HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use EPIDUO Gel safely and effectively. See full prescribing information for EPIDUO Gel.

EPIDUO™ (adapalene and benzoyl peroxide) Gel 0.1%/2.5%
For topical use only
Initial U.S. Approval: 2008

----------INDICATIONS AND USAGE----------
EPIDUO Gel is a combination of adapalene, a retinoid, and benzoyl peroxide, and is indicated for the topical treatment of acne vulgaris in patients 12 years of age and older.(1)

----------DOSAGE AND ADMINISTRATION---------
Apply a thin film of EPIDUO Gel to affected areas of the face and/or trunk once daily after washing. Use a pea-sized amount for each area of the face (e.g. forehead, chin, each cheek). Avoid the eyes, lips and mucous membranes. (2)

EPIDUO Gel is not for oral, ophthalmic, or intravaginal use. (2)

----------DOSAGE FORMS AND STRENGTHS----------
Each gram of EPIDUO Gel contains 1 mg (0.1%) adapalene and 25 mg (2.5%) benzoyl peroxide in an aqueous based gel. (3)

----------CONTRAINDICATIONS----------
None. (4)

----------WARNINGS AND PRECAUTIONS----------
Ultraviolet Light and Environmental Exposure: Avoid exposure to sunlight and sunlamps. Wear sunscreen when sun exposure cannot be avoided. (5.1)
Erythema, scaling, dryness, and stinging/burning may occur with use of EPIDUO Gel. (5.2)

----------ADVERSE REACTIONS----------
Observed local adverse reactions in patients treated with EPIDUO Gel were erythema, scaling, dryness, stinging, and burning. Other most commonly reported adverse events (≥ 1% in patients treated with EPIDUO Gel were dry skin, contact dermatitis, application site burning, application site irritation, skin irritation.(6)

To report SUSPECTED ADVERSE REACTIONS, contact Galderma Laboratories L.P. at 1-866-735-4137 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

----------DRUG INTERACTIONS----------
Exercise caution in using preparations containing sulfur, resorcinol, or salicylic acid in combination with EPIDUO Gel. (7.1)

Concomitant use of topical products with a strong drying effect can increase irritation. Use with caution. (7.1)

See 17 for PATIENT COUNSELING INFORMATION

Revised: 12/2008

FULL PRESCRIBING INFORMATION: CONTENTS*

***Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

EPIDUO Gel is indicated for the topical treatment of acne vulgaris in patients 12 years of age and older.

2 DOSAGE AND ADMINISTRATION

Apply a thin film of EPIDUO Gel to affected areas of the face and/or trunk once daily after washing. Use a pea-sized amount for each area of the face (e.g. forehead, chin, each cheek). Avoid the eyes, lips and mucous membranes.

EPIDUO Gel is not for oral, ophthalmic, or intravaginal use.

3 DOSAGE FORMS AND STRENGTHS

Each gram of EPIDUO Gel contains 1 mg (0.1%) adapalene and 25 mg (2.5%) benzoyl peroxide in an aqueous based gel.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Ultraviolet Light and Environmental Exposure

Exposure to sunlight, including sunlamps, should be minimized during the use of EPIDUO Gel. Patients with high levels of sun exposure and those with inherent sensitivity to sun should exercise particular caution. Use of sunscreen products and protective apparel, (e.g., hat) are recommended when exposure cannot be avoided. Weather extremes, such as wind or cold, may be irritating to patients under treatment with EPIDUO Gel.

5.2 Local Cutaneous Reactions

Erythema, scaling, dryness, and stinging/burning may be experienced with use of EPIDUO GEL. These are most likely to occur during the first four weeks of treatment, are mostly mild to moderate in intensity, and usually lessen with continued use of the medication. Depending upon the severity of these side effects, patients should be instructed to use a moisturizer, reduce the frequency of the application of EPIDUO GEL, or discontinue use.

The product should not be applied to cuts, abrasions, eczematous or sunburned skin. As with other retinoids, use of “waxing” as a depilatory method should be avoided on skin treated with EPIDUO Gel.

Avoid concomitant use of other potentially irritating topical products (medicated or abrasive soaps and cleansers, soaps and cosmetics that have strong skin-drying effect and

products with high concentrations of alcohol, astringents, spices, or limes).

6 ADVERSE REACTIONS

6.1 Clinical Studies Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

During clinical trials, 1401 subjects were exposed to EPIDUO Gel. A total of 1036 subjects with acne vulgaris, 12 years and older, were treated once daily for 12 weeks to 12 months. Related adverse events reported within 12 weeks of treatment and in at least 1% of subjects treated with EPIDUO Gel and those reported in subjects treated with the vehicle gel are presented in Table 1:

Table 1 Drug Related Adverse Events Reported in Clinical Trials by At Least 1% of Patients Treated For 12 Weeks

System Organ Class/Preferred Term	Epiduo Gel N = 564	Vehicle Gel N = 489
Subjects with AE(s)	14%	4%
Dry skin	7%	2%
Contact dermatitis	3%	<1%
Application site burning	2%	<1%
Application site irritation	1%	<1%
Skin irritation	1%	0%

Local tolerability evaluations, presented in Table 2, were conducted at each study visit in clinical trials by assessment of erythema, scaling, dryness, burning, and stinging.

Table 2 Incidence of Local Cutaneous Irritation in Controlled Clinical Studies (N=553) Treatment Emergent Signs and Symptoms

	Maximum Severity During Treatment			End of Treatment Severity (12 Weeks)		
	Mild	Moderate	Severe	Mild	Moderate	Severe
Erythema	27%	13%	1%	8%	2%	1%
Scaling	35%	11%	1%	9%	1%	<1%
Dryness	41%	13%	1%	10%	2%	<1%
Stinging/burning	41%	15%	3%	7%	2%	1%

Analysis over the 12-week period showed that local tolerability scores for erythema, scaling, dryness, and stinging/burning peaked at Week 1 of therapy and decreased thereafter.

7 DRUG INTERACTIONS

Concomitant topical acne therapy should be used with caution because a possible cumulative irritancy effect may occur, especially with the use of peeling, desquamating, or abrasive agents.

No formal drug-drug interaction studies were conducted with EPIDUO GEL.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy category C. There are no well-controlled trials in pregnant women treated with EPIDUO Gel. Animal reproduction studies have not been conducted with the combination gel or benzoyl peroxide. Furthermore, such studies are not always predictive of human response; therefore, EPIDUO Gel should be used during pregnancy only if the potential benefit justifies the risk to the fetus.

No teratogenic effects were observed in rats treated with oral doses of 0.15 to 5.0 mg adapalene/kg/day, up to 25 times (mg/m^2/day) the maximum recommended human dose (MRHD) of 2 grams of EPIDUO Gel. However, teratogenic changes were observed in rats and rabbits when treated with oral doses of ≥ 25 mg adapalene/kg/day representing 123 and 246 times MRHD, respectively. Findings included cleft palate, microphthalmia, encephalocele and skeletal abnormalities in rats; and umbilical hernia, exophthalmos and kidney and skeletal abnormalities in rabbits.

Dermal teratology studies conducted in rats and rabbits at doses of 0.6-6.0 mg adapalene/kg/day [25-59 times (mg/m^2) the MRHD] exhibited no fetotoxicity and only minimal increases in supernumerary ribs in both species and delayed ossification in rabbits.

8.3 Nursing Mothers

It is not known whether adapalene or benzoyl peroxide is excreted in human milk following use of EPIDUO Gel. Because many drugs are excreted in human milk, caution should be exercised when EPIDUO Gel is administered to a nursing woman.

8.4 Pediatric Use

Safety and effectiveness of EPIDUO Gel in pediatric patients under the age of 12 have not been established.

8.5 Geriatric Use

Clinical studies of EPIDUO Gel did not include sufficient numbers of subjects

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