HIGHLIGHTS OF PRESCRIBING INFORMATION

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

ELIDEL® (pimecrolimus) Cream, 1% for topical use
Initial U.S. Approval: 2001

WARNING: LONG-TERM SAFETY OF TOPICAL CALCINEURIN INHIBITORS HAS NOT BEEN ESTABLISHED
See full prescribing information for complete boxed warning.

Although a causal relationship has not been established, rare cases of malignancy (e.g., skin and lymphoma) have been reported in patients treated with topical calcineurin inhibitors, including ELIDEL Cream, 1%. (5.1)
Therefore:

- **Continuous long-term use of topical calcineurin inhibitors, including ELIDEL Cream, 1%, in any age group should be avoided, and application limited to areas of involvement with atopic dermatitis. (2, 5.1)**
- **ELIDEL Cream, 1% is not indicated for use in children less than 2 years of age. (1, 5.1, 8.4)**

----------INDICATIONS AND USAGE----------

ELIDEL Cream, 1% is a calcineurin inhibitor immunosuppressant indicated as *second-line therapy* for the short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised adults and children 2 years of age and older, who have failed to respond adequately to other topical prescription treatments, or when those treatments are not advisable. (1)

----------DOSAGE AND ADMINISTRATION----------

- Apply a thin layer of ELIDEL Cream, 1% to the affected skin twice daily. (2)
- If signs and symptoms persist beyond 6 weeks, patients should be re-examined. (2)
- Continuous long-term use of ELIDEL Cream, 1% should be avoided. (2)
- Avoid use with occlusive dressings. (2)

----------DOSAGE FORMS AND STRENGTHS----------

Cream, 1%. (3)

----------CONTRAINDICATIONS----------

ELIDEL® (pimecrolimus) Cream 1% is contraindicated in individuals with a history of hypersensitivity to pimecrolimus or any of the components of the cream. (4, 6.2)

----------WARNINGS AND PRECAUTIONS----------

- Should not be used in immunocompromised adults and children, including patients on systemic immunosuppressive medications. (5.1)
- Avoid treatment on malignant or pre-malignant skin conditions, as these can present as dermatitis. (5.2)
- Should not be used in patients with Netherton's Syndrome or skin diseases with a potential for increased systemic absorption. (5.2)

----------ADVERSE REACTIONS----------

The most commonly reported adverse reactions (≥1%) were application site burning, headache, nasopharyngitis, cough, influenza, pyrexia and viral infection. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Valeant Pharmaceuticals North America LLC at 1-800-321-4576 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide

Revised: 03/2014

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

WARNING: LONG-TERM SAFETY OF TOPICAL CALCINEURIN INHIBITORS HAS NOT BEEN ESTABLISHED

Although a causal relationship has not been established, rare cases of malignancy (e.g., skin and lymphoma) have been reported in patients treated with topical calcineurin inhibitors, including ELIDEL Cream, 1% [see *Warnings and Precautions (5.1)*].
Therefore:

- **Continuous long-term use of topical calcineurin inhibitors, including ELIDEL Cream, 1%, in any age group should be avoided, and application limited to areas of involvement with atopic dermatitis [see *Dosage and Administration (2), Warnings and Precautions (5.1)*].**
- **ELIDEL Cream, 1% is not indicated for use in children less than 2 years of age [see *Warnings and Precautions (5.1), Use in Specific Populations (8.4)*].**

1 INDICATIONS AND USAGE

ELIDEL® (pimecrolimus) Cream, 1% is indicated as second-line therapy for the short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised adults and children 2 years of age and older, who have failed to respond adequately to other topical prescription treatments, or when those treatments are not advisable.

ELIDEL Cream, 1% is not indicated for use in children less than 2 years of age [see *Warnings and Precautions (5.1), Use in Specific Populations (8.4)*].

2 DOSAGE AND ADMINISTRATION

Apply a thin layer of ELIDEL (pimecrolimus) Cream, 1% to the affected skin twice daily. The patient should stop using ELIDEL Cream, 1% when signs and symptoms (e.g., itch, rash and redness) resolve and should be instructed on what actions to take if symptoms recur.

If signs and symptoms persist beyond 6 weeks, patients should be re-examined by their health care provider to confirm the diagnosis of atopic dermatitis.

Continuous long-term use of ELIDEL Cream, 1% should be avoided, and application should be limited to areas of involvement with atopic dermatitis [see *Warnings and Precautions (5.1)*].

The safety of ELIDEL Cream, 1% under occlusion, which may promote systemic exposure, has not been evaluated. Avoid use of ELIDEL Cream, 1% with occlusive dressings.

3 DOSAGE FORMS AND STRENGTHS

Cream, 1%.

Each gram of ELIDEL Cream, 1% contains 10 mg of pimecrolimus in a whitish cream base.

4 CONTRAINDICATIONS

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

5 WARNINGS AND PRECAUTIONS

5.1 Risk of Immunosuppression

Prolonged systemic use of calcineurin inhibitors for sustained immunosuppression in animal studies and transplant patients following systemic administration has been associated with an increased risk of infections, lymphomas, and skin malignancies. These risks are associated with the intensity and duration of immunosuppression.

Based on this information and the mechanism of action, there is a concern about a potential risk with the use of topical calcineurin inhibitors, including ELIDEL Cream, 1%. While a causal relationship has not been established, rare cases of skin malignancy and lymphoma have been reported in patients treated with topical calcineurin inhibitors, including ELIDEL Cream, 1%. Therefore:

- Continuous long-term use of topical calcineurin inhibitors, including ELIDEL Cream, 1%, in any age group should be avoided, and application limited to areas of involvement with atopic dermatitis
- ELIDEL Cream, 1% is not indicated for use in children less than 2 years of age
- ELIDEL Cream, 1% should not be used in immunocompromised adults and children, including patients on systemic immunosuppressive medications.
- If signs and symptoms of atopic dermatitis do not improve within 6 weeks, patients should be re-examined by their healthcare provider and their diagnosis be confirmed.
- The safety of ELIDEL Cream, 1% has not been established beyond one year of non-continuous use.

5.2 Application to Malignant or Pre-malignant Skin Conditions

The use of ELIDEL Cream, 1% should be avoided on malignant or pre-malignant skin conditions. Malignant or pre-malignant skin conditions, such as cutaneous T-cell lymphoma (CTCL), can present as dermatitis.

ELIDEL Cream, 1% should not be used in patients with Netherton's Syndrome or other skin diseases where there is the potential for increased systemic absorption of pimecrolimus. The safety of ELIDEL Cream, 1% has not been established in patients with generalized erythroderma.

The use of ELIDEL Cream, 1% may cause local symptoms such as skin burning (burning sensation, stinging, soreness) or pruritus. Localized symptoms are most common during the first few days of ELIDEL Cream, 1% application and typically improve as the lesions of atopic dermatitis resolve [see *Adverse Reactions (6.1)*].

5.3 Bacterial and Viral Skin Infections

Before commencing treatment with ELIDEL Cream, 1%, bacterial or viral infections at treatment sites should be resolved. Trials have not evaluated the safety and efficacy of ELIDEL Cream, 1% in the treatment of clinically infected atopic dermatitis.

While patients with atopic dermatitis are predisposed to superficial skin infections including eczema herpeticum (Kaposi's varicelliform eruption), treatment with ELIDEL Cream, 1% may be independently associated with an increased risk of varicella zoster virus infection (chicken pox or shingles), herpes simplex virus infection, or eczema herpeticum.

In clinical trials, 15/1,544 (1%) cases of skin papilloma (warts) were observed in subjects using ELIDEL Cream, 1%. The youngest subject 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, 1% should be considered until complete resolution of the warts is achieved.

5.4 Patients with Lymphadenopathy

In clinical trials, 14/1,544 (0.9%) cases of lymphadenopathy were reported while using ELIDEL Cream, 1%. 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, 1% 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, ELIDEL Cream, 1% should be discontinued. Patients who develop lymphadenopathy should be monitored to ensure that the lymphadenopathy resolves.

5.5 Sun Exposure

During the course of treatment, it is prudent for patients to minimize or avoid natural or artificial sunlight exposure, even while ELIDEL Cream, 1% is not on the skin. The potential effects of ELIDEL Cream, 1% on skin response to ultraviolet damage are not known.

5.6 Immunocompromised Patients

The safety and efficacy of ELIDEL Cream, 1% in immunocompromised patients have not been studied.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

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

No phototoxicity and no photoallergenicity were detected in clinical trials with 24 and 33 normal volunteers, respectively. In human dermal safety trials, ELIDEL (pimecrolimus) Cream, 1% did not induce contact sensitization or cumulative irritation.

In a one-year safety trial in pediatric subjects age 2-17 years old involving sequential use of ELIDEL Cream, 1% and a topical corticosteroid, 43% of ELIDEL Cream, 1% treated subjects and 68% of vehicle -treated subjects used corticosteroids during the trial. Corticosteroids were used for more than 7 days by 34% of ELIDEL Cream, 1% treated subjects and 54% of vehicle -treated subjects. An increased incidence of impetigo, skin infection, superinfection (infected atopic dermatitis), rhinitis, and urticaria were found in the subjects that had used ELIDEL Cream, 1% and topical corticosteroid sequentially as compared to ELIDEL Cream, 1% alone.

In 3 randomized, double-blind vehicle-controlled pediatric trials and one active-controlled adult trial, 843 and 328 subjects respectively, were treated with ELIDEL Cream, 1%. In these clinical trials, 48 (4%) of the 1,171 ELIDEL treated subjects and 13 (3%) of 408 vehicle-treated subjects 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 subjects treated with ELIDEL Cream, 1%.

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

Table 1. Treatment Emergent Adverse Events (≥1%) in Elidel® Treatment Groups

	Pediatric Subjects* Vehicle-Controlled (6 weeks)		Pediatric Subjects* Open-Label (20 weeks)	Pediatric Subjects* Vehicle-Controlled (1 year)		Adult Active Comparator (1 year)
	Elidel® Cream (N=267) N (%)	Vehicle (N=136) N (%)	Elidel® Cream (N=335) 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 (19.6%)	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%)
Rhinorrhea	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%)	1 (1.3%)	0
Sinus Congestion	3 (1.1%)	1 (0.7%)	2 (0.6%)	<1%	<1%	3 (0.9%)

	Pediatric Subjects* Vehicle-Controlled (6 weeks)		Pediatric Subjects* Open-Label (20 weeks)	Pediatric Subjects* Vehicle-Controlled (1 year)		Adult Active Comparator (1 year)
	Elidel® Cream (N=267) N (%)	Vehicle (N=136) N (%)	Elidel® Cream (N=335) 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%)
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 (5.4%)	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	1 (0.4%)	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%)
Arthralgias	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

Two cases of septic arthritis have been reported in infants less than one year of age in clinical trials conducted with ELIDEL Cream, 1% (n = 2,443). Causality has not been established.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of ELIDEL Cream, 1%. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

General: Anaphylactic reactions, ocular irritation after application of the cream to the eye lids or near the eyes, angioneurotic edema, facial edema, skin flushing associated with alcohol use, skin discoloration.

Hematology/Oncology: Lymphomas, basal cell carcinoma, malignant melanoma, squamous cell carcinoma.

7 DRUG INTERACTIONS

Potential interactions between ELIDEL Cream, 1% and other drugs, including immunizations, have not been systematically evaluated. Due to 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.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

There are no adequate and well-controlled studies with ELIDEL Cream, 1% in pregnant women. Therefore, ELIDEL Cream, 1% should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

In dermal embryofetal developmental studies, no maternal or fetal toxicity was observed up to the highest practicable doses tested, 10 mg/kg/day (1% pimecrolimus cream) in rats (0.14X MRHD based on body surface area) and 10 mg/kg/day (1% pimecrolimus cream) in rabbits (0.65X MRHD based on AUC comparisons). The 1% pimecrolimus cream was administered topically for 6 hours/day during the period of organogenesis in rats and rabbits (gestational days 6-21 in rats and gestational days 6-20 in rabbits).

A second dermal embryofetal development study was conducted in rats using pimecrolimus cream applied dermally to pregnant rats (1 g cream/kg body weight of 0.2%, 0.6% and 1.0% pimecrolimus cream) from gestation day 6 to 17 at doses of 2, 6, and 10 mg/kg/day with daily exposure of approximately 22 hours. No maternal, reproductive, or embryo-fetal toxicity attributable to pimecrolimus was noted at 10 mg/kg/day (0.66X MRHD based on AUC comparisons), the highest dose evaluated in this study. No teratogenicity was noted in this study at any dose.

A combined oral fertility and embryofetal developmental study was conducted in rats and an oral embryofetal developmental study was conducted in rabbits. Pimecrolimus was administered during the period of organogenesis (2 weeks prior to mating until gestational day 16 in rats, gestational days 6-18 in rabbits) up to dose levels of 45 mg/kg/day in rats and 20 mg/kg/day in rabbits. In the absence of maternal toxicity, indicators of embryofetal toxicity (post-implantation loss and reduction in litter size) were noted at 45 mg/kg/day (38X MRHD based on AUC comparisons) in the oral fertility and embryofetal developmental study conducted in rats. No malformations in the fetuses were noted at 45 mg/kg/day (38X MRHD based on AUC comparisons) in this study. No maternal toxicity, embryotoxicity or teratogenicity were noted in the oral rabbit embryofetal developmental toxicity study at 20 mg/kg/day (3.9X MRHD based on AUC comparisons), which was the highest dose tested in this study.

A second oral embryofetal development study was conducted in rats. Pimecrolimus was administered during the period of organogenesis (gestational days 6 – 17) at doses of 2, 10 and 45 mg/kg/day. Maternal toxicity, embryolethality and fetotoxicity were noted at 45 mg/kg/day (271X MRHD based on AUC comparisons). A slight increase in skeletal variations that were indicative of delayed skeletal ossification was also noted at this dose. No maternal toxicity, embryolethality or fetotoxicity were noted at 10 mg/kg/day (16X MRHD based on AUC comparisons). No teratogenicity was noted in this study at any dose.

A second oral embryofetal development study was conducted in rabbits. Pimecrolimus was administered during the period of organogenesis (gestational days 7 – 20) at doses of 2, 6 and 20 mg/kg/day. Maternal toxicity, embryotoxicity and fetotoxicity were noted at 20 mg/kg/day (12X MRHD based on AUC comparisons). A slight increase in skeletal variations that were indicative of delayed skeletal ossification was also noted at this dose. No maternal toxicity, embryotoxicity or fetotoxicity were noted at 6 mg/kg/day (5X MRHD based on AUC comparisons). No teratogenicity was noted in this study at any dose.

An oral peri- and post-natal developmental study was conducted in rats. Pimecrolimus was administered from gestational day 6 through lactational day 21 up to a dose level of 40 mg/kg/day. Only 2 of 22 females delivered live pups at the highest dose of 40 mg/kg/day. Postnatal survival, development of the F1 generation, their subsequent

maturation and fertility were not affected at 10 mg/kg/day (12X MRHD based on AUC comparisons), the highest dose evaluated in this study.

Pimecrolimus was transferred across the placenta in oral rat and rabbit embryofetal developmental studies.

8.3 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.

8.4 Pediatric Use

ELIDEL Cream, 1% is not indicated for use in children less than 2 years of age.

The long-term safety and effects of ELIDEL Cream, 1% on the developing immune system are unknown

Three Phase 3 pediatric trials were conducted involving 1,114 subjects 2-17 years of age. Two trials were 6-week randomized vehicle-controlled trials with a 20-week open-label phase and one was a vehicle-controlled (up to 1 year) safety trial with the option for sequential topical corticosteroid use. Of these subjects 542 (49%) were 2-6 years of age. In the short-term trials, 11% of ELIDEL subjects did not complete these trials and 1.5% of ELIDEL subjects discontinued due to adverse events. In the one-year trial, 32% of ELIDEL subjects did not complete this trial and 3% of ELIDEL subjects discontinued due to adverse events. Most discontinuations were due to unsatisfactory therapeutic effect.

The most common local adverse event in the short-term trials of ELIDEL Cream, 1% in pediatric subjects ages 2-17 was application site burning (10% vs. 13% vehicle); the incidence in the long-term trial was 9% ELIDEL vs. 7% vehicle [see Adverse Reactions (6.1)]. Adverse events that were more frequent (>5%) in subjects treated with ELIDEL Cream, 1% 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 trial [see Adverse Reactions (6.1)]. In 843 subjects ages 2-17 years treated with ELIDEL Cream, 1%, 9 (0.8%) developed eczema herpeticum (5 on ELIDEL Cream, 1% alone and 4 on ELIDEL Cream, 1% used in sequence with corticosteroids). In 211 subjects on vehicle alone, there were no cases of eczema herpeticum. The majority of adverse events were mild to moderate in severity.

Two Phase 3 trials were conducted involving 436 infants age 3 months-23 months. One 6-week randomized vehicle-controlled trial with a 20-week open-label phase and one safety trial, up to one year, were conducted. In the 6-week trial, 11% of ELIDEL and 48% of vehicle subjects did not complete this trial; no subject in either group discontinued due to adverse events. Infants on ELIDEL Cream, 1% had an increased incidence of some adverse events compared to vehicle. In the 6-week vehicle-controlled trial 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 trial, for infants who switched to ELIDEL Cream, 1% from vehicle, the incidence of the above-cited adverse events approached or equaled the incidence of those subjects who remained on ELIDEL Cream, 1%. In the 6 month safety data, 16% of ELIDEL and 35% of vehicle subjects discontinued early and 1.5% of ELIDEL and 0% of vehicle subjects discontinued due to adverse events. Infants on ELIDEL Cream, 1% 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 systemic exposure to pimecrolimus from ELIDEL (pimecrolimus) Cream, 1% was investigated in 28 pediatric subjects with atopic dermatitis (20%-80% BSA involvement) between the ages of 8 months-14 yrs. Following twice daily application for three weeks, blood concentrations of pimecrolimus were <2 ng/mL with 60% (96/161) of the blood samples having blood concentration below the limit of quantification (0.5 ng/mL). However, more children (23 children out of the total 28 children investigated) had at least one detectable blood level as compared to the adults (12 adults out of the total 52 adults investigated) over a 3-week treatment period. Due to the erratic nature of the blood levels observed, no correlation could be made between amount of cream, degree of BSA involvement, and

blood concentrations. In general, the blood concentrations measured in adult atopic dermatitis subjects were comparable to those seen in the pediatric population.

In a second group of 30 pediatric subjects aged 3-23 months with 10%-92% BSA involvement, following twice daily application for three weeks, blood concentrations of pimecrolimus were <2.6 ng/mL with 65% (75/116) of the blood samples having blood concentration below 0.5ng/mL, and 27% (31/116) below the limit of quantification (0.1 ng/mL) for these trials.

Overall, a higher proportion of detectable blood levels was seen in the pediatric subject population as compared to adult population. This increase in the absolute number of positive blood levels may be due to the larger surface area to body mass ratio seen in these younger subjects. In addition, a higher incidence of upper respiratory symptoms/infections was also seen relative to the older age group in the PK trials. At this time, a causal relationship between these findings and ELIDEL use cannot be ruled out.

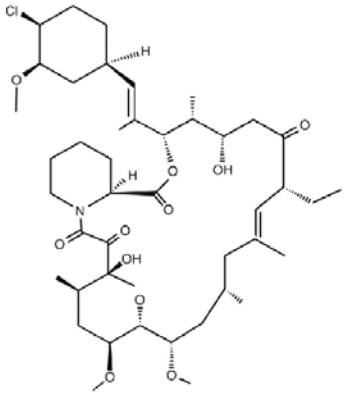
8.5 Geriatric Use

Nine (9) subjects ≥65 years old received ELIDEL Cream, 1% in Phase 3 trials. Clinical trials of ELIDEL Cream, 1% did not include sufficient numbers of subjects aged 65 and over to assess efficacy and safety.

11 DESCRIPTION

ELIDEL® (pimecrolimus) Cream, 1%, for topical use, contains the compound pimecrolimus, the immunosuppressant 33-epi-chloro-derivative of the macrolactam ascomycin.

Chemically, pimecrolimus is (1R,9S,12S,13R,14S,17R,18E,21S,23S,24R,25S,27R)-12-[(1E)-2-{(1R,3R,4S)-4-chloro-3-methoxycyclohexyl}-1-methylvinyl]-17-ethyl-1,14-dihydroxy-23,25-dimethoxy-13,19,21,27-tetramethyl-11,28-dioxa-4-aza-tricyclo[22.3.1.04,9]octacos-18-ene-2,3,10,16-tetraone. The compound has the empirical formula C43H68CINO11 and the molecular weight of 810.47. The structural formula is:



Pimecrolimus is a white to off-white fine crystalline powder. It is soluble in methanol and ethanol and insoluble in water.

Each gram of ELIDEL Cream, 1% contains 10 mg of pimecrolimus in a whitish cream base of benzyl alcohol, cetyl alcohol, citric acid anhydrous, mono- and di-glycerides, oleyl alcohol, propylene glycol, sodium cetostearyl sulphate, sodium hydroxide, stearyl alcohol, triglycerides, and water.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The mechanism of action of pimecrolimus in atopic dermatitis is not known. While the following have been observed, the clinical significance of these observations in atopic dermatitis is not known. It has been demonstrated that pimecrolimus binds with high affinity to macrophilin-12 (FKBP-12) and inhibits the calcium-dependent phosphatase, calcineurin. As a consequence, it inhibits T cell activation by blocking the transcription of early cytokines. In particular, pimecrolimus inhibits at nanomolar concentrations Interleukin-2 and interferon

gamma (Th1-type) and Interleukin-4 and Interleukin-10 (Th2-type) cytokine synthesis in human T-cells. In addition, pimecrolimus prevents the release of inflammatory cytokines and mediators from mast cells in vitro after stimulation by antigen/IgE.

12.3 Pharmacokinetics

Absorption

In adult subjects (n=52) being treated for atopic dermatitis [13%-62% Body Surface Area (BSA) involvement] for periods up to a year, a maximum pimecrolimus concentration of 1.4 ng/mL was observed among those subjects with detectable blood levels. In the majority of samples in adult (91%; 1,244/1,362) subjects, blood concentrations of pimecrolimus were below 0.5 ng/mL. Data on blood levels of pimecrolimus measured in pediatric subjects are described in Use in Specific Populations (8.4).

Distribution

Laboratory in vitro plasma protein binding studies using equilibrium gel filtration have shown that 99.5% of pimecrolimus in plasma is bound to proteins over the pimecrolimus concentration range of 2-100 ng/mL tested. The major fraction of pimecrolimus in plasma appears to be bound to various lipoproteins. As with other topical calcineurin inhibitors, it is not known whether pimecrolimus is absorbed into cutaneous lymphatic vessels or in regional lymph nodes.

Metabolism

Following the administration of a single oral radiolabeled dose of pimecrolimus numerous circulating O-demethylation metabolites were seen. Studies with human liver microsomes indicate that pimecrolimus is metabolized in vitro by the CYP3A sub-family of metabolizing enzymes. No evidence of skin mediated drug metabolism was identified in vivo using the minipig or in vitro using stripped human skin.

Elimination

Based on the results of the aforementioned radiolabeled study, following a single oral dose of pimecrolimus ~81% of the administered radioactivity was recovered, primarily in the feces (78.4%) as metabolites. Less than 1% of the radioactivity found in the feces was due to unchanged pimecrolimus.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

In a 2-year rat dermal carcinogenicity study using ELIDEL Cream, 1%, a statistically significant increase in the incidence of follicular cell adenoma of the thyroid was noted in low, mid and high dose male animals compared to vehicle and saline control male animals. Follicular cell adenoma of the thyroid was noted in the dermal rat carcinogenicity study at the lowest dose of 2 mg/kg/day [0.2% pimecrolimus cream; 1.5X the Maximum Recommended Human Dose (MRHD) based on AUC comparisons]. No increase in the incidence of follicular cell adenoma of the thyroid was noted in the oral carcinogenicity study in male rats up to 10 mg/kg/day (66X MRHD based on AUC comparisons). However, oral studies may not reflect continuous exposure or the same metabolic profile as by the dermal route. In a mouse dermal carcinogenicity study using pimecrolimus in an ethanolic solution, no increase in incidence of neoplasms was observed in the skin or other organs up to the highest dose of 4 mg/kg/day (0.32% pimecrolimus in ethanol) 27X MRHD based on AUC comparisons. However, lymphoproliferative changes (including lymphoma) were noted in a 13 week repeat dose dermal toxicity study conducted in mice using pimecrolimus in an ethanolic solution at a dose of 25 mg/kg/day (47X MRHD based on AUC comparisons). No lymphoproliferative changes were noted in this study at a dose of 10 mg/kg/day (17X MRHD based on AUC comparison). However, the latency time to lymphoma formation was shortened to 8 weeks after dermal administration of pimecrolimus dissolved in ethanol at a dose of 100 mg/kg/day (179-217X MRHD based on AUC comparisons).

In a mouse oral (gavage) carcinogenicity study, a statistically significant increase in the incidence of lymphoma was noted in high dose male and female animals compared to vehicle control male and female animals. Lymphomas were noted in the oral mouse carcinogenicity study at a dose of 45 mg/kg/day (258-340X MRHD based on AUC comparisons). No drug-related tumors were noted in the mouse oral carcinogenicity study at a dose of 15 mg/kg/day (60-133X MRHD based on AUC comparisons).

In an oral (gavage) rat carcinogenicity study, a statistically significant increase in the incidence of benign thymoma was noted in 10 mg/kg/day pimecrolimus treated male and female animals compared to vehicle control treated male and female animals. In addition, a significant increase in the incidence of benign thymoma was noted in another oral (gavage) rat carcinogenicity study in 5 mg/kg/day pimecrolimus treated male animals compared to vehicle control treated male animals. No drug-related tumors were noted in the rat oral carcinogenicity study at a dose of 1 mg/kg/day male animals (1.1X MRHD based on AUC comparisons) and at a dose of 5 mg/kg/day for female animals (21X MRHD based on AUC comparisons).

In a 52-week dermal photo-carcinogenicity study, the median time to onset of skin tumor formation was decreased in hairless mice following chronic topical dosing with concurrent exposure to UV radiation (40 weeks of treatment followed by 12 weeks of observation) with the ELIDEL Cream, 1% vehicle alone. No additional effect on tumor development beyond the vehicle effect was noted with the addition of the active ingredient, pimecrolimus, to the vehicle cream.

A 39-week oral monkey toxicology study was conducted with pimecrolimus doses of 15, 45 and 120 mg/kg/day. A dose dependent increase in expression of immunosuppressive-related lymphoproliferative disorder (IRLD) associated with lymphocryptovirus (a monkey strain of virus related to human Epstein Barr virus) was observed. IRLD in monkeys mirrors what has been noted in human transplant patients after chronic systemic immunosuppressive therapy, post transplantation lymphoproliferative disease (PTLD), after treatment with chronic systemic immunosuppressive therapy. Both IRLD and PTLD can progress to lymphoma, which is dependent on the dose and duration of systemic immunosuppressive therapy. A dose dependent increase in opportunistic infections (a signal of systemic immunosuppression) was also noted in this monkey study. A no observed adverse effect level (NOAEL) for IRLD and opportunistic infections was not established in this study. IRLD occurred at the lowest dose of 15 mg/kg/day for 39 weeks [31X the Maximum Recommended Human Dose (MRHD) of ELIDEL Cream, 1% based on AUC comparisons] in this study. A partial recovery from IRLD was noted upon cessation of dosing in this study.

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.

An oral fertility and embryofetal developmental study in rats revealed estrus cycle disturbances, post-implantation loss and reduction in litter size at the 45 mg/kg/day dose (38X MRHD based on AUC comparisons). 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.

A second oral fertility and embryofetal developmental study in rats revealed reduced testicular and epididymal weights, reduced testicular sperm counts and motile sperm for males and estrus cycle disturbances, decreased corpora lutea, decreased implantations and viable fetuses for females at 45 mg/kg/day dose (123X MRHD for males and 192X MRHD for females based on AUC comparisons). No effect on fertility in female rats was noted at 10 mg/kg/day (5X MRHD based on AUC comparisons). No effect on fertility in male rats was noted at 2 mg/kg/day (0.7X MRHD based on AUC comparisons).

14 CLINICAL STUDIES

Three randomized, double-blind, vehicle-controlled, multi-center, Phase 3 trials were conducted in 589 pediatric subjects ages 3 months-17 years old to evaluate ELIDEL (pimecrolimus) Cream, 1% for the treatment of mild to moderate atopic dermatitis. Two of the three trials support the use of ELIDEL Cream, 1% in subjects 2 years and older with mild to moderate atopic dermatitis [see *Warnings and Precautions (5.1)*]. Three other trials in 1,619 pediatric and adult subjects provided additional data regarding the safety of ELIDEL Cream, 1% in the treatment of atopic dermatitis. Two of these other trials were vehicle-controlled with optional sequential use of a medium potency topical corticosteroid in pediatric subjects and one trial was an active comparator trial in adult subjects with atopic dermatitis [see *Warnings and Precautions (5.1)* and *Adverse Reactions (6.1)*].

Two identical 6-week, randomized, vehicle-controlled, multi-center, Phase 3 trials were conducted to evaluate ELIDEL Cream, 1% for the treatment of mild to moderate atopic dermatitis. A total of 403 pediatric subjects 2-17 years old were included in the trials. The male/female ratio was approximately 50% and 29% of the subjects were African American. At trial entry, 59% of subjects had moderate disease and the mean body surface area (BSA)

affected was 26%. About 75% of subjects had atopic dermatitis affecting the face and/or neck region. In these trials, subjects applied either ELIDEL Cream, 1% or vehicle cream twice daily to 5% to 96% of their BSA for up to 6 weeks. At endpoint, based on the physician's global evaluation of clinical response, 35% of subjects treated with ELIDEL Cream, 1% were clear or almost clear of signs of atopic dermatitis compared to only 18% of vehicle-treated subjects. More ELIDEL subjects (57%) had mild or no pruritus at 6 weeks compared to vehicle subjects (34%). The improvement in pruritus occurred in conjunction with the improvement of the subjects' atopic dermatitis.

In these two 6-week trials of ELIDEL, the combined efficacy results at endpoint are presented in Table 2 as follows:

Table 2. Combined Efficacy Results at Endpoint for Two 6-week Trials of ELIDEL Cream

	% Subjects	
	Elidel® (N= 267)	Vehicle (N= 136)
Global Assessment		
Clear	28 (10%)	5 (4%)
Clear or Almost Clear	93 (35%)	25 (18%)
Clear to Mild Disease	180 (67%)	55 (40%)

In the two pediatric trials that independently support the use of ELIDEL Cream, 1% in mild to moderate atopic dermatitis, a significant treatment effect was seen by day 15. Of the key signs of atopic dermatitis, erythema, infiltration/papulation, lichenification, and excoriations were reduced at day 8 when compared to vehicle.

Figure 1 depicts the time course of improvement in the percent body surface area affected as a result of treatment with ELIDEL Cream, 1% in 2-17 year olds.

Figure 1

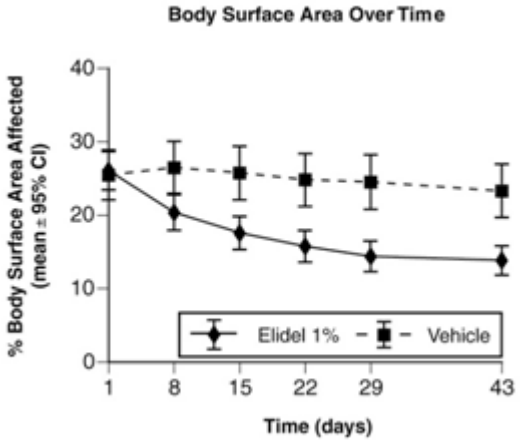
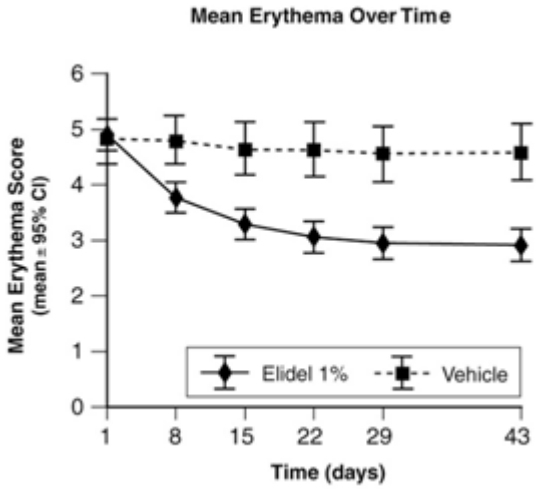


Figure 2 shows the time course of improvement in erythema as a result of treatment with ELIDEL Cream, 1% in 2-17 year olds.

Figure 2



16 HOW SUPPLIED/STORAGE AND HANDLING

ELIDEL (pimecrolimus) Cream, 1% is a whitish cream available in tubes of 30 grams, 60 grams, and 100 grams.

30 gram tube……NDC 0187-5100-01

60 gram tube……NDC 0187-5101-02

100 gram tube……..NDC 0187-5102-03

Store at 25°C (77°F); excursions permitted to 15°C-30°C (59°F-86°F) [USP Controlled Room Temperature]. Do not freeze.

17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Medication Guide)

Patients using ELIDEL Cream, 1% should receive the following information and instructions:

- **ELIDEL Cream, 1% may cause serious side effects.** It is not known if ELIDEL Cream, 1% is safe to use for a long period of time. A very small number of people who have used ELIDEL Cream, 1% have had cancer (for example, skin or lymphoma). However, a link with ELIDEL Cream, 1% use has not been shown. Because of this concern:
- A patient should not use ELIDEL Cream, 1% continuously for a long time.
- ELIDEL Cream, 1% should be used only on areas of skin that have eczema.
- ELIDEL Cream, 1% is not for use on a child under 2 years old.
- A patient should not use sun lamps, tanning beds, or get treatment with ultraviolet light therapy during treatment with ELIDEL Cream, 1%.
- A patient should limit sun exposure during treatment with ELIDEL Cream, 1% even when the medicine is not on the skin. If a patient needs to be outdoors after applying ELIDEL Cream, 1%, the patient should wear loose fitting clothing that protects the treated area from the sun. The physician should advise the patient about other types of protection from the sun.
- A patient should not cover the skin being treated with bandages, dressings or wraps. A patient can wear normal clothing.
- ELIDEL Cream, 1% is for use on the skin only. Do not get ELIDEL Cream, 1% in your eyes, nose, mouth, vagina, or rectum (mucous membranes). If you get ELIDEL Cream, 1% in any of these areas, burning or

irritation can happen. Wipe off any ELIDEL Cream, 1% from the affected area and then rinse the area well with cold water. ELIDEL Cream, 1% is for external use only.

- A patient should use ELIDEL Cream, 1% for short periods, and if needed, treatment may be repeated with breaks in between.
- Wash hands before using ELIDEL Cream, 1%. When applying ELIDEL Cream, 1% after a bath or shower, the skin should be dry.
- Apply a thin layer of ELIDEL Cream, 1% only to the affected skin areas, twice a day, as directed by the physician.
- Use the smallest amount of ELIDEL Cream, 1% needed to control the signs and symptoms of eczema.
- A patient should not bathe, shower or swim right after applying ELIDEL Cream, 1%. This could wash off the cream.
- A patient can use moisturizers with ELIDEL Cream, 1%. They should be sure to check with the physician first about the products that are right for them. Because the skin of patients with eczema can be very dry, it is important they keep up good skin care practices. If a patient uses moisturizers, he or she should apply them after ELIDEL Cream, 1%.

Manufactured for:
Valeant Pharmaceuticals North America LLC
Bridgewater, NJ 08807

Manufactured by:
Contract Pharmaceutical Limited,
Mississauga, Ontario L5N 6L6

Made in Canada

U.S. Patents 5,912,238; 6,352,998; and 6,423,722
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XXXXXXXXXXXX

MEDICATION GUIDE

ELIDEL® (EĹ-ee-del)

(pimecrolimus)

Cream, 1%

Important: ELIDEL Cream, 1% is for use on the skin only (topical). Do not get ELIDEL Cream, 1% in your eyes, nose, mouth, vagina, or rectum.

What is the most important information I should know about ELIDEL Cream, 1%?

It is not known if ELIDEL Cream, 1% is safe to use for a long period of time. A very small number of people who have used ELIDEL Cream, 1% have developed cancer (for example, skin cancer or lymphoma). But a link that ELIDEL Cream, 1% use caused these cancers has not been shown. Because of this concern:

- Do not use ELIDEL Cream, 1% continuously for a long time.
- Use ELIDEL Cream, 1% only on areas of your skin that have eczema.
- Do not use ELIDEL Cream, 1% on a child under 2 years of age.

What is ELIDEL Cream, 1%?

ELIDEL Cream, 1% is a prescription medicine used on the skin (topical) to treat mild to moderate eczema (atopic dermatitis). ELIDEL Cream, 1% is for adults and children age 2 years and older who do not have a weakened immune system. ELIDEL Cream, 1% is used on the skin for short periods, and if needed, treatment may be repeated with breaks in between. ELIDEL Cream, 1% is for use after other prescription medicines have not worked for you or if your doctor recommends that other prescription medicines should not be used.

It is not known if ELIDEL Cream, 1% is safe and effective in people who have a weakened immune system.

ELIDEL Cream, 1% is not for use in children under 2 years of age.

Who should not use ELIDEL Cream, 1%?

Do not use ELIDEL Cream, 1% if you are allergic to pimecrolimus or any of the ingredients in ELIDEL Cream, 1%. See the end of this Medication Guide for a complete list of ingredients in ELIDEL Cream, 1%.

What should I tell my doctor before using ELIDEL Cream, 1%?

Before using ELIDEL Cream, 1%, tell your doctor about all of your medical conditions, including if you:

- have a skin disease called Netherton's syndrome (a rare inherited condition)
- have any infection on your skin including chicken pox or herpes
- have been told you have a weakened immune system

- are pregnant or plan to become pregnant. It is not known if ELIDEL Cream, 1% will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if ELIDEL Cream, 1% passes into your breast milk. You and your doctor should decide if you will use ELIDEL Cream, 1% or breastfeed. You should not do both.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Tell your doctor about all the skin medicines and products you use.

Know the medicines you take. Keep a list of them with you to show your doctor and pharmacist each time you get a new medicine.

How should I use ELIDEL Cream, 1%?

- Use ELIDEL Cream, 1% exactly as your doctor tells you to use it.
- Stop ELIDEL Cream, 1% when the signs and symptoms of eczema, such as itching, rash, and redness go away, or as directed by your doctor.
- Wash your hands before using ELIDEL Cream, 1%. If you apply ELIDEL Cream, 1% after a bath or shower, make sure your skin is dry.
- Apply a thin layer of ELIDEL Cream, 1% only to the affected skin areas, two times each day, as directed by your doctor.
- Use the smallest amount of ELIDEL Cream, 1% to help control the signs and symptoms of eczema.
- If you apply ELIDEL Cream, 1% to another person, or if you have eczema and are not treating your hands, it is important for you to wash your hands with soap and water after applying ELIDEL Cream, 1%. This should remove any cream left on your hands.
- Do not bathe, shower or swim right after applying ELIDEL Cream, 1%. This could wash off the cream.
- You can use moisturizers with ELIDEL Cream, 1%. Ask your doctor first about the products that are right for you. People with eczema can have very dry skin, so it is important to keep up good skin care practices. If you use moisturizers, apply them after ELIDEL Cream, 1%.
- **Call your doctor if your symptoms get worse with ELIDEL Cream, 1% or your symptoms do not improve after 6 weeks of treatment.**

What should I avoid while using ELIDEL Cream, 1%?

- You should not use sun lamps, tanning beds, or get treatment with ultraviolet light therapy during treatment with ELIDEL Cream, 1%.
- Limit your time in the sun during treatment with ELIDEL Cream, 1% even when the medicine is not on your skin. If you need to be outdoors after applying ELIDEL Cream, 1%, wear loose fitting clothing that protects the treated area from the sun. Ask your doctor what other types of protection from the sun you

should use. It is not known how ELIDEL Cream, 1% may affect your skin with exposure to ultraviolet light.

- Do not cover the skin being treated with bandages, dressings or wraps. You can wear normal clothing.
- ELIDEL Cream, 1% is for use on the skin only. Do not get ELIDEL Cream, 1% in your eyes, nose, mouth, vagina, or rectum (mucous membranes). If you get ELIDEL Cream, 1% in any of these areas, burning or irritation can happen. Wipe off any ELIDEL Cream, 1% from the affected area and then rinse the area well with cold water.
- Do not swallow ELIDEL Cream, 1%. If you do, call your doctor.
    - Avoid using ELIDEL Cream, 1% on skin areas that have cancers or pre-cancers.

What are the possible side effects of ELIDEL Cream, 1%?

ELIDEL Cream, 1% may cause serious side effects.

- See “What is the most important information I should know about ELIDEL Cream, 1%?”
- The most common side effect at the skin application site is burning or a feeling of warmth. These side effects are usually mild or moderate, happen during the first few days of treatment, and usually clear up in a few days.

Other common side effects include:

- headache
- common cold or stuffy nose, sore throat
- cough
- flu (influenza)
- fever
- viral infection. Some people may get viral skin infections (like cold sores, chicken pox, shingles, or warts) or swollen lymph nodes (glands).

Tell your doctor if you get a skin infection or if you have any side effect (for example, swollen glands) that bothers you or that does not go away.

These are not all the possible side effects with ELIDEL Cream, 1%. Ask your doctor or pharmacist for more information.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store ELIDEL Cream, 1%?

- Store ELIDEL Cream, 1% at room temperature between 68° to 77°F (20° to 25°C).
- Do not freeze ELIDEL Cream, 1%.

Keep ELIDEL Cream, 1% and all medicines out of the reach of children.

General information about the safe and effective use of ELIDEL Cream, 1%

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use ELIDEL Cream, 1% for conditions other than which it was prescribed. Do not give ELIDEL Cream, 1% to other people even if they have the same symptoms you have. It may harm them.

You can ask your doctor or pharmacist for information about ELIDEL Cream, 1% that is written for health professionals.

For more information, go to www.Elidel.com or call 1-800-321-4576.

What are the ingredients in ELIDEL Cream, 1%?

Active ingredient: pimecrolimus
Inactive ingredients: benzyl alcohol, cetyl alcohol, citric acid anhydrous, mono- and di-glycerides, oleyl alcohol, propylene glycol, sodium cetostearyl sulphate, sodium hydroxide, stearyl alcohol, triglycerides, and water

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Manufactured for:
Valeant Pharmaceuticals North America LLC
Bridgewater, NJ 08807

Manufactured by:
Contract Pharmaceutical Limited,
Mississauga, Ontario L5N 6L6

Made in Canada

U.S. Patents 5,912,238; 6,352,998; and 6,423,722

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