

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-903

PROPRIETARY NAME REVIEW(S)

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

PROPRIETARY NAME REVIEW

DATE OF REVIEW: February 14, 2005
IND#: 59,778
NAME OF DRUG: NeoProfen (primary name)
(ibuprofen L-Lysine) Injection
IND HOLDER: Farmacon-IL, LLC

I. INTRODUCTION:

This consult was written in response to a request from the Division of Cardio-Renal Drug Products (HFD-110) for a review of the proprietary names, "NeoProfen" regarding potential name confusion with other proprietary and/or established drug names. Package insert labeling was provided for review and comment. However, container labels and carton labeling were not provided for review and comment at this time.

PRODUCT INFORMATION

NeoProfen (ibuprofen L-Lysine) is a non-steroidal anti-inflammatory agent (NSAID) under investigation for the early treatment of patent ductus arteriosus (PDA) in premature infants with respiratory distress syndrome (RDS). Although the exact mechanism of action through which ibuprofen causes closure of a PDA is not known, it is believed to be through inhibition of prostaglandin synthesis of which ibuprofen has been shown to be a potent inhibitor both in vitro and in vivo. The dose recommendation is dependent on the infant's weight. A course of therapy is defined as three intravenous doses. An initial dose of 10 mg/kg is followed by two doses of 5 mg/kg, at 24 and 48 hours after the initial infusion. NeoProfen will be supplied in a vial box containing three 2 mL single use vials, each containing 10 mg/mL Ibuprofen L-Lysine.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts^{1,2} as well as several FDA databases³ for existing drug names which sound-alike or look-alike to NeoProfen [REDACTED] 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 conducted⁴. The SAEGIS⁵ Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies for each NeoProfen [REDACTED] consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary names NeoProfen [REDACTED]. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. DDMAC did not have concerns from a promotional perspective regarding the proposed names, NeoProfen [REDACTED].
2. The Expert Panel identified nine proprietary names that were thought to have the potential for confusion with NeoProfen. Additionally, the Expert Panel identified four names that have potential for confusion with [REDACTED]. These products are listed in Table 1 and Table 2, respectively, along with the dosage forms available and usual dosage (see pages 4 & 5).

¹ MICROMEDEX Integrated Index, 2005, 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, Missouri.

³ AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-05, and the electronic online version of the FDA Orange Book.

⁴ www location <http://www.uspto.gov/tmdb/index.html>.

⁵ Data provided by Thomson & Thomson's SAEGIS™ Online service, available at www.thomson-thomson.com

Table 2: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel for

Product Name	Dosage forms and strengths	Other similar names	Other**
NeoProfen	Ibuprofen Tablets 100 mg/mL, 2 mL vials	Ibuprofen Injection 10 mg/kg or 24 mg/kg	
Intropin Rx	Dopamine Injection 40 mg/mL, 80 mg/mL, 160 mg/mL Dopamine Injection Premixed Bags 0.8 mg/mL, 1.6 mg/mL, 3.2 mg/mL	The hemodynamic effects of dopamine are dose-dependent. In general, low doses of less than 2 mcg/kg/min may increase renal blood flow and urine output. Moderate to higher doses of 2—10 mcg/kg/min increase cardiac output. Doses greater than 10 mcg/kg/min result in mainly alpha-adrenergic effects such as vasoconstriction and increased blood pressure.	LA/SA
Ivoqualine (INN)	Ivoqualine	Potential psychotropic agent. Selective serotonin releaser.	LA/SA
Lupron Rx	Leuprolide Injection (SQ) 1 mg/0.2 mL Leuprolide Depot Suspension (IM) 3.75 mg, 7.5 mg, 11.25 mg, 15 mg, 22.5 mg, 30 mg	Dose varies based on indication. Injection: 1 mg SQ daily Depot: 3.75mg, 7.5mg IM monthly Depot-Ped: 7.5mg, 11.25mg, 15 mg IM monthly Depot 3: 11.25mg, 22.5mg IM every three months Depot 4: 30mg IM every four months	LA
Ibuprofen Rx and OTC	Ibuprofen Tablets 200 mg, 400 mg, 600 mg, 800 mg Ibuprofen Chewable Tablets 50 mg, 100 mg Ibuprofen Capsules 200 mg Ibuprofen Suspension 100 mg/5 mL, 50 mg/1.25 mL	Adults: 200—800 mg PO 3—4 times a day.	LA/SA
*Frequently used, not all-inclusive. **LA (look-alike), SA (sound-alike)			

B. PHONETIC and ORTHOGRAPHIC COMPUTER ANALYSIS (POCA)

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. The phonetic search module returns a numeric score to the search engine based on the phonetic similarity to the input text. Likewise, an orthographic algorithm exists which operates in a similar fashion. All names considered to have significant phonetic or orthographic similarities to NeoProfen **NeoProfen** were discussed by the Expert Panel (EPD).

C. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within the Centers of the FDA for each proposed proprietary name to determine the degree of confusion of NeoProfen and **NeoProfen** with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation

of the drug name. These studies employed a total of 123 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for NeoProfen and ~~_____~~ (see below). These prescriptions were optically scanned and one prescription was delivered to a 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.

NeoProfen

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
<p>Outpatient RX:</p> <p>7/7/04 Decrease NeoProfen to 10mg IV per infusion daily</p>	<p>Decrease NeoProfen to 10 mg IV per infusion.</p>
<p>Inpatient RX:</p> <p>2/7/04 Decrease NeoProfen to 10mg IV per infusion</p>	

IVprofen

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
<p>Outpatient RX:</p> <p>_____</p> <p>Buspense 2 vials Decrease to 10mg IV per infusion</p>	<p>Decrease _____ to 10 mg IV per infusion.</p>
<p>Inpatient RX:</p> <p>_____ Decrease to 10mg IV per infusion</p>	

2. Results for NeoProfen:

The study sample was written with incorrect directions for use "... 10 mg IV per infusion day" rather than the intended "... 10 mg IV per infusion, today"; however, this does not appear to have had an affect on the results. Six respondents in the inpatient study interpreted the proposed name, NeoProfen as "Neoproxen", "Neoprosen", "Neoproxen", "Neoprozen", "Neoproxen", and "Neoproxen", which are all orthographically and phonetically similar to Naproxen, a currently marketed US prescription and OTC product. In addition, "Neoprosen" and "Neoprozen" are phonetically similar to the trade name Naprosyn, a currently marketed US prescription product. Furthermore one respondent commented "sounds a lot like ibuprophen" and another commented "could this possibly be a combination of Neomycin and Ibuprofen?". The remaining incorrect name interpretations were misspelled/phonetic variations of "NeoProfen". See Appendix A for the complete listing of interpretations from the verbal and written studies.

3. Results for [REDACTED]

A total of eleven respondents (nine from the inpatient written study, one from the outpatient study, and one from the verbal study) interpreted the proposed name, [REDACTED] as "Ibuprofen", which is a currently marketed US prescription and OTC product. Additionally, one respondent from the inpatient study interpreted the proposed name [REDACTED] as "Ibruprofen", which is orthographically and phonetically similar to ibuprofen. Furthermore one respondent commented "Too close to ibuprofen, although I guess the part emphasizes this is IV" and another commented "This proposed name seems ripe for errors especially if not spoken carefully (ibuprofen). Also, it does not seem reasonable to [REDACTED]". The remaining incorrect name interpretations were misspelled/phonetic variations of [REDACTED]. See Appendix B for the complete listing of interpretations from the verbal and written studies.

D. SAFETY EVALUATOR RISK ASSESSMENT

1. NeoProfen Name Evaluation

In reviewing the proprietary name NeoProfen, the primary concerns related to look-alike and sound-alike confusion with Naprosyn, Naproxen, Neosporin, Meprospan, Vicoprofen, Ibuprofen, Neo-Fradin, Neotrofin, and Neopterin. Upon further review of the names gathered from EPD, the names Meprospan and Neopterin were not reviewed further. Meprospan (meprobamate) has been discontinued by the manufacturer. Generic meprobamate is available and the name Meprospan is retrievable in drug information resources; however, due to the numerous differentiating product characteristics such as product strength, indication for use, frequency of administration, and available dosage forms it will not be reviewed further. Neopterin is a lab test for renal function and viral infections used primarily in transplant patients. Thus the differing context of use for Neopterin should minimize the potential for confusion.

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, the interpretations "Neoproxen", "Neoprosen", "Neoproxen", "Neoprozen", "Neoproxen", and Neoproxen" look and/or sound similar to the following drug products respectively: Naproxen and Naprosyn. In addition, one respondent commented "sounds a lot like ibuprophen" and another commented "could this possibly be a combination of Neomycin and Ibuprofen?". Thus, DMETS will assess if the "Neo" portion of the name infers "Neomycin". The majority of the remaining misinterpretations were misspelled/phonetic variations of the proposed name, NeoProfen.

a. NOMENCLATURE CONCERNS WITH "NEO"

Concern was raised with respect to the "NEO" portion of the proposed tradename NeoProfen. The prefix "Neo" may imply "Neomycin"; as stated by one participant in the inpatient written prescription study "...combination of Neomycin and...". Additionally, one respondent in the verbal prescription study commented "sounds a lot like ibuprophen, neosporin". However, there are products on the U.S. market that begin with the letters "NEO" that do not contain Neomycin (i.e. Neopap, Neo Tect Kit, Neoral, Neosar). Additionally, the prefix "Neo" may imply "Neonatal". Since this product is intended for use in the neonatal patient population, this possible interpretation is not of concern at this time. DMETS searched the FDA Adverse Event Reporting System (AERS) for cases of medication errors associated with product names beginning with the letters "NEO" using the preferred term "medication error". No reports have been sent to the Agency indicating confusion or concern regarding misinterpretation of the active ingredients. Therefore, DMETS has no objections to the use of the prefix "NEO" for this product.

b. LOOK-ALIKE AND SOUND-ALIKE NAMES

- i. Naprosyn was identified as having look-alike and sound-alike potential with NeoProfin. Naprosyn (naproxen) is a non-steroidal anti-inflammatory agent indicated for use in rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, tendonitis, bursitis, gout, dysmenorrhea, fever, headache, and pain. Naprosyn is available as 250 mg, 375 mg, and 500 mg tablets, 375 mg and 500 mg delayed-release tablets, and 125 mg/5 mL oral suspension. Although naproxen is not commercially available as an injection, it may be compounded as an injection in hospital pharmacies. A method of preparation for Naproxen Sodium 100 mg/mL Injection has been published in the International Journal of Pharmaceutical Compounding Jan/Feb 2005 edition. Naprosyn is completely bioavailable; therefore, oral and intravenous doses are similar. One study evaluated intravenous doses of 275 mg to 550 mg of naproxen sodium.⁶ The usual dosage range for Naprosyn is 500 mg to

⁶ Silvano, A, Elpis S, Maurizo C, et al: Intravenous sodium naproxen: bioavailability in man and relief from pain in rheumatic diseases. *Curr Ther Res* 1982; 32:952-961.

1100 mg per day in divided doses. Pediatric doses of Naprosyn are 2.5 – 7.5 mg/kg every 8 – 12 hours. Naprosyn and NeoProfen share a similar placement of five overlapping letters, "NAPROSYN" and "NEOPROFEN" which contributes to the look-alike characteristics of the two names. Additionally, prescribers may not capitalize the "P" when writing NeoProfen, which further contributes to the orthographic similarities (see sample below). The beginnings of the two names may sound similar if pronounced (NAAP-RO vs. NEAP-RO). The endings (SYN vs. FEN) rhyme which also contributes to the phonetic similarities of these two names. Furthermore, the outpatient prescription study showed that two participants misinterpreted the name as Neoprofen and Neoprofen which both look and sound similar to Naprosyn. In addition to the look-alike and sound-alike similarities between Naprosyn and NeoProfen, these two products share the same drug classification (NSAID). Although naproxen injection is not commercially available, it can be compounded as an injection, and thus, an overlap of this dosage form (injection) may increase the potential for error. The injectable dosage form also shares overlapping numerals in their concentrations (100 mg/mL vs. 10 mg/mL) and a potential for overlap in dose (20 mg) may occur in the pediatric population (i.e. an 8 kg patient would require 20 mg of Naprosyn at the lowest recommended dose of 2.5 mg/kg). DMETS notes that there are different product characteristics such as commercially available dosage forms (tablets, delayed-release tablets, suspension vs. injection), route of administration (oral vs. injection), and dosing frequency (once to thrice daily vs. three doses, 24 hours apart). However, these differences may not be sufficient to prevent potential confusion since the two names are so orthographically similar.

Naprosyn 20mg 10x1
Neoprofen 20mg 10x1

- ii. Naproxen was identified as having look-alike and sound-alike potential with NeoProfen. Naproxen is a non-steroidal anti-inflammatory agent indicated for use in rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, tendonitis, bursitis, gout, dysmenorrhea, fever, headache, and pain. It is available via prescription as 250 mg, 375 mg, and 500 mg tablets, 375 mg and 500 mg delayed-release tablets, 125 mg/5 mL suspension, and 250 mg and 500 mg naproxen sodium tablets. It is also available over-the-counter in 200 mg naproxen sodium tablets. Although naproxen is not commercially available as an injection, it may be compounded as an injection in hospital pharmacies. A method of preparation for Naproxen Sodium 100 mg/mL Injection has been published in the International Journal of Pharmaceutical Compounding Jan/Feb 2005 edition. Naproxen is completely bioavailable; therefore, oral and intravenous doses are similar. One study evaluated intravenous doses of 275 mg to 550 mg of naproxen sodium.⁷ The usual dosage range for naproxen is 500 mg to 1100 mg per day in divided doses. Pediatric doses of naproxen are 2.5 – 7.5 mg/kg every 8 – 12 hours. Naproxen and NeoProfen

⁷ Silvano A, Elpis S, Maurizo C, et al: Intravenous sodium naproxen: bioavailability in man and relief from pain in rheumatic diseases. *Curr Ther Res* 1982; 32:952-961.

share a similar placement of five overlapping letters, "NAPROXEN" and "NEOPROFEN" which contributes to the look-alike characteristics of the two names (see sample, page 10). Additionally, prescribers may not capitalize the "P" when writing NeoProfen, which further contributes to the orthographic similarities. The beginnings of the two names may sound similar if pronounced (NAAP-RO vs. NEAP-RO). The endings (XEN vs. FEN) rhyme which contribute to phonetic similarities between these two names. Furthermore, the outpatient prescription study showed that six participants misinterpreted the name as Neoprofen, Neoprosen, Neoprofen, Neoprofen, Neoprofen, and Neoprofen which all look and sound similar to naproxen. In addition to the look-alike and sound-alike similarities between naproxen and NeoProfen, these two products share the same drug classification (NSAID). Although naproxen injection is not commercially available, it can be compounded as an injection, and thus, an overlap of this dosage form (injection) may increase the potential for error. The injectable dosage form also shares overlapping numerals in their concentrations (100 mg/mL vs. 10 mg/mL) and a potential for overlap in dose (20 mg) may occur in the pediatric population (i.e. an 8 kg patient would require 20 mg of Naproxen at the lowest recommended dose of 2.5 mg/kg). DMETS notes that there are different product characteristics such as commercially available dosage forms (tablets, delayed-release tablets, suspension vs. injection), route of administration (oral vs. injection), and dosing frequency (once to thrice daily vs. three doses, 24 hours apart). However, these differences may not be sufficient to prevent potential confusion since the two names are so orthographically similar.

neoprofen
naproxen

- iii. Neosporin was found to have look-alike and sound-alike potential with NeoProfen. Neosporin (bacitracin/neomycin/polymixin B) is available as an OTC topical anti-infective agent indicated for use as first aid prevention of infection in minor cuts, scrapes, and burns and is to be applied sparingly to the affected area one to three times daily. As an ophthalmic solution (gramicidin/neomycin/polymixin B) and ophthalmic ointment (bacitracin/neomycin/polymixin B), Neosporin is indicated for the treatment of conjunctivitis, keratitis, keratoconjunctivitis, blepharitis and blepharoconjunctivitis and is to be applied into the affected eye(s) every four hours for 7 to 10 days. Neosporin and NeoProfen have the same number of letters (nine) and syllables (four). Both names contain the same three initial letters (NEO-), the same final letter (-N), and a "P", "R", and "O" in similar positions in the middle of the name (NEOSP[R]IN vs. NEOP[R]FEN), which contribute to the look-alike and sound-alike similarities. In addition, their second to last letters ("I" vs. "E") sound similar and may look similar when scripted.

neoprofen
neosporin

Additionally, both products may share the same dosing frequency (one to three times ~~per~~ vs. three doses ~~24 hours apart~~). However, there are different product characteristics such as dosage forms (topical ointment, ophthalmic solution, ophthalmic ointment vs. injection), route of administration (topical, ophthalmic vs. injection), and drug classification (anti-infective vs. NSAID), which may help avert name confusion and error. Thus, DMETS believes the potential for name confusion resulting in medication errors involving Neosporin and NeoProfen is minimal.

- iv. Vicoprofen and NeoProfen may look-alike when scripted. Vicoprofen (Hydrocodone/Ibuprofen) is a combination of an opioid analgesic and an NSAID indicated for the short-term management of acute pain. Vicoprofen is a schedule III controlled substance, is available as 7.5 mg/200 mg tablet, and is usually dosed 1 tablet every 4 to 6 hours as needed. Both drug names contain seven identical ending letters (-OPROFEN), which contribute to the look-alike characteristics. Additionally the initial letters "VIC-" and "NE-" may look-alike when scripted (see sample below). In addition to the look-alike similarities, both products are available in one strength (7.5 mg/200 mg vs. 10 mg/mL); however, since two different doses of NeoProfen are administered, the dose would be required on a prescription for NeoProfen prior to dispensing, which helps differentiate the two products. Furthermore, DMETS notes that there are different product characteristics such as dosage forms (tablet vs. injection) and route of administration (oral vs. injection) that may help prevent name confusion. Due to the aforementioned product differences, DMETS believes the likelihood for name confusion between Vicoprofen and NeoProfen is minimal.

neoprofen
vicoprofen

- v. Ibuprofen has potential for look-alike confusion with NeoProfen. Ibuprofen is a NSAID and is available as 200 mg tablets and capsules, 50 mg and 100 mg chewable tablets, and 100 mg/5 mL and 50 mg/1.25 mL oral suspension over-the-counter (OTC) and as 400 mg, 600 mg, and 800 mg tablets with a prescription. Ibuprofen is indicated for use in rheumatoid arthritis, osteoarthritis, primary dysmenorrhea, fever, headache, and pain. The usual dosage range is 200 to 800 mg 3 to 4 times daily as needed. The usual pediatric dose is 4 to 10 mg/kg every 6 to 8 hours as needed, with a maximum of 50 mg/kg/day. Both drug names contain the same number of letters (nine) and six identical ending letters (-PROFEN), which contribute to the look-alike characteristics. The initial letters "IBU-" and "NEO-" may look-alike when scripted (see sample below); however, the "B" in ibuprofen and the initial "N" in NeoProfen provide an orthographic distinction.

neoprofen
ibuprofen

Ibuprofen and NeoProfen contain the same active ingredient (ibuprofen), may overlap in dose (5 mg/kg and 10 mg/kg), and may be written as one time orders. However, since NeoProfen will likely be written in an inpatient setting, the presence of the route of administration will decrease the potential for name confusion between Ibuprofen and NeoProfen.

- vi. Neo-Fradin and NeoProfen may look-alike when scripted. Neo-Fradin is an oral aminoglycoside antimicrobial indicated for the treatment of hepatic coma and is dosed 4 to 12 grams per day in 4 divided doses, treatment for longer than 2 weeks is not recommended. Neo-Fradin is available as a 125 mg/5 mL suspension. Both names share the same number of letters (nine), the same three beginning letters (NEO-) and end with the letter "N". Additionally the middle letters (-FRADI- vs. -PROFE-) may look similar when scripted (see sample below). However, several differentiating product characteristics may help avert confusion between the two products, such as dosage form (suspension vs. injection), frequency of use (four times daily vs. three doses 24 hours apart), and drug classification (antimicrobial vs. NSAID). Although both products are available in one strength (125 mg/5 mL vs. 10 mg/mL); NeoProfen is administered in two different doses; therefore, the dose is required on a prescription for NeoProfen prior to dispensing, thus differentiating the two products. DMETS believes the likelihood for confusion between Neo-Fradin and NeoProfen is minimal due to their differing product characteristics.

Neoprofen
Neofradin

- vii. Neotrofin was found to have look-alike and sound-alike similarities with NeoProfen. Neotrofin (AIT-034 (Letepirinim)) is _____

_____ ⁹ The name Neotrofin is an active trademark on the USPTO. Dosage ranges and product information is not available for this proposed agent. The two names are identical aside from the middle and second to last letters (**NEOTROFIN** vs. **NEOPROFEN**). The middle letters "T" and "P" can look similar when written (see sample below) and also sound similar when spoken. The second to last letters "I" and "E" both look and sound very similar. Due to the lack of available information, DMETS is unable to fully evaluate the potential for confusion between Neotrofin and NeoProfen.

Neoprofen
Neotrofin

⁸ Wang X, Hauptmann N, Taylor E, et.al: Neotrofin increases heme oxygenase-1 selectively in neurons. Brain Res. 2003 Feb 7;962(1-2):1-14.

⁹ www.alz.org, www.alsa.org, www.mdausa.org

3 Page(s) Withheld

Trade Secret / Confidential

Draft Labeling

Deliberative Process

Proprietary name
Review 5

III. COMMENTS TO THE SPONSOR

DMETS does not recommend the use of the proprietary names, NeoProfen due to their potential to look and sound similar to Naprosyn, Naproxen, and Ibuprofen.

A. NEOPROFEN LOOK-ALIKE AND SOUND-ALIKE CONCERNS

1. Naprosyn was identified as having look-alike and sound-alike potential with NeoProfen. Naprosyn (naproxen) is a non-steroidal anti-inflammatory agent indicated for use in rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, tendonitis, bursitis, gout, dysmenorrhea, fever, headache, and pain. Naprosyn is available as 250 mg, 375 mg, and 500 mg tablets, 375 mg and 500 mg delayed-release tablets, and 125 mg/5 mL oral suspension. Although naproxen is not commercially available as an injection, it may be compounded as an injection in hospital pharmacies. A method of preparation for Naproxen Sodium 100 mg/mL Injection has been published in the International Journal of Pharmaceutical Compounding Jan/Feb 2005 edition. Naprosyn is completely bioavailable; therefore, oral and intravenous doses are similar. One study evaluated intravenous doses of 275 mg to 550 mg of naproxen sodium.¹⁰ The usual dosage range for Naprosyn is 500 mg to 1100 mg per day in divided doses. Pediatric doses of Naprosyn are 2.5 – 7.5 mg/kg every 8 – 12 hours. Naprosyn and NeoProfen share a similar placement of five overlapping letters, "NAPROSYN" and "NEOPROFEN" which contributes to the look-alike characteristics of the two names. Additionally, prescribers may not capitalize the "P" when writing NeoProfen, which further contributes to the orthographic similarities (see sample).

Naprosyn 20mg 10x1
NeoProfen 20mg 10x1

The beginnings of the two names may sound similar if pronounced (NAAP-RO vs. NEAP-RO). The endings (SYN vs. FEN) rhyme which also contributes to the phonetic similarities of these two names. Furthermore, the outpatient prescription study showed that two participants misinterpreted the name as Neoprosen and Neoprozen which both look and sound similar to Naprosyn. In addition to the look-alike and sound-alike similarities between Naprosyn and NeoProfen, these two products share the same drug classification (NSAID). Although naproxen injection is not commercially available, it can be compounded as an injection, and thus, an overlap of this dosage form (injection) may increase the potential for error. The

¹⁰ Silvano, A, Elpis S, Maurizo C, et al: Intravenous sodium naproxen: bioavailability in man and relief from pain in rheumatic diseases. Curr Ther Res 1982; 32:952-961.

injectable dosage form also shares overlapping numerals in their concentrations (100 mg/mL vs. 10 mg/mL) and a potential for overlap in dose (20 mg) may occur in the pediatric population (i.e. an 8 kg patient would require 20 mg of Naprosyn at the lowest recommended dose of 2.5 mg/kg). DMETS notes that there are different product characteristics such as commercially available dosage forms (tablets, delayed-release tablets, suspension vs. injection), route of administration (oral vs. injection), and dosing frequency (once to thrice daily vs. three doses, 24 hours apart). However, these differences may not be sufficient to prevent potential confusion since the two names are so orthographically similar.

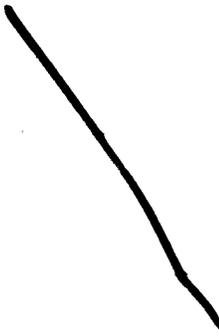
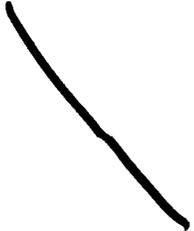
2. Naproxen was identified as having look-alike and sound-alike potential with NeoProfen. Naproxen is a non-steroidal anti-inflammatory agent indicated for use in rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, tendonitis, bursitis, gout, dysmenorrhea, fever, headache, and pain. It is available via prescription as 250 mg, 375 mg, and 500 mg tablets, 375 mg and 500 mg delayed-release tablets, 125 mg/5 mL suspension, and 250 mg and 500 mg naproxen sodium tablets. It is also available over-the-counter in 200 mg naproxen sodium tablets. Although naproxen is not commercially available as an injection, it may be compounded as an injection in hospital pharmacies. A method of preparation for Naproxen Sodium 100 mg/mL Injection has been published in the International Journal of Pharmaceutical Compounding Jan/Feb 2005 edition. Naproxen is completely bioavailable; therefore, oral and intravenous doses are similar. One study evaluated intravenous doses of 275 mg to 550 mg of naproxen sodium.¹¹ The usual dosage range for naproxen is 500 mg to 1100 mg per day in divided doses. Pediatric doses of naproxen are 2.5 – 7.5 mg/kg every 8 – 12 hours. Naproxen and NeoProfen share a similar placement of five overlapping letters, "NAPROXEN" and "NEOPROFEN" which contributes to the look-alike characteristics of the two names (see sample below).

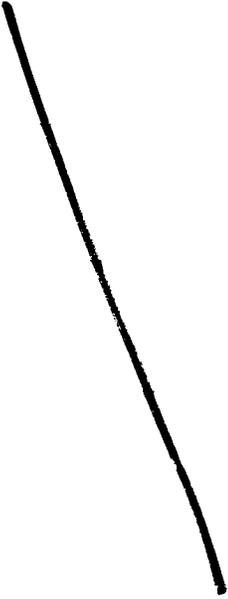
neoprofen
naproxen

Additionally, prescribers may not capitalize the "P" when writing NeoProfen, which further contributes to the orthographic similarities. The beginnings of the two names may sound similar if pronounced (NAAP-RO vs. NEAP-RO). The endings (XEN vs. FEN) rhyme which contribute to phonetic similarities between these two names. Furthermore, the outpatient prescription study showed that six participants misinterpreted the name as Neoprofen, Neoprosen, Neoprofen, Neoprozen, Neoprofen, and Neoprofen which all look and sound similar to naproxen. In addition to the look-alike and sound-alike similarities between naproxen and NeoProfen, these two products share the same drug classification (NSAID). Although naproxen injection is not commercially available, it can be compounded as an injection, and thus, an overlap of this dosage form (injection) may increase the potential for error. The injectable dosage form also shares overlapping numerals in their concentrations (100 mg/mL vs. 10 mg/mL) and a potential for overlap in dose (20 mg) may occur in the pediatric population (i.e. an 8 kg patient would require

¹¹ Silvano A, Elpis S, Maurizo C, et al: Intravenous sodium naproxen: bioavailability in man and relief from pain in rheumatic diseases. *Curr Ther Res* 1982; 32:952-961.

20 mg of Naproxen at the lowest recommended dose of 2.5 mg/kg). DMETS notes that there are different product characteristics such as commercially available dosage forms (tablets, delayed-release tablets, suspension vs. injection), route of administration (oral vs. injection), and dosing frequency (once to thrice daily vs. three doses, 24 hours apart). However, these differences may not be sufficient to prevent potential confusion since the two names are so orthographically similar.





Additionally, DMETS reviewed the package insert labeling of NeoProfen from a safety perspective. DMETS has identified the following area of possible improvement, which might minimize potential user error.

DMETS notes the established name is expressed inconsistently throughout the package insert labeling. The established name is currently expressed in the following manners: "...L-Lysin^{ate} **IV**", "...L-Lysin^{ate} **IV**", "...L-Lysin^{ate} **IV**" and "...L-Lysin^{ate} **IV**". We recommend consulting Guiragos Poochikian, Acting Chair, of the CDER Labeling and Nomenclature Committee on the proper designation of the established name. Upon proper designation of the established name, revise consistently throughout the labels and labeling.

IV. RECOMMENDATIONS

- A. DMETS does not recommend the use of the proprietary names, NeoProfen or
- B. DMETS recommends implementation of the package insert labeling revision outlined in section III of this review in order to minimize potential errors with the use of this product. Container labels and carton labeling were not submitted for review and comment. Please submit the labels and labeling when available for review and comment.
- C. DDMAC finds the proprietary names NeoProfen acceptable from a promotional perspective.
- D. Consult Guiragos Poochikian, Acting Chair, of the CDER Labeling and Nomenclature Committee on the proper designation of the established name.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Diane Smith, project manager, at 301-827-3242.

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Appendix A – DMETS Prescription Study Results for NeoProfen

<u>Voicemail</u>	<u>Outpatient</u>	<u>Inpatient</u>
Neoprofen	Neoprofen	Neoprofen NeoProfen (NeoProfen could this possibly be a combination of Neomycin and Ibuprofen?)
Neoprofin	NeoPropen	
Neoprofen	NeoProfen	NeoProfen
Neoprophen	Neoprophen	NeoProfen
Neoprophen	Neoprofen	Neoprofen
Neoprofin	NeoProfen	Neoprofen
Neoprophen		
(Neoprophen sounds a lot like ibuprophen, neosporin)	NeoProfen	Neoprofen
Neoprofen	NeoProfen	Neoprofen
Neoprofin	Neoproxen	Neoprofen
Neoprofen	Neoprosen	Neoprofen
Neoprofen	Neoproxen	Neoprofen
Neoprofen	NeoPropen	NeoProfen
Neoprofen	NeoProfen	Neoprofen
	Neoprozen	NeoProfen
	neoproxen	
	Neoprofen	
	Neoproxen	
	NeoProfen	

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 ✓ Trade Secret / Confidential

 Draft Labeling

 Deliberative Process

*Proprietary Name
Review*

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

/s/

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