

Acne Subject Preference for Pump Over Tube for Dispensing Fixed-Dose Combination Adapalene 0.1%–Benzoyl Peroxide 2.5% Gel

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ABSTRACT

Introduction: Acne is a chronic inflammatory disease. Key to a patient's success on fixed-dose adapalene–benzoyl peroxide (BPO) gel is ensuring adherence. Use of a pump system to deliver a pre-measured amount of gel with each pressure enables application of a more consistent dose vs. the tube, which should improve adherence. In the present study, we evaluate patient preference for two different containers for dispensing adapalene–BPO gel.

Methods: In this 15-day, open-label study, 300 subjects were asked to treat their acne using fixed-dose adapalene 0.1%–BPO 2.5% gel dispensed in either a tube or a pump once-daily for up to 7 days. At week 1, subjects

switched to the alternative packaging design for the same timeframe. At the end of the treatment period, subjects were asked to complete a subject preference survey.

Results: Among subjects completing the survey ($n = 291$), 79.0% ($n = 230$) preferred the pump for dispensing adapalene–BPO gel and 21.0% ($n = 61$) preferred the tube ($p < 0.001$). The top three characteristics of the pump were that it was easy to use (89.0%; $n = 259/291$), clean (73.2%; $n = 213/291$) and convenient (69.4%; $n = 202/291$). When asked to rate their experience with using the pump, 91.8% ($n = 267/291$; $p < 0.001$) of subjects reported being satisfied on a self-assessment scale. The majority of subjects stated they would tell their doctor about their preference for the pump next time adapalene–BPO gel was prescribed (76.6%; $n = 223/291$; $p < 0.001$) and would prefer the pump if both containers cost the same amount (80.1%; $n = 233/291$; $p < 0.001$).

Conclusion: Patients prefer using a pump instead of a tube to dispense adapalene–BPO gel. This delivery mechanism helps to ensure consistent application and thus may improve patient adherence to the prescribed acne treatment regimen.

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INTRODUCTION

Acne is a chronic inflammatory disease of the pilosebaceous unit, with a long duration and a pattern of recurrence or relapse [1, 2]. An individual's adherence to their medication has a prominent role in the success of any acne therapy [1]. However, adherence to acne treatment regimens is traditionally poor [3, 4]. For example, one large study involving 3,339 acne subjects from the Americas, Europe and Asia demonstrated that among subjects treated with topical therapy only, poor adherence occurred in 40% of cases. When a combination of both systemic and topical therapies was used, poor adherence to at least one treatment increased to 60% [5]. Several different factors affect adherence. Poor adherence is independently correlated with young age, at least one adverse reaction, high Dermatology Life Quality Index score, previous systemic treatment, lack of improvement as evaluated by the dermatologist, lack of patient satisfaction with treatment, lack of knowledge about acne treatment and consultation with a primary care physician [5, 6].

Patients prefer topical acne therapies that are available as gel formulations, can be used once-daily, are applied with the fingers and can be stored at room temperature [7]. Furthermore, fixed-dose combinations provide convenience for patients, which improves adherence [1].

Patient preference for one container over another for dispensing their acne treatment may also impact adherence. However, such data are limited. A previous study by Fried and Nighland in acne patients dissatisfied with

their current therapy assessed the impact of a new acne treatment dispensed from a pump [8]. They found that more than three-quarters of patients rated the pump as an excellent or very good way to dispense their medication, and a similar proportion of patients were very satisfied or extremely satisfied with the pump treatment application [8].

Key to a patient's success on fixed-dose adapalene–benzoyl peroxide (BPO) gel is consistent application. This means not only ensuring patients apply their treatment as frequently as prescribed, but also ensuring patients apply the right amount of product with each application. The use of a pump delivering a pre-measured and more consistent amount of drug at each dose may help to further improve the efficacy of this treatment option vs. use of less consistent amounts dispensed from a tube.

The objective of the present study was to evaluate patient preference for two different containers used to dispense fixed-dose adapalene–BPO gel (tube vs. pump).

MATERIALS AND METHODS

Study Design

This open-label study was conducted by two investigative sites in the US. The total study duration was 15 days. At baseline (visit 1), eligible subjects were randomized into two groups: one was asked to treat their acne using Epiduo[®] (adapalene 0.1%–BPO 2.5%) gel (Quebec: Galderma Production Canada, Inc.) dispensed in either a 45-g laminate tube or a 45-g bottle with a dispensing pump once-daily (in the evening) for up to 7 days. At week 1 (visit 2), subjects returned to the site and, upon returning the study product, were given the

alternative package to use for up to 7 days. At the end of the second treatment period, subjects were asked to return the study product to the site (visit 3), at which time they completed an online preference survey. All adverse events (AEs) or product technical complaints were collected.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 and 2008. Informed consent was obtained from all patients for being included in the study.

Subject Selection

Eligible subjects had to meet all the inclusion criteria and none of the exclusion criteria in order to qualify for enrollment in the study. Key inclusion criteria were (1) male or female subjects of any race, aged 12–35 years inclusive; (2) diagnosis of acne and eligible for treatment with adapalene–BPO; (3) subject willingness to use adapalene–BPO dispensed in either a tube or a pump for up to 7 days and to switch to using adapalene–BPO dispensed in the alternative packaging design for up to 7 days; and (4) informed consent by the subject (or guardian if <18 years of age) prior to any study-related procedures. Exclusion criteria included (1) female subjects who were pregnant, nursing or planning a pregnancy; and (2) known or suspected allergy to the study products.

Statistical Analysis

All analyses were performed on the safety population (all subjects who were enrolled and received at least one dose of study products). A total of 300 subjects were planned for

enrollment with the prediction that a minimum of 200 subjects would complete the survey. This sample size ensured that the margin of error was no larger than 7%.

The response to question 1 in the subject preference survey was summarized as tube or pump. Question 5 was summarized for all responses (very satisfied, satisfied, no opinion, dissatisfied and very dissatisfied) and also dichotomized responses (satisfied or not satisfied), with the definition of satisfied being a response of satisfied or very satisfied. A subject was classified as not satisfied if the response was either no opinion, dissatisfied or very dissatisfied. The Rao–Scott Chi square test was applied to the responses to questions 3, 4 and 5 to test differences between the responses. An exact binomial test was used to determine differences in responses to questions 1, 2 and the dichotomized version of question 5. Additionally, responses for questions 2 and the dichotomized responses of question 5 were analyzed using Fisher's Exact test, grouping subjects according to their response to question 1. Question 6 was summarized by frequencies and percentages.

No statistical analyses were conducted on reported AEs or reported product technical complaints.

RESULTS

Subject Disposition

A total of 300 enrolled subjects receiving at least one dose of study product were included in the safety population. Nine subjects (3%) withdrew from the study at their own request and 291 subjects (97%) completed the study. Demographic characteristics were comparable among both groups (Table 1).

Table 1 Demographic characteristics

Characteristic	Measure	Safety population (<i>n</i> = 300)
Gender	Female	178 (59.3%)
	Male	122 (40.7%)
Ethnicity	Hispanic or Latino	46 (15.3%)
	Not Hispanic or Latino	254 (84.7%)
Race	White	200 (66.7%)
	Black or African American	43 (14.3%)
	Asian	19 (6.3%)
	American Indian or Alaska Native	5 (1.7%)
	Native Hawaiian or Other Pacific Islander	3 (1.0%)
	Other or mixed	30 (10.0%)
Age (years)	Mean (standard deviation)	21.5 (7.16)
	Median	19.5
	Min, max	12.0, 35.0

Subject Preference Survey

Among subjects who completed the preference survey (*n* = 291), 79.0% (*n* = 230) preferred the pump for dispensing adapalene–BPO gel and 21.0% (*n* = 61) preferred the tube (*p* < 0.001).

Subjects felt that all the statements listed within the preference survey better described the pump over the tube. They included that the pump made it easier to give a consistent amount for the face every time (81.8%; *n* = 238/291; *p* < 0.001) and made it easier to know how much to apply to the face (74.9%; *n* = 218/291; *p* < 0.001). In addition, subjects reported the pump was easier to use (82.1%; *n* = 239/291; *p* < 0.001), did not waste gel (72.9%; *n* = 212/291; *p* < 0.001) and made less of a mess (86.9%; *n* = 253/291; *p* < 0.001) (Table 2).

Results were then analyzed according to subject preference for the pump or the tube. Among the subset of subjects who preferred the

pump, the main reasons were because it made less of a mess (95.2%; *n* = 219/230; *p* < 0.001), was more convenient to use (93.5%; *n* = 215/230; *p* < 0.001) and was easier to use (93.5%; *n* = 215/230; *p* < 0.001) (Table 3).

All subjects who completed the survey were asked to select the characteristics they felt described the adapalene–BPO pump. The three characteristics cited most frequently were easy to use (89.0%; *n* = 259/291), clean (73.2%; *n* = 213/291) and convenient (69.4%; *n* = 202/291) (Fig. 1).

A total of 91.8% (*n* = 267/291) of subjects were satisfied (very satisfied or satisfied) with their experience using the pump (*p* < 0.001). Among subjects who preferred the pump, the majority of subjects were satisfied (very satisfied or satisfied) with their experience using the pump (98.7%; *n* = 227/230; *p* < 0.001).

Just over three-quarters of subjects (76.6%; *n* = 223/291) stated that they would tell their

Table 2 Subject belief on whether statements better described the attributes of the tube or pump

Statement	Response	All subjects ($n = 291$)	p value*
Easy to know how much to apply to my face	Tube	73 (25.1%)	<0.001
	Pump	218 (74.9%)	
Easy to give me a consistent amount for my face every time	Tube	53 (18.2%)	<0.001
	Pump	238 (81.8%)	
Does not waste adapalene–BPO gel	Tube	79 (27.1%)	<0.001
	Pump	212 (72.9%)	
Does not drip or leak as much	Tube	67 (23.0%)	<0.001
	Pump	224 (77.0%)	
Makes less of a mess	Tube	38 (13.1%)	<0.001
	Pump	253 (86.9%)	
Easy to store	Tube	120 (41.2%)	0.002
	Pump	171 (58.8%)	
Easy to handle	Tube	66 (22.7%)	<0.001
	Pump	225 (77.3%)	
Easy to use	Tube	52 (17.9%)	<0.001
	Pump	239 (82.1%)	
Easy to take with me when I'm not home	Tube	124 (42.6%)	0.007
	Pump	167 (57.4%)	
Saves time	Tube	56 (19.2%)	<0.001
	Pump	235 (80.8%)	
Makes it easy to follow my doctor's instructions	Tube	68 (23.4%)	<0.001
	Pump	223 (76.6%)	
Attractive looking	Tube	35 (12.0%)	<0.001
	Pump	256 (88.0%)	
The one you are more likely to leave out on the counter	Tube	57 (19.6%)	<0.001
	Pump	234 (80.4%)	
More convenient to use	Tube	59 (20.3%)	<0.001
	Pump	232 (79.7%)	

BPO benzoyl peroxide

* p value was associated with the exact binomial test against the null hypothesis of 50% for each response

doctor about their preference for the pump the next time their doctor prescribed adapalene–BPO gel ($p < 0.001$). The majority of subjects

(80.1%; $n = 233/291$) indicated they would prefer the pump if the tube and pump cost the same amount ($p < 0.001$).

Table 3 Subject belief on whether statements better described the attributes of the tube or pump based on preference for the tube or pump

Statement	Response	Product preference		<i>p</i> value*
		Tube (<i>n</i> = 61)	Pump (<i>n</i> = 230)	
Easy to know how much to apply to my face	Tube	43 (70.5%)	30 (13.0%)	<0.001
	Pump	18 (29.5%)	200 (87.0%)	
Easy to give me a consistent amount for my face every time.	Tube	33 (54.1%)	20 (8.7%)	<0.001
	Pump	28 (45.9%)	210 (91.3%)	
Does not waste adapalene–BPO gel	Tube	38 (62.3%)	41 (17.8%)	<0.001
	Pump	23 (37.7%)	189 (82.2%)	
Does not drip or leak as much	Tube	38 (62.3%)	29 (12.6%)	<0.001
	Pump	23 (37.7%)	201 (87.4%)	
Makes less of a mess	Tube	27 (44.3%)	11 (4.8%)	<0.001
	Pump	34 (55.7%)	219 (95.2%)	
Easy to store	Tube	43 (70.5%)	77 (33.5%)	<0.001
	Pump	18 (29.5%)	153 (66.5%)	
Easy to handle	Tube	37 (60.7%)	29 (12.6%)	<0.001
	Pump	24 (39.3%)	201 (87.4%)	
Easy to use	Tube	37 (60.7%)	15 (6.5%)	<0.001
	Pump	24 (39.3%)	215 (93.5%)	
Easy to take with me when I'm not home	Tube	47 (77.0%)	77 (33.5%)	<0.001
	Pump	14 (23.0%)	153 (66.5%)	
Saves time	Tube	37 (60.7%)	19 (8.3%)	<0.001
	Pump	24 (39.3%)	211 (91.7%)	
Makes it easy to follow my doctor's instructions	Tube	41 (67.2%)	27 (11.7%)	<0.001
	Pump	20 (32.8%)	203 (88.3%)	
Attractive looking	Tube	18 (29.5%)	17 (7.4%)	<0.001
	Pump	43 (70.5%)	213 (92.6%)	
The one you are more likely to leave out on the counter	Tube	20 (32.8%)	37 (16.1%)	0.006
	Pump	41 (67.2%)	193 (83.9%)	
More convenient to use	Tube	44 (72.1%)	15 (6.5%)	<0.001
	Pump	17 (27.9%)	215 (93.5%)	

BPO benzoyl peroxide

* *p* value was associated with the Fisher's exact test against the null hypothesis of the independence between product preference and survey response

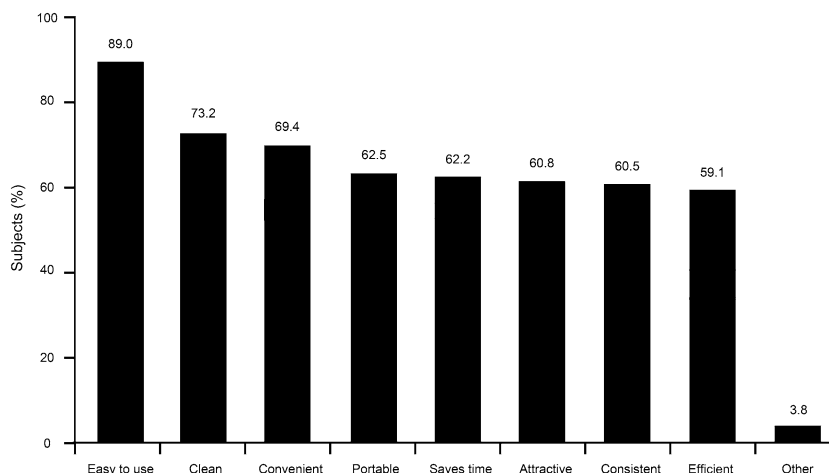


Fig. 1 Characteristics describing the adapalene–benzoyl peroxide (BPO) gel pump ($n = 291$) (subjects were asked to choose all that apply). The figure shows characteristics

selected by subjects who completed the survey that they felt described the adapalene–BPO pump

Adverse Events

In the safety population ($n = 300$), 13 subjects (4.3%) reported 22 events. The AEs were mild (68.2%; $n = 15/22$) or moderate (31.8%; $n = 7/22$) in severity and most considered by the investigators to be probably related (95.5%; $n = 21/22$) to the study medication. The AEs were classified largely as skin and subcutaneous tissue disorders ($n = 21/22$) and included dry skin ($n = 5/22$), erythema ($n = 2/22$), pain of skin ($n = 8/22$), pruritus ($n = 1/22$), rash ($n = 1/22$), scab ($n = 1/22$), skin exfoliation ($n = 2/22$) and skin tightness ($n = 1/22$). One report of a toothache was deemed definitely unrelated to the study medication. No serious AEs were reported and no subjects withdrew from the study due to an AE.

Product Technical Complaints

There were no product technical complaints about the dispensing container with a pump. There was one report of a product technical complaint about the tube relating to automatic dispensing of the product.

DISCUSSION

In this analysis of 300 subjects, we demonstrated that the majority of acne subjects prefer the pump over the tube for dispensing adapalene–BPO gel and a similar proportion would tell their doctor about this preference at the time of their next prescription. Furthermore, over 90% of subjects reported being satisfied or very satisfied with the pump on a patient self-assessment scale. These results align with those of another study showing that 86% of patients dissatisfied with their current acne therapy who received a new treatment dispensed from a pump were very satisfied or extremely satisfied with the pump treatment application at the end of the 12-week study period [8].

Since poor adherence is independently correlated with a lack of patient satisfaction with their acne treatment [5], it is hoped that use of a pump instead of a tube to dispense adapalene–BPO gel may further encourage patient adherence to this treatment option. In fact, one study has shown that 95% of acne patients using a pump dispenser over a 3-month

period took 75–100% of their prescribed doses [9]. Such findings are important in all acne patients, but especially when treating patients with long-term chronic disease who require maintenance therapy, as good adherence may help to reduce the risk of relapse. The combination of two effective medications into one fixed-dose adapalene–BPO regimen helps to reduce the complexity of acne management by reducing the number of treatments a patient has to remember to take on a daily basis and is another effective approach to enhancing adherence [10].

It is important to ensure the patient uses their medication as directed. Application of the same amount each time encourages an even spread and distribution of topical acne medication on each occasion, which allows for consistency of application [11]. The use of a system to deliver a pre-measured amount of adapalene–BPO gel with each pressure (approximately 0.5 ml) enables patients to apply a more consistent dose each time vs. the tube, i.e. a thin film of gel across the entire acne-affected areas and not just individual pimples [12, 13]. Critically, over 90% of subjects who preferred the pump found it was an easy way to deliver a consistent amount each time, helping to optimize patient outcomes [14, 15]. Furthermore, doctors should be able to more accurately predict how long a prescription will last when the gel is dispensed from a pump instead of a tube [11].

In addition to medication use as directed, successful management of acne also involves choosing the right medication. As such, efficacy is a critical parameter when treating patients with acne and individuals often need long-term maintenance therapy [1, 2, 14, 15]. Treatment with adapalene–BPO results in a significant reduction in total, inflammatory and non-inflammatory lesions at week 1. Further

improvements observed to week 12 can be sustained to week 52 [16–18]. In cases of more severe disease, there is clinical benefit in combining adapalene–BPO with lymecycline or doxycycline for 12 weeks [19, 20]. Longer term adapalene–BPO treatment for a further 6 months prevents relapse and continues to reduce acne lesions over the same timeframe [14, 15].

Just over 75% of all subjects stated that use of the pump instead of the tube made it easier to follow their doctor's instructions, which increased to over 88% in subjects who preferred the pump. As a result, patients will be using the gel as directed and are more likely to have a safer treatment experience. Use of a more consistent amount of adapalene–BPO gel dispensed from a pump may help to reduce the occurrence of adverse reactions, compared with possible over-application of the gel if dispensed from a tube [11]. The safety profile of adapalene–BPO gel demonstrated in this study is consistent with the findings of previous studies [17, 18, 21, 22].

Product waste increases the cost of therapy [11]. Almost three-quarters of subjects preferred the pump over the tube because it did not result in as much waste. Product waste may manifest as drips and leaks from the container and excess product being dispensed. Use of a pump to dispense a more consistent amount of adapalene–BPO gel vs. the tube avoids both of these potential issues. Furthermore, waste may also result from medication left in the dispenser when it appears empty. The pump has a better product restitution rate compared with the tube (>95% and >90%, respectively) [13, 23].

The open-label study design introduces significant bias, which limits the generalizability of the results. However, the order of the response choices to the survey questions was randomized to avoid bias. In

addition, all therapies were authorized so subjects were able to use previous and concomitant therapies as part of their individualized treatment plan. Since the aim was to assess subject preference for the dispensing container and not the medication itself, no diaries were used to assess treatment compliance. Collation of such information would have facilitated further analysis of the impact of the pump as a preferred dispensing route.

CONCLUSION

Patients prefer using a pump instead of a tube to dispense adapalene–BPO gel. This delivery mechanism helps to ensure consistent application and thus may improve patient adherence to the prescribed acne treatment regimen.

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Additional informed consent was obtained from all patients for whom identifying information is included in this article.

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