

Study Finds Teen Immunizations Are Increasing

BY LORINDA BULLOCK
Associate Editor

Twenty-five percent of girls aged 13-17 had received at least one dose of the human papillomavirus vaccine, according to results from the second National Immunization Survey (NIS-Teen).

"This was very good for a first-year measurement for a new vaccine," Dr. Lance Rodewald, director of the division of immunization services at the Centers

for Disease Control and Prevention's National Center for Immunization and Respiratory Diseases, said during a briefing.

But while coverage rates for routinely recommended vaccines among U.S. teens are increasing, the number of adolescents fully immunized against diseases such as pertussis and meningitis is not yet at the 90% goal set by a government-led initiative.

The Healthy People 2010 initiative set goals for youths 13-15 years of age with three doses of hepatitis B vaccine, two doses

of measles, mumps, and rubella vaccine, one dose of tetanus-diphtheria or tetanus, diphtheria, and acellular pertussis vaccine, and one dose of varicella vaccine for those who had not had chickenpox.

Healthy People 2010 did not include a goal for the HPV vaccine because it is still so new. The quadrivalent human papillomavirus (HPV4) is complete at three doses. Dr. Rodewald said an estimated 2.5 million 13- to 17-year-old girls have received the vaccine to date.

Dr. Rodewald presented results from the second NIS-Teen, which he described as a national "report card on the implementation of the vaccines." During the last quarter of 2007, parents of children between the ages of 13 and 17 were interviewed about their child's vaccination history. The survey included 3,000 adolescents as participants, split almost evenly between boys and girls.

The 13- to 17-year-old age group was selected because, according to Dr. Rodewald, the vaccines are targeted to 11- and 12-year-olds.

For HPV in particular, Dr. Rodewald said, 11- and 12-year-olds have a "very strong and robust" immune response that adds further protection that will last through the later, riskier periods. He also said the HPV vaccine can provide up to 6 years of protection.

"You always want to vaccinate before the period where there could be disease, and so it's very important to vaccinate before the onset of sexual activity, and 11- and 12-year-olds, of course, is before the onset of sexual activity, so this provides protection in anticipation of exposure later on in life," he said.

The numbers for the Tdap were also particularly encouraging. Vaccinations increased from 10.8% in 2006 to 30.4% in 2007, very good for a new vaccine.

Compared with the 2006 estimates, Dr. Rodewald said, other areas of improvement included the following:

- Vaccination coverage levels for three or more doses of hepatitis B and two or more doses of MMR vaccine were more than 80%, very close to the Healthy People 2010 goal.

- The one dose coverage of varicella vaccine, which protects against chickenpox, was 75.7%, but coverage with the new recommended two doses was low at 18.8% among preteens and teens without previous history of the disease.

- Of the adolescents surveyed, 32.4% received the meningococcal conjugate vaccination, compared with 11.7% in 2006.

Dr. Rodewald thanked and congratulated parents, doctors, and nurses for actively getting young children and adolescents vaccinated to improve the survey numbers, but he also encouraged them to continue to make sure these patients get the proper immunizations.

"The bottom line for the report card is we've got a great start for teens, but we need to keep this positive momentum going in order to provide the protection from infectious diseases that all teens should have."

DIFFERIN® (adapalene) Cream, 0.1%

Rx Only

BRIEF SUMMARY

For topical use only. Not for ophthalmic, oral, or intravaginal use.

INDICATIONS AND USAGE: DIFFERIN® Cream is indicated for the topical treatment of acne vulgaris.

CONTRAINDICATIONS: DIFFERIN® Cream should not be administered to individuals who are hypersensitive to adapalene or any of the components in the cream vehicle.

PRECAUTIONS: General: If a reaction suggesting sensitivity or chemical irritation occurs, use of the medication should be discontinued. Exposure to sunlight, including sunlamps, should be minimized during use of adapalene. Patients who normally experience high levels of sun exposure, and those with inherent sensitivity to sun, should be warned to exercise caution. Use of sunscreen products and protective clothing over treated areas is recommended when exposure cannot be avoided. Weather extremes, such as wind or cold, also may be irritating to patients under treatment with adapalene.

Avoid contact with the eyes, lips, angles of the nose, and mucous membranes. 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 adapalene.

Information for Patients: Patients using DIFFERIN® Cream should receive the following information and instructions:

1. This medication is to be used only as directed by the physician.
2. It is for external use only.
3. Avoid contact with the eyes, lips, angles of the nose, and mucous membranes.
4. Cleanse area with a mild or soapless cleanser before applying this medication.
5. Moisturizers may be used if necessary; however, products containing alpha hydroxy or glycolic acids should be avoided.
6. Exposure of the eye to this medication may result in reactions such as swelling, conjunctivitis, and eye irritation.
7. This medication should not be applied to cuts, abrasions, eczematous or sunburned skin.
8. Wax epilation should not be performed on treated skin due to the potential for skin erosions.
9. During the early weeks of therapy, an apparent exacerbation of acne may occur. This is due to the action of this medication on previously unseen lesions and should not be considered a reason to discontinue therapy. Overall clinical benefit may be noticed after two weeks of therapy, but at least eight weeks are required to obtain consistent beneficial effects.

Drug Interactions: As DIFFERIN® Cream has the potential to produce local irritation in some patients, concomitant use of other potentially irritating topical products (medicated or abrasive soaps and cleansers, soaps and cosmetics that have a strong drying effect, and products with high concentrations of alcohol, astringents, spices or lime rind) should be approached with caution. Particular caution should be exercised in using preparations containing sulfur, resorcinol, or salicylic acid in combination with DIFFERIN® Cream. If these preparations have been used, it is advisable not to start therapy with DIFFERIN® Cream until the effects of such preparations in the skin have subsided.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Carcinogenicity studies with adapalene have been conducted in mice at topical doses of 0.4, 1.3, and 4.0 mg/kg/day, and in rats at oral doses of 0.15, 0.5, and 1.5 mg/kg/day. These doses are up to 8 times (mice) and 6 times (rats) in terms of mg/m²/day the maximum potential exposure at the recommended topical human dose (MRHD), assumed to be 2.5 grams DIFFERIN® Cream, which is approximately 1.5 mg/m² adapalene. In the oral study, increased incidence of benign and malignant pheochromocytomas in the adrenal medullas of male rats was observed.

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

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

Reproductive function and fertility studies were conducted in rats administered oral doses of adapalene in amounts up to 20 mg/kg/day (up to 80 times the MRHD based on mg/m² comparisons). No effects of adapalene were found on the reproductive performance or fertility of the F₂ males or females. There were also no detectable effects on the growth, development and subsequent reproductive function of the F₂ generation.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when DIFFERIN® Cream is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in pediatric patients below the age of 12 have not been established.

ADVERSE REACTIONS: In controlled clinical trials, local cutaneous irritation was monitored in 285 acne patients who used DIFFERIN® Cream once daily for 12 weeks. The frequency and severity of erythema, scaling, dryness, pruritus and burning were assessed during these studies. The incidence of local cutaneous irritation with DIFFERIN® Cream from the controlled clinical studies is provided in the following table:

	None	Mild	Moderate	Severe
Erythema	52% (148)	38% (108)	10% (28)	<1% (1)
Scaling	58% (166)	35% (100)	6% (18)	<1% (1)
Dryness	48% (136)	42% (121)	9% (26)	<1% (2)
Pruritus (persistent)	74% (211)	21% (61)	4% (12)	<1% (1)
Burning/Stinging (persistent)	71% (202)	24% (69)	4% (12)	<1% (2)

Other reported local cutaneous adverse events in patients who used DIFFERIN® Cream once daily included: sunburn (2%), skin discomfort-burning and stinging (1%) and skin irritation (1%). Events occurring in less than 1% of patients treated with DIFFERIN® Cream included: acne flare, dermatitis and contact dermatitis, eyelid edema, conjunctivitis, erythema, pruritus, skin discoloration, rash, and eczema.

OVERDOSAGE: DIFFERIN® Cream is intended for cutaneous use only. If the medication is applied excessively, no more rapid or better results will be obtained and marked redness, scaling, or skin discomfort may occur. The acute oral toxicity of DIFFERIN® Cream in mice and rats is greater than 10 mL/kg. Chronic ingestion of the drug may lead to the same side effects as those associated with excessive oral intake of Vitamin A.

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of 0.6, 2.0, and 6.0 mg/kg/day, up to 150 times the maximal daily human topical dose exhibited no fetotoxicity and only minimal increases in supernumerary ribs in rats. There are no adequate and well-controlled studies in pregnant women. Adapalene should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when DIFFERIN® Gel is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in pediatric patients below the age of 12 have not been established.

ADVERSE REACTIONS: Some adverse effects such as erythema, scaling, dryness, pruritus, and burning will occur in 10-40% of patients. Pruritus or burning immediately after application also occurs in approximately 20% of patients. The following additional adverse experiences were reported in approximately 1% or less of patients: skin irritation, burning/stinging, erythema, sunburn, and acne flares. These are most commonly seen during the first month of therapy and decrease in frequency and severity thereafter. All adverse effects with use of DIFFERIN® Gel during clinical trials were reversible upon discontinuation of therapy.

OVERDOSAGE: DIFFERIN® Gel is intended for cutaneous use only. If the medication is applied excessively, no more rapid or better results will be obtained and marked redness, peeling, or discomfort may occur. The acute oral toxicity of DIFFERIN® Gel in mice and rats is greater than 10 mL/kg. Chronic ingestion of the drug may lead to the same side effects as those associated with excessive oral intake of Vitamin A.

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DIFFERIN® (adapalene gel) Gel, 0.1%

Rx Only

BRIEF SUMMARY

INDICATIONS AND USAGE: DIFFERIN® Gel is indicated for the topical treatment of acne vulgaris.

CONTRAINDICATIONS: DIFFERIN® Gel should not be administered to individuals who are hypersensitive to adapalene or any of the components in the vehicle gel.

WARNINGS: Use of DIFFERIN® Gel should be discontinued if hypersensitivity to any of the ingredients is noted. Patients with sunburn should be advised not to use the product until fully recovered.

PRECAUTIONS: General: If a reaction suggesting sensitivity or chemical irritation occurs, use of the medication should be discontinued. Exposure to sunlight, including sunlamps, should be minimized during the use of adapalene. Patients who normally experience high levels of sun exposure, and those with inherent sensitivity to sun, should be warned to exercise caution. Use of sunscreen products and protective clothing over treated areas is recommended when exposure cannot be avoided. Weather extremes, such as wind or cold, also may be irritating to patients under treatment with adapalene.

Avoid contact with the eyes, lips, angles of the nose, and mucous membranes. The product should not be applied to cuts, abrasions, eczematous skin, or sunburned skin.

Certain cutaneous signs and symptoms such as erythema, dryness, scaling, burning, or pruritus may be experienced during treatment. These are most likely to occur during the first two to four weeks and will usually lessen with continued use of the medication. Depending upon the severity of adverse events, patients should be instructed to reduce the frequency of application or discontinue use.

Drug Interactions: As DIFFERIN® Gel has the potential to produce local irritation in some patients, concomitant use of other potentially irritating topical products (medicated or abrasive soaps and cleansers, soaps and cosmetics that have a strong drying effect, and products with high concentrations of alcohol, astringents, spices, or lime) should be approached with caution. Particular caution should be exercised in using preparations containing sulfur, resorcinol, or salicylic acid in combination with DIFFERIN® Gel. If these preparations have been used, it is advisable not to start therapy with DIFFERIN® Gel until the effects of such preparations in the skin have subsided.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Carcinogenicity studies with adapalene have been conducted in mice at topical doses of 0.3, 0.9, and 2.6 mg/kg/day and in rats at oral doses of 0.15, 0.5, and 1.5 mg/kg/day, approximately 4-75 times the maximal daily human topical dose. In the oral study, positive linear trends were observed in the incidence of follicular cell adenomas and carcinomas in the thyroid glands of female rats, and in the incidence of benign and malignant pheochromocytomas in the adrenal medullas of male rats.

No photocarcinogenicity studies were conducted. 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 to sunlight. Although the significance of these studies to human use is not clear, patients should be advised to avoid or minimize exposure to either sunlight or artificial UV irradiation sources.

In a series of *in vivo* and *in vitro* studies, adapalene did not exhibit mutagenic or genotoxic activities.

Pregnancy: Teratogenic effects. Pregnancy Category C. No teratogenic effects were seen in rats at oral doses of adapalene 0.15 to 5.0 mg/kg/day, up to 120 times the maximal daily human topical dose. Cutaneous route teratology studies conducted in rats and rabbits at doses

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