

10 New Substances Added to Patch Test Tray

BY DAMIAN McNAMARA

SINT MAARTEN, NETHERLANDS ANTILLES — The North American Contact Dermatitis Group removed 5 allergens from its 2007-2008 standard North American patch test tray and replaced them with 10 new substances to test for in 2009-2010.

The group removed imidazolidinyl urea, 2%; dimethylol dimethyl hydan-

toin, 1%; diazolidinyl urea, 1%; bisphenol F epoxy resin, 0.025%; and triamcinolone acetonide, 1%, Dr. Kathryn A. Zug reported at the Caribbean Dermatology Symposium.

The 10 allergens added are:

► Dimethylaminopropylamine (DMA-PA), 1%. “You may be hearing more about this allergen. DMAPA is found in body wash, shampoos, and detergents and can cause face, neck, and eyelid der-

matitis,” said Dr. Zug, a dermatologist at Dartmouth-Hitchcock Medical Center in Lebanon, N.H. She said she had no relevant disclosures to report.

► D-Limonene, 3%.

► Shellac, 20%. “This has been described previously for eyelid dermatitis from mascara,” Dr. Zug said.

► Majantole, 5%. She described this as “a new, important fragrance allergen” from a synthetic source.

► Oleamidopropyl dimethylamine, 0.1%.
► Carvone, 5%.

► *Lavandula angustifolia* (lavender) oil, 2%.

► Decyl glucoside, 5%. “This plant-derived surfactant is included in more ‘natural’ products,” Dr. Zug said. “It’s an uncommon allergen, but the North American Contact Dermatitis Group is now monitoring it.”

► *Jasminum officinale* oil (*Jasminum grandiflorum*), 2%.

► *Mentha piperita* (peppermint) oil, 2%.

An allergen that sounds new, but is not, is *Myroxylon pereirae* resin. “This is one of our familiar allergens, balsam of Peru,” Dr. Zug said. “What has happened? We’ve taken a simple name—balsam of Peru—and made it more complicated by adopting the botanical name.”

She added, “Hopefully you will all be familiar with it when you see it on a standard tray.”

In discussing the results of a study of allergies to fragrances, Dr. Zug noted that a Lyral sensitization frequency of 2.3% was reported in a comprehensive study of 26 fragrances patch tested in a total of 21,325 patients in Germany (Contact Derm. 2007;57:1-10). Lyral is a component of fragrances and detergents included in the Fragrance Mix II patch test kit.

“Europeans are very interested in figuring out the frequency of [fragrance] allergies,” Dr. Zug said.

Other fragrances not on the standard series that were associated with stronger or more frequent patch test results in the study included tree moss (2.4%), oak moss (2.0%), hydroxycitronellal (1.3%), isoeugenol (1.1%), and cinnamic aldehyde (1.0%).

Because of studies like this, Dr. Zug said, “we may be able to better hone down which fragrance components our patients are allergic to, rather than just telling them they have a fragrance allergy.” ■

EPIDUO™

(adapalene and benzoyl peroxide) Gel 0.1% / 2.5%

For Topical Use Only

Not For Ophthalmic, Oral, or Intravaginal Use.

BRIEF SUMMARY

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.

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

Ultraviolet Light and Environmental Exposure: Avoid exposure to sunlight and sunlamps. Wear sunscreen when sun exposure cannot be avoided.

Erythema, scaling, dryness, and stinging/burning may occur with use of EPIDUO Gel.

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 ($\geq 1\%$) in patients treated with EPIDUO Gel were dry skin, contact dermatitis, application site burning, application site irritation, skin irritation.

DRUG INTERACTIONS

Exercise caution in using preparations containing sulfur, resorcinol, or salicylic acid, medicated or abrasive soaps and cleansers and products with high concentrations of alcohol or astringents in combination with EPIDUO Gel. Concomitant use of topical products with a strong drying effect can increase irritation. Use with caution.

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/m²/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, encephalocoele 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/m²) the MRHD] exhibited no fetotoxicity and only minimal increases in supernumerary ribs in both species and delayed ossification in rabbits.

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.

Pediatric Use

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

Geriatric Use

Clinical studies of EPIDUO Gel did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

Carcinogenesis, Mutagenesis, Impairment of Fertility

No carcinogenicity, photocarcinogenicity, genotoxicity, or fertility studies were conducted with EPIDUO Gel.

Carcinogenicity studies with adapalene have been conducted in mice at topical doses of 0.4, 1.3, and 4.0 mg/kg/day (1.2, 3.9, and 12 mg/m²/day), and in rats

Rx only

at oral doses of 0.15, 0.5, and 1.5 mg/kg/day (0.9, 3.0, and 9.0 mg/m²/day). In terms of body surface area, the highest dose levels are 9.8 (mice) and 7.4 times (rats) the MRHD of 2 grams of EPIDUO Gel. In the rat study, an increased incidence of benign and malignant pheochromocytomas in the adrenal medulla of male rats was observed.

No significant increase in tumor formation was observed in rodents topically treated with 15-25% benzoyl peroxide carbopol gel (6-10 times the concentration of benzoyl peroxide in EPIDUO Gel) for two years. Rats received maximum daily applications of 138 (males) and 205 (females) mg benzoyl peroxide/kg. In terms of body surface area, these levels are 27-40 times the MRHD. Similar results were obtained in mice topically treated with 25% benzoyl peroxide carbopol gel for 56 weeks followed by intermittent treatment with 15% benzoyl peroxide carbopol gel for rest of the 2 years study period, and in mice topically treated with 5% benzoyl peroxide carbopol gel for two years.

The role of benzoyl peroxide as a tumor promoter has been well established in several animal species. However, the significance of this finding in humans is unknown.

In a photocarcinogenicity study conducted with 5% benzoyl peroxide carbopol gel, no increase in UV-induced tumor formation was observed in hairless mice topically treated for 40 weeks.

No photocarcinogenicity studies were conducted with adapalene. However, animal studies have shown an increased tumorigenic risk with the use of pharmacologically similar drugs (e.g., retinoids) when exposed to UV irradiation in the laboratory or sunlight. Although the significance of these findings to humans is not clear, patients should be advised to avoid or minimize exposure to either sunlight or artificial irradiation sources.

Adapalene did not exhibit mutagenic or genotoxic effects *in vitro* (Ames test, Chinese hamster ovary cell assay, mouse lymphoma TK assay) or *in vivo* (mouse micronucleus test).

Bacterial mutagenicity assays (Ames test) with benzoyl peroxide has provided mixed results, mutagenic potential was observed in a few but not in a majority of investigations. Benzoyl peroxide has been shown to produce single-strand DNA breaks in human bronchial epithelial and mouse epidermal cells, it has caused DNA-protein cross-links in the human cells, and has also induced a dose-dependent increase in sister chromatid exchanges in Chinese hamster ovary cells. In rat oral studies, 20 mg adapalene/kg/day (120 mg/m²/day; 98 times the MRHD based on mg/m²/day comparison) did not affect the reproductive performance and fertility of F₀ males and females, or growth, development and reproductive function of F₁ offspring.

No fertility studies were conducted with benzoyl peroxide.

PATIENT COUNSELING INFORMATION

— Advise patients to cleanse the area to be treated with a mild or soapless cleanser; pat dry. Apply EPIDUO Gel as a thin layer, avoiding the eyes, lips and mucous membranes.

— Advise patients not to use more than the recommended amount and not to apply more than once daily as this will not produce faster results, but may increase irritation.

— EPIDUO Gel may cause irritation such as erythema, scaling, dryness, stinging or burning.

— Advise patients to minimize exposure to sunlight, including sunlamps. Recommend the use of sunscreen products and protective apparel, (e.g., hat) when exposure cannot be avoided.

— EPIDUO Gel may bleach hair and colored fabric.

Marketed by:

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Manufactured by:

Galderma Production Canada Inc.

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Made in Canada.

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References: 1. Data on file. Galderma Laboratories, L.P. Phase 3 data. 2. 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.

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Source: Dr. Zug