

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-612

PROPRIETARY NAME REVIEW(S)

MEMORANDUM

Division of Medication Errors and Technical Support
Office of Drug Safety
HFD-420; White Oak, Mail Stop 4447
Center for Drug Evaluation and Research

DATE: December 16, 2005

TO: David Orloff, MD
Director, Division of Metabolism and Endocrinology Products, HFD-510

FROM: Denise Toyer, PharmD, Deputy Director
Carol Holquist, RPh, Director
Division of Medication Errors and Technical Support, HFD-420

SUBJECT: ODS Consult 04-0076-01; Lipofen (Fenofibrate Capsules) 50 mg, 100 mg, and 150 mg
NDA 21-612

This memorandum is written in response to the attached DMETS Proprietary Name Review conducted on Lipofen for the Division of Metabolism and Endocrinology Products (HFD-510). We have reviewed the safety evaluator's comments and agree that there is a potential for confusion between Lipofen and Lipitor and therefore we do not recommend the use of the name Lipofen. However, we do not agree with the reviewer that there is potential for confusion between Liposin and Lipofen. Specifically, the written review states:

"Liposin may sound like Lipofen when spoken. In fact, two participants of the Rx Study interpreted a verbal order for Lipofen as "Liposin". Liposin is an over-the-counter preparation formulated as a complement to "low-fat" diets to help maintain normal blood cholesterol levels. The recommended dosage is one or two capsules after each meal...In addition to phonetic and orthographic similarities, Liposin and Lipofen share product similarities including, route of administration (oral), dosage form (capsule), and indications for use (both products are used to reduce lipids and cholesterol)... Overall, due to product characteristic overlap, and strong sound-alike characteristics between Liposin and Lipofen, DMETS believes there is potential for confusion between the products.

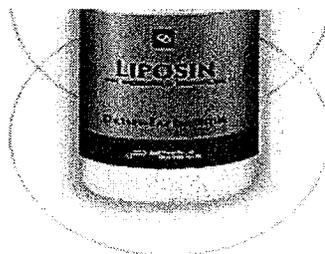
We have identified two citations referencing Liposin on the Internet. The first is a technology as a "new lipid system for safe delivery of genetic material into cells and tissues." This technology is being developed by Qugen Therapeutics PTE, LTD in Singapore. The second citation refers to the nutritional product included in the safety evaluator's review. This citation is identified on the Internet and the product is manufactured by Metabolic Nutrition.

References to purchase this product could only be located on the internet (<http://www.metabolicsnutrition.com>). Information pertaining to Liposin could not be found at commonly recognized electronic pharmacy sites (e.g., www.Walgreens.com, www.Rx.com; www.drugstore.com; www.cvs.com) nor in the electronic PDR, Facts and Comparison, and Clinical Pharmacology Online. Additionally, a search of the 2005 Red Book, a reference commonly used by pharmacists, did not reveal references to Liposin.

We agree there is similarity in the phonetic and orthographic presentation of the names, Lipofen and Liposin. The names are identical in length (seven letters) and share all of the same letters except for the letters 'fe' vs. 'si.' The last syllable when pronounced 'fen vs. sin' contributes to

the phonetic similarities. Orthographically the names look similar except for the upstroke from the letter 'f' in Lipofen. As noted by the reviewer there are also product characteristics that overlap such as route of administration (oral), dosage form (capsule), and indications for use (both products are used to reduce lipids and cholesterol). However, we disagree on the following points where the reviewer notes that confusion may occur.

- Liposin is a combination product with two active ingredients. Therefore, Liposin is likely to be ordered without the indication of strength since it is not needed to distinguish the product. The bottle clearly does not provide any references to the strength of the product on the main display panel (see below). The reviewer notes that an order for Lipofen 150 mg or Lipofen 50 mg could be misinterpreted as Liposin 150 mg or 50 mg where the 150 mg and 50 mg represent the amounts of L-Carnitine and Glucomannan respectively. We disagree with this conclusion especially because there are multiple active ingredients in this product and the strengths are not prominently displayed in the marketing (labels, website, etc) of this product. Therefore, we believe that it is more likely that the product is known as Liposin without regard to the strength.



- Liposin is not a prescription product but an over-the-counter product. We acknowledge that practitioners oftentimes provide patients with prescriptions that contain information on OTC products as reminders. However, we note that Liposin appears to only be available on the Metabolic Nutrition website. Therefore, if a prescriber is treating a patient for hypercholesterolemia with Liposin they will know that the product is not available at the neighborhood pharmacy and inform the patient of how to obtain the product. Despite this, there is the possibility that a pharmacy could receive a reminder on a prescription form for Liposin and it could be confused for Lipofen. However, as noted above it is unlikely that strength will be present on this form and thus the pharmacist/nurse would need to contact the prescriber for further information.

In summary, we agree the proposed name Lipofen is unacceptable but, we do not agree with the reviewer that there is potential for confusion between Liposin and Lipofen.

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CONSULTATION RESPONSE

DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT

OFFICE OF DRUG SAFETY

(WO: 22, Mailstop 4447, HFD-420)

DATE RECEIVED: July 27, 2005	DESIRED COMPLETION DATE: October 27, 2005	ODS CONSULT #: 04-0076-01
DATE OF DOCUMENT: July 4, 2005	PDUFA DATE: January 11, 2006	

TO: David Orloff, M.D.
Director, Division of Metabolism and Endocrinology Products
HFD-510

THROUGH: Margaret Simoneau
Project Manager, Division of Metabolism and Endocrinology Products
HFD-510

PRODUCT NAME: Lipofen Fenofibrate Capsules, 50 mg, 100 mg, and 150 mg NDA#: 21-612	NDA SPONSOR: Cipher Pharmaceuticals Ltd.
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SAFETY EVALUATOR: Charlie Hoppes, R.Ph., M.P.H.

RECOMMENDATIONS:

1. DMETS does not recommend the use of the proprietary name, Lipofen.
2. DMETS recommends implementation of the label and labeling revisions outlined in Section III. of this review in order to minimize potential errors with the use of this product.
3. DDMAC objects to the proposed trade name "Lipofen" as overly fanciful and suggestive of some unique effectiveness or composition attributable to the product. However, the Division did not concur with DDMAC's objection to Lipofen.

Denise Toyer, Pharm.D. Deputy Director Division of Medication Errors and Technical Support Office of Drug Safety	Carol Holquist, R.Ph. Director Division of Medication Errors and Technical Support Office of Drug Safety Phone: (301) 796-2360 Fax: (301) 796-9865
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is 150 mg daily and hypertriglyceridemia ranges from 50 mg to 150 mg daily. The maximum recommended dose is 150 mg daily. Lipofen will be available as 50 mg, 100 mg, and 150 mg capsules, packaged in ~~30, and 90 count bottles.~~ b(4)

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 Lipofen 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. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies for each of the proposed names 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 Lipofen ~~_____~~. Potential concerns regarding drug marketing and promotion related to the proposed names 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. b(4)

1. Refer to ODS Consult 04-0076-2 in reference to DDMAC's objections with ~~_____~~ DDMAC objects to the proposed trade name "Lipofen" as overly fanciful and suggestive of some unique effectiveness or composition attributable to the product. The active ingredient of this product is the common substance fenofibrate. This composition does not support the implication of unique effectiveness or composition, rendering the proposed trade name as overly fanciful. Furthermore, the prefix of the word, "lipo," strongly suggests lipids, and alludes to the therapeutic category of this product. Additionally, "fen" can be considered a b(4)

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, 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 98-05, and the electronic online version of the FDA Orange Book.

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

truncated version of “fen”ofibrate. Combining the two word portions that imply both the therapeutic category and the identification of the common ingredient is particularly problematic in and of itself, as it could preclude the sponsor from disseminating reminder advertisements or labeling, which are both prohibited from making any suggestions or representations about the drug being advertised (21 CFR 201.100(f), 202.1(e)(2)(i)).

2. The Expert Panel identified six proprietary names that were thought to have the potential for confusion with Lipofen. After further review, one additional name was identified. These products are listed in Table 1 (see page 4), along with the dosage forms available and usual dosage. Panelists commented that Lipofen sounds like an NSAID and could be associated with a “profen” (e.g., ibuprofen).

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

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
Proposed Proprietary Name	Fenofibrate Capsules 50 mg, 100 mg, and 150 mg	50 mg to 150 mg given once daily. 50 to 150 mg for hypertriglyceridemia and 150 mg for hypercholesterolemia.	
Liposyn	Fat Emulsion for total parenteral nutrition, 10% and 20%, 100 mL, 200 mL, and 500 mL	Infuse intravenously at a rate of 1 mL/minute. May increase to 2 mL/ minute	SA/LA
Lipitor	Atorvastatin Calcium Tablets, 10 mg, 20 mg, 40 mg, and 80 mg	Take 10 mg to 80 mg once a day.	LA
Lidopen	Lidocaine Hydrochloride Injection 300 mg/3 mL	Inject 300 mg intramuscularly to prevent myocardial infarction.	SA/LA
Naprosyn/ Naproxen	Naproxen Tablets USP, 250 mg, 375 mg, and 500 mg Naproxen Suspension, 125 mg/5 mL	Take 250 mg to 500 mg twice daily.	LA
Ibuprofen	Ibuprofen Tablets USP, 200 mg, 400 mg, 600 mg, 800 mg Ibuprofen Suspension, 100 mg/5 mL	Take 200 mg to 800 mg every six to eight hours not to exceed 3.2 g per day.	LA
Profen	Ibuprofen Tablets USP, 400 mg Ibuprofen Suspension, 100 mg/5 mL	Take 200 mg to 800 mg every six to eight hours not to exceed 3.2 g per day.	SA/LA
Liposin	Vitamin C (as Ascorbic Acid) 200 mg Chitosan (pH modified) 500 mg Psyllium Husk (Plantago husk) 200 mg L-Carnitine 150 mg Glucomannan (Amorphophallus konjac) (root) 50 mg	Take one to two capsules before each meal with 8 oz. of water.	SA

*Frequently used, not all-inclusive.

**L/A (look-alike), S/A (sound-alike)

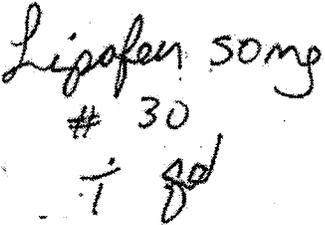
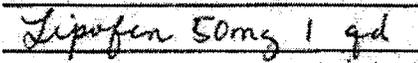
B. PHONETIC and ORTHOGRAPHIC COMPUTER ANALYSIS (POCA)

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 Lipofen 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 the proposed proprietary name to determine the degree of confusion of Lipofen 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 119 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 Lipofen (see table 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.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
<p>Outpatient RX:</p> 	<p>Lipofen 50 mg # 30 Take one every day.</p>
<p>Inpatient RX:</p> 	

2. Results:

Three respondents of the Verbal Study interpreted the proposed name as Liposyn. Liposyn is a currently marketed U.S. product. Additionally, two respondents interpreted the proposed name as Liposin. Liposin is a currently marketed U.S. product. See Appendix A for the complete listing of interpretations from the verbal and written studies.

D. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name Lipofen, the primary concerns related to look-alike and sound-alike confusion with Liposyn, Lidopen, Naprosyn/Naproxen, Ibuprofen, Profen, Lipitor, and Liposin.

Upon further analysis of the names gathered from EPD, the names Naprosyn and Naproxen were not reviewed further due to a lack of convincing look-alike/sound-alike similarities with Lipofen in addition to differentiating product characteristics such as the product strength, indication for use, and frequency of administration.

Additionally, DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was confirmation that Lipofen could be confused with Liposyn and Liposin. Three respondents from the verbal study misinterpreted the name for the already existing marketed drug product, Liposyn and two respondents for the marketed drug product, Liposin. Although there are limitations to the predictive value of these studies, primarily due to sample size, we have acquired safety concerns due to the positive interpretation with this drug product. A positive finding in a study with a small sample size may indicate a high risk and potential for medication errors when extrapolated to the general U.S. population.

- a. Lipitor has been identified as a name with similar appearance to Lipofen when scripted. Lipitor is atrovastatin calcium tablets indicated for reducing elevated lipid and cholesterol thereby reducing the risk of myocardial infarction. The usual adult dosage is 10 mg to 80 mg once a day. Look-alike properties of the names Lipitor and Lipofen may be attributed to the shared letters, "Lip". The "t" and "r" in Lipitor may also look very much like the "f" and "n" in Lipofen (see writing sample below).



The image shows a handwritten writing sample. On the left, the word "Lipofen" is written in a cursive script. Below it, the word "Lipitor" is also written in a cursive script. A vertical line is drawn to the right of the word "Lipitor", separating the two words for comparison.

In addition to orthographic similarities, Lipitor and Lipofen share product similarities including, route of administration (oral), dosage form (both are available as solid oral dosage forms), dosing regimen (both are once-a-day products), and indications for use (both products are used to reduce lipids and cholesterol). Lipitor and Lipofen also share numeric similarities in strength 10 mg vs. 100 mg, respectively. Postmarketing experience has shown confusion as a result of numerical similarities in strength. It is possible, for example, for an order for Lipitor 100 mg daily to be misinterpreted as Lipofen 10 mg daily especially if the last zero on the Lipofen dose lacks prominence or if a blemish on the order makes it

appear as though there is a decimal point, "10.0". In the event that a patient gets Lipitor rather than Lipofen or vice versa, they may be at risk of unintended side effects since there are adverse event profile differences between the two products. Overall, DMETS believes there is potential for these products to be confused.

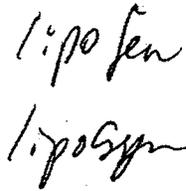
- b. Liposin may sound like Lipofen when spoken. In fact, two participants of the Rx Study interpreted a verbal order for Lipofen as "Liposin". Liposin is an over-the-counter preparation formulated as a complement to "low-fat" diets to help maintain normal blood cholesterol levels. The recommended dosage is one or two capsules after each meal. Liposin and Lipofen owe sound-alike characteristics to shared letters, "Lipo" and "n". The fricatives "s" in Liposin and "f" in Lipofen, in addition to the short vowel "i" in Liposin and "e" in Lipofen may also sound alike. Shared letters also contribute to look-alike similarities between Liposin and Lipofen (see writing sample below).

The image shows two handwritten words, "Liposin" and "Lipofen", written in cursive. The words are written one above the other, separated by a vertical line. The handwriting is somewhat slanted and the letters are connected, illustrating the visual similarity between the two words.

In addition to phonetic and orthographic similarities, Liposin and Lipofen share product similarities including, route of administration (oral), dosage form (capsule), and indications for use (both products are used to reduce lipids and cholesterol). Liposin and Lipofen also have product differences including, dosing regimen (before meals vs. once-a-day) and prescriptive status (OTC vs. Rx only). Liposin, having multiple active ingredients, would most likely be ordered without reference to strength, thus possibly leading to clarifying questions which might in turn prevent errors. However, an order for Lipofen referencing the strengths, 50 mg or 150 mg, might be confused with Liposin due to strength commonalities with some of the active ingredients in Liposin: L-Carnitine 150 mg, and Glucomannan (Amorphophallus konjac) (root) 50 mg. Also, it is common practice for prescribers to write an order for OTC products as a reminder for the patient or phone a request for such items to a pharmacy. In that scenario, these two products could be confused due to strong orthographic and phonetic similarities. Overall, due to product characteristic overlap, and strong sound-alike characteristics and orthographic similarities between Liposin and Lipofen, DMETS believes there is potential for confusion between the products.

- c. Liposyn may sound similar to Lipofen when spoken and look similar when scripted. In fact, three participants of the Rx studies responded with "Liposyn" to a Lipofen verbal prescription order. Liposyn is a fat emulsion for total parenteral nutrition, and is available in 10% and 20% strengths in the following sizes, 100 mL, 200 mL, and 500 mL. Liposyn, a source of calories and essential fatty acids for patients requiring parenteral nutrition for extended periods of time (usually for > 5 days), is usually infused intravenously at a rate of 1 or 2 mL/minute. Sound-alike properties of the names Liposyn and Lipofen may be attributed to the shared beginnings, "Lipo", and terminal "n" sound. The "y" in Liposyn also sounds like the short "i", and is therefore similar in sound to the

short "e" of Lipofen. The names also look very much alike when scripted, especially in cursive writing with downstroke "f" in Lipofen similar to downstroke "y" in Liposyn (see writing sample below).

The image shows two lines of handwritten text in cursive. The first line reads "Lipofen" and the second line reads "Liposyn". Both words are written in a fluid, cursive style where the downstrokes of the letters 'f' and 'y' are very similar, making them look alike when scripted.

In addition to phonetic and orthographic similarities, Liposyn and Lipofen share product similarities including, numeric alignment of one size of Liposyn (100 mL) with one strength of Lipofen (100 mg). It is also possible for both products to be given once a day. However, Liposyn and Lipofen also have product differences including, route of administration (intravenous vs. oral), dosage form (injection vs. capsule), and dose (10% and 20% vs. 50 mg, 100 mg, and 150 mg), respectively. These differences will minimize the potential for error.

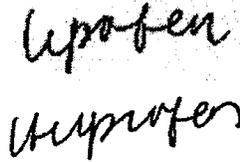
- d. Lidopen may sound similar to Lipofen when spoken and look similar when scripted. Lidopen is lidocaine hydrochloride injection, for prevention of myocardial infarction. Lidocaine (300 mg) from the Lidopen device is intended for self-administration by intramuscular injection. Sound-alike properties of the names Lidopen and Lipofen may be attributed to the shared letters, "Li,o,en", and the rhyming qualities of the names. The names also look similar when scripted, especially in cursive writing with downstroke "f" in Lipofen similar to downstroke "p" in Lidopen (see writing sample below).

The image shows two lines of handwritten text in cursive. The first line reads "Lidopen" and the second line reads "Lipofen". Both words are written in a fluid, cursive style. The downstroke of the 'p' in "Lidopen" is similar to the downstroke of the 'f' in "Lipofen", making them look alike when scripted.

However, the upstroke "d" in Lidopen may serve to orthographically differentiate the name from Lipofen with downstroke "p". Despite phonetic and orthographic similarities, Lidopen and Lipofen have product differences which may serve to distinguish the products including, route of administration (intramuscular vs. oral), dosage form (injection vs. capsule), dose (300 mg vs. 50 mg, 100 mg, and 150 mg), and dosing interval (situational use vs. chronically, once daily), respectively. These differences will minimize the potential for error.

- e. Ibuprofen has been identified as a name with similar appearance to Lipofen when scripted. Ibuprofen, the active ingredient in various Rx and OTC products

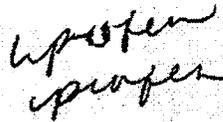
including, Motrin and Advil, is indicated for relief of signs and symptoms of rheumatoid arthritis (RA) and osteoarthritis (OA), relief of mild-to-moderate pain, treatment of primary dysmenorrhea, and reduction of fever. The usual adult dosage is 200 mg to 800 mg every six to eight hours not to exceed 3.2 grams in one day. The names look similar when scripted, due to shared letters, "l", "p", and "ofen" (see writing sample below).



The image shows two lines of handwritten text. The first line is "Lipofen" and the second line is "Ibuprofen". Both are written in a cursive, slanted script.

However, the relatively longer name, ibuprofen, with distinctive "b" and "r" may serve to differentiate the names orthographically. In addition to phonetic and orthographic similarities, Ibuprofen and Lipofen share product similarities including, numeric alignment of one strength (100 mg), route of administration (oral), and similarities in dosage form (both are available as a solid oral dosage form). However, ibuprofen and Lipofen also have product differences including, indications for use (analgesic/antipyretic vs. lipid/cholesterol lowering), and dosing regimen (every six to eight hours vs. once daily), respectively. These differences and lack of convincing look-alike properties will minimize the potential for error.

- f. Profen may sound similar to Lipofen when spoken and look similar when scripted. Profen is the proprietary name for ibuprofen, indicated for relief of signs and symptoms of rheumatoid arthritis (RA) and osteoarthritis (OA), relief of mild-to-moderate pain, treatment of primary dysmenorrhea, and reduction of fever. The usual adult dosage is 200 mg to 800 mg every six to eight hours not to exceed 3.2 grams in one day. Sound-alike properties of the names Profen and Lipofen may be attributed to the shared letters, "p", "o", and "fen". However, the distinctive "r" in Profen and relative brevity (two syllables vs. three), may contribute to differentiate the names phonetically. The names also look alike, especially if the "li" beginning Lipofen lack prominence (see writing sample below).



The image shows two lines of handwritten text. The first line is "Lipofen" and the second line is "Profen". Both are written in a cursive, slanted script.

However, the relatively longer name, lipofen, and distinctive "r" in Profen may serve to differentiate the names orthographically. Profen and Lipofen share product similarities including, numeric alignment of one strength (100 mg, an Over-The-Counter dose for Profen), route of administration (oral), and similarities in dosage form (both are available as a solid oral dosage form). However, Profen and Lipofen also have product differences including, indications for use (analgesic/antipyretic vs. lipid/cholesterol lowering), and dosing regimen (every six to eight hours vs. once daily), respectively. These product differences as well

as prescriptive differences on the overlapping strength (Profen is OTC at that strength), and lack of convincing sound-alike/look-alike properties will minimize the potential for error.

III. COMMENTS TO THE SPONSOR:

DMETS does not recommend the use of the proprietary name Lipofen. In reviewing the proprietary name, the primary concerns related to look-alike and/or sound-alike confusion with Lipofen/Lipitor, and Lipofen/Liposin.

1. Lipitor has been identified as a name with similar appearance to Lipofen when scripted. Lipitor is atrovastatin calcium tablets indicated for reducing elevated lipid and cholesterol thereby reducing the risk of myocardial infarction. The usual adult dosage is 10 mg to 80 mg once a day. Look-alike properties of the names Lipitor and Lipofen may be attributed to the shared letters, "Lip". The "t" and "r" in Lipitor may also look very much like the "f" and "n" in Lipofen (see writing sample below).

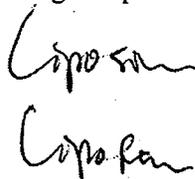


The image shows two lines of handwritten text in cursive. The top line reads "Lipofen" and the bottom line reads "Lipitor". The letters are slanted and connected, making the two words appear very similar in appearance.

In addition to orthographic similarities, Lipitor and Lipofen share product similarities including, route of administration (oral), dosage form (both are available as solid oral dosage forms), dosing regimen (both are once-a-day products), and indications for use (both products are used to reduce lipids and cholesterol). Lipitor and Lipofen also share numeric similarities in strength 10 mg vs. 100 mg, respectively. Postmarketing experience has shown confusion as a result of numerical similarities in strength. It is possible, for example, for an order for Lipitor 100 mg daily to be misinterpreted as Lipofen 10 mg daily especially if the last zero on the Lipofen dose lacks prominence or if a blemish on the order makes it appear as though there is a decimal point, "10.0". In the event that a patient gets Lipitor rather than Lipofen or vice versa, they may be at risk of unintended side effects since there are adverse event profile differences between the two products. Overall, DMETS believes there is potential for these products to be confused.

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2. Liposin may sound like Lipofen when spoken. In fact, two participants of the Rx Study interpreted a verbal order for Lipofen as "Liposin". Liposin is an over-the-counter preparation formulated as a complement to "low-fat" diets to help maintain normal blood cholesterol levels. The recommended dosage is one or two capsules after each meal. Liposin and Lipofen owe sound-alike characteristics to shared letters, "Lipo" and "n". The fricatives "s" in Liposin and "f" in Lipofen, in addition to the short vowel "i" in Liposin and "e" in Lipofen may also sound alike. Shared letters also contribute to look-alike similarities between Liposin and Lipofen (see writing sample below).



The image shows two handwritten words, 'Liposin' and 'Lipofen', written in cursive. They are positioned one above the other, separated by a vertical line. The words are written in dark ink on a light background.

In addition to phonetic and orthographic similarities, Liposin and Lipofen share product similarities including, route of administration (oral), dosage form (capsule), and indications for use (both products are used to reduce lipids and cholesterol). Liposin and Lipofen also have product differences including, dosing regimen (before meals vs. once-a-day) and prescriptive status (OTC vs. Rx only). Liposin, having multiple active ingredients, would most likely be ordered without reference to strength, thus possibly leading to clarifying questions which might in turn prevent errors. However, an order for Lipofen referencing the strengths, 50 mg or 150 mg, might be confused with Liposin due to strength commonalities with some of the active ingredients in Liposin: L-Carnitine 150 mg, and Glucomannan (Amorphophallus konjac) (root) 50 mg. Also, it is common practice for prescribers to write an order for OTC products as a reminder for the patient or phone a request for such items to a pharmacy. In that scenario, these two products could be confused due to strong orthographic and phonetic similarities. Overall, due to product characteristic overlap, and strong sound-alike characteristics and orthographic similarities between Liposin and Lipofen, DMETS believes there is potential for confusion between the products.

Additionally, DMETS reviewed the labels and labeling from a safety perspective. DMETS has identified the following areas of possible improvement, which might minimize potential user error.

A. GENERAL COMMENT

DMETS reviewed labels and labeling with the previously proposed proprietary name, "CIP-Fenofibrate", and was therefore unable to assess the effect the newly proposed proprietary name, "Lipofen" has on readability.

B. CONTAINER LABELS

[50 mg, 100 mg, 150 mg, _____, packaged in _____ 30, and 90]

1. _____

b(4)

2. Relocate "Rx only", so that it does not appear with the expression of strength for the sample size (7's) and container of 30's.
3. Increase the prominence of the established name.
4. To prevent confusion, separate the statement of strength and net quantity of contents.
5. Decrease the prominence of the manufacturer's name.

C. INSERT LABELING

1. Please ensure that the conditions of 21 CFR 201.10(g)(1) are met such that the established name of this drug product appears at least once in association with the proprietary name in each column of running text of the insert labeling.
2. We note that there is no Information for Patients subsection in the PRECAUTIONS section of insert labeling. Is there any pertinent information that needs to be presented?

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IV. RECOMMENDATIONS:

- A. DMETS does not recommend the use of the proprietary name, Lipofen.
- B. DMETS recommends implementation of the label and labeling revisions outlined in Section III of this review that might lead to safer use of the product. We would be willing to revisit these issues if the Division receives another draft of the labeling from the manufacturer.
- C. DDMAC objects to the proposed trade name "Lipofen" as overly fanciful and suggestive of some unique effectiveness or composition attributable to the product. However, the Division did not concur with DDMAC's objection to Lipofen.

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 301-796-0538.

Charlie Hoppes, RPh, MPH
Safety Evaluator
Division of Medication Errors and Technical Support
Office of Drug Safety

Concur:

Alina Mahmud, RPh, MS
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

Appendix A. Prescription Studies for Lipofen

Verbal	Inpatient	Outpatient
Liposin	Lipofen	Lipofen
Liposin	Lipofen	Lipofen
Lipofin	Lipofen	Lipofen
Liposyn	Lipofen	Lipofen
Liposyn	Lipfen	Lipofen
Libosen	Lipofen	Lipofen
Liposen	Lipofin	Lipofen
Liposon	Lipofen	Lipofen
Lipo-son	Lipofen	Lipofen
Lipofin	Lipofen	Lipofen
Liposun	Lipofen	Lipofen
Lipo-Syn	Lipofen	Lopfen
Liposen	Lipofen	Lipofen
	Lipofen	Lipofen
	Lipofin	Lipofen
	Lipofen	

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/s/

Charles Hoppes
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