

# Evaluation of a Solubilized Benzoyl Peroxide Gel: A Pooled Analysis From 3 Randomized Investigator-Blinded Clinical Trials



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A 3-step acne-treatment system has been developed utilizing a novel solubilized 5% benzoyl peroxide (BPO) gel along with 2% salicylic acid toner and 2% salicylic acid cleanser. According to data from 3 comparative clinical trials that included 111 actively treated subjects with acne vulgaris, monotherapy with the 3-step acne-treatment system and modified regimens of the system that included the solubilized serum gel appear to be more effective than the combination BPO and clindamycin gel (jar gel formulation) in reducing noninflammatory lesions, and at least as effective as the BPO and clindamycin gel in reducing inflammatory lesions.<sup>1-3</sup> Favorable skin tolerability and high levels of patient satisfaction were also observed in clinical trials with solubilized BPO gel regimens. The 3-step acne-treatment system is not available over the counter and can be obtained only through a physician.

The bioavailability of BPO in many commercially successful formulations may be variable or inconsistent owing to its poor solubility. BPO particulate size may vary markedly, resulting in inconsistent or suboptimal follicular penetration. These are important characteristics, as a major goal of BPO therapy is to reduce *Propionibacterium acnes* organisms. A novel formulation of solubilized BPO has been developed that helps maximize the bioavailability of BPO and enhances its penetration into follicles. This formulation is available

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as part of a 3-step acne-treatment system that also incorporates the use of a proprietary toner and cleanser, both of which contain 2% salicylic acid.<sup>4</sup>

## Methods

### Treatment Regimens

Data were pooled from 111 patients who participated in 1 of 3 randomized investigator-blinded trials (Table 1) evaluating the use of solubilized 5% BPO gel alone, the solubilized 5% BPO gel along with 2% salicylic acid toner and 2% salicylic acid cleanser (3-step acne-treatment system), and a combination BPO and clindamycin gel product (jar gel formulation).<sup>2,3</sup> Depending on the trial, each treatment was applied once or twice daily for 2 to 4 weeks. Patients were evaluated at weekly intervals.

### Inclusion Criteria

Patients included in the trials were 11 to 45 years of age with mild to moderate acne consisting of 17 to 100 inflammatory lesions and 10 to 100 noninflammatory lesions. Descriptions of the tolerability ratings of “none,” “mild,” “moderate,” and “severe,” can be found in Table 2. Subjects were willing to refrain from sunbathing and using other acne medications during the study.

### Exclusion Criteria

The exclusion criteria for the trials were allergies to BPO, papulopustular rosacea and other skin diseases on the face (other than acne) that might interfere with the study evaluations, a beard if it might interfere with the study evaluations, facial sunburn at the screening visit, and uncontrolled systemic diseases as determined by the investigator.

### Washout Periods

The washout periods required before enrollment and randomization were as follows: 1 week for medicated facial cleansers; 2 weeks for topical  $\alpha$ -hydroxy acids and

TABLE 1

## Studies From Which the Data Were Pooled to Evaluate the Use of Various Regimens of the 3-Step Acne-Treatment System Compared With Benzoyl Peroxide/Clindamycin Gel in Reducing Acne Lesions

Study	Treatments Evaluated	Regimen	Patients Evaluated, No.		
			Solubilized 5% BPO Gel	Solubilized 5% BPO Gel + 2% Salicylic Acid Toner ± 2% Salicylic Acid Cleanser	Prescription BPO/Clindamycin Combination Gel Product
NOA009B* <sup>2</sup>	Solubilized 5% BPO gel + 2% salicylic acid toner 5% BPO/clindamycin combination product	Twice daily for 2 wk	NA	34	34
NOA010A* <sup>1</sup>	Solubilized 5% BPO gel Solubilized 5% BPO gel + 2% salicylic acid toner + 2% salicylic acid cleanser 5% BPO/clindamycin combination product	Twice daily for 4 wk	23	13	23
NOA013 <sup>3</sup>	Solubilized 5% BPO gel + 2% salicylic acid toner + 2% salicylic acid cleanser	Once or twice daily for 3 wk	NA	41	0
<b>Total</b>			<b>23</b>	<b>88</b>	<b>57</b>

Abbreviations: BPO, benzoyl peroxide; NA, not applicable.

\*All or some patients treated in split-face manner. Such patients provide 2 sets of treatment data (one for the left facial side and one for the right facial side).

antiacne medications (except topical retinoids and antibiotics); and 4 weeks for topical retinoids, topical and systemic antibiotics, and topical and systemic corticosteroids.

### Outcome Measures

#### Efficacy

Outcome measures related to efficacy were changes in noninflammatory lesion count (mean percent reduction) and inflammatory lesion count (mean percent reduction).

#### Local Tolerability

Local tolerability was assessed by capturing potential reactions, including stinging and burning, erythema, dryness, and itching. The rating scale definitions for these specific findings are included in Table 2.

### Patient Satisfaction Assessment

Patient satisfaction was evaluated in 2 of the 3 trials, NOA013 and NOA010A, and was not assessed in study NOA009B. Parameters were evaluated separately in studies NOA010A and NOA013 owing to differences in the scales used. Both studies assessed satisfaction with the improvement in acne (rated as “very satisfied,” “satisfied,” “somewhat satisfied,” “neutral/indifferent,” or “dissatisfied”). In the NOA013 study, the following assessment was included: products leave the skin feeling refreshed and have acceptable tolerability (rated as “agree completely,” “somewhat agree,” “neither agree nor disagree,” “somewhat disagree,” or “disagree completely”). In the NOA010A study, the following assessment was included: products leave the skin feeling refreshed and feel like

TABLE 2

### Tolerability Scale Used to Assess Stinging and Burning, Erythema, Dryness, and Itching in Patients With Mild to Moderate Acne

Score	Stinging/Burning	Erythema	Dryness	Itching
0	None	None—no erythema (may be minor discoloration)	None	None
1	Mild—light, warm tingling sensation, not really bothersome	Mild—light pink, noticeable	Mild—slight but definite roughness	Mild—occasional, slight itching
2	Moderate—definite warmth, tingling/stinging sensation that is somewhat bothersome	Moderate—pink-red, noticeable	Moderate—moderate roughness	Moderate—constant or intermittent itching that is somewhat bothersome
3	Severe—hot tingling/stinging sensation that is disturbing normal activity	Severe—deep or bright red, may be warm to the touch	Severe—marked roughness	Severe—bothersome itching that is disturbing normal activity

they are working (rated as “excellent,” “good,” “fair,” or “poor”).

#### Patient Demographics

The mean age of included subjects was 20 years. Most were white (82.7%), and the remainder were African American (15.7%) and Asian American (16%).<sup>2,3</sup> The distribution of females and males was proportionally comparable (52% vs 48%, respectively). Half of the subjects were Fitzpatrick skin type III.

#### Statistical Analysis

Intent-to-treat analyses were used for statistical evaluation of study results. A *P* value of  $\leq .05$  was considered to signify statistical significance. Efficacy data are reported here; however, owing to the differing designs of the studies in this pooled analysis (split-face versus full-face), the statistical significance of between-group differences in efficacy and tolerability parameters could not be reliably evaluated. Patient satisfaction data did allow for between-group differences to be evaluated using the Wilcoxon rank-sum test.

#### Efficacy Results

##### Noninflammatory Lesions

The mean percent reduction in noninflammatory lesion count was greater with the solubilized 5% BPO regimens

than with BPO and clindamycin gel at both week 2 and week 4 (Figure 1). Mean reductions were as follows: 37% with the 3-step acne-treatment system, 29% with solubilized BPO gel, and 16% with BPO and clindamycin gel at week 2. The results at week 4 were 47%, 42%, and 28%, respectively.

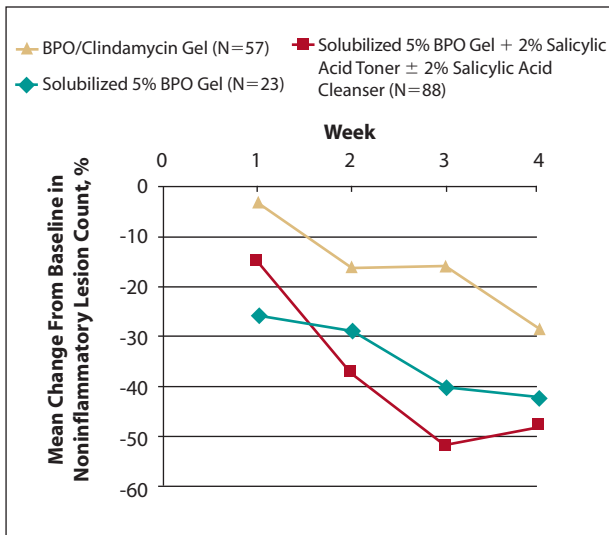
##### Inflammatory Lesions

The mean reduction in inflammatory lesion count was comparable across all 3 regimens at week 2, exhibiting a range of 48% to 52% (Figure 2). At week 4, the mean reduction in inflammatory lesions was 65% with the 3-step acne-treatment system, 70% with solubilized BPO gel, and 61% with BPO and clindamycin gel.

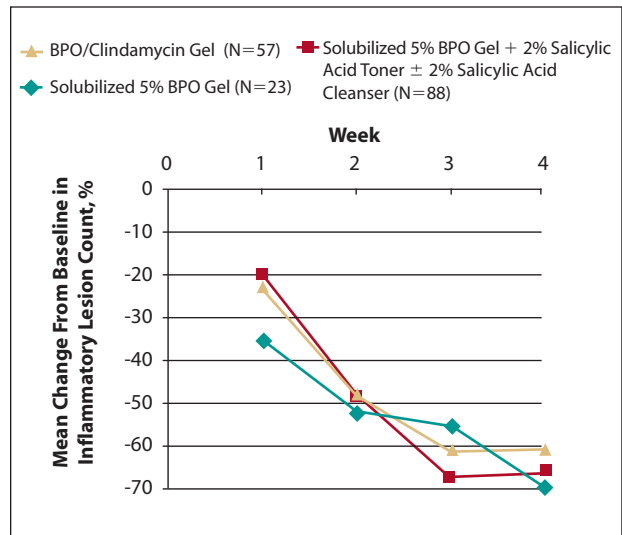
##### Patient Satisfaction

Data from the NOA013 study demonstrated good patient satisfaction with the 3-step acne-treatment system. At week 3, overall mean scores showed that patients were “satisfied” to “very satisfied” with the improvement in their acne, “somewhat agreed” to “completely agreed” that both the toner and the cleanser in the system leave the skin feeling refreshed, and “somewhat agreed” to “completely agreed” that each of the component parts of the acne system (the solubilized 5% BPO gel, the toner, and the cleanser) have acceptable tolerability. Additionally, in the NOA010A study, the solubilized

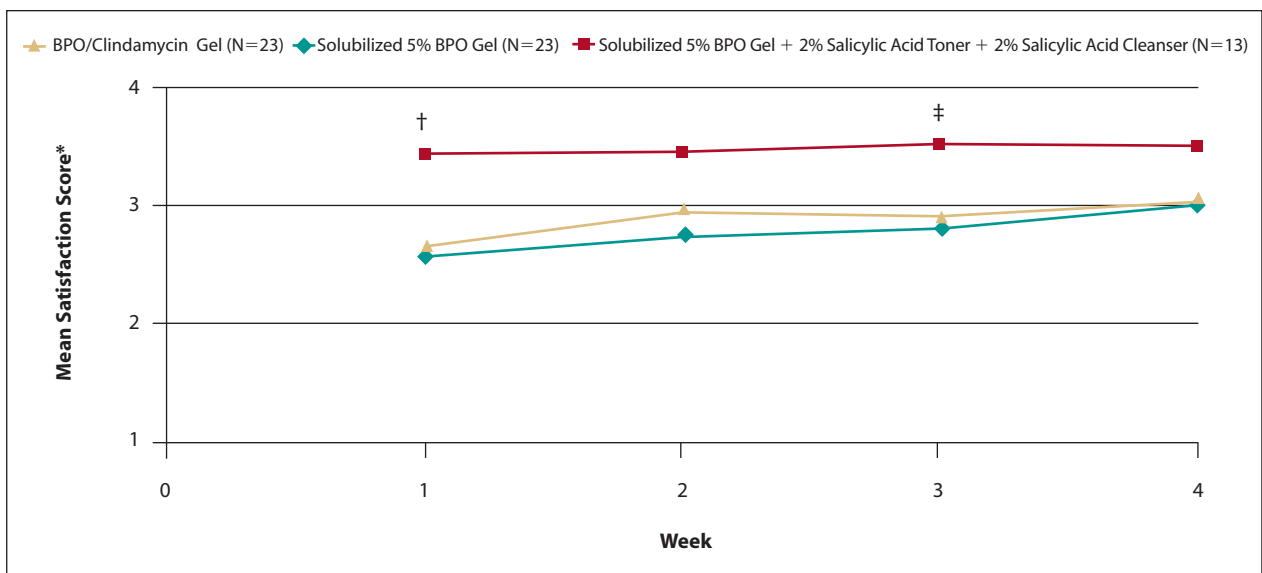
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**Figure 1.** Mean reduction in noninflammatory acne lesion count.



**Figure 2.** Mean reduction in inflammatory acne lesion count.



**Figure 3.** Patient satisfaction that benzoyl peroxide (BPO)/clindamycin gel, solubilized 5% BPO gel, and solubilized 5% BPO gel with 2% salicylic acid toner and 2% salicylic acid cleanser leave the skin feeling refreshed and that the products feel like they are working. Asterisk indicates scale where 1=poor, 2=fair, 3=good, 4=excellent; dagger,  $P \leq .01$  vs BPO/clindamycin gel; double dagger,  $P \leq .05$  vs BPO/clindamycin gel.

5% BPO gel along with 2% salicylic acid toner and 2% salicylic acid cleanser (3-step acne-treatment system) was significantly superior to BPO and clindamycin gel for satisfaction with the improvement in acne ( $P \leq .05$  at week 2) and satisfaction that the products leave the skin feeling refreshed and feel like they are working ( $P \leq .01$  at week 1,  $P \leq .05$  at week 3; Figure 3).

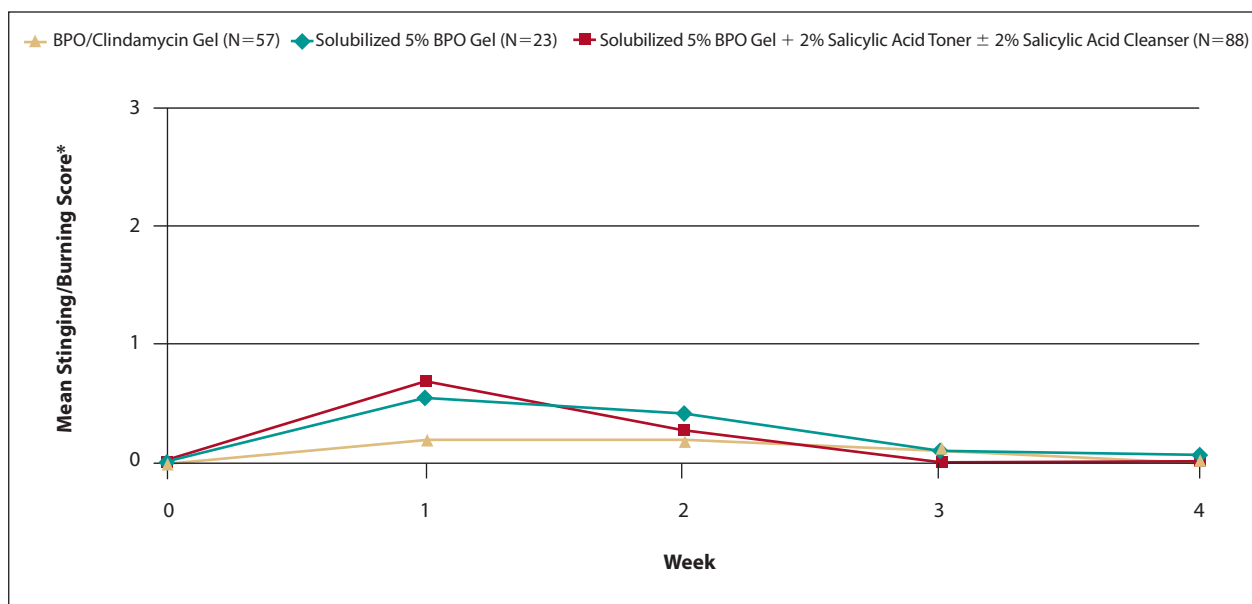
## Tolerability

Importantly, the mean levels of stinging and burning, erythema, dryness, and itching remained less than mild with all regimens at all time points (Figures 4–7). The

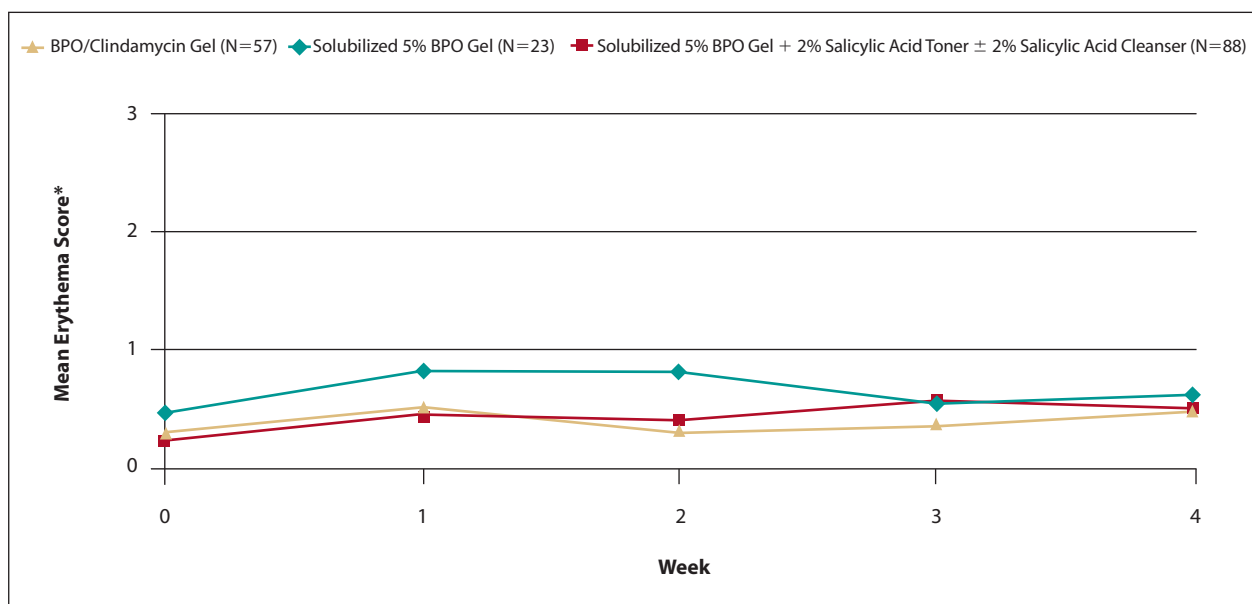
mean level of stinging and burning was slightly higher with the solubilized 5% BPO regimens than with BPO and clindamycin gel at week 1. However, by week 4, stinging and burning were completely absent in all groups (Figure 4). In the first 2 weeks, the mean levels of erythema and dryness were slightly higher with solubilized 5% BPO alone than with BPO and clindamycin gel (Figures 5 and 6).

## Conclusion

A 3-step acne-treatment system has been developed utilizing a novel solubilized 5% BPO gel along with 2% salicylic



**Figure 4.** Mean score for stinging/burning in patients using benzoyl peroxide (BPO)/clindamycin gel, solubilized 5% BPO gel, and solubilized 5% BPO gel with 2% salicylic acid toner and 2% salicylic acid cleanser. Asterisk indicates scale where 0=none, 1=mild, 2=moderate, 3=severe.

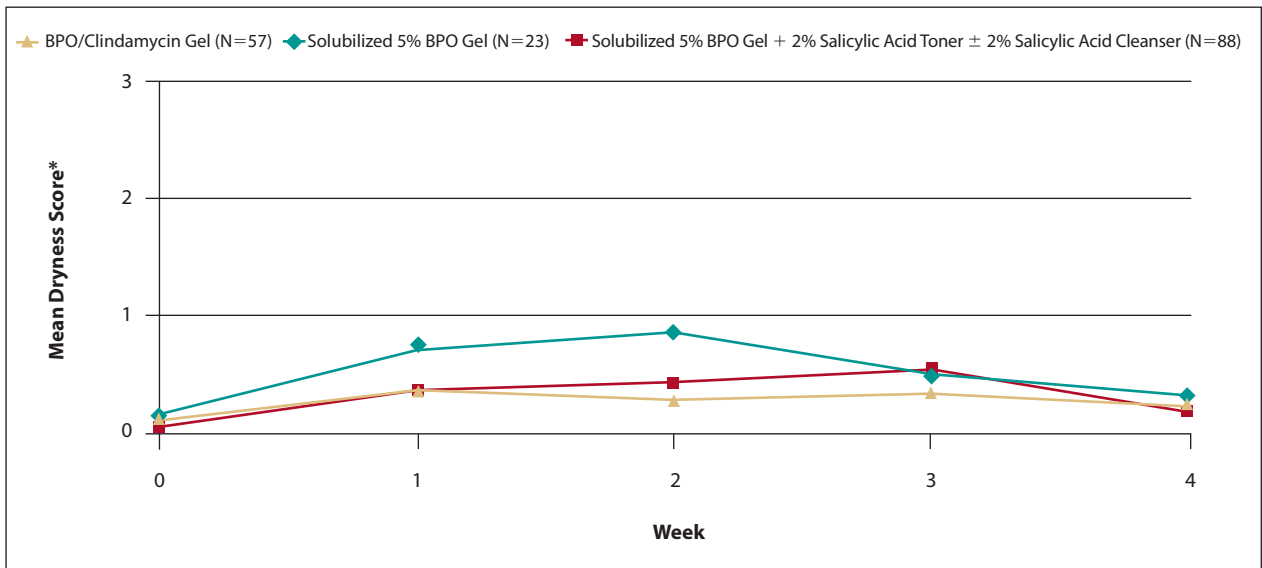


**Figure 5.** Mean score for erythema in patients using benzoyl peroxide (BPO)/clindamycin gel, solubilized 5% BPO gel, and solubilized 5% BPO gel with 2% salicylic acid toner and 2% salicylic acid cleanser. Asterisk indicates scale where 0=none, 1=mild, 2=moderate, 3=severe.

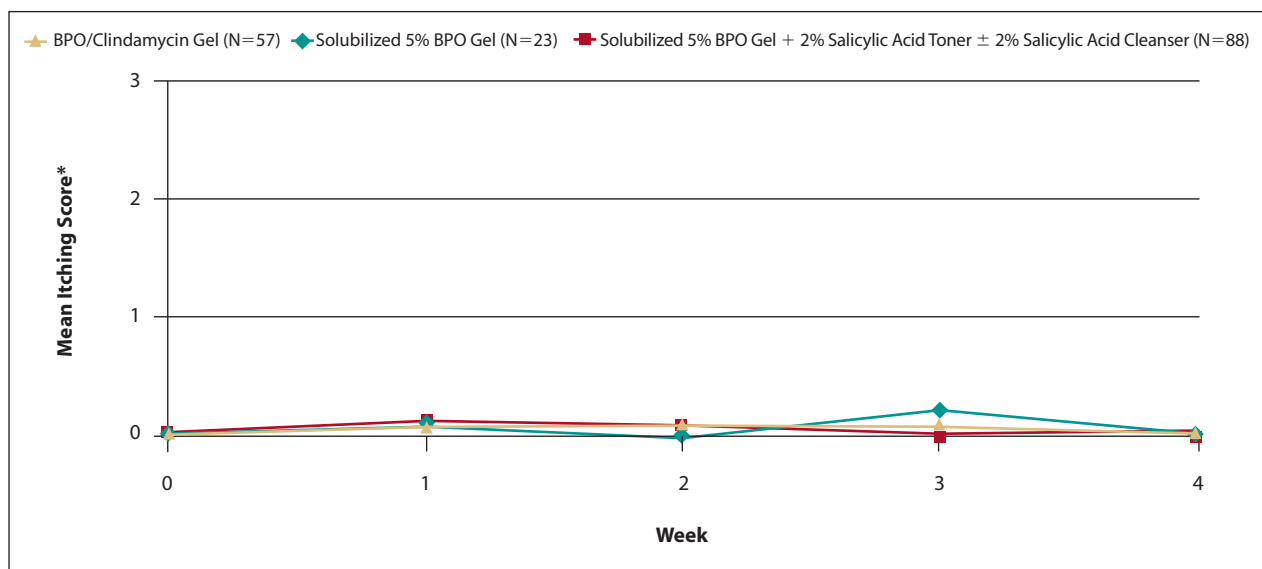
acid toner and 2% salicylic acid cleanser. According to data from 3 comparative clinical trials that included 111 actively treated subjects, monotherapy with the 3-step acne-treatment system in patients with acne vulgaris appears to be more effective than the combination BPO and clindamycin gel (jar gel formulation) in reducing noninflammatory lesions, and at least as effective as the BPO and clindamycin gel in reducing inflammatory

lesions.<sup>2,3</sup> The solubilized BPO gel—used alone or as part of the 3-step acne-treatment system—offers an effective and well-tolerated approach to treating acne vulgaris, demonstrating enhanced follicular penetration of BPO and rapid reduction in acne lesion counts. Favorable skin tolerability and high levels of patient satisfaction were also observed in clinical trials with solubilized BPO gel regimens. This branded 3-step acne-

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**Figure 6.** Mean score for dryness in patients using benzoyl peroxide (BPO)/clindamycin gel, solubilized 5% BPO gel, and solubilized 5% BPO gel with 2% salicylic acid toner and 2% salicylic acid cleanser. Asterisk indicates scale where 0=none, 1=mild, 2=moderate, 3=severe.



**Figure 7.** Mean score for itching in patients using benzoyl peroxide (BPO)/clindamycin gel, solubilized 5% BPO gel, and solubilized 5% BPO gel with 2% salicylic acid toner and 2% salicylic acid cleanser. Asterisk indicates scale where 0=none; 1=mild, 2=moderate, 3=severe.

treatment system is not available over the counter and can only be obtained through the office of a physician.

## References

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