



Pediatric cardiovascular research a priority for NHLBI

The National Heart, Lung and Blood Institute (NHLBI) released in May a comprehensive report on current research on pediatric cardiovascular disease, and outlined the top eight research priorities reflecting scientific opportunities in the field. NHLBI found research needs in areas span-

ning from stem cell biology to the relationship between genetic and environmental factors in the development of heart defects.

Identifying the research needs in pediatric heart diseases is only one responsibility NHLBI takes on as an organization. It also coordinates the

National Asthma Education and Prevention Program that recently released long-awaited updated guidelines for asthma management (see page 92).

The institute offers numerous other services for those with pediatric concerns. Its Web site has several interac-

tive pages to help parents make sure their child is healthy. With activities like "Garfield's Games for Star Sleepers," children can learn the importance of a good night's rest and how much sleep they should be getting. The site also has information on asthma prevention, sleep disorders, healthy weight management and other health concerns affecting children.

In response to the federal government's Healthy People 2010 program, which outlines the steps toward a healthier American public, NHLBI's Web site features a section to promote education in four specific areas: cardiovascular health, asthma, sleep and minority populations. This gateway offers institutional information and resources on these health topics.

Along with the National Recreation and Park Association, NHLBI also supports a national program called Hearts N' Parks that works to educate children and adults on the importance of a healthy diet and daily activity. The community-based initiative aims to help decrease obesity and the risk of coronary heart disease by providing information on positive lifestyle choices as part of the activities at parks and recreational facilities.

— Erin Verkler

For more information on the task force report, other research publications or additional community efforts by NHLBI, visit www.nhlbi.nih.gov. For publication information, call (800) 575-WELL. For questions, call (301) 592-8573.

Correction

Health professional memberships in the Food Allergy & Anaphylaxis Network (FAAN) (Agency ABCs, June AAP News) do not cover the cost of items such as videos and cookbooks. Call FAAN at (800) 929-4040 for the most current membership benefits.



Muscular Dystrophy Association
Jerry Lewis, National Chairman
1-800-572-1717
www.mdaua.org

Elidel® (pimecrolimus) Cream 1%

FOR DERMATOLOGIC USE ONLY
NOT FOR OPHTHALMIC USE

Rx only

BRIEF SUMMARY: Please see package insert for full prescribing information.

INDICATIONS AND USAGE: Elidel® (pimecrolimus) Cream 1% is indicated for short-term and intermittent long-term therapy in the treatment of mild to moderate atopic dermatitis in non-immunocompromised patients 2 years of age and older, in whom the use of alternative, conventional therapies is deemed inadvisable because of potential risks, or in the treatment of patients who are not adequately responsive to or intolerant of alternative, conventional therapies (see DOSAGE AND ADMINISTRATION in the full prescribing information).

CONTRAINDICATIONS: Elidel® (pimecrolimus) Cream 1% is contraindicated in individuals with a history of hypersensitivity to pimecrolimus or any of the components of the cream.

PRECAUTIONS: General: Elidel® (pimecrolimus) Cream 1% should not be applied to areas of active cutaneous viral infections. Studies have not evaluated the safety and efficacy of Elidel Cream in the treatment of clinically infected atopic dermatitis. Before commencing treatment with Elidel Cream, clinical infections at treatment sites should be cleared. While patients with atopic dermatitis are predisposed to superficial skin infections including eczema herpeticum (Kaposi's varicelliform eruption), treatment with Elidel Cream may be associated with an increased risk of varicella zoster virus infection (chicken pox or shingles), herpes simplex virus infection, or eczema herpeticum. In the presence of these skin infections, the balance of risks and benefits associated with Elidel Cream use should be evaluated. In clinical studies, 14 cases of lymphadenopathy (0.9%) were reported while using Elidel Cream. These cases of lymphadenopathy were usually related to infections and noted to resolve upon appropriate antibiotic therapy. Of these 14 cases, the majority had either a clear etiology or were known to resolve. Patients who receive Elidel Cream and who develop lymphadenopathy should have the etiology of their lymphadenopathy investigated. In the absence of a clear etiology for the lymphadenopathy, or in the presence of acute infectious mononucleosis, discontinuation of Elidel Cream should be considered. Patients who develop lymphadenopathy should be monitored to ensure that the lymphadenopathy resolves. In clinical studies, 15 cases of skin papillomas or warts (1%) were observed in patients using Elidel Cream. The youngest patient was age 2 and the oldest was age 12. In cases where there is worsening of skin papillomas or they do not respond to conventional therapy, discontinuation of Elidel Cream should be considered until complete resolution of the warts is achieved. The enhancement of ultraviolet carcinogenicity is not necessarily dependent on phototoxic mechanisms. Despite the absence of observed phototoxicity in humans (see ADVERSE REACTIONS), Elidel Cream shortened the time to skin tumor formation in an animal photo-carcinogenicity study (see Carcinogenesis, Mutagenesis, Impairment of Fertility). Therefore, it is prudent for patients to minimize or avoid natural or artificial sunlight exposure. The use of Elidel Cream in patients with Netherton's Syndrome is not recommended due to the potential for increased systemic absorption of pimecrolimus. There are no data to support use of Elidel in immunocompromised patients. The use of Elidel Cream may cause local symptoms such as skin burning. Localized symptoms are most common during the first few days of Elidel Cream application and typically improve as the lesions of atopic dermatitis resolve. Most application site reactions lasted no more than 5 days, were mild to moderate in severity, and started within 1-5 days of treatment. (See ADVERSE REACTIONS.)

Information for Patients: Patients using Elidel should receive the following information and instructions:

- Patients should use Elidel Cream as directed by the physician. Elidel Cream is for external use on the skin only. As with any topical medication, patients or caregivers should wash hands after application if hands are not an area for treatment.
- Patients should minimize or avoid exposure to natural or artificial sunlight (tanning beds or UVAB treatment) while using Elidel Cream.
- Patients should not use this medication for any disorder other than that for which it was prescribed.
- Patients should report any signs or symptoms of adverse reactions to their physician.
- Therapy should be discontinued after signs and symptoms of atopic dermatitis have resolved. Treatment with Elidel should be resumed at the first signs or symptoms of recurrence.
- Use of Elidel may cause reactions at the site of application such as a mild to moderate feeling of warmth and/or sensation of burning. Patients should see a physician if an application site reaction is severe or persists for more than 1 week.
- The patient should contact the physician if no improvement in the atopic dermatitis is seen following 6 weeks of treatment, or if at any time the condition worsens.

Drug Interactions: Potential interactions between Elidel and other drugs, including immunizations, have not been systematically evaluated. Due to the very low blood levels of pimecrolimus detected in some patients after topical application, systemic drug interactions are not expected, but cannot be ruled out. The concomitant administration of known CYP3A family of inhibitors in patients with widespread and/or erythrodermic disease should be done with caution. Some examples of such drugs are erythromycin, itraconazole, ketoconazole, fluconazole, calcium channel blockers and cimetidine.

Carcinogenesis, Mutagenesis, Impairment of Fertility: A battery of *in vitro* genotoxicity tests, including Ames assay, mouse lymphoma L5178Y assay, and chromosome aberration test in V79 Chinese hamster cells and an *in vivo* mouse micronucleus test revealed no evidence for a mutagenic or clastogenic potential for the drug. No effect on fertility in female rats was noted at 10 mg/kg/day (12X MRHD based on AUC comparisons). No effect on fertility in male rats was noted at 45 mg/kg/day (23X MRHD based on AUC comparisons), which was the highest dose tested in this study.

Pregnancy: Teratogenic Effects: Pregnancy Category C: There are no adequate and well-controlled studies of topically administered pimecrolimus in pregnant women. The experience with Elidel Cream when used by pregnant women is too limited to permit assessment of the safety of its use during pregnancy. Pimecrolimus was transferred across the placenta in oral rat and rabbit embryofetal developmental studies. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used only if clearly needed during pregnancy.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from pimecrolimus, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: Elidel Cream may be used in pediatric patients 2 years of age and older. Three Phase 3 pediatric studies were conducted involving 1114 patients 2-17 years of age. Two studies were 6-week randomized vehicle-controlled studies with a 20-week open-label phase and one was a vehicle-controlled long-term (up to 1 year) safety study with the option for sequential topical corticosteroid use. Of these patients 542 (49%) were 2-6 years of age. In the short-term studies, 11% of Elidel patients did not complete these studies and 1.5% of Elidel patients discontinued due to adverse events. In the one-year study, 32% of Elidel patients did not complete this study and 3% of Elidel patients discontinued due to adverse events. Most discontinuations were due to unsatisfactory therapeutic effect. The most common local adverse event in the short-term studies of Elidel Cream in pediatric patients ages 2-17 was application site burning (10% vs. 13% vehicle); the incidence in the long-term study was 9% Elidel vs. 7% vehicle (see ADVERSE REACTIONS). Adverse events that were more frequent (>5%) in patients treated with Elidel Cream compared to vehicle were headache (14% vs. 9%) in the short-term trial, nasopharyngitis (26% vs. 21%), influenza (13% vs. 4%), pharyngitis (8% vs. 3%), viral infection (7% vs. 1%), pyrexia (13% vs. 5%), cough (16% vs. 11%), and headache (25% vs. 16%) were increased over vehicle in the 1-year safety study (see ADVERSE REACTIONS). In 843 patients ages 2-17 years treated with Elidel Cream, 9 (0.8%) developed eczema herpeticum (5 on Elidel Cream alone and 4 on Elidel Cream used in sequence with corticosteroids). In 211 patients on vehicle alone, there were no cases of eczema herpeticum. The majority of adverse events were mild to moderate in severity. Elidel Cream is not recommended for use in pediatric patients below the age of 2 years. Two Phase 3 studies were conducted involving 436 infants age 3 months - 23 months. One 6-week randomized vehicle-controlled study with a 20-week open-label phase and one long-term safety study were conducted. In the 6-week study, 11% of Elidel and 48% of vehicle patients did not complete this study; no patient in either group discontinued due to adverse events. Infants on Elidel Cream had an increased incidence of some adverse events compared to vehicle. In the 6-week vehicle-controlled study these adverse events included pyrexia (32% vs. 13% vehicle), URI (24% vs. 14%), nasopharyngitis (15% vs. 8%), gastroenteritis (7% vs. 3%), otitis media (4% vs. 0%), and diarrhea (8% vs. 0%). In the open-label phase of the study, for infants who switched to Elidel Cream from vehicle, the incidence of the above-cited adverse events approached or equaled the incidence of those patients who remained on Elidel Cream. In the 6-month safety data, 16% of Elidel and 35% of vehicle patients discontinued early and 1.5% of Elidel and 0% of vehicle patients discontinued due to adverse events; infants on Elidel Cream had a greater incidence of some adverse events as compared to vehicle. These included pyrexia (30% vs. 20%), URI (21% vs. 17%), cough (15% vs. 9%), hypersensitivity (8% vs. 2%), teething (27% vs. 22%), vomiting (9% vs. 4%), rhinitis (13% vs. 9%), viral rash (4% vs. 0%), rhinorrhea (4% vs. 0%), and wheezing (4% vs. 0%). The effects of Elidel Cream on the developing immune system in infants are unknown.

Geriatric Use: Nine (9) patients ≥ 65 years old received Elidel Cream in Phase 3 studies. Clinical studies of Elidel did not include sufficient numbers of patients aged 65 and over to assess efficacy and safety.

ADVERSE REACTIONS: In human dermal safety studies, Elidel® (pimecrolimus) Cream 1% did not induce contact sensitization, phototoxicity, or photoallergy, nor did it show any cumulative irritation. In a one-year safety study in pediatric patients age 2-17 years old involving sequential use of Elidel Cream and a topical corticosteroid, 43% of Elidel patients and 68% of vehicle patients used corticosteroids during the study. Corticosteroids were used for more than 7 days by 34% of Elidel patients and 54% of vehicle patients. An increased incidence of impetigo, skin infection, superinfection (infected atopic dermatitis), rhinitis, and urticaria were found in the patients that had used Elidel Cream and topical corticosteroid sequentially as compared to Elidel Cream alone. In 3 randomized, double-blind vehicle-controlled pediatric studies and one active-controlled adult study, 843 and 320 patients respectively, were treated with Elidel Cream. In the clinical trials, 48 (4%) of the 111 Elidel patients and 13 (2%) of 408 vehicle-treated patients discontinued therapy due to adverse events. Discontinuations for AEs were primarily due to application site reactions, and cutaneous infections. The most common application site reaction was application site burning, which occurred in 8%-26% of patients treated with Elidel Cream. The following

table depicts the incidence of adverse events pooled across the 2 identically designed 6-week studies with their open label extensions and the 1-year safety study for pediatric patients ages 2-17. Data from the adult active-controlled study is also included in this table. Adverse events are listed regardless of relationship to study drug.

	Treatment Emergent Adverse Events (≥1%) in Elidel® Treatment Groups						
	Pediatric Patients* Vehicle-Controlled (6 weeks)		Pediatric Patients* Open-Label (20 weeks)		Pediatric Patients* Vehicle-Controlled (1 year)		Adult Active Comparator (1 year)
	Elidel® Cream (N=267) N (%)	Vehicle (N=136) N (%)	Elidel® Cream (N=325) N (%)	Elidel® Cream (N=272) N (%)	Vehicle (N=75) N (%)	Elidel® Cream (N=328) N (%)	
At least 1 AE	182 (68.2%)	97 (71.3%)	240 (72.0%)	230 (84.6%)	56 (74.7%)	256 (78.0%)	
Infections and Infestations							
Upper Respiratory							
Tract Infection NOS	38 (14.2%)	18 (13.2%)	65 (19.4%)	13 (4.8%)	6 (8.0%)	14 (4.3%)	
Nasopharyngitis	27 (10.1%)	10 (7.4%)	32 (9.8%)	72 (26.5%)	16 (21.3%)	25 (7.6%)	
Skin Infection NOS	8 (3.0%)	9 (5.1%)	18 (5.4%)	6 (2.2%)	3 (4.0%)	21 (6.4%)	
Influenza	8 (3.0%)	1 (0.7%)	22 (6.6%)	36 (13.2%)	3 (4.0%)	32 (9.8%)	
Ear Infection NOS	6 (2.2%)	2 (1.5%)	19 (5.7%)	9 (3.3%)	1 (1.3%)	2 (0.6%)	
Otitis Media	6 (2.2%)	1 (0.7%)	10 (3.0%)	8 (2.9%)	4 (5.3%)	2 (0.6%)	
Impetigo	5 (1.9%)	3 (2.2%)	12 (3.6%)	11 (4.0%)	4 (5.3%)	8 (2.4%)	
Bacterial Infection	4 (1.5%)	3 (2.2%)	4 (1.2%)	3 (1.1%)	0	6 (1.8%)	
Folliculitis	3 (1.1%)	1 (0.7%)	3 (0.9%)	6 (2.2%)	3 (4.0%)	20 (6.1%)	
Sinusitis	3 (1.1%)	1 (0.7%)	11 (3.3%)	6 (2.2%)	1 (1.3%)	2 (0.6%)	
Pneumonia NOS	3 (1.1%)	1 (0.7%)	5 (1.5%)	0	1 (1.3%)	1 (0.3%)	
Pharyngitis NOS	2 (0.7%)	2 (1.5%)	3 (0.9%)	22 (8.1%)	2 (2.7%)	3 (0.9%)	
Pharyngitis Streptococcal	2 (0.7%)	2 (1.5%)	10 (3.0%)	0	<1%	0	
Molluscum Contagiosum	2 (0.7%)	0	4 (1.2%)	5 (1.8%)	0	0	
Staphylococcal Infection	1 (0.4%)	5 (3.7%)	7 (2.1%)	0	<1%	3 (0.9%)	
Bronchitis NOS	1 (0.4%)	3 (2.2%)	4 (1.2%)	29 (10.7%)	6 (8.0%)	8 (2.4%)	
Herpes Simplex	1 (0.4%)	0	4 (1.2%)	9 (3.3%)	2 (2.7%)	13 (4.0%)	
Tonsillitis NOS	1 (0.4%)	0	3 (0.9%)	17 (6.3%)	0	2 (0.6%)	
Viral Infection NOS	2 (0.7%)	1 (0.7%)	1 (0.3%)	18 (6.6%)	1 (1.3%)	0	
Gastroenteritis NOS	0	3 (2.2%)	2 (0.6%)	20 (7.4%)	2 (2.7%)	6 (1.8%)	
Chickenpox	2 (0.7%)	0	3 (0.9%)	8 (2.9%)	3 (4.0%)	1 (0.3%)	
Skin Papilloma	1 (0.4%)	0	2 (0.6%)	9 (3.3%)	<1%	0	
Tonsillitis Acute NOS	0	0	0	7 (2.6%)	0	0	
Upper Respiratory Tract							
Infection Viral NOS	1 (0.4%)	0	3 (0.9%)	4 (1.5%)	0	1 (0.3%)	
Herpes Simplex Dermatitis	0	0	1 (0.3%)	4 (1.5%)	0	2 (0.6%)	
Bronchitis Acute NOS	0	0	0	4 (1.5%)	0	0	
Eye Infection NOS	0	0	0	3 (1.1%)	<1%	1 (0.3%)	
General Disorders and Administration Site Conditions							
Application Site Burning	28 (10.4%)	17 (12.5%)	5 (1.5%)	23 (8.5%)	5 (6.7%)	85 (25.9%)	
Pyrexia	20 (7.5%)	12 (8.8%)	41 (12.2%)	34 (12.5%)	4 (5.3%)	4 (1.2%)	
Application Site							
Reaction NOS	8 (3.0%)	7 (5.1%)	7 (2.1%)	9 (3.3%)	2 (2.7%)	48 (14.6%)	
Application Site Irritation	8 (3.0%)	8 (5.9%)	3 (0.9%)	1 (0.4%)	3 (4.0%)	21 (6.4%)	
Influenza Like Illness	1 (0.4%)	0	2 (0.6%)	5 (1.8%)	2 (2.7%)	6 (1.8%)	
Application Site Erythema	1 (0.4%)	0	0	6 (2.2%)	0	7 (2.1%)	
Application Site Pruritus	3 (1.1%)	2 (1.5%)	2 (0.6%)	5 (1.8%)	0	18 (5.5%)	
Respiratory, Thoracic and Mediastinal Disorders							
Cough	31 (11.6%)	11 (8.1%)	31 (9.3%)	43 (15.8%)	8 (10.7%)	8 (2.4%)	
Nasal Congestion	7 (2.6%)	2 (1.5%)	6 (1.8%)	4 (1.5%)	1 (1.3%)	2 (0.6%)	
Rhinorrhoea	5 (1.9%)	1 (0.7%)	3 (0.9%)	1 (0.4%)	1 (1.3%)	0	
Asthma Aggravated	4 (1.5%)	3 (2.2%)	13 (3.9%)	3 (1.1%)	0	0	
Sinus Congestion	3 (1.1%)	1 (0.7%)	2 (0.6%)	<1%	<1%	3 (0.9%)	
Rhinitis	1 (0.4%)	0	5 (1.5%)	12 (4.4%)	5 (6.7%)	7 (2.1%)	
Wheezing	1 (0.4%)	1 (0.7%)	4 (1.2%)	2 (0.7%)	<1%	0	
Asthma NOS	2 (0.7%)	1 (0.7%)	11 (3.3%)	10 (3.7%)	2 (2.7%)	8 (2.4%)	
Epistaxis	0	1 (0.7%)	0	9 (3.3%)	1 (1.3%)	1 (0.3%)	
Dyspnea NOS	0	0	0	5 (1.8%)	1 (1.3%)	2 (0.6%)	
Gastrointestinal Disorders							
Abdominal Pain Upper	11 (4.1%)	6 (4.4%)	10 (3.0%)	15 (5.5%)	5 (6.7%)	1 (0.3%)	
Sore Throat	9 (3.4%)	5 (3.7%)	15 (4.4%)	22 (8.1%)	4 (5.3%)	12 (3.7%)	
Vomiting NOS	8 (3.0%)	6 (4.4%)	14 (4.2%)	18 (6.6%)	6 (8.0%)	2 (0.6%)	
Diarrhea NOS	3 (1.1%)	1 (0.7%)	2 (0.6%)	21 (7.7%)	4 (5.3%)	7 (2.1%)	
Nausea	1 (0.4%)	3 (2.2%)	4 (1.2%)	11 (4.0%)	5 (6.7%)	6 (1.8%)	
Abdominal Pain NOS	4 (1.5%)	1 (0.7%)	5 (1.5%)	12 (4.4%)	3 (4.0%)	1 (0.3%)	
Toothache	1 (0.4%)	1 (0.7%)	2 (0.6%)	7 (2.6%)	1 (1.3%)	2 (0.6%)	
Constipation	1 (0.4%)	0	2 (0.6%)	10 (3.7%)	<1%	0	
Loose Stools	0	1 (0.7%)	4 (1.2%)	<1%	<1%	0	
Reproductive System and Breast Disorders							
Dysmenorrhea	3 (1.1%)	0	5 (1.5%)	3 (1.1%)	1 (1.3%)	4 (1.2%)	
Eye Disorders							
Conjunctivitis NEC	2 (0.7%)	1 (0.7%)	7 (2.1%)	6 (2.2%)	3 (4.0%)	10 (3.0%)	
Skin & Subcutaneous Tissue Disorders							
Urticaria	3 (1.1%)	0	1 (0.3%)	1 (0.4%)	<1%	3 (0.9%)	
Acne NOS	0	1 (0.7%)	1 (0.3%)	4 (1.5%)	<1%	6 (1.8%)	
Immune System Disorders							
Hypersensitivity NOS	11 (4.1%)	6 (4.4%)	16 (4.8%)	14 (5.1%)	1 (1.3%)	11 (3.4%)	
Injury and Poisoning							
Accident NOS	3 (1.1%)	1 (0.7%)	1 (0.3%)	<1%	1 (1.3%)	0	
Laceration	2 (0.7%)	1 (0.7%)	5 (1.5%)	<1%	<1%	0	
Musculoskeletal, Connective Tissue and Bone Disorders							
Back Pain	1 (0.4%)	2 (1.5%)	1 (0.3%)	<1%	0	6 (1.8%)	
Arthralgia	0	0	1 (0.3%)	3 (1.1%)	1 (1.3%)	5 (1.5%)	
Ear and Labyrinth Disorders							
Earache	2 (0.7%)	1 (0.7%)	0	8 (2.9%)	2 (2.7%)	0	
Nervous System Disorders							
Headache	37 (13.9%)	12 (8.8%)	38 (11.3%)	69 (25.4%)	12 (16.0%)	23 (7.0%)	

*Ages 2-17 years

DOSAGE AND ADMINISTRATION: Apply a thin layer of Elidel® (pimecrolimus) Cream 1% to the affected skin twice daily and rub in gently and completely. Elidel may be used on all skin surfaces, including the head, neck, and intertriginous areas. Elidel should be used twice daily for as long as signs and symptoms persist. Treatment should be discontinued if resolution of disease occurs. If symptoms persist beyond 6 weeks, the patient should be re-evaluated. The safety of Elidel Cream under occlusion, which may promote systemic exposure, has not been evaluated. Elidel Cream should not be used with occlusive dressings.

Store at 25°C (77°F); excursions permitted to 15°C-30°C (59°F-86°F). Do not freeze.

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