

Memorandum

**Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research**

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SUBJECT: Pediatric Drug use analysis for Topical Calcineurin Inhibitors
Pimecrolimus Topical Cream (Elidel[®]): NDA 21-302
Tacrolimus Topical Ointment (Protopic[®]): NDA 50-777

EXECUTIVE SUMMARY

This consult examines nationwide drug utilization trends for Elidel[®] and Protopic[®] with primary focus on the pediatric population.

During June 2003 – May 2004, there were a total of 3.9 million Elidel[®] prescriptions (2.81 million new, 1.04 million refills) and 1.0 million total Protopic[®] prescriptions dispensed (707,000 new, 332,000 refills). Total prescriptions dispensed increased 47% for Elidel[®] and 16% for Protopic[®] as compared to the previous year. Pediatricians were the most frequent prescribers of Elidel[®] for the period June 2003 – May 2004 accounting for 31% (1.1 million prescriptions) of prescribing, followed by dermatologists accounting for 23% (843,000 prescriptions). Protopic[®] was most commonly prescribed by dermatologists who accounted for 54% of prescribing (529,000 prescriptions) and pediatricians with 17% (163,000 prescriptions).

Participants ages 1-16 years accounted for 41% of Elidel[®] Claims and 35% of Protopic[®] Claims processed by Caremark and available in the Dimension Rx[™] system during June 2003 – May 2004. Among all pediatric participants (1-16 years) prescribed these products in the year June 2003 – May 2004, claims for Elidel[®] in participants age 1-2 years accounted for 12.7%, participants ages 3-16 years accounted for 28.7%, and participants ages 17+ years accounted for 58.6%. For Protopic[®], participants age 1-2 years accounted for 8.0% of claims, participants age 3-16 years accounted for 26.6% of claims and adults accounted for 65.4% of claims. The proportion of pediatric prescriptions dispensed was relatively stable throughout the 3 years analyzed; however, the

increasing total prescription volume appears to be resulting in increasing numbers of prescriptions to pediatric participants.

When we applied the proportions of all pediatric Elidel[®] and Protopic[®] prescriptions from AdvancePCS to IMS Health, NPA Plus[™] data to approximate the number of prescriptions dispensed nationwide to children, it was estimated that approximately 1.6 million Elidel[®] prescriptions and 359,000 Protopic[®] prescriptions were dispensed persons ages 1-16 years in the U.S. during June 2003 – May 2004.

The most common diagnoses for Elidel[®] and Protopic[®] for patients seen by office based physicians during the period June 2003 – May 2004 was “dermatitis with eczema, unspecified cause” (ICD-9 692.9) which accounted for 55% of total Elidel[®] use and 39% of Protopic[®] use. “Atopic Dermatitis + Related conditions” (ICD-9 691.8) was the second most common indication for all age groups accounting for 24% of the total Elidel[®] use and 29% of the Protopic[®] use.

INTRODUCTION

Pimecrolimus (Elidel[®] NDA 21-302) approved on 12/13/2001, and tacrolimus (Protopic[®]) approved 12/8/2000, are topical calcineurin inhibitors 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, who have had inadequate response to conventional therapy or in whom the use of alternative, conventional therapies is inadvisable.

This review describes outpatient drug use patterns in the pediatric population as compared to the adult population in the years after approval. Proprietary drug use databases licensed by the Agency were used to conduct this analysis.

DATA SOURCES

This analysis describes the outpatient drug use patterns for Elidel[®] and Protopic[®] as measured by two IMS Health audits and prescription claims information from Caremark Pharmacy Benefit Management Company’s, DimensionRx[™] system. Total prescriptions dispensed annually and prescriber specialties were obtained from IMS Health, National Prescription Audit *Plus*[™] (NPA *Plus*[™]), indications for use were obtained from the IMS Health, National Disease and Therapeutic Index[™] (NDTI[™]), and patient demographics were obtained from prescription claims for a 36-month period of time from Caremark DimensionRx[™].

IMS HEALTH, NATIONAL PRESCRIPTION AUDIT PLUS[™] (NPA PLUS[™])

NPA Plus[™] measures the retail dispensing of prescriptions, or the frequency with which drugs move out of retail pharmacies into the hands of consumers via formal prescriptions. These retail pharmacies include chain, independent, food store, mail order, discount houses, and mass merchandiser pharmacies, as well as nursing home (long-term care) pharmacy providers. Information on the specialty of the prescribing physician can also be collected; however this information is not available on prescriptions dispensed in the long-term care and mail order pharmacy settings.

The number of dispensed prescriptions is obtained from a sample of approximately 22,000 pharmacies throughout the U.S. and projected nationally. The pharmacies in the database account for approximately 40% of all pharmacy stores and represent approximately 45% of all prescriptions dispensed in the U.S.

Sales data is given in terms of eaches which is the smallest unit of a shipping package which is labeled for sale. For Elidel and Protopic, this would be tubes.

Data for this analysis include prescriptions dispensed from May 1, 2000 through April 30, 2004, inclusive.

Caremark, DIMENSION RX™

Caremark is one of the largest pharmacy benefit management (PBM) companies in the U.S., currently managing drug benefits for over 70 million lives and processing over 545 million prescription claims annually. FDA has on-line access to Caremark's Dimension Rx database consisting of a subset of total Caremark paid claims representing 350 million claims per year for prescriptions filled in 57,000 pharmacies across the country. Participants whose claims are processed by Caremark include those covered under various types of insurance plans that cover prescription drugs, including some employers' self-insured plans, selected managed care plans, Blue Cross/Blue Shield plans, and selected other traditional insurers. Demographically, these participants appear to represent all 50 states, and include substantial numbers of the elderly, children and women of childbearing age. Their representativeness of all participants receiving dispensed prescriptions in the U.S., however, is not known at this time.

For this analysis, annual prescription claims in the Dimension Rx™ system were examined from June 1, 2001 through May 31, 2004, inclusive.

IMS HEALTH, NATIONAL DISEASE AND THERAPEUTIC INDEX™ (NDTI™)

The National Disease and Therapeutic Index™ (NDTI™) is an ongoing survey designed and conducted by IMS Health to provide descriptive information on the patterns and treatment of disease encountered in office-based practice in the continental U.S. by collecting data on drug products mentioned during visits to office-based physicians. The data are gathered by a panel of approximately 3,000 office-based physicians who complete and submit a survey of their practice patterns to IMS Health for two consecutive days per quarter. These data may include profiles and trends of diagnoses, patients, and treatment patterns and are collected and projected nationally to reflect national prescribing patterns.

NDTI™ uses the term drug uses for mentions of a drug in association with a diagnosis during an office-based patient visit. This term may be duplicated by the number of diagnoses for which the drug is mentioned. It is important to note that a drug use does not necessarily result in a prescription being generated. Rather, the term drug use indicates that a given drug was mentioned during an office visit and could result in a prescription given, a refill authorized, or a sample given to the patient.

For this analysis, we examined annual mentions during office-based physician visits from June 1, 2001 through May 31, 2004, inclusive.

RESULTS

I. Sales Distribution and Dispensed Prescriptions

Elidel® and Protopic® are primarily distributed through retail channels (chain, independent, food store, and mail service pharmacies). The retail channels accounted for a combined 95% (4.09 million eaches or tubes) of Elidel® sales and 94% (1.24 million eaches) of Protopic® sales during June 2003 – April 2004¹. Use of topical calcineurin inhibitors has increased from 164,000 total prescriptions in the period June 2000 – May 2001 to 4.9 million total prescriptions in June 2003 – May 2004 (Table 1). In the year ending May 2004, Elidel® was the most commonly dispensed product in this class with 3.9 million prescriptions dispensed, compared to Protopic® with 1 million prescriptions dispensed. New prescriptions accounted for 72% of the total dispensing for these topical calcineurin inhibitors during June 2003 – May 2004 (Elidel® 73% and Protopic® 68%), a small decrease from 74% of the previous year (calculated from table 1).

Pediatricians were responsible for approximately 31% of Elidel® prescribing (1.1 million prescriptions) followed by dermatologists with 23% (843,000 prescriptions) during June 2003 – May 2004 (Table 2). During the same period, Protopic® was most commonly prescribed by dermatologists which accounted for 54% of prescriptions (529,000) followed by pediatricians who accounted for 17% (163,000 prescriptions). Compared to the previous year, the

¹ IMS Health, National sales Perspectives, Combined, Data Extracted 6/2004 File: 0406tc3.dvr, Data not shown.

relative number of prescriptions rose 46% for Elidel[®] and 16% for Protopic[®] while prescribing by pediatricians grew 62% for Elidel[®] and 29% for Protopic[®] (calculated from Table 2).

II. Patient Demographics

Prescription claims for Elidel[®] and Protopic[®] in the Caremark Dimension Rx data show trends of increasing use among adult and pediatric participants over the 3 years analyzed (Table 3). Participants ages 1-16 years accounted for 41% of Elidel dispensing and 35% of Protopic dispensing in June 2003 – May 2004. Among all participants in the year June 2003 – May 2004, claims for Elidel[®] in participants age 1-2 years accounted for 12.7% of claims, participants ages 3-16 years accounted for 28.7%, and participants ages 17+ years accounted for 58.6%. For Protopic[®], participants age 1-2 years accounted for 8% of claims, participants age 3-16 years accounted for 27% of claims and adults accounted for 65% of claims. The proportion of pediatric prescriptions dispensed was relatively stable throughout the 3 years analyzed for both products. Claims for Elidel and Protopic 0.1% ointment had the greatest increases in the pediatric population.

When we applied the proportions of all pediatric Elidel[®] and Protopic[®] prescriptions from Caremark Dimension Rx[™] (Table 3) to IMS Health, NPA Plus[™] data (Table 1) to approximate the number of prescriptions dispensed nationwide to children, it was estimated that approximately 1.6 million Elidel[®] prescriptions and 359,000 Protopic[®] prescriptions were dispensed persons ages 1-16 years in the U.S. during June 2003 – May 2004.

Estimated Nationwide Prescriptions by Age Group for Elidel [®] and Protopic [®]							
		June 2001 - May 2002		June 2002 - May 2003		June 2003 - May 2004	
		Percentage of Caremark Dimension Rx [™] Claims (From Table 3)	Estimated Number of Prescriptions in the U.S.*	Percentage of Caremark Dimension Rx [™] Claims (From Table 3)	Estimated Number of Prescriptions in the U.S.*	Percentage of Caremark Dimension Rx [™] Claims (From Table 3)	Estimated Number of Prescriptions in the U.S.*
ELIDEL			303,000		2,625,000		3,852,000
	Age 1-2	9.6%	29,088	12.1%	317,625	12.7%	489,204
	Age 3-16	25.0%	75,750	28.4%	745,500	28.7%	1,105,524
	Age 17+	65.4%	198,162	59.5%	1,561,875	58.6%	2,257,272
PROTOPIC			866,000		892,000		1,039,000
	Age 1-2	8.3%	71,878	8.3%	74036	8.0%	83120
	Age 3-16	26.9%	232,954	26.7%	238164	26.6%	276374
	Age 17+	64.8%	561,168	65.0%	579800	65.4%	679506
*Total number of prescriptions obtained from IMS NPA+ (Table 1), projected prescriptions for age strata are calculated.							

III. Intended Duration of Therapy

The IMS measure, “Days of Therapy” is the intended duration of a prescription as written by the physician during a patient visit. During June 2003 – May 2004, Elidel[®] prescriptions written for 60 days or less accounted for 98% of prescriptions written for patients age 0-2 years, 95% of prescriptions for ages 3-16 years, and 91% of prescriptions for adults (Table 4). During the same period, Protopic[®] prescriptions were written for 60 days or less accounted for 100% of prescriptions for patients age 0-2 years, 79% of prescriptions for patients 3-16 years of age, and 78% of prescriptions for adults.

IV. Indications for Use

With the exception of the Protopic[®] 0-2 year age group, which was too small to evaluate, the most common diagnosis associated with the use of both Elidel[®] and Protopic[®] for patients seen by office based physicians during the period June 2003 – May 2004 was “dermatitis with eczema, unspecified cause” (ICD-9 692.9) which accounted

for 55% of total Elidel use and 39% of Protopic[®] use (Table 5). “Atopic Dermatitis + Related conditions” (ICD-9 691.8) was the second most common indication for all age groups accounting for 24% of the total Elidel use and 29% of the Protopic[®] use.

DISCUSSION

IMS Health, NPA *Plus*[™] data provide an estimate of the total number of prescriptions dispensed in the U.S. However, NPA *Plus*[™] does not include demographic information for each prescription, such as age and gender. The inclusion of prescriber specialty data in this report does not include the mail order and long-term care channels, which in this analysis comprised only 4.5% of prescriptions dispensed during June 2003 – May 2004².

Sales of Elidel and Protopic were predominately through the retail channels (mail order, independent, food store, chain, and long term care pharmacies) which accounted for 95-95% of total sales volume (tubes or eaches of product)³. Therefore, use in the inpatient setting was not analyzed.

Caremark Dimension Rx[™] data cannot be projected to make national level estimates of use, but its large sample size can be helpful for replicating findings in IMS Health’s NDTI[™], where sample sizes are often small. Although the data from Caremark may not be nationally representative, they provide a useful description of prescription drug use in the U.S. for a large proportion of the population with prescription drug coverage. Estimates of the number of prescriptions dispensed nationally to pediatric populations based on the proportion dispensed to pediatric patients in the Caremark system are dependent upon the assumption that these patterns are similar across populations with and without prescription drug coverage. The accuracy of this assumption is not known at this time. In addition, reliable information for patients less than the age of 1 year is not available from this data source.

IMS Health, NDTI[™] data provide estimates of patient demographics and indications for use of medicinal products in the U.S. Due to its sampling and data collection methodologies, the small sample size can make these data unstable, especially in populations where use is low. The NDTI[™] intended duration of therapy measure records the physician’s intent at the time of the patient’s office visit and neither reflects what the patient received, nor how long the patient used the product.

CONCLUSIONS

During June 2003 – May 2004, there were a total of 3.9 million Elidel[®] prescriptions (2.81 million new, 1.04 million refills) and 1.0 million total Protopic[®] prescriptions dispensed (707,000 new, 332,000 refills). Total prescriptions dispensed increased 47% for Elidel[®] and 16% for Protopic[®] as compared to the previous year. Pediatricians were the most frequent prescribers of Elidel[®] for the period June 2003 – May 2004 accounting for 31% (1.1 million prescriptions) of prescribing, followed by dermatologists accounting for 23% (843,000 prescriptions). Protopic[®] was most commonly prescribed by dermatologists who accounted for 54% of prescribing (529,000 prescriptions) and pediatricians with 17% (163,000 prescriptions).

Participants ages 1-16 years accounted for 41% of Elidel[®] Claims and 35% of Protopic[®] Claims represented in Caremark’s Dimension Rx system during June 2003 – May 2004. Among all pediatric participants (1-16 years) prescribed these products in the year June 2003 – May 2004, claims for Elidel[®] in participants age 1-2 years accounted for 12.7%, participants ages 3-16 years accounted for 28.7%, and participants ages 17+ years accounted for 58.6%. For Protopic[®], participants age 1-2 years accounted for 8.0% of claims, participants age 3-16 years accounted for 26.6% of claims and adults accounted for 65.4% of claims. The proportion of pediatric prescriptions dispensed was relatively stable throughout the 3 years analyzed; however, the increasing total prescription volume appears to be resulting in increasing numbers of prescriptions to pediatric participants.

² Percent difference derived from total sales (table 1) and total prescriptions by physician specialty (table 2)

³ IMS Health, National sales Perspectives, Combined, Data Extracted 6/2004 File: 0406tc13.dvr, Data not shown. An each is defined as an individual dispensing package labeled for sale, in this case, tubes.

When we applied the proportions of all pediatric Elidel[®] and Protopic[®] prescriptions from AdvancePCS to IMS Health, NPA Plus[™] data to approximate the number of prescriptions dispensed nationwide to children, it was estimated that approximately 1.6 million Elidel[®] prescriptions and 359,000 Protopic[®] prescriptions were dispensed persons ages 1-16 years in the U.S. during June 2003 – May 2004.

The most common diagnoses for Elidel[®] and Protopic[®] for patients seen by office based physicians during the period June 2003 – May 2004 was “dermatitis with eczema, unspecified cause” (ICD-9 692.9) which accounted for 55% of total Elidel[®] use and 39% of Protopic[®] use. “Atopic Dermatitis + Related conditions” (ICD-9 691.8) was the second most common indication for all age groups accounting for 24% of the total Elidel[®] use and 29% of the Protopic[®] use.

ACCOMPANYING TABLES AND FIGURES

Table 1: Number of New and Refill Prescriptions Dispensed in Retail Pharmacy Settings in the US for Elidel and Protopic, June 1, 2001 through May 31, 2004 (IMS Health, National Prescription Audit Plus™ - Data Extracted June 2004)

Copyright IMS HEALTH													
Projected Number of Total, New, and Refill Prescriptions Dispensed													
by Retail Pharmacies													
(Chain, Independent, Food Stores, Long Term Care, and Mail Order) in the US													
for Product Elidel, Protopic													
Stratified by product, strength													
Distributed by Moving Annual Total June 2000 - May 2004 (no data for 2000)													
(in thousands; ADD THREE 0's TO EACH FIGURE)													
Copyright IMS HEALTH													
		June 2000 - May 2001 Estimated Prescriptions			June 2001 - May 2002 Estimated Prescriptions			June 2002 - May 2003 Estimated Prescriptions			June 2003 - May 2004 Estimated Prescriptions		
		Total	New	Refill	Total	New	Refill	Total	New	Refill	Total	New	Refill
TOTAL		164	135	29	1,169	852	317	3,517	2,613	904	4,891	3,518	1,373
ELIDEL					303	269	34	2,625	2,020	605	3,852	2,811	1,041
	1%				303	269	34	2,625	2,020	605	3,852	2,811	1,041
PROTOPIC		164	135	29	866	583	283	892	593	299	1,039	707	332
	0.1%	109	89	20	560	367	193	635	418	217	774	520	254
	0.03%	55	46	9	306	216	90	257	175	82	263	186	77
SOURCE: IMS HEALTH; National Prescription Audit Plus™, On-line													
Notes: Run Date: 06/30/2004 Source File: 0406tci.dvr													
* a blank means no data; a zero means less than 500 total projected													
¹ Total includes New and Refill prescriptions													

Table 2: Top 10 Physician Specialties Prescribing Elidel and Protopic June 1, 2000 through May 31, 2004 (IMS Health National Prescription Audit Plus™ - Data Extracted June 2004)

Copyright IMS HEALTH					
Projected Number of Total ¹ Prescriptions Dispensed					
by Retail Pharmacies					
(Chain, Independent, Food Stores) in the US					
for Product Elidel, Protopic					
Stratified by product, provider speciality					
Distributed by Moving Annual Total June 2000 - May 2004 (no data for 2000)					
(in thousands; ADD THREE 0's TO EACH FIGURE)					
Copyright IMS HEALTH					
		June 2000 - May 2001	June 2001 - May 2002	June 2002 - May 2003	June 2003 - May 2004
TOTAL			1,125	3,381	4,672
ELIDEL	0202 NVR		294	2,531	3,689
	PEDIATRICS		57 (19.4%)	707 (27.9%)	1,143 (31.0%)
	DERMATOLOGY		125 (42.5%)	731 (28.9%)	843 (22.9%)
	FAMILY PRACTICE		24 (8.2%)	292 (11.5%)	465 (12.6%)
	OSTEOPATHIC MEDICINE		23 (7.8%)	189 (7.5%)	272 (7.4%)
	INTERNAL MEDICINE		16 (5.4%)	162 (6.4%)	268 (7.3%)
	UNKNOWN		12 (4.1%)	117 (4.6%)	169 (4.6%)
	ALLERGY		12 (4.1%)	84 (3.3%)	101 (2.7%)
	NURSE PRACTITIONER		03 (1.0%)	36 (1.4%)	82 (2.2%)
	PHYSICIAN ASSISTANT		03 (1.0%)	32 (1.3%)	67 (1.8%)
	GENERAL PRACTICE		03 (1.0%)	33 (1.3%)	45 (1.2%)
	TOTAL OTHERS		16 (5.4%)	149 (5.9%)	234 (6.3%)
PROTOPIC	0101 FUW	158	831	850	983
	DERMATOLOGY	109 (69.0%)	493 (59.3%)	470 (55.3%)	529 (53.8%)
	PEDIATRICS	10 (6.3%)	106 (12.8%)	126 (14.8%)	163 (16.6%)
	UNKNOWN	09 (5.7%)	56 (6.7%)	65 (7.6%)	72 (7.3%)
	OSTEOPATHIC MEDICINE	07 (4.4%)	34 (4.1%)	35 (4.1%)	40 (4.1%)
	ALLERGY	08 (5.1%)	45 (5.4%)	37 (4.4%)	36 (3.7%)
	FAMILY PRACTICE	03 (1.9%)	21 (2.5%)	27 (3.2%)	32 (3.3%)
	INTERNAL MEDICINE	03 (1.9%)	20 (2.4%)	25 (2.9%)	29 (3.0%)
	PHYSICIAN ASSISTANT	01 (0.6%)	07 (0.8%)	09 (1.1%)	15 (1.5%)
	NURSE PRACTITIONER	01 (0.6%)	05 (0.6%)	07 (0.8%)	12 (1.2%)
	OBSTETRICS/GYNECOLOGY	01 (0.6%)	04 (0.5%)	05 (0.6%)	06 (0.6%)
	TOTAL OTHERS	07 (4.4%)	40 (4.8%)	44 (5.2%)	49 (5.0%)
SOURCE: IMS HEALTH; National Prescription Audit Plus™, On-line					
Notes: Run Date: 06/30/2004 Source File: 0406tci2.dvr					
* a blank means no data; a zero means less than 500 total projected					
¹ Total includes New and Refill prescriptions					
**NOTE: DATA NOT TO BE SHARED OUTSIDE OF FDA OR WITH non-FDA STAFF					
WITHOUT PRIOR CLEARANCE BY IMS HEALTH.					
Clearance must be requested from IMS HEALTH through the FDA Office of Drug Safety					

Table 3: Total Prescription Claims Paid for Elidel and Protopic by Age Group in a Large U.S. Pharmacy Benefit Manager, June 1, 2001 through May 31, 2004 (Caremark, Dimension Rx™ – Data Extracted July 2004)

Copyright ADVANCE PCS Dimension Rx				
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WITHOUT PRIOR CLEARANCE BY ADVANCEPCS.				
Clearance must be requested from AdvancePCS through the FDA Office of Drug Safety*				
Total number of prescription claims				
Dispensed by Retail Pharmacies in the Advance PCS™ pharmacy claims processing network ² for Elidel and Protopic				
Stratified by Drug Label Name, Age Band				
Time Period 6/1/2001 and 5/31/2004				
Counts are ACTUAL. DO NOT ADD ANY ZEROS. Data are NOT projected to represent a national estimate.				
Drug Label Name	Jun 2001 - May 2002	Jun 2002 - May 2003	Jun 2003 - May 2004	
Total Elidel 1% Cream	34,697	302,026	450,606	
Age 1-2	3,337 (9.6%)	36,636 (12.1%)	57,418 (12.7%)	
Age 3-16	8,679 (25.0%)	85,693 (28.4%)	129,281 (28.7%)	
Age 17+	22,681 (65.4%)	179,697 (59.5%)	263,907 (58.6%)	
Total Protopic 0.03% Ointmen	36,268	30,755	29,936	
Age 1-2	7,857 (21.7%)	7,072 (23.0%)	6,818 (22.8%)	
Age 3-16	17,865 (49.3%)	15,104 (49.1%)	14,348 (47.9%)	
Age 17+	10,546 (29.1%)	8,579 (27.9%)	8,770 (29.3%)	
Total Protopic 0.1% Ointment	80,627	93,705	112,873	
Age 1-2	1,826 (2.3%)	3,209 (3.4%)	4,648 (4.1%)	
Age 3-16	13,600 (16.9%)	18,144 (19.4%)	23,634 (20.9%)	
Age 17+	65,201 (80.9%)	72,352 (77.2%)	84,591 (74.9%)	
Total Protopic Ointment	116,895	124,460	142,809	
Age 1-2	9,683 (8.3%)	10,281 (8.3%)	11,466 (8.0%)	
Age 3-16	31,465 (26.9%)	33,248 (26.7%)	37,982 (26.6%)	
Age 17+	75,747 (64.8%)	80,931 (65.0%)	93,361 (65.4%)	
SOURCE: AdvancePCS™ Dimension Rx				
Notes: Run Date 07/01/2004				
* A blank cell indicates that "zero" claims were processed for that drug product.				
¹ Total prescriptions are all new prescriptions plus all subsequent refills				
² AdvancePCS™ is a pharmacy benefits manager in the U.S. that processes 450 million third-party mail order Rx claims, claims annually and covers 75 million Patient Lives throughout the U.S.				
Data are NOT projected to represent a national total, do not include non-AdvancePCS reimbursed Rxs or and do not include prescriptions where the patient paid cash at the pharmacy without subsequent third-party insurance reimbursement.				
*NOTE: NOT TO BE SHARED OUTSIDE OF FDA OR WITH NON-FDA STAFF				
WITHOUT PRIOR CLEARANCE BY ADVANCEPCS.				
Clearance must be requested from AdvancePCS through the FDA Office of Drug Safety*				

**Table 4: Intended Duration of Elidel and Protopic Prescriptions Written by Office Based Physicians during June 2001 – May 2004
(IMS Health National Disease and Therapeutic Index™, extracted 7/2004)**

Copyright IMS HEALTH			
Projected Number of Total Drug Appearances 1, 2			
During Patient Visits 3 in Office-Based Practices in the Continental US for Elidel, Protopic			
Stratified by Age band (grouped 0-2, 3-16, 17+), Days of Therapy (grouped 1-30, 31-60, over 60)			
Distributed by Moving Annual Total June 2001 - May 2004 (all values are absolute numbers, do not add zeros)			
	June 2001 - May 2002	June 2002 - May 2003	June 2003 - May 2004
ELIDEL	203,283	1,123,666	1,344,387
Age 00-2	15,563 (7.7%)	189,543 (16.9%)	268,460 (20.0%)
1-30 days of therapy	8,139 (52.3%)	163,790 (86.4%)	255,600 (95.2%)
31-60 Days of Therapy	---	23,983 (12.7%)	6,390 (2.4%)
Over 60 days of therapy	7,424 (47.7%)	1,770 (0.9%)	6,470 (2.4%)
Age 03-16	89,411 (44.0%)	412,904 (36.7%)	535,522 (39.8%)
1-30 days of therapy	69,383 (77.6%)	352,226 (85.3%)	487,949 (91.1%)
31-60 Days of Therapy	15,977 (17.9%)	43,869 (10.6%)	21,232 (4.0%)
Over 60 days of therapy	4,051 (4.5%)	16,809 (4.1%)	26,341 (4.9%)
Age 17+	98,309 (48.4%)	521,219 (46.4%)	540,405 (40.2%)
1-30 days of therapy	80,545 (81.9%)	428,420 (82.2%)	427,092 (79.0%)
31-60 Days of Therapy	12,562 (12.8%)	59,079 (11.3%)	63,461 (11.7%)
Over 60 days of therapy	5,202 (5.3%)	33,720 (6.5%)	49,852 (9.2%)
PROTOPIC	358,398	311,010	386,525
Age 00-2	20,684 (5.8%)	22,842 (7.3%)	45,310 (11.7%)
1-30 days of therapy	17,327 (83.8%)	16,074 (70.4%)	33,838 (74.7%)
31-60 Days of Therapy	3,357 (16.2%)	2,450 (10.7%)	11,472 (25.3%)
Over 60 days of therapy	---	4,318 (18.9%)	---
Age 03-16	146,360 (40.8%)	115,031 (37.0%)	125,379 (32.4%)
1-30 days of therapy	106,819 (73.0%)	71,877 (62.5%)	81,053 (64.6%)
31-60 Days of Therapy	21,434 (14.6%)	15,028 (13.1%)	18,387 (14.7%)
Over 60 days of therapy	18,107 (12.4%)	28,126 (24.5%)	25,939 (20.7%)
Age 17+	191,354 (53.4%)	173,137 (55.7%)	215,836 (55.8%)
1-30 days of therapy	116,228 (60.7%)	124,882 (72.1%)	116,890 (54.2%)
31-60 Days of Therapy	47,616 (24.9%)	31,802 (18.4%)	50,428 (23.4%)
Over 60 days of therapy	27,510 (14.4%)	16,453 (9.5%)	48,518 (22.5%)
SOURCE: IMS HEALTH; National Disease and Therapeutic Index™, CD-ROM June 2001 - May 2004			
NOTES: NDTI bull 06-30-2004 D040389 Elidel-Protopic days of therapy.dvw extracted 7/2004			
* --- means no data; a zero means less than 500 total projected			
¹ A drug appearance roughly translates to a mention of a drug during a patient visit (unduplicated by number of diagnoses for which it may be used);			
² A drug appearance can result from a prescription written, a refill authorized, a sample given, the drug administered in the office, a prescription issued by a dispensing physician, hospital order written, recommendation given to purchase OTC product, patient on drug and no action taken, or a combination of these;			
³ Every patient contact reported is considered a patient visit, regardless of location			
**NOTE: DATA NOT TO BE SHARED OUTSIDE OF FDA OR WITH non-FDA STAFF WITHOUT PRIOR CLEARANCE Clearance must be requested from IMS HEALTH through the FDA Office of Drug Safety			

Table 5: Elidel and Protopic Indications for Use During Office Visits by Diagnoses and Age Group, June 1, 2001 – May 30, 2004 (IMS Health, National Disease and Therapeutic Index™ - Data Extracted July 2004)

Copyright IMS Health			
Projected Total Number of Drug Uses ¹			
During Patient Visits ² in Office-Based Practices in the Continental US			
For product Elidel and Protopic			
Stratified by Custom age band (0-2, 3-16, 17+), Diag 4			
For moving annual total June 2001 - May 2004			
(in thousands; ADD THREE 0's TO EACH FIGURE)			
(percents are absolute numbers)			
	June 2001 -May 2002	June 2002 -May 2003	June 2003 -May 2004
ELIDEL NVR 02-02	312 (33.7%)	1,950 (77.6%)	2,509 (78.1%)
Age 00-2	29 (9.3%)	342 (17.6%)	510 (20.3%)
6929 DERM+ECZ UNSPEC CAUSE	16 (55.9%)	169 (49.5%)	267 (52.5%)
6918 ATOP DERM+RELAT COND OTH	08 (25.9%)	132 (38.4%)	184 (36.1%)
7821 RASH+OTH NONSP SKIN ERUP	05 (18.2%)	30 (8.7%)	42 (8.3%)
Total Others (6)	---	12 (3.4%)	16 (3.1%)
Age 03-16	113 (36.1%)	709 (36.4%)	874 (34.8%)
6929 DERM+ECZ UNSPEC CAUSE	62 (55.0%)	389 (54.8%)	547 (62.6%)
6918 ATOP DERM+RELAT COND OTH	41 (36.7%)	222 (31.3%)	240 (27.5%)
7821 RASH+OTH NONSP SKIN ERUP	05 (4.7%)	29 (4.1%)	31 (3.5%)
Total Others (25)	04 (3.6%)	69 (9.7%)	56 (6.4%)
Age 17+	152 (48.7%)	819 (42.0%)	943 (37.6%)
6929 DERM+ECZ UNSPEC CAUSE	76 (49.8%)	381 (46.5%)	462 (49.0%)
6918 ATOP DERM+RELAT COND OTH	23 (15.4%)	145 (17.7%)	151 (16.0%)
6900 ERYTHEMATOSQUAMOUS DERMA	04 (2.8%)	40 (4.9%)	57 (6.0%)
Total Others (60)	49 (32.0%)	252 (30.8%)	273 (28.9%)
All Patients	312 (100.0%)	1,950 (100.0%)	2,509 (100.0%)
6929 DERM+ECZ UNSPEC CAUSE	163 (52.0%)	992 (50.9%)	1,385 (55.2%)
6918 ATOP DERM+RELAT COND OTH	77 (24.7%)	517 (26.5%)	610 (24.3%)
7821 RASH+OTH NONSP SKIN ERUP	15 (4.9%)	76 (3.9%)	104 (4.2%)
Total Others (72)	57 (18.3%)	365 (18.7%)	410 (16.3%)
PROTOPIC FUW 01-01	615 (66.3%)	562 (22.4%)	706 (21.9%)
Age 00-2	59 (9.7%)	38 (6.7%)	90 (12.8%)
6918 ATOP DERM+RELAT COND OTH	28 (47.6%)	20 (54.2%)	60 (66.5%)
6929 DERM+ECZ UNSPEC CAUSE	20 (33.6%)	14 (36.2%)	24 (26.7%)
3730 BLEPHARITIS	---	---	05 (5.6%)
Total Others (3)	11 (18.7%)	04 (9.6%)	01 (1.2%)
Age 03-16	183 (29.8%)	187 (33.3%)	221 (31.3%)
6929 DERM+ECZ UNSPEC CAUSE	40 (21.5%)	63 (33.8%)	108 (48.8%)
6918 ATOP DERM+RELAT COND OTH	112 (61.3%)	97 (52.1%)	86 (39.0%)
7090 DYSCHROMIA	03 (1.4%)	12 (6.4%)	13 (5.9%)
Total Others (15)	29 (15.7%)	14 (7.7%)	14 (6.3%)
Age 17+	330 (53.7%)	324 (57.6%)	356 (50.5%)
6929 DERM+ECZ UNSPEC CAUSE	125 (37.8%)	129 (39.9%)	125 (35.1%)
6918 ATOP DERM+RELAT COND OTH	88 (26.8%)	49 (15.2%)	46 (12.8%)
7090 DYSCHROMIA	03 (1.0%)	19 (5.7%)	33 (9.1%)
Total Others (54)	114 (34.5%)	127 (39.1%)	153 (43.0%)
All Patients	615 (100.0%)	562 (100.0%)	706 (100.0%)
6929 DERM+ECZ UNSPEC CAUSE	203 (33.0%)	210 (37.3%)	275 (39.0%)
6918 ATOP DERM+RELAT COND OTH	234 (38.1%)	171 (30.4%)	204 (28.8%)
7090 DYSCHROMIA	09 (1.4%)	31 (5.4%)	45 (6.4%)
Total Others (61)	169 (27.5%)	151 (26.9%)	182 (25.8%)
SOURCE: IMS HEALTH; National Disease and Therapeutic Index, CD-ROM June 2001 - May 2004			
NOTES: NDTI bull 06-30-2004 D040389 Elidel-Protopic indications.dvw Extracted 7/2004			
* --- means no data; a zero means less than 500 total projected;			
¹ A drug use is the mention of a drug in association with a diagnosis during a patient visit. The drug uses are duplicated by the number of diagnoses for which the drug is mentioned.			
² Every patient contact reported is considered a patient visit, regardless of location			
**NOTE: DATA NOT TO BE SHARED OUTSIDE OF FDA OR WITH non-FDA STAFF WITHOUT PRIOR CLEARANCE BY IMS HEALTH.			
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