

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-070

PROPRIETARY NAME REVIEW(S)

**Division of Medication Errors and Technical Support (DMETS)
Office of Surveillance and Epidemiology
HFD-420; PKLN Rm. 6-34
Center for Drug Evaluation and Research**

PROPRIETARY NAME REVIEW

DATE OF REVIEW: June 5, 2007

NDA #: 22-070

NAME OF DRUG: **Atralin**
(Tretinoin Gel)
0.05%

NDA HOLDER: Coria Laboratories Ltd

*****NOTE: This review contains proprietary and confidential information that should not be released to the public.*****

I. INTRODUCTION:

This review was written in response to a request from the Division of Dermatology and Dental Products, for assessment of the proprietary name, Atralin, regarding potential name confusion with other proprietary or established drug names. Container labels, carton and insert labeling were reviewed in DMETS review #2007-1163, dated June 13, 2007.

PRODUCT INFORMATION

Atralin is an aqueous formulation containing 0.05% tretinoin for topical treatment of acne vulgaris. The usual dosage is an application of a thin layer of Atralin once a day, before bedtime, to skin where lesions occur. Atralin should be kept away from eyes, mouth, nasal creases, and mucous membranes. Atralin is a translucent to opaque, smooth, pale yellow gel that will be available as — g and 45 g tubes. b(4)

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of the internet, several standard published drug product reference texts^{1,2} as well as several FDA databases^{3,4} for existing drug names which sound-alike or look-alike to Atralin to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted⁵. The Saegis⁶ Pharma-

¹ MICROMEDEX Integrated Index, 2007, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

² Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

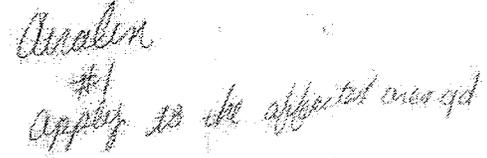
³ AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-07, and the electronic online version of the FDA Orange Book.

⁴ Phonetic and Orthographic Computer Analysis (POCA)

⁵ WWW location <http://www.uspto.gov/tmdb/index.html>.

⁶ Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at www.thomson-thomson.com

random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
<p><u>Outpatient RX:</u></p> 	<p>Atralin #1 Apply to affected area daily.</p>
<p><u>Inpatient RX:</u></p> 	

2. Results:

None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed U.S. product. There was one participant from the outpatient written study who interpreted the proposed name as “Naprosyn”, however, we believe this to be an oversight as Naprosyn was another name immediately above Atralin in the written study. See appendix A for the complete listing of interpretations from the verbal and written studies.

C. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name, Atralin, the following eighteen names and one medical term were identified as having the potential to look and/or sound similar to Atralin: Adderall, Atralin, Aralen, Atrovent, Atropen, Atropine, _____^{***}, Agrylin, Astelin, Alphalin, Arestin, Unico Atralin Weed Killer, Atrial (medical term), _____^{***}, Atridox, Ativan, and Atripla.

b(4)

Additionally, DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that the proposed name could be confused with any of the aforementioned names. However, negative findings are not predicative as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to a small sample size. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Atralin.

Upon initial analysis of the aforementioned names, the following eight names and one medical term will not be considered further because of the lack of convincing look-alike and sound alike similarities with Atralin and numerous differentiating product characteristics such as product strength, indication for use, frequency of administration, route of administration, patient population, therapeutic class, unit of measure, and/or dosage formulation. : Adderall, _____^{***}, _____^{***}, Unico Atralin Weed Killer, Atrial (medical term), _____^{***}, Atripla, and Ativan. The name, Atralin, is a foreign drug that is an identical match in appearance and sound to Atralin. Atralin (sertraline) is available in Bangladesh for the treatment of depression. We have

b(4)

*** Name pending approval. Not FOI releasable.

safety concerns with the fact that this drug name, Atralin, is an exact match and is marketed in another country containing a different active ingredient. Through literature review and postmarketing surveillance, DMETS is aware of confusion between products marketed domestically and abroad which have similar or identical proprietary names, but different active ingredients. The Institute of Safe Medication Practices (ISMP) published an article citing such examples of confusion, including, Dilacor XR (U.S. - extended-release diltiazem) vs. Dilacor (Serbia – digoxin) ⁷. Another example of such confusion is the case of Palladone (U.S. - extended-release hydromorphone) vs. Pallidone (New Zealand – methadone) ⁸. DMETS recommends that the sponsor be made aware of this foreign product with the proprietary name, Atralin. We are willing to meet with the sponsor for further discussion.

The remaining nine (n=9) names, Aralen, Atrovent, Atropen, Atropine, Agrylin, Astelin, Alphalin, Arestin, and Atridox, were reviewed in depth because of their increased orthographic/phonetic similarity and potential overlapping product characteristics. Upon further analysis, these nine names were assessed as having minimal risk of confusion because of the differentiating product characteristics listed in the “Reason for Discard” column in Table 1 below and page 6.

Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**	Reason for Discard
Atralin	Tretinoin Gel, 0.05%	Apply a thin layer once a day, before bedtime, to skin where lesions occur. Keep away from eyes, mouth, nasal creases, and mucous membranes.		
Aralen Phosphate	Chloroquine Phosphate Tablets 500 mg (equiv. to 300 mg base)	<i>Malaria Prophylaxis:</i> 500 mg (300 mg base) on exactly the same day of each week. <i>Malaria Treatment (acute attack):</i> Initial dose of 1g (600 mg base) followed by an additional 500 mg (300 mg base) after 6 to 8 hours and a single dose of 500 mg (300 mg base) on each of 2 consecutive days. <i>Extraintestinal amebiasis:</i> 1 g (600 mg) daily for 2 days, followed by 500 mg (300 mg base) daily for at least 2 to 3 weeks. Treatment usually combined with an effective intestinal amebicide.	LA/SA	<ul style="list-style-type: none"> • Route of administration • Indications of use • Dosage form • Indications of use • The letter “t” has a very prominent sound when enunciated and its upstroke characteristic helps to differentiate it from Aralen.
Atrovent HFA	Ipratropium Bromide Metered Aerosol Inhalation 17 mcg per actuation	2 inhalations 4 times a day.	SA	<ul style="list-style-type: none"> • Strength • Dosage Form • Route of Administration • Dosing frequency • Indications of use • The “v” in Atrovent has a very prominent sound and when pronounced sounds different than Atralin.
Atrovent	Ipratropium Bromide Nasal Spray 0.03%, 0.06%	For 0.03% - 2 sprays per nostril 2 or 3 times daily. For 0.06% - 2 sprays per nostril 4 times daily.		
AtroPen	Atropine Injectable 0.25 mg/0.3 mL, 0.5 mg/0.7 mL, 1 mg/0.7 mL, 2 mg/0.7 mL	One pen (2 mg strength for adults) if two or more mild symptoms of nerve agent or insecticide exposure appear in situations where exposure is known or suspected. Two additional injections given in rapid succession 10 minutes after receiving first injection if the victim develops any of the severe symptoms.	LA/SA	<ul style="list-style-type: none"> • Strength • Dosage Form • Dosing frequency • Route of Administration • Indications of use • The downstroke in “p” is prominent in sound and appearance. Also, the upstroke in “t” is prominent in appearance.
Atropine Sulfate	Atropine Sulfate Injection 0.05 mg/mL, 0.1 mg/mL,	Hypotonic radiography: 1 mg IM Surgery: 0.5 mg (0.4 mg to 0.6 mg) SC, IM, or IV.		<ul style="list-style-type: none"> • Strength • Dosage Form

⁷ New Dangers in the Drug Re-Importation Process: Will we know what our patients are taking?. ISMP Safety Alert! January 27, 2005, 10(2), 1-2.

⁸ Safety Briefs, Foreign Influence. ISMP Safety Alert! Community/Ambulatory Care Issue. June 2005, 4(6), 2.3.

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**	Reason for Discard
Atralin	Tretinoin Gel 0.05%	Apply a thin layer once a day, before bedtime, to skin where lesions occur. Keep away from eyes, mouth, nasal creases, and mucous membranes.		
	0.4 mg/mL, 0.5 mg/mL, 0.8 mg/mL	Bradyarrhythmias: 0.4 mg to 1 mg IV every 1 to 2 hours as needed; larger doses up to a maximum of 2 mg, may be required.		<ul style="list-style-type: none"> • Route of Administration • Dosing frequency • Indications of use • The downstroke in "p" is prominent in sound and when pronounced sounds different than Atralin.
Agrylin	Anagrelide HCl Capsules 0.5 mg, 1 mg	Starting dosage: 0.5 mg four times daily or 1 mg two times daily, which should be maintained for at least 1 week. Dosage should be increased by not more than 0.5 mg/day in any 1 week and should not exceed 10 mg/day or 2.5 mg in a single dose.	SA	<ul style="list-style-type: none"> • Dosage Form • Route of Administration • Dosing frequency • Indications of use • The letter "g" is prominent in sound and is distinct when compared to "t".
Astelin	Azelastine HCl Metered Nasal Spray 0.125 mg	2 sprays per nostril twice daily.	LA	<ul style="list-style-type: none"> • Strength • Dosage Form • Route of Administration • Dosing frequency • Indications of use • The presence of the letter "s" following Astelin helps to differentiate it from Atralin.
Alphalin (discontinued but available in generic form)	Vitamin A Palmitate Capsules 50,000 Units	For severe deficiency, 100,000 units orally, followed by 50,000 units daily for 2 weeks; follow-up therapy, 10,000 to 20,000 units for 2 months.	SA	<ul style="list-style-type: none"> • Strength • Dosage Form • Route of Administration • Indications of use • The letters "ph" in Alphalin help to distinguish it in sound from Atralin.
Arestin	Minocycline HCl Extended-release Dental Powder 1 mg	This is administered by an oral health care professional and is a variable dose product.	LA	<ul style="list-style-type: none"> • Strength • Dosage Form • Route of Administration • Dosing frequency • Indications of use • The upstroke letter "t" in Atralin in conjunction with the cross stroke of the "t" in Arestin help to differentiate the two names from one another.
Atridox	Doxycycline Hyclate Injection 42.5 mg	200 mg on the 1 st day, administered in 1 or 2 infusions. Subsequent daily dosage is 100 mg to 200 mg depending on the severity of the infection, with 200 mg administered in 1 or 2 infusions.	LA	<ul style="list-style-type: none"> • Strength • Dosage Form • Route of Administration • Dosing frequency • Indications of use • The endings of each name are distinct.
<p>*Frequently used, not all-inclusive. **L/A (look-alike), S/A (sound-alike)</p>				

Appendix A: Prescription Study Results for Atralin

Inpatient

Atralin
Atralin
Atralin
Antralin
Atralin
Atralin
Atralin
Atralin
Atralin
Atrolin
Citralin
Atralin
Atralin
Atralin
Atralin
Atralin
Atralin
Atralin
Atralin

Outpatient

Atralin
Atralin
Atralin
Naprosyn
Airalin
Atralin
Atralin
Atralin
Atralin
Atralin
Airalin or Aeralin
Atralin
Atralin

Voice

Atrolin
Atrilin
Atrolin
Atrelin
Atrolin
Atrolin
Atrolyn
Atrolyn

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Jinhee Jahng
7/13/2007 12:08:30 PM
DRUG SAFETY OFFICE REVIEWER

Todd Bridges
7/13/2007 12:13:18 PM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
7/13/2007 04:28:46 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
7/13/2007 04:33:47 PM
DRUG SAFETY OFFICE REVIEWER