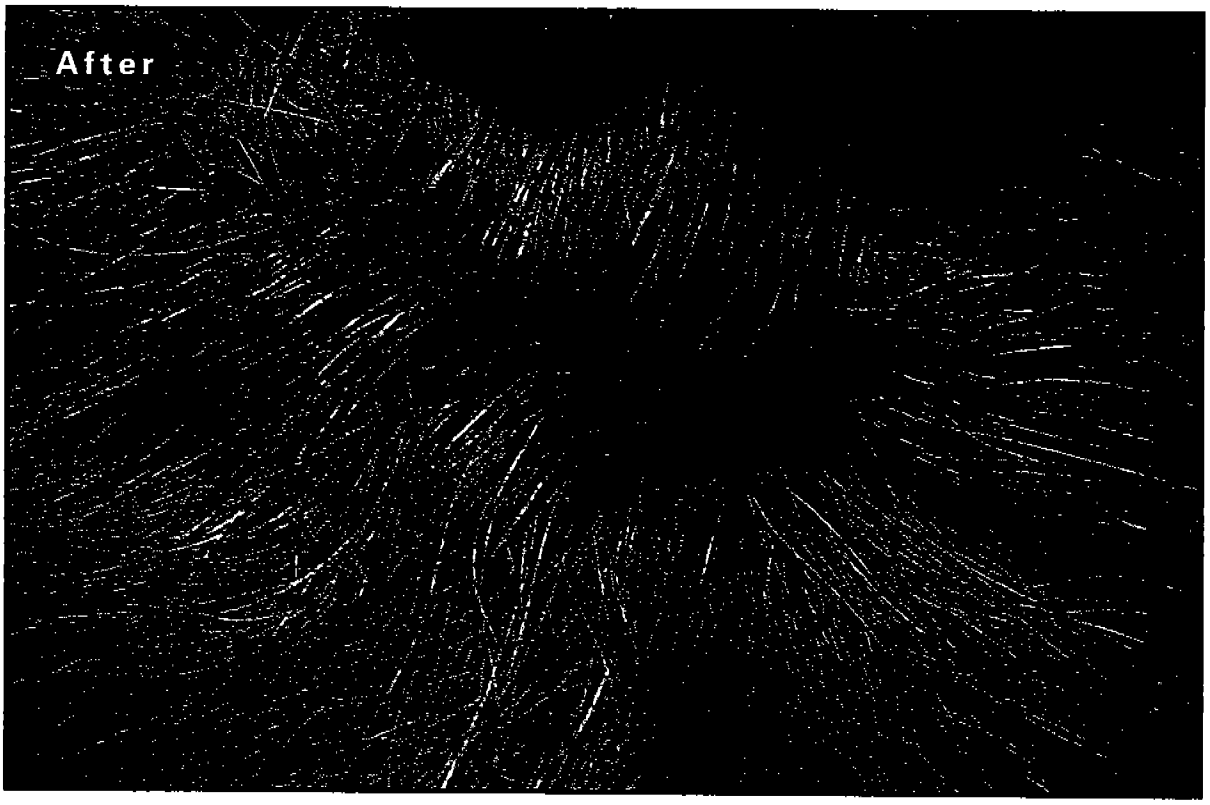
Diagnosis
- Moderate psoriasis

Prior Treatments
- The patient had received no prior treatment.

Treatment Plan
- Luxíq, BID for 1 month

Physician author: Brett C. Shulman, MD, Clinical Assistant Professor
Clinic/hospital affiliation: The University of Rochester
Rochester, NY

Patient cleared of scalp psoriasis following treatment with Luxíq Foam



Outcome and Discussion

- Following 1 month of treatment, patient no longer exhibited scaling, plaque thickness, erythema, and pruritus.
- Physician's and patient's global assessments rated Luxíq as providing significant improvement.
- Patient's acceptance of Luxíq was very high.

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