POSTER 115

# COMPARING FACIAL TOLERABILITY OF A 3-STEP ACNE SYSTEM CONTAINING A NOVEL SOLUBILIZED 5% BENZOYL PEROXIDE LOTION FOR NORMAL TO DRY SKIN WITH THAT OF A BENZOYL PEROXIDE/CLINDAMYCIN COMBINATION PRESCRIPTION PRODUCT

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## INTRODUCTION

A 3-step acne system containing a novel solubilized 5% benzoyl peroxide (BPO) lotion is now available for treating acne vulgaris in patients with normal to dry skin.[1] The system also contains a proprietary gentle cream cleanser and a proprietary therapeutic moisturizer containing 20% glycerin and 1% dimethicone. (A related 3-step system is also available for normal to oily skin—containing solubilized 5% BPO in a gel formulation together with a proprietary 2% salicylic acid cleanser and a proprietary 2% salicylic acid toner.)

Both systems have the potential to enhance the follicular penetration of BPO, and thus enhance clinical efficacy, as a result of patented technology which solubilizes BPO. (Other BPO products typically contain insoluble macrocrystals of BPO which may be too large to enter the follicles.)
A split-face study was performed to compare the tolerability of the new 3-step system for normal to dry skin with that of a BPO/clindamycin prescription product in an optimized vehicle.

## METHODS

### *Study design*

- Split-face, investigator-blind, randomized study

### *Inclusion criteria*

- Healthy female volunteers
- 18-45 years of age
- Caucasian
- Clear facial skin (no irritation or rashes etc.)
- If of childbearing potential, agreement to use birth control for the duration of the study

### *Exclusion criteria*

- History of unusual skin reactions to cosmetics or tretinoin products
- Actinic keratoses visible on face
- Concomitant condition or therapy that might interfere with evaluation of the study products
- Pregnancy or breastfeeding

### *Washout periods*

- 24 hours for facial use of emollients and cosmetics
- 1 week for facial use of moisturizers, topical medications, toners, and astringents
- 30 days for systemic retinoids, systemic steroids, systemic antibiotics, or experimental drugs or devices

### *Treatment regimen*

- Volunteers were randomly assigned to apply one of the following on one facial side, and the other on the contralateral facial side, once daily for 3 weeks:
  - 3-step acne system (proprietary gentle cream cleanser + solubilized 5% BPO lotion + proprietary therapeutic moisturizer)
  - 5% BPO/1% clindamycin combination prescription product containing two emollients (applied after using a specified over-the-counter cleanser).
- Each facial side was first washed with the cleanser assigned to that facial side, rinsed well, and dried before the relevant BPO-containing study product was applied. In the case of the 3-step acne system, the solubilized 5% BPO lotion was applied 10 minutes after washing and, once this was completely absorbed, the therapeutic moisturizer was applied.
- On weekdays, study monitors dispensed the coded products to each volunteer and supervised their application. The volunteers were instructed to squeeze out a pea-sized amount of the designated product onto a cotted fingertip and then to spread it gently over the assigned facial side (including the sensitive nasolabial fold). Using a new finger cot, the same procedure was followed for the contralateral facial side. At weekends, the volunteers applied the products unsupervised at home.
- The volunteers were instructed not to tamper with the application sites.
- If marked erythema or dryness, or severe burning or stinging, were reported on either side of the face—i.e. a score of 6 for erythema or dryness (see Table 1), or a score of 4 for burning or stinging (see Table 2)—treatments were stopped on the affected side(s) and both facial sides were evaluated. Treatment continued on any facial side not reaching these termination scores.

### *Outcome measures*

- Each facial side was assessed in terms of:
  - Erythema and dryness (by an expert grader) (Table 1)
  - Burning or stinging, and comfort (self-assessment by the volunteer) (Table 2).

### *Follow-on evaluation*

- In order to better understand the burning or stinging responses in this study (which occurred with a higher incidence than those reported in clinical trials), a follow-on study was performed to further evaluate 13 of the volunteers—the 3 who reached termination score plus 10 others who reported a sensation of burning for at least 10 minutes.
- First, the degree of stinging they felt in response to 10% lactic acid was graded as none, mild, moderate, or severe.
- Second, the degree of burning they felt 1, 5, and 15 minutes after applying the solubilized 5% BPO lotion—to one facial side without prior washing and to the contralateral facial side after washing with the proprietary cleanser—was graded on a 10-point scale.

**TABLE 1** Scales used by the expert grader to assess erythema and dryness on each facial side.

| Score | Erythema | Dryness |
|---|---|---|
| 0 | None | None |
| 2 | Mild erythema | Slight flaking |
| 4 | Moderate confluent erythema | Moderate flaking/scaling |
| 6 | Marked erythema, slight edema* | Marked scaling, slight fissuring* |
| 8 | Marked erythema, edema, flare, possible erosion | Severe scaling, fissuring |

*Termination score for test products on relevant facial side (last score carried forward in analyses).

**TABLE 2** Scales used by the volunteer to assess burning or stinging, and comfort, on each facial side.

| Score | Burning or stinging | Comfort** |
|---|---|---|
| 0 | None | Very comfortable |
| 1 | Barely perceivable | Comfortable |
| 2 | Slight | Somewhat comfortable |
| 3 | Moderate | Somewhat uncomfortable |
| 4 | Severe* | Uncomfortable |

*Termination score for test products on relevant facial side (last score carried forward in analyses).
**Comfort was an overall integrated evaluation that included erythema, dryness, burning or stinging, and tightness.

## RESULTS

### *Subjects*

- 50 female volunteers were enrolled, of whom:
  - 47 (94%) completed the study
  - 2 discontinued as a result of allergic contact dermatitis to BPO proven by patch test (and their data were excluded from analyses)
  - 1 discontinued due to a non-study reason.
- The volunteers had a mean age of 27 years.
- Of the 47 completers:
  - 44 completed both regimens
  - 3 reached termination score for burning or stinging with the acne system (however, all 3 rated that facial side as "very comfortable" throughout the study including at the point of discontinuation).

### *Facial tolerability*

- The incidence of subjects rating the facial tolerability of the novel solubilized 5% BPO acne system as "very comfortable" was consistently greater than that with the combination product containing BPO/clindamycin and two emollients (Figure 1).
- Compared with the BPO/clindamycin prescription product, the solubilized 5% BPO acne system also resulted in:
  - Lower mean levels of dryness (P≤.05 at day 14) (Figure 2)
  - Comparable mean levels of erythema (Figure 3)
  - Higher mean levels of burning or stinging (P≤.05 at days 7, 14, and 21) (Figure 4).
- With the solubilized 5% BPO acne system, mean dryness levels were not only significantly lower than BPO/clindamycin at day 14, but—unlike BPO/clindamycin—dryness was completely absent in all subjects at day 21.
- Importantly, despite the increased level of burning or stinging, patients rated the comfort of the facial side treated with the acne system more favorably than the side treated with BPO/clindamycin (P≤.05 at day 14) (Figure 1). This may be because burning or stinging was typically transient (including in those who reached the termination score), whereas dryness may be more prolonged.

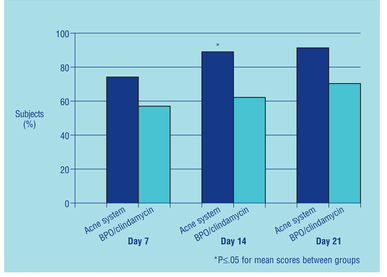


**Figure 1.** Proportion of subjects reporting their treated skin to be "very comfortable" (N = 47).

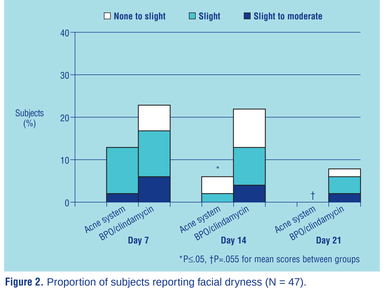


**Figure 2.** Proportion of subjects reporting facial dryness (N = 47).

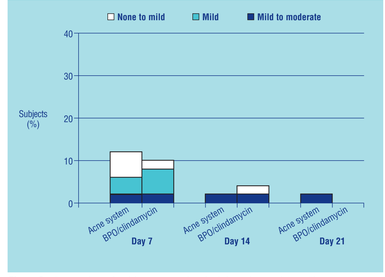


**Figure 3.** Proportion of subjects reporting facial erythema (N = 47).

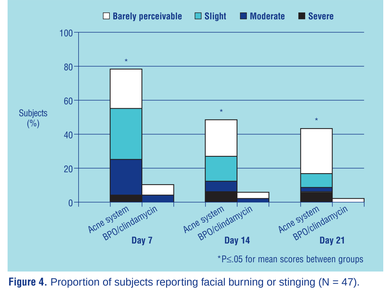


**Figure 4.** Proportion of subjects reporting facial burning or stinging (N = 47).

- With both products, burning was greatest in the first week (but typically no more than slight) and lessened with continued treatment.

### *Follow-on evaluation*

- The follow-on evaluation revealed that burning tended to be:
  - Stronger in subjects who had stronger stinging on the lactic acid skin sensitivity test than in those who had only mild stinging
  - Stronger when the solubilized 5% BPO lotion was applied after washing than when applied without pre-washing.
- It is possible that the incidence of burning was higher in this study than in previous clinical trials in patients with acne because:
  - In the study reported here, the amount of product to be applied was specified and could not be modified, and its application was supervised on most days—whereas in most studies (and in clinical practice) subjects are able to adjust dosing at the first sign of any burning
  - Burning occurs primarily in the upper cheek/suborbital area and, because acne lesions are uncommon in this area, susceptible patients may learn to avoid applying the product to this part of their face.

## CONCLUSIONS

Compared with the BPO/clindamycin product, the solubilized 5% BPO acne system was associated with significantly superior comfort ratings and significantly less dryness at day 14. Transient burning and stinging were reported but did not negatively affect overall comfort ratings.

Among susceptible subjects—i.e. those with strong stinging in response to a lactic acid test (which is estimated to occur in approximately 10% of the population)—burning may perhaps be minimized by avoiding washing the face immediately before applying the solubilized 5% BPO lotion and by avoiding application of the lotion to the suborbital area.

## REFERENCES

1. CLENZIderm M.D. – Product Detail. Available at: http://www.obagi.com/article/forpatients/obagiclenzidermmd/products/products.html. Accessed November 9, 2007.

## DISCLOSURE

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