

New Drug Reviews

# Adapalene/Benzoyl Peroxide (Epiduo) for Acne Vulgaris

HEATHER PICKETT, DO, FAAFP, and SCOTT WILTZ, MD, MPH Nellis Air Force Base Family Medicine Residency, Nellis Air Force Base, Nevada

STEPS new drug reviews cover Safety, Tolerability, Effectiveness, Price, and Simplicity. Each independent review is provided by authors who have no financial association with the drug manufacturer.

The series coordinator for *AFP* is Allen F. Shaughnessy, PharmD, Tufts University Family Medicine Residency Program at Cambridge Health Alliance, Malden, Mass.

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Epiduo is a combination of topical adapalene 0.1% and benzoyl peroxide 2.5% in a gel formulation. It is labeled for the treatment of acne vulgaris in patients at least 12 years of age. Benzoyl peroxide releases oxygen free radicals to oxidize bacterial proteins and decrease anaerobic bacteria in the sebaceous follicles, and produces a keratolytic effect. The mechanism of adapalene, a retinoid-type compound, is not known; however, it may work by decreasing inflammation, keratinization, and cellular differentiation, thereby reducing microcomedone development.

| Drug   | Dosage                              | Dose form   | Approximate cost*     |
|--|-------------------------------------|---|-----------------------|
| Adapalene/benzoyl<br>peroxide (Epiduo)   | Pea-sized amount applied once daily | Adapalene 0.1%/benzoyl<br>peroxide 2.5% topical gel | \$237 for a 45-g tube |
| *—Estimated retail price of full treatment course based on information obtained at http://www.drugstore.com (accessed May 10, 2011). |                                     |   |                       |

### SAFETY

Limited studies have not identified significant safety issues. Combining adapalene and benzoyl peroxide produces adverse effects similar to those of each drug used alone.<sup>2,3</sup> Adapalene can increase the risk of photosensitivity; patients using this drug should minimize their exposure to sun and other sources of ultraviolet light.<sup>3</sup> No studies have been performed in children younger than 12 years. Adapalene/benzoyl peroxide is a U.S. Food and Drug Administration pregnancy category C drug, and its safety in lactating women is not known.<sup>1</sup>

## **TOLERABILITY**

Epiduo, which contains benzoyl peroxide 2.5%, is less likely to cause adverse effects compared with products containing benzoyl peroxide 5 to 10%.<sup>2,4</sup> The addition of adapalene has not been shown to increase the risk of adverse effects compared with benzoyl peroxide alone.<sup>4</sup> Erythema, scaling, dryness, stinging, and burning commonly occur at the beginning of therapy and usually subside

within four weeks.<sup>1,2</sup> Sun and wind exposure will increase these symptoms, especially in patients who are sensitive to sunlight. As with other topical acne medications, less frequent application; use of moisturizers; and avoidance of alcohol-containing products, other acne products, and abrasive cleaners may minimize adverse effects. Avoiding mucous membranes and the corners of the eyes, nose, and mouth when applying the product is thought to decrease the likelihood of irritation. Adapalene/benzoyl peroxide can cause bleaching if it is transferred to clothing or bedding.<sup>1</sup>

# EFFECTIVENESS

In patients with mild to moderate noninflammatory acne, the combination product may produce greater lesion reduction than either medication alone. However, three randomized controlled trials (two of which were sponsored by the drug manufacturer) showed only a 10 to 15 percent improvement.<sup>3-5</sup> A sponsored study with 1,668 patients found a somewhat greater reduction in the number of lesions among participants who used the ▶ combination product compared with those who used either medication alone (62 percent versus 50 to 55 percent).<sup>3</sup> A second study, not sponsored by the manufacturer, showed that the combination of adapalene and benzoyl peroxide 2.5% was somewhat less effective than the combination of clindamycin and benzoyl peroxide 5%.<sup>6</sup> Reductions in lesions may be noted in as little as one week<sup>3-5</sup> and may persist over at least 12 months of use.<sup>2-4</sup>

### PRICE

A 45-g tube of adapalene/benzoyl peroxide costs about \$237; no generic formulation is available. Comparative amounts of prescription products clindamycin/benzoyl peroxide (Benzaclin), erythromycin/benzoyl peroxide (Benzamycin), and adapalene (Differin) cost about \$204, \$230, and \$280, respectively, for brand name formulations, and \$150, \$101, and \$160, respectively, for generic formulations. Nonprescription benzoyl peroxide products cost \$10 to \$15 per month.

### SIMPLICITY

A pea-sized portion of the gel should be applied once daily, after washing, to each cheek, the forehead, and the chin. No other topical acne products should be used at the same time. Application in the morning can help avoid bleaching of bedding.<sup>1</sup>

#### **Bottom Line**

Adapalene/benzoyl peroxide is as effective as other combination products for the treatment of acne. Once-daily application is an advantage in terms of simplicity and adherence to therapy, but the cost is much higher than that of the individual components sold

separately; this may create a barrier to adherence. Patients should start with less expensive options and use more expensive combinations only if the initial regimens do not work or if adherence is an issue.

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the U.S. Air Force Medical Department or the U.S. Air Force at large.

Address correspondence to Heather Pickett, DO, FAAFP, at heather.pickett@nellis.af.mil. Reprints are not available from the authors.

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#### REFERENCES

- Epiduo [package insert]. Baie d'Urfé, Quebec: Galderma Production Canada, Inc.; 2009. http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=41207. Accessed May 10, 2011.
- Pariser DM, Westmoreland P, Morris A, Gold MH, Liu Y, Graeber M. Long-term safety and efficacy of a unique fixed-dose combination gel of adapalene 0.1% and benzoyl peroxide 2.5% for the treatment of acne vulgaris. J Drugs Dermatol. 2007;6(9):899-905.
- Gold LS, Tan J, Cruz-Santana A, et al.; Adapalene-BPO Study Group. A North American study of adapalenebenzoyl peroxide combination gel in the treatment of acne. Cutis. 2009;84(2):110-116.
- Thiboutot DM, Weiss J, Bucko A, et al.; Adapalene-BPO Study Group. Adapalene-benzoyl peroxide, a fixed-dose combination for the treatment of acne vulgaris: results of a multicenter, randomized double-blind, controlled study. J Am Acad Dermatol. 2007;57(5):791-799.
- 5. Loesche C, Pernin C, Poncet M. Adapalene 0.1% and benzoyl peroxide 2.5% as a fixed-dose combination gel is as well tolerated as the individual components alone in terms of cumulative irritancy. *Eur J Dermatol.* 2008;18(5):524-526.
- Zouboulis CC, Fischer TC, Wohlrab J, Barnard J, Alió AB. Study of the efficacy, tolerability, and safety of 2 fixed-dose combination gels in the management of acne vulgaris. *Cutis.* 2009;84(4):223-229.
- 7. Drugstore.com. http://www.drugstore.com. Accessed May 11, 2011. ■