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Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology**

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To: Russell Katz, MD, Director
Division of Neurology Products

Through: Todd Bridges, RPh, Team Leader
Carol Holquist, RPh, Director
Division of Medication Error Prevention and Analysis

From: Zachary Oleszczuk, PharmD, Safety Evaluator
Division of Medication Error Prevention

Subject: Medication Error Postmarketing Safety Review

Drug Name(s): Lamictal (Lamotrigine) Tablets
Application Type/Number: 25 mg, 100 mg, 150 mg, and 200 mg
NDA 20-241

Lamictal CD (Lamotrigine) Chewable Dispersible Tablets
2 mg, 5 mg, and 25 mg
NDA 20-764

Applicant: GlaxoSmithKline

OSE RCM #: 2007-388 and 2007-350

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EXECUTIVE SUMMARY

The pediatric exclusivity has not had an impact on the medication errors reported to date with Lamictal. In total, DMEPA analyzed one hundred thirty four (n=134) cases of medication errors involving Lamictal. The largest number of cases reported are the result of proprietary name confusion between Lamictal and Lamisil tablets. Name confusion between Lamictal and Lamisil has been the focus of a communication plan submitted by GlaxoSmithKline as an alternative to the Agency's request to change the proprietary name of Lamictal. Despite the efforts of the communication plan medication errors involving Lamictal and Lamisil continue to be reported. Additionally, confusion with other drug products, which do not have a specific communication plans, have resulted in outcomes from no adverse event to hospitalizations. Similar efforts to the Lamictal and Lamisil confusion should be made to raise awareness for potential confusion of Lamictal and these names. Furthermore, the Division of Medication Error Prevention and Analysis notes that the established name lamotrigine may also be vulnerable to name confusion as three products lamivudine, levothyroxine, and levetiracetam have been reported as being confused with lamotrigine. DMEAP will need to strategize with the review Division on how best to minimize confusion with these other products. See section 5 for our recommendations.

1 BACKGROUND

1.1 INTRODUCTION

This postmarketing safety review of medication errors is written in response to a request from the Office of Pediatric Therapeutics and the Office of Pediatric and Maternal Health Staff to evaluate medication errors of name confusion involving Lamictal. This summary was requested in preparation for the November 17, 2008 Advisory Committee scheduled under the Best Pharmaceuticals for Children Act.

1.2 REGULATORY HISTORY

Lamictal (lamotrigine) tablets was approved on December 27, 1994 for NDA 20-241. A subsequent formulation Lamictal chewable dispersible tablet, Lamictal CD (lamotrigine chewable dispersible) tablets (NDA 20-764) was approved on August 24, 1998 (see Appendix A). Pediatric Exclusivity was granted to Lamictal tablets and Lamictal CD tablets on February 14, 2007.

Lamisil (terbinafine hydrochloride) is an allylamine antifungal. The currently marketed Lamisil products with their status, dosage form, strength, indications, and usual dosages can be found in Appendix B.

Following the approval of Lamisil 250 mg tablets in 1996 medication errors began to be reported because of name confusion between Lamisil and Lamictal. A "Dear Pharmacist" letter was distributed by GlaxoSmithKline in June 1998 to highlight the name confusion.

Reports of name confusion between Lamictal and Lamisil continued into 2000 and thus efforts were made to reduce confusion between Lamictal and Lamisil. Originally, the sponsor was requested to consider revision of the proprietary name. The sponsor submitted justification to retain the name and these other provisions for proprietary name confusion were implemented. GlaxoSmithKline distributed “Dear Healthcare Professional” letters in June 2000, July 2000, and August 2000. Additionally, a formal communication plan was developed by GlaxoSmithKline in 2001, as an alternative to the Agency suggesting that GlaxoSmithKline change the proprietary name of Lamictal, that included activities planned to promote awareness of name confusion to pharmacists, physicians and patients. Some of the planned actions include annual communication to healthcare professionals, computer flagging programs in chain pharmacies, error monitoring, shelf shouters, promotion of name confusion at pharmacy meetings, placing error messages in promotional materials, placing error messages in advertisements in medical journals, promotion of name confusion at physician conventions, placing an error message on the company website and providing brochures for epilepsy and bipolar disorders for patients.

1.3 PRODUCT INFORMATION

Lamictal (lamotrigine) tablets are an antiepileptic drug used in the treatment of epilepsy and bipolar disorder and is manufactured by GlaxoSmithKline. Lamictal is supplied as 25 mg, 100 mg, 150 mg, and 200 mg tablets and 2 mg, 5 mg, and 25 mg chewable dispersible tablets. Lamictal requires that a patient be titrated over several weeks. The dose and speed at which a patient is titrated is dependent upon which other medication the patient is taking and which indication is being treated. Once a patient has been titrated a usual adult dose can range from 100 mg orally once per day to 500 mg orally in two divided doses.

2 METHODS AND MATERIALS

2.1 ADVERSE EVENT REPORTING SYSTEM (AERS) SELECTION OF CASES AND PERIODIC REPORTS SUBMITTED BY GLAXOSMITHKLINE

The Division of Medication Error Prevention and Analysis searched the FDA Adverse Event Reporting System (AERS) database on June 25, 2008 to identify post-marketing cases involving name confusion associated with Lamictal. The MedDRA Higher Level Terms (HLT) “Maladministration”, and “Medication Errors NEC”; Preferred Terms “Overdose”, “Accidental overdose”, “Accidental exposure”, “Transmission of drug via semen”, “Accidental drug intake by child”, “Drug exposure before pregnancy”, and “Pharmaceutical complaint”; and tradename “Lamictal”, active ingredient “Lamotrigine”, and verbatim “Lam%” and was used as search criteria. Due to the number of reports the pregnancy related categories were removed from the search of Lamictal.

A separate AERS search was also conducted on June 25, 2008 to identify post-marketing cases involving name confusion associated with Lamisil. The MedDRA Higher Level Terms (HLT) “Maladministration”, and “Medication Errors NEC”; Preferred Terms “Overdose”, “Accidental overdose”, “Accidental exposure”, “Drug exposure via breast milk”, “Drug exposure during pregnancy”, “Transmission of drug via semen”, “Unspecified agent exposure during pregnancy”, “Accidental drug intake by child”, “Drug exposure before pregnancy”, and “Pharmaceutical complaint”; and tradename “Lamisil”, active ingredient “Terbinafine”, and verbatim “Lam%” and “Terbin%” were used as search criteria. The Lamisil cases were manually searched for errors only related to Lamictal and Lamisil name confusion. Other medication errors for Lamisil were excluded from this review and are discussed in OSE review #2008-701.

Duplicate cases and those not involving a medication error were excluded from evaluation.

Additionally, the Division of Medication Error Prevention and Analysis evaluated periodic reports submitted by GlaxoSmithKline since the 4th quarter of 2003. These periodic reports were cross referenced to AERS cases. All duplicate cases were eliminated.

2.2 MEDMARX DATABASE***

The Division of Medication Error Prevention and Analysis requested a search of the USP MEDMARX*** database to identify reports of medication errors involving name confusion associated with Lamictal.

2.3 INSTITUTE OF SAFE MEDICATION PRACTICE DATABASES***

Upon the Division of Medication Error Prevention and Analysis's request, the Institute for Safe Medication Practice (ISMP) searched their database for medication errors involving name confusion with Lamictal.

3 RESULTS

3.1 ADVERSE EVENT REPORTING SYSTEM (AERS) AND PERIODIC REPORTS SUBMITTED BY GLAXOSMITHKLINE

A total of 134 cases were identified following the elimination of duplicate cases (see Appendix E). The medication errors cases describe proprietary name confusion between Lamictal and other drug products. In total, fourteen proprietary names have been reported in AERS as being confused with Lamictal. The largest number of which involve Lamictal and Lamisil.

3.2 LAMICTAL NAME CONFUSION WITH NAMES OTHER THAN LAMISIL (N=55)

Fifty-five cases described proprietary name confusion between Lamictal and 14 various products other than Lamisil. Six (n=6) cases were foreign and forty nine (n=49) were domestic. Of the domestic cases the largest number occurred with Lomotil, Labetalol, Lamivudine, Topamax, and Trileptal. The remaining names only had one reported occurrence of error.

Causality reported with these errors were similar names, close proximity on the pharmacy shelf, work environment distracted the person involved in the error, stocking error or an illegible prescription. See Table 1 for a breakdown of these cases. The outcomes were dependent on which drug Lamictal was confused with and whether or not the error was caught prior to administration. The outcomes ranged from no adverse event to hospitalization.

Table 1:

Proprietary Names confused with Lamictal that were Reported More Than Once						
Drug Name	Location	Years Errors Occurred	Outcomes	Intended Medication Received Medication	Ages	Causality
Trileptal (oxcarbazepine) n=1	1 Domestic	2000	Hospitalization	Intended: Lamictal Received: Trileptal	Unknown	Stress (busy time at the pharmacy)
Topamax (topiramate) n=3	3 Domestic	2002	Minor Adverse Events	Intended: Topamax Received: Lamictal	Unknown	None Reported
		2007	Minor Adverse Events	Intended: Lamictal Received: Topamax	15 years of age	None Reported
		Unknown	Minor Adverse Events	Intended: Topamax Received: Lamictal	Unknown	None Reported
Epivir (Lamivudine) n=7	7 Domestic	1996	Hospitalization	Intended: Lamivudine Received: Lamictal	45 years of age	Shelf Proximity
		1997	Unknown	Intended: Lamivudine Received: Lamictal	Unknown	None Reported
		1997	Hospitalization	Intended: Lamivudine Received: Lamictal	39 years of age	None Reported
		2000	Unknown	Intended: Lamivudine Received: Lamictal	Unknown	Misspelled Prescription
		2002	Seizure	Intended: Lamictal Received: Lamivudine	10 years of age	None Reported
		2002	Minor Adverse Events	Intended: Lamivudine Received: Lamictal	24 years of age	None Reported
		2005	Minor Adverse Events	Intended: Lamivudine Received: Lamictal	Unknown	None Reported

Table 1 (continued):

Proprietary Names confused with Lamictal that were Reported More Than Once (continued)						
Drug Name	Location	Years Errors Occurred	Outcomes	Intended Medication Received Medication	Ages	Causality
Normodyne (labetalol) n=11	11 Domestic	1999	Patient did not receive any doses	Intended: Labetalol Received: Lamictal	Unknown	Stocking Error
		2002	Hospitalization	Intended: Lamictal Received: Labetalol	15 years of age	None Reported
		2002	Unknown	Intended: Lamictal Received: Labetalol	67 years of age	None Reported
		2002	Monitoring	Intended: Lamictal Received: Labetalol	Unknown	Stocking Error
		2005	Unknown	Intended: Labetalol Received: Lamictal	30 years of age	Similar Names
		2007	Patient did not receive any doses	Intended: Labetalol Received: Lamictal	Unknown	Stress (busy workload)
		2008	Patient did not receive any doses	Intended: Labetalol Received: Lamictal	Unknown	Stocking Error
		Unknown	Unknown	Intended: Labetalol Received: Lamictal	30 years of age	None Reported
		Unknown	Minor Adverse Events	Intended: Labetalol Received: Lamictal	55 years of age	None Reported
		Unknown	Patient did not receive any doses	Intended: Labetalol Received: Lamictal	Unknown	None Reported
		Unknown	Rash	Intended: Labetalol Received: Lamictal	Unknown	None Reported

Table 1 (continued):

Proprietary Names confused with Lamictal that were Reported More Than Once (continued)						
Drug Name	Location	Years Errors Occurred	Outcomes	Intended Medication Received Medication	Ages	Causality
Lomotil (diphenoxylate hydrochloride with atropine sulfate) n=11	11 Domestic	1995	Patient did not receive any doses	Intended: Lamictal Received: Lomotil	Unknown	None Reported
		1997	Patient did not receive any doses	Intended: Lomotil Received: Lamictal	Unknown	None Reported
		1998	Patient did not receive any doses	Intended: Lamictal Received: Lomotil	Unknown	None Reported
		2000	Hospitalization	Intended: Lamictal Received: Lomotil	59 years of age	None Reported
		2004	Minor Adverse Events	Intended: Lomotil Received: Lamictal	76 years of age	Transcription Error
		2005	Minor Adverse Events	Intended: Lomotil Received: Lamictal	76 years of age	None Reported
		2006	Patient did not receive any doses	Intended: Lomotil Received: Lamictal	Unknown	Similar Names
		Unknown	Patient did not receive any doses	Intended: Lamictal Received: Lomotil	10 years of age	None Reported
		Unknown	Patient did not receive any doses	Intended: Lomotil Received: Lamictal	Unknown	Illegible Prescription
		Unknown	Patient did not receive any doses	Intended: Lomotil Received: Lamictal	Unknown	Illegible Prescription
Unknown	Unknown	Intended: Lamictal Received: Lomotil	Unknown	Similar Names		

Table 1 (continued):

Proprietary Names confused with Lamictal that were Reported More Than Once (continued)						
Drug Name	Location	Years Errors Occurred	Outcomes	Intended Medication Received Medication	Ages	Causality
Unknown n=8	8 Domestic	2003	Seizure	Intended: Lamictal Received: Unknown	1 year of age	None Reported
		2005	Minor Adverse Events	Intended: Unknown Received: Lamictal	54 years of age	None Reported
		2006	Hospitalization	Intended: Lamictal Received: Unknown	Unknown	None Reported
		2007	Intervention	Intended: Unknown Received: Lamictal	Unknown	None Reported
		Unknown	Minor Adverse Events	Intended: Lamictal Received: Unknown	58 years of age	None Reported
		Unknown	Monitored	Intended: Unknown Received: Lamictal	Unknown	None Reported
		Unknown	Intervention	Intended: Unknown Received: Lamictal	Unknown	None Reported
		Unknown	Hospitalization	Intended: Unknown Received: Unknown	Unknown	None Reported

3.3 LAMICTAL AND LAMISIL PROPRIETARY NAME CONFUSION (N=79)

Seventy nine cases of Lamictal and Lamisil name confusion were reported between 1996 through 2008. See Appendix C for a breakdown of the case by year. There was a range of outcomes and reported causality (See Section 3.2.2) When an age was reported, the majority of cases occurred in patients greater than 17 years of age. Only 4 errors occurred (1 foreign and 3 Domestic) in patients under the age of 16. Because the review division was interested in errors involving pediatric patients these cases are described in Table 2 page 10.

Table 2:

Lamictal Name Confusion with Lamisil in Patients less than or equal to 16 Years of age (n=4)						
Age Range	Actual age	Medication Ordered Medication Received	Years in which Errors reported	Outcome	Causality	Location
0 years to 1 year	1 year of age	Ordered: Lamictal Received: Lamisil	2001	Intervention required Inflamed eye and an abnormal ECG	None Reported	Foreign
2 years to 5 years	NA	NA	NA	NA	NA	NA
6 years to 11 years	8 years of age	Ordered: Lamictal Received: Lamisil	1998	None reported	None Reported	Domestic
	9 years of age	Ordered: Lamisil Received: Lamictal	2001	Hospitalization	Similar Names	Domestic
12 years to 16 years	16 years of age	Ordered: Lamictal Received: Lamisil	1997	Increase seizures	None Reported	Domestic

3.2.1 Reported Outcomes and Related Causality of Lamictal and Lamisil Confusion

Seventy five (n=75) of the 79 cases of reported confusion occurred in patients 17 years of age and older. Sixty (n=60) of the cases were domestic, fourteen (n=14) were foreign, and one (n=1) case was from an unknown origin. All seventy five of the cases involved the oral tablet formulation of Lamictal and Lamisil. When causality was reported the confusion was attributed to similar names, close proximity on the pharmacy shelf, incorrect selection from a computer screen, illegible prescription or the work environment distracted the person involved in the error (see table 3).

Table 3:**Name Confusion between Lamisil and Lamictal Identified in AERS for Patient 17 years of Age and Older or Unknown**

Outcome	Location	Year	Medication Ordered	Medication Received	Causality
Death (n=5)	Foreign	2004	Lamisil	Lamictal	Computer Selection Error
	Foreign	2004	Lamisil	Lamictal	Computer Selection Error
	Foreign	2005	Lamisil	Lamictal	None Reported
	Domestic	2005	Lamictal	Lamisil	None Reported
	Domestic	2007	Lamictal	Lamisil	None Reported
Initial or Prolonged Hospitalization (n=6)	Domestic	1998	Lamisil	Lamictal	None Reported
	Domestic	2000	Lamictal	Lamisil	None Reported
	Foreign	2004	Lamisil	Lamictal	None Reported
	Domestic	2006	Lamisil	Lamictal	None Reported
	Domestic	2006	Lamisil	Lamictal	None Reported
	Foreign	2007	Lamisil	Lamictal	None Reported
Increase in Seizures (n=3)	Domestic	1997	Lamictal	Lamisil	None Reported
	Domestic	1998	Lamictal	Lamisil	Similar Names
	Domestic	2000	Lamictal	Lamisil	None Reported

Table 3 Continued:**Name Confusion between Lamisil and Lamictal Identified in AERS for Patient 17 years of Age and Older or Unknown**

Outcome	Location	Year	Medication Ordered	Medication Received	Causality
Rash (n=7)	Domestic	1998	Lamisil	Lamictal	None Reported
	Domestic	1999	Lamisil	Lamictal	None Reported
	Domestic	1999	Lamisil	Lamictal	None Reported
	Domestic	2003	Lamisil	Lamictal	None Reported
	Domestic	2003	Lamisil	Lamictal	None Reported
	Domestic	2004	Lamisil	Lamictal	None Reported
	Foreign	2004	Lamisil	Lamictal	None Reported
Intervention Required (n=6)	Foreign	1996	Lamisil	Lamictal	None Reported
	Domestic	1997	Lamisil	Lamictal	None Reported
	Domestic	2000	Lamisil	Lamictal	Similar Names
	Domestic	2003	Lamisil	Lamictal	None Reported
	Domestic	2003	Lamisil	Lamictal	Stress (distracted by putting away order)
	Foreign	2005	Lamisil	Lamictal	None Reported
Delay in Treatment (n=3)	Domestic	2006	Lamictal	Lamisil	Similar Names
	Foreign	2007	Lamisil	Lamictal	None Reported
	Domestic	2008	Lamisil	Lamictal	Computer Selection Error

Table 3 Continued:

Name Confusion between Lamisil and Lamictal Identified in AERS for Patient 17 years of Age and Older or Unknown					
Outcome	Location	Year	Medication Ordered	Medication Received	Causality
Suicidal (n=1)	Domestic	2002	Lamictal	Lamisil	None Reported
Minor Adverse Events (n=12)	Foreign	1996	Lamisil	Lamictal	None Reported
	Foreign	1996	Lamisil	Lamictal	None Reported
	Domestic	1999	Lamictal	Lamisil	None Reported
	Domestic	1999	Unknown	Unknown	None Reported
	Domestic	2000	Lamisil	Lamictal	None Reported
	Domestic	2003	Lamictal	Lamisil	None Reported
	Foreign	2004	Lamictal	Lamisil	Similar Tablets
	Domestic	2004	Lamisil	Lamictal	None Reported
	Domestic	2004	Lamictal	Lamisil	None Reported
	Domestic	2004	Lamictal	Lamisil	None Reported
	Foreign	2005	Lamictal	Lamisil	None Reported
	Domestic	2006	Lamisil	Lamictal	None Reported

Table 3 Continued:

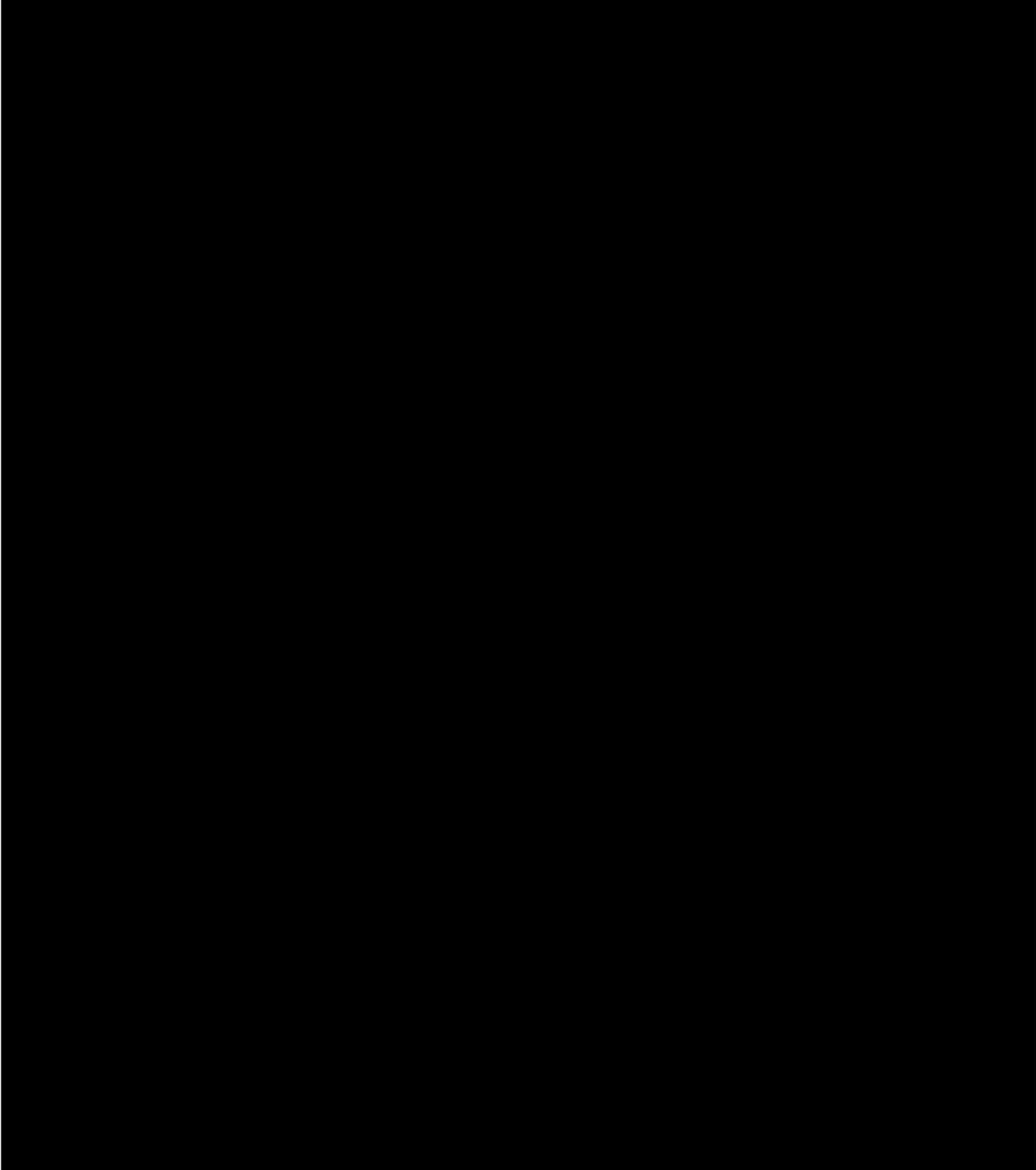
Name Confusion between Lamisil and Lamictal Identified in AERS for Patient 17 years of Age and Older or Unknown

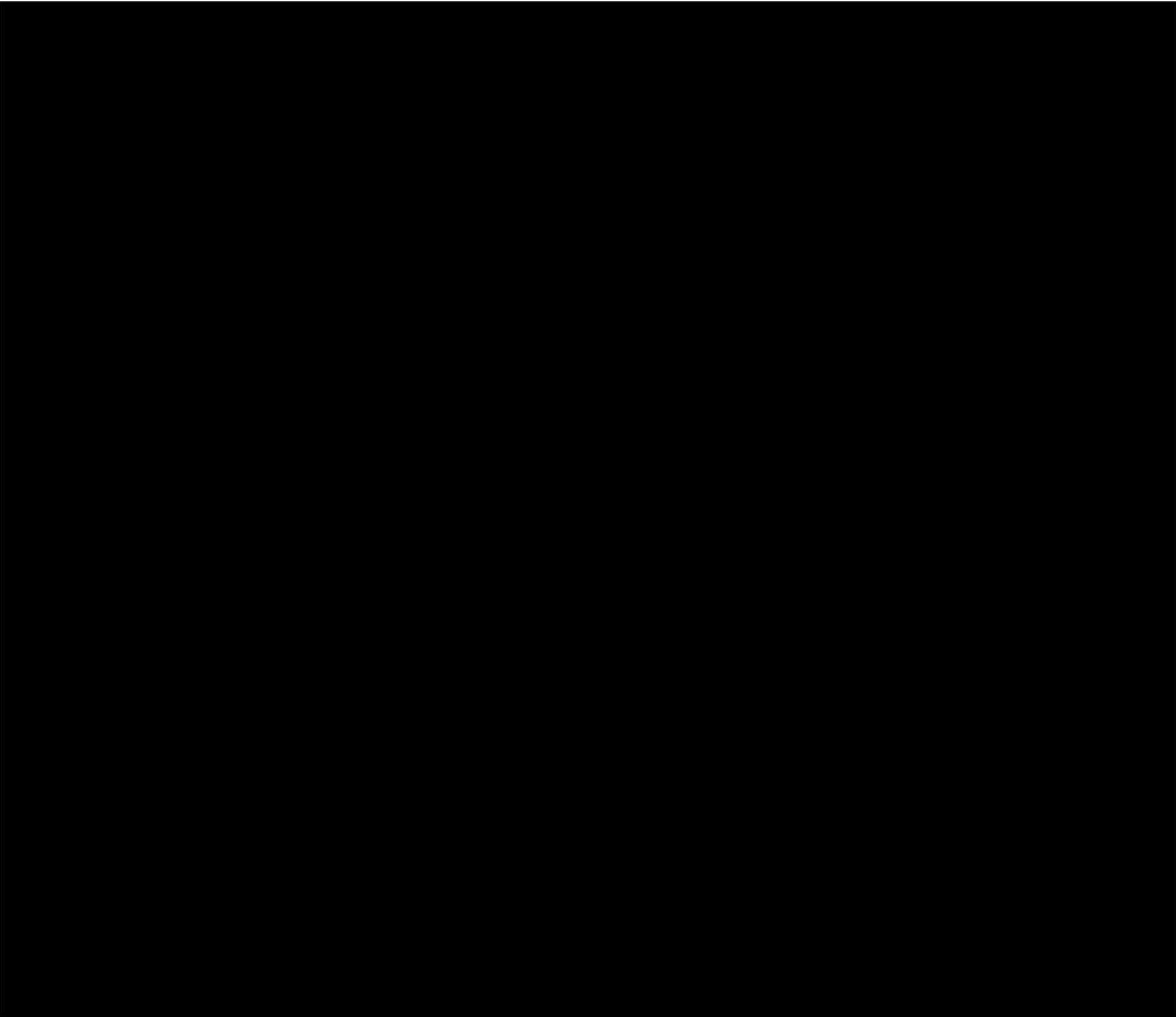
Outcome	Location	Year	Medication Ordered	Medication Received	Causality
Patient Did Not Receive Any Doses (n=16)	Domestic	1996	Unknown	Unknown	Similar Names
	Domestic	1996	Unknown	Unknown	Similar Names
	Domestic	1996	Lamisil	Lamictal	None Reported
	Domestic	1997	Unknown	Unknown	Similar Names
	Domestic	1998	Lamictal	Lamisil	None Reported
	Domestic	1998	Unknown	Unknown	Close Proximity to each other on Shelf
	Domestic	1999	Unknown	Unknown	Similar Names
	Domestic	1999	Lamictal	Lamisil	None Reported
	Domestic	1999	Lamisil	Lamictal	Computer Selection Error
	Domestic	1999	Lamisil	Lamictal	Computer Selection Error
	Domestic	2000	Lamictal	Lamisil	None Reported
	Foreign	2001	Unknown	Unknown	Similar Names
	Domestic	2003	Lamictal	Lamisil	None Reported
	Domestic	2004	Lamisil	Lamictal	Misspelled Names and Similar Names
	Domestic	2006	Lamisil	Lamictal	Illegible prescription
	Domestic	2006	Lamisil	Lamictal	None Reported

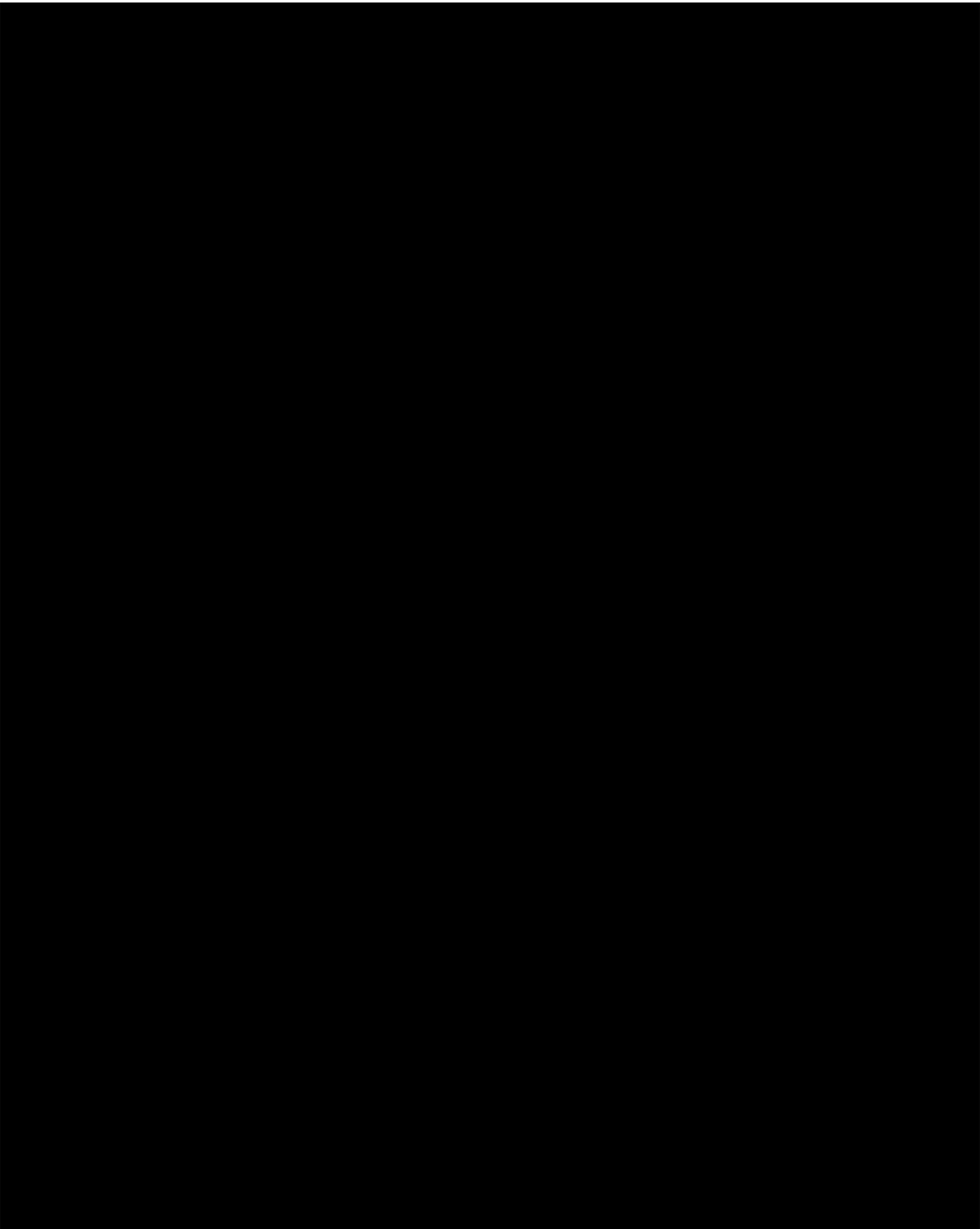
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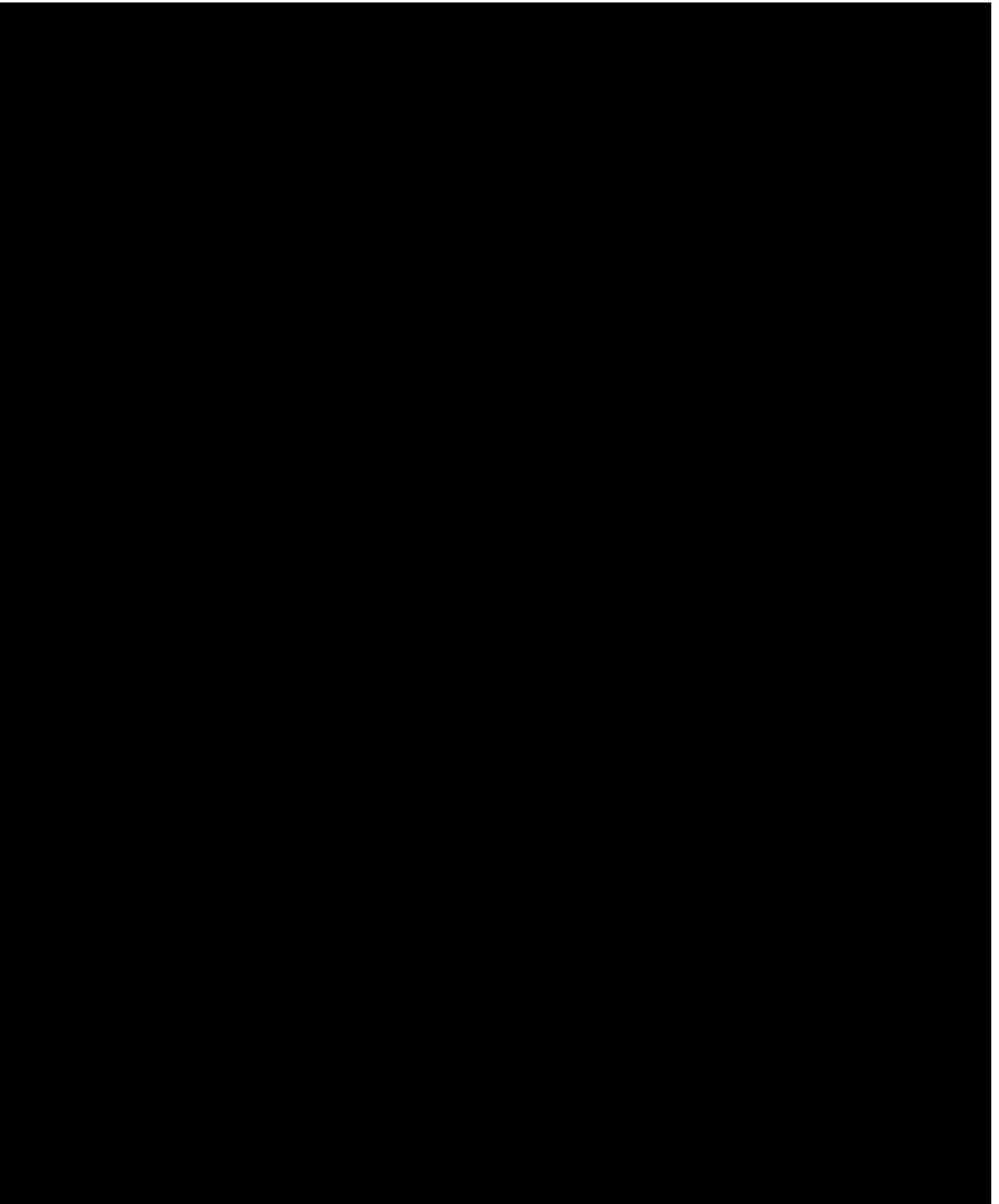
Name Confusion between Lamisil and Lamictal Identified in AERS for Patient 17 years of Age and Older or Unknown					
Outcome	Location	Year	Medication Ordered	Medication Received	Causality
No Adverse Event Reported (n=5)	Domestic	1997	Lamictal	Lamisil	None Reported
	Domestic	2005	Lamictal	Lamisil	None Reported
	Domestic	2006	Lamictal	Lamisil	None Reported
	Domestic	2006	Lamisil	Lamictal	None Reported
	Domestic	2007	Lamictal	Lamisil	None Reported
Unknown (n=11)	Domestic	1996	Lamisil	Lamictal	None Reported
	Domestic	1997	Lamisil	Lamictal	Stress (Workload)
	Domestic	1997	Lamisil	Lamictal	None Reported
	Domestic	1997	Unknown	Unknown	Similar Names
	Domestic	1999	Lamisil	Lamictal	None Reported
	Domestic	2000	Lamisil	Lamictal	Similar Names
	Domestic	2001	Lamisil	Lamictal	None Reported
	Domestic	2001	Lamisil	Lamictal	None Reported
	Domestic	2004	Lamisil	Lamictal	None Reported
	Domestic	2005	Lamictal	Lamisil	None Reported
	Unknown	2005	Lamisil	Lamictal	None Reported

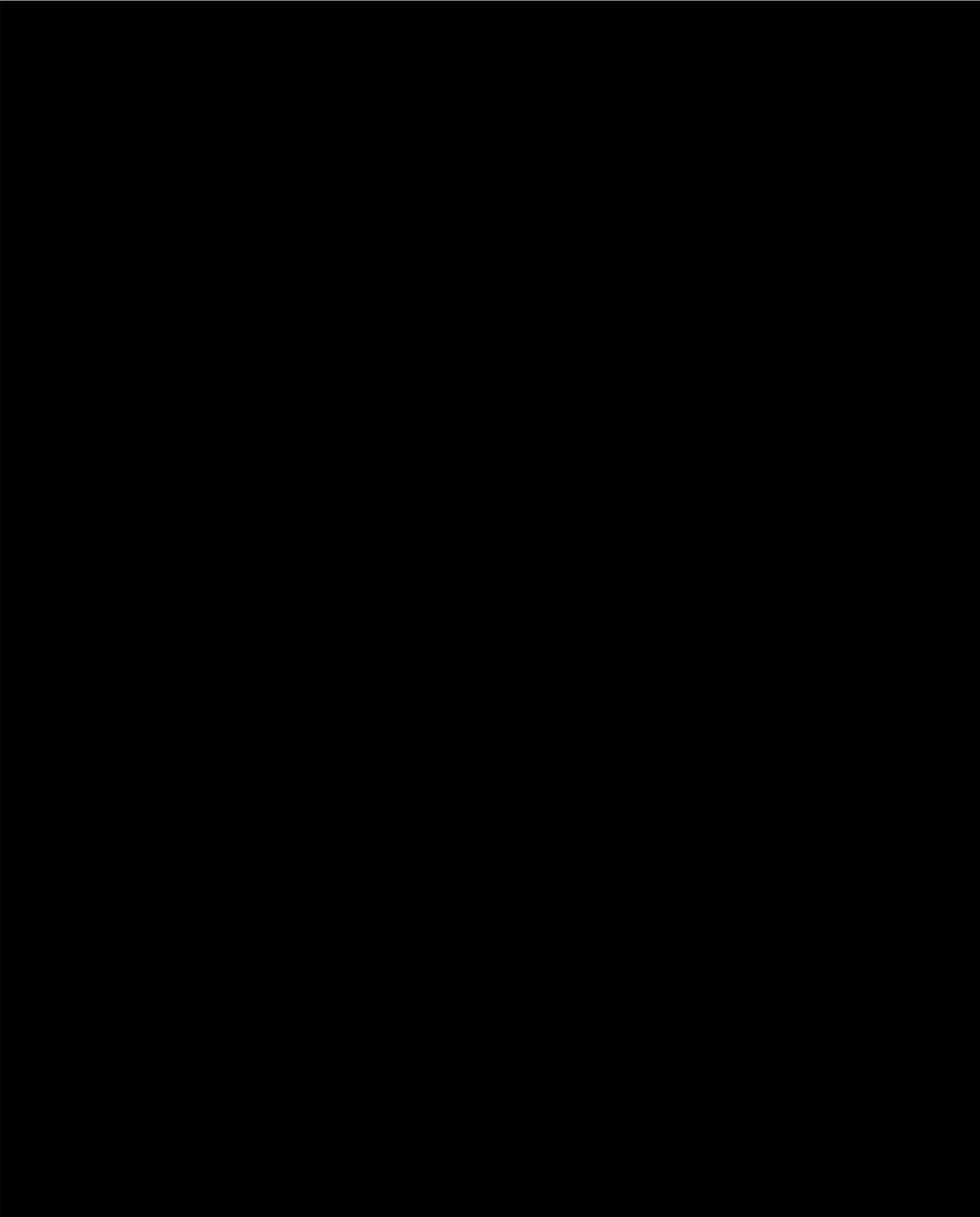
3.4 MEDMARX DATABASE***











3.5 INSTITUTE OF SAFE MEDICATION PRACTICES DATABASES***

4 DISCUSSION

We evaluated all cases of name confusion reported with the proprietary name Lamictal. In addition to summarizing all cases of name confusion, we were asked to assess whether or not the pediatric exclusivity had any impact on the medication errors reported with Lamictal. Our analysis demonstrates no evidence to support that the pediatric exclusivity for Lamictal has increased the risk of errors seen with Lamictal name confusion.

Name confusion has been reported between Lamictal products and seventeen (n=17) different names since 1995. All of the cases involved the oral dosage form, primarily the tablet of Lamisil. Fourteen (n=14) of the seventeen names report proprietary name confusion with Lamictal, while three names report established name confusion with Lamotrigine.

4.1 ESTABLISHED NAME CONFUSION

Although the majority of reported errors occur with the proprietary name Lamictal, DMEPA notes that the established name, Lamotrigine is also vulnerable to error. The 3 products that are most often confused with Lamotrigine are Lamivudine, Levetiracetam, and Levothyroxine. There has been at least one reported transcription error and at least one reported selection error for each of the three established names. The causality of this confusion can be attributed to the orthographic and phonetic similarities of these names in addition to overlapping product characteristics (see Appendix C).

Of the 3 names, Lamivudine, has been reported most frequently and presents a clear and consistent trend of medication error. Thus, due to the overlapping characteristics and the postmarketing evidence DMEPA has identified that these two products are being confused active steps must be taken to reduce the risk for medication errors due to name confusion between Lamotrigine and Lamivudine.

4.2 PROPRIETARY NAME CONFUSION

Fourteen proprietary names have reportedly been confused with Lamictal. Eight (n=8) of the names (Loxitane, Amitriptyline, Cymbalta, Dilantin, Ludiomil, Neurontin, Seroquel and Xeloda) were only reported once or twice and have not demonstrated continued confusion.

One name, Largactil (Chlorpromazine), a foreign proprietary name, has also been reported to be confused with Lamictal. We acknowledge that this particular error may occur while American citizens are traveling to foreign countries, but the risk of domestic cases of name confusion are minimized since the proprietary name is not marketed in the United States.

The remaining five (n=5) proprietary names Lamisil, Trileptal, Lomotil, Labetalol, and Topamax have orthographic and phonetic similarities in addition to overlapping product characteristics (see Appendix A) that contribute to continued name confusion leading to error. These five names are discussed in more detail below.

4.2.1 Lamictal and Lamisil Confusion

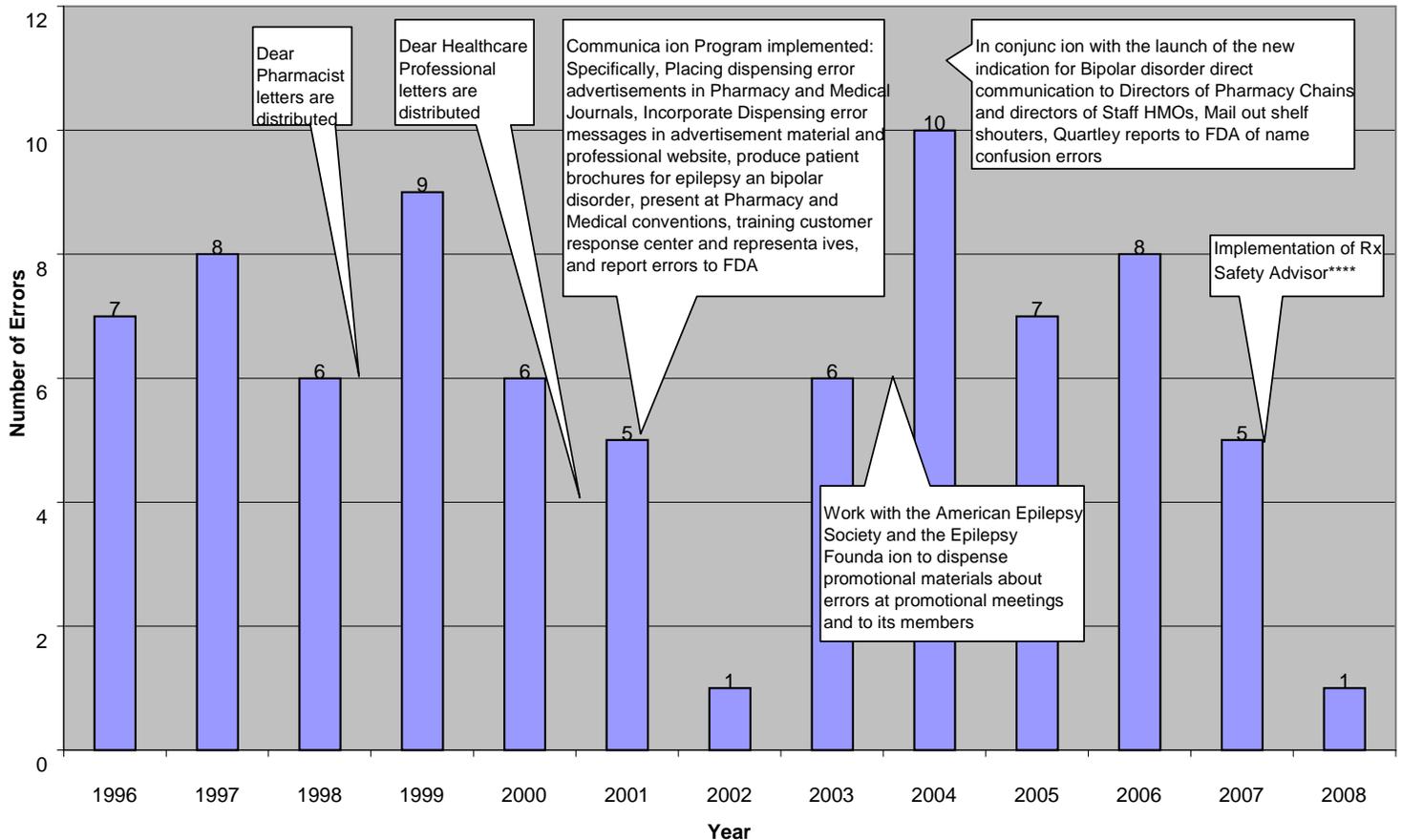
Name confusion between Lamictal and Lamisil has been reported multiple times in multiple databases and continues to occur despite efforts to reduce medication errors between this name pair.

It is interesting to note that name confusion between Lamictal and Lamisil was not reported until after the approval of Lamisil oral tablets on March 10, 1996. The confusion appears to be limited to the tablet formulation. Lamictal and Lamisil were co-marketed for several years without confusion. However, the approval of the tablets provided new and similar overlapping product characteristics (see Appendix A) that provided a greater similarity to this name pair than what had previously existed. The tablet formulation provided for overlap in dosage form, frequency of dosing (once daily), and a numerical similarity in dosage strength (25 mg vs. 250 mg). These new product characteristic in combination with the orthographic and phonetic similarities of the names and similar use environment collectively contributes to these errors.

The cases of proprietary name confusion do not appear to be linked to any particular practice setting of care as errors were reported from all practice settings.

Although, efforts have been taken to raise awareness of the potential name confusion between Lamictal and Lamisil, such as Dear Healthcare Professional letters, “shelf shouters”, and implementation of computer software that monitors for name confusion of Lamisil and Lamictal, errors continue to occur. The graph on page 24 illustrates the time frame in which these interventions were employed as compared to the number of reports received in AERS and the periodic reports. The data from outside sources show a comparable number of reports per year.

Lamisil and Lamictal Confusion



4.2.2 Lamictal Confusion with Trileptal

Trileptal and Lamictal share several overlapping product characteristics such as prescription status (prescription), dosage form (tablets), strength (150 mg), frequency of dose (twice daily), route of administration (orally), indication (epilepsy), patient population (adults and pediatric patients 4 to 16 years old with epilepsy), and prescriber population (primary care physician or neurologist).

Since two cases of name confusion were reported prior to pediatric exclusivity being granted to Lamictal and one case was reported after Lamictal was granted pediatric exclusivity, DMEPA's analysis shows that the pediatric exclusivity does not appear to have an impact on medication errors involving Lamictal and Trileptal. Based on the limited information available there does not appear to be a continued trend of confusion between this name pair. However, due to the overlapping characteristics and postmarketing evidence DMEPA has identified that these two products are being confused, DMEPA will continue to monitor this name pair.

**** Safety RX Advisor is a software program that alerts Pharmacist to potential Look-alike or sound-alike names. A warning message is displayed prior to the claim being made and after the claim is accepted. An override code must be entered to bypass the message. Unlike many pharmacy warning systems this message cannot be paged through.

4.2.3 Lamictal Confusion with Topamax

Topamax and Lamictal share several overlapping product characteristics such as prescription status (prescription), dosage form (tablets), strength (25 mg, 100 mg, and 200 mg), frequency of administration (twice daily), route of administration (orally), indication (epilepsy), and prescriber population (primary care physician or neurologist). Although Topamax and Lamictal have overlapping product characteristics that contribute to product confusion the orthographic and phonetic differences in the name help to minimize the potential for error.

Since all three cases of name confusion identified in postmarketing searches were reported prior to pediatric exclusivity being granted to Lamictal a DMEPA's analysis shows that the pediatric exclusivity did not have an impact on medication errors involving Lamictal and Topamax. Based on the limited number of cases and information available there does not appear to be a continued trend of confusion between this name pair. However, due to the overlapping characteristics and postmarketing evidence DMEPA has identified that these two products are being confused, DMEPA will continue to monitor this name pair.

4.2.4 Lamictal Confusion with Lomotil

Lomotil and Lamictal share several overlapping product characteristics such as prescription status (prescription), dosage form (tablets), route of administration (orally), and patient population (adults and pediatric patients 4 to 16 years old). Additionally, although Lomotil and Lamictal do not share a direct overlap in strength the two medications do share a numerical overlap with the 2.5 mg strength of Lomotil and the 25 mg strength of Lamictal especially if the decimal point on the Lomotil prescription is not prominent. Lomotil and Lamictal have orthographic and phonetic similarities in addition to overlap in product characteristics that contribute to name and product confusion.

Name confusion between Lamictal and Lomotil has been reported steadily since 1995. While DMEPA's analysis shows that pediatric exclusivity has not impacted medication errors involving Lamictal and Lomotil, the overlapping orthographic and phonetic similarities and the overlapping product characteristics, show that name confusion between Lamictal and Lomotil leading to medication errors will continue to occur and to be reported.

4.2.5 Lamictal Confusion with Labetalol

Labetalol and Lamictal share several overlapping product characteristics such as prescription status (prescription), dosage form (tablets), strength (100 mg and 200 mg), frequency of dose (twice daily), and the route of administration (orally). Labetalol and Lamictal have orthographic and phonetic similarities in addition to overlap in product characteristics that contribute to name and product confusion.

Name confusion between Lamictal and Labetalol has been reported steadily since 1999. While DMEPA's analysis shows that pediatric exclusivity has not impacted medication errors involving Lamictal and Labetalol, the overlapping orthographic and phonetic similarities and the overlapping product characteristics, show that name confusion between Lamictal and Labetalol leading to medication errors will continue to occur and to be reported. Since reported errors have not decreased with this name pair over the years active intervention will be necessary to decrease the risk of name confusion.

5 CONCLUSION AND RECOMMENDATIONS

The pediatric indication of use for the oral granules has not been shown to exacerbate existing medication errors reported due to proprietary or established name confusion with Lamictal. The largest number of medication errors reported with Lamisil are the result of proprietary name confusion between Lamisil and Lamictal.

The interventions to date have not been effective in minimizing these errors. However, the RX Safety Advisor component of the sponsor's interventions has just been implemented in 2007. More information needs to be gathered regarding the computer software before a final determination can be made as to the effectiveness the software program has had on this confusion. If the errors with Lamictal and Lamisil continue to occur over the next years we will need to consider other alternative methods to minimize the occurrence of these errors. We recommend the following:

1. Continue the communication program developed by GlaxoSmithKline.
2. Continue to monitor the effectiveness of the RX Safety Advisor. If the RX Safety Advisor does not have a positive impact on the reduction of the name confusion, consider additional options to minimize this risk.
3. Work with the Institute for Safe Medication Practices to have the name pair Lamisil and Lamictal placed on the Joint Commission list of Look-alike and Sound-alike names.
4. Monitor name confusion with the established name.
5. Include Labetalol and Lomotil in the future communications involving name confusion with Lamictal.
6. Include Lamivudine in the future communication plans as having been confused with Lamictal due to the established names.

Additionally, one other proprietary name (Lomotil) and two established names (Labetalol and Lamivudine) have been identified as sources of errors related to name confusion with Lamictal and Lamotrigine that will require active intervention to minimize medication errors.

6 REFERENCES

6.1 ADVERSE EVENTS REPORTING SYSTEM (AERS)

AERS is a database application in CDER FDA that contains adverse event reports for approved drugs and therapeutic biologics. These reports are submitted to the FDA mostly from the manufactures that have approved products in the U.S. The main utility of a spontaneous reporting system that captures reports from health care professionals and consumers, such as AERS, is to identify potential postmarketing safety issues. There are inherent limitations to the voluntary or spontaneous reporting system, such as underreporting and duplicate reporting; for any given report, there is no certainty that the reported suspect product(s) caused the reported adverse event(s); and raw counts from AERS cannot be used to calculate incidence rates or estimates of drug risk for a particular product or used for comparing risk between products.

6.2 MEDMARX ([HTTPS://WWW.MEDMARX.COM](https://www.medmarx.com))***

MEDMARX® is a national, Internet-accessible database that hospitals and health care systems use to track and trend adverse drug events and medication errors. Hospitals and health care systems participate in MEDMARX voluntarily and subscribe to it on an annual basis. MEDMARX is a quality improvement tool, which facilitates productive and efficient documentation, reporting, analysis, tracking, trending, and prevention of adverse drug events.

6.3 ISMP DATABASES***

The data provided to FDA comes from a Memorandum of Understanding agreement between the Division of Medication Error Prevention and the Institute for Safe Medication Practices (ISMP) and cannot be shared outside the FDA

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/s/

Zachary A Oleszczuk
10/23/2008 12:47:54 PM
DRUG SAFETY OFFICE REVIEWER

Todd Bridges
10/23/2008 01:06:44 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
10/23/2008 04:35:52 PM
DRUG SAFETY OFFICE REVIEWER