CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 22-033

PROPRIETARY NAME REVIEW(S)

MEMORANDUM	Division of Medication Errors and Technical Support Office of Surveillance and Epidemiology HFD-420; WO22, Mail Stop 4447 Center for Drug Evaluation and Research

To: Thomas Laughren, MD
Director, Division of Psychiatry Products
HFD-130

Through: Linda Y. Kim-Jung, PharmD, Team Leader
Denise P. Toyer, PharmD, Deputy Director
Carol A. Holquist, RPh, Director
Division of Medication Errors and Technical Support, HFD-420

From: Loretta Holmes, BSN, PharmD, Safety Evaluator
Division of Medication Errors and Technical Support, HFD-420

Date: December 2, 2007

Subject: **DMETS Proprietary Name, Label, and Labeling Review**
Drug: Luvox CR (Fluvoxamine Maleate) Extended-Release Tablets
NDA#: 22-033
Sponsor: Solvay Pharmaceuticals

Review #: 2007-2315

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

This review was written in response to a request from the Division of Psychiatry Products (HFD-130), for a re-review of the proposed proprietary name, Luvox CR, regarding potential name confusion with other proprietary or established drug names. Revised container labels, carton and insert labeling were provided for review and comment.

DMETS notes that in our previous review of the name (OSE Review 06-0193, dated January 31, 2007), DMETS identified a proposed name ([redacted] pending review by the Agency, that had the potential for confusion with Luvox CR and we recommended that the application that received approval first have rights to the name. However, the name [redacted] is no longer viable because that product was approved with a different name. Since our previous review of the name, the following additional names have been identified as having a similar appearance and/or sound to Luvox CR: Lovaza, Videx, [redacted], NuOx, and Rulox.

Upon initial review of the five names identified as having similar appearance and/or sound to Luvox CR, it was determined that they lacked convincing look-alike and/or sound-alike similarities with Luvox CR in addition to having differentiating product characteristics such as:

- Videx (didanosine): Differs in dosage form (chewable tablets, powder for oral solution) and indication of use (treatment of HIV).
- [redacted]

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

- Rulox (aluminum hydroxide and magnesium hydroxide): Differs in dose (10 mL to 20 mL), dosage form (oral suspension), frequency of administration (four times per day), strength (aluminum hydroxide 225 mg and magnesium hydroxide 200 mg per 5 mL), and indication of use (treatment of gastric hyperacidity). Additionally, Rulox is an over-the-counter product.
- NuOx (benzoyl peroxide and sulfur): Differs in strength (benzoyl peroxide 6% and sulfur 3%), dosage form (topical gel) and indication of use (treatment of acne vulgaris). DMETS was unable to obtain dosage information for this product.
- Lovaza (omega-3-acid ethyl esters): Differs in strength (1 gm), dose (2 gm or 4 gm), number of strengths available (one), and indication of use (treatment of hypertriglyceridemia).

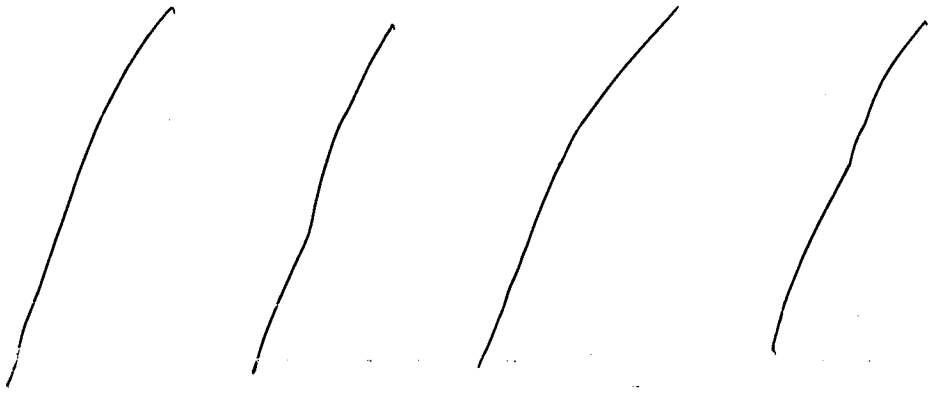
Thus the name remains acceptable.

In the review of the container labels, carton and insert labeling of Luvox CR, DMETS has applied principles of human factors, conducted a FMEA (Failure Modes and Effects Analysis) and identified the following areas of needed improvement.

A. GENERAL COMMENTS

1. Relocate the dosage form statement "extended-release capsules" so that it immediately follows the established name (since it is part of the established name). Additionally, use a darker font for the established name and the dosage form to increase their prominence.

2. Relocate the usual dosage statement from the principal display panel to one of the side panels.

3. 

4. Since the product is an extended-release capsule, include instructions that state the capsule should not be crushed or chewed.

5. DMETS recommends the sponsor launch an educational campaign prior to and after marketing Luvox CR in order to alert healthcare professionals to the availability of this new formulaton and its similarities and differences to Luvox which is to be reintroduced into the marketplace.

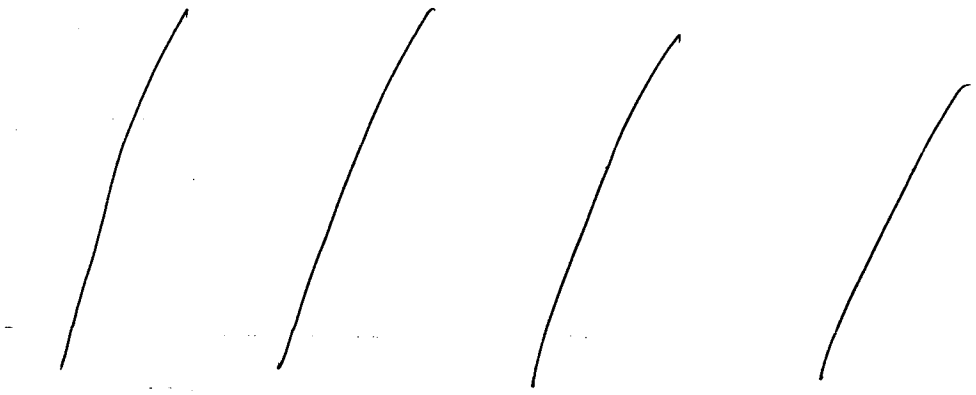
2 Page(s) Withheld

1 Trade Secret / Confidential

_____ Draft Labeling

_____ Deliberative Process

D. INSERT LABELING



2. The product is an extended-release capsule, however, there is no wording in the Dosage and Administration Section that states that the capsule should not be crushed or chewed. Please include this information.

In summary, DMETS has no objections to the use of the proposed proprietary name, Luvox CR. However, if approval of the NDA is delayed beyond 90 days from the signature date of this review, the name must be re-evaluated. A re-review of the name before NDA approval will rule out any objections based upon approvals of other proprietary/established names from the signature date of this document. DMETS recommends implementation of the label and labeling recommendations as outlined above. Additionally, the Division of Drug Marketing, Advertising, and Communications (DDMAC) finds the proprietary name, Luvox CR, acceptable from a promotional perspective.

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. Please copy DMETS on any correspondence to the sponsor pertaining to this issue. If you have further questions or need clarification, please contact Daniel Brounstein, OSE Project Manager, at 301-796-0674.

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

/s/

Loretta Holmes
12/13/2007 09:03:39 AM
DRUG SAFETY OFFICE REVIEWER

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12/13/2007 09:12:59 AM
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12/13/2007 09:15:47 AM
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CONSULTATION RESPONSE

DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY
(DMETS; WO22, Mailstop 4447)

DATE RECEIVED: June 30, 2006 DATE OF DOCUMENT: April 28, 2006	DESIRED COMPLETION DATE: January 31, 2007 PDUFA DATE: January 31, 2007	OSE REVIEW #: 06-0193

TO: Thomas Laughren, MD
Director, Division of Psychiatry Products
HFD-130

THROUGH: Linda Y. Kim-Jung, PharmD, Team Leader
Denise P. Toyer, PharmD, Deputy Director
Carol A. Holquist, RPh, Director
Division of Medication Errors and Technical Support

FROM: Loretta Holmes, PharmD, Safety Evaluator
Division of Medication Errors and Technical Support

PRODUCT NAME: **Luvox CR**
(Fluvoxamine Maleate) Extended-release Capsules
100 mg and 150 mg

NDA #: **22-033**

SPONSOR: Solvay Pharmaceuticals

RECOMMENDATIONS:

1. DMETS identified a proposed name, [redacted] that has the potential for confusion with Luvox CR. DMETS does not believe that Luvox CR and [redacted] can safely co-exit in the marketplace. Therefore, DMETS recommends that only one of these names be approved. The application that receives approval first will have rights to the name. If the approval of this application is delayed beyond 90 days from the signature date of this document, the name Luvox CR must be re-evaluated.

2. DMETS also recommends that the sponsor launch an educational campaign to inform practitioners of the existence of this new product and to the fact that it has overlapping characteristics with the currently marketed fluvoxamine immediate-release products. Practitioners need to be forewarned of these similarities prior to being exposed to new prescriptions for Luvox CR.

3. DMETS recommends implementation of the label and labeling revisions outlined in Section III of this review to minimize potential errors with the use of this product. Additionally, DMETS strongly recommends that the sponsor adds a " [redacted] on the container label and carton labeling in order to minimize confusion between Luvox CR and the existing immediate release fluvoxamine product.

4. DMETS recommends consulting Richard Lostritto, Chair of the CDER Labeling and Nomenclature Committee (LNC) for guidance on the established name with respect to ' [redacted] " is not a dosage form recognized by the United States Pharmacopeia.

5. DDMAC finds the proprietary name, Luvox CR, acceptable from a promotional perspective.

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 Angela Robinson, Project Manager, at 301-796-2284.

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

Division of Medication Errors and Technical Support (DMETS)
Office of Surveillance and Epidemiology
White Oak Bldg #22, Mailstop 4447
Center for Drug Evaluation and Research

PROPRIETARY NAME, LABEL AND LABELING REVIEW

DATE OF REVIEW: July 7, 2006

NDA#: **22-033**

NAME OF DRUG: **Luvox CR**
(Fluvoxamine Maleate) Extended-release Capsules
100 mg and 150 mg

NDA HOLDER: Solvay Pharmaceuticals, Inc.

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

I. INTRODUCTION:

This consult was written in response to a request from the Division of Psychiatry Products (HFD-130), for assessment of the proprietary name, Luvox CR, regarding potential name confusion with other proprietary or established drug names. Luvox CR will be a product extension of the Luvox product line. Although the reference listed drug, "Luvox", is no longer available, the generic equivalent, fluvoxamine maleate, is currently available from various manufacturers. The sponsor is proposing Luvox CR, an extended-release form of fluvoxamine maleate, which is to be dosed once daily, whereas the currently marketed fluvoxamine maleate is an immediate-release dosage form which can be dosed once or twice daily. See Table 1 below for a side-by-side comparison of both products. Container labels, carton and package insert labeling were provided for review and comment.

Table 1. Product Comparison (Luvox CR vs. Fluvoxamine maleate)

Product Name	Dosage form	Strengths	Indication	Adult Dose
Luvox CR (Proposed proprietary name)	Extended release Capsule	100 mg and 150 mg	Generalized social anxiety disorder and obsessive-compulsive disorder	100 mg once daily at bedtime. Increase in 50 mg increments as needed to a maximum of 300 mg per day
Fluvoxamine maleate (Established name—generic products available only)	Tablet	25 mg, 50 mg and 100 mg	Obssessive-compulsive disorder	50 mg once daily at bedtime. Increase the dose in 50 mg increments as needed to a maximum of 300 mg per day. Give total daily doses greater than 100 mg in 2 divided doses.

PRODUCT INFORMATION

Luvox CR contains fluvoxamine maleate, a selective serotonin (5-HT) reuptake inhibitor (SSRI). It is indicated for the treatment of Generalized Social Anxiety Disorder and Obsessive-Compulsive Disorder (OCD). The recommended starting dose in adult patients is 100 mg administered as a single daily dose

at bedtime. The dose should be increased in 50 mg increments every week, as tolerated, until maximum therapeutic benefit is achieved, not to exceed 300 mg per day. Luvox CR will be available in 100 mg and 150 mg strengths and supplied in bottles [redacted] containing 30 capsules.

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 databases[3,4] for existing drug names which sound-alike or look-alike to Luvox CR 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 conducted[5]. The Saegis[6] 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 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 name, Luvox CR. 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 finds the proprietary name, Luvox CR, acceptable from a promotional perspective.

2. The Expert Panel identified ten proprietary names and one established name that were thought to have the potential for confusion with Luvox CR. These products are listed in Table 2 (pages 4 and 5), along with the dosage forms available and usual dosage.

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[1] MICROMEDEX Integrated Index, 2006, 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 98-06, 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

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

Luvox (Discontinued in 2003) Generics available	Fluvoxamine maleate Tablets 25 mg, 50 mg and 100 mg	Obsessive-Compulsive Disorder: 50 mg as a single daily dose at bedtime. Increase the dose in 50 mg increments every 4 to 7 days, as tolerated, until maximum therapeutic benefit is achieved, not to exceed 300 mg per day. Give total daily doses greater than 100 mg in 2 divided doses; if doses are unequal, give larger dose at bedtime.	LA/SA
Lasix	Furosemide Tablets (brand and generics available): 20 mg, 40 mg, and 80 mg Oral Solution (generics availabe only): 10 mg/mL and 40 mg/5 mL Injection (generics available only): 10 mg/mL	Edema, congestive heart failure, or hypertension (diuresis): *Oral*: 20 mg to 80 mg per dose initially, increased in increments of 20 mg to 80 mg per dose at intervals of 6 to 8 hours; usual maintenance interval is once or twice daily. *Intramuscular or Intravenous (IV)*: 20 mg to 40 mg per dose, may be repeated in 1 to 2 hours as needed and increased by 20 mg per dose with each succeeding dose up to 1000 mg per day; usual dosing interval is 6 to 12 hours. *Continuous intravenous infusion*: Initial IV bolus dose of 20 mg to 40 mg, followed by continuous IV infusion doses of 10 mg to 40 mg per hour.	LA
			LA
Levoxyl	Levothyroxine sodium Tablets 25 mcg, 50 mcg, 75 mcg, 88 mcg, 100 mcg, 112 mcg, 125 mcg, 137 mcg, 150 mcg, 175 mcg, 200 mcg, and 300 mcg	Hypothyroidism: Healthy adults <50 years old, 1.7 mcg/kg/d (e.g., 100 mcg to 125 mcg/day for a 70 kg adult). Older patients may require less than 1 mcg/kg/day. Dose should be adjusted based on clinical response and laboratory parameters. TSH suppression: *Well differentiated thyroid cancer*: Dose should be individualized. Doses >2 mcg/kg/day may be needed to suppress TSH to <0.1 mU/L. *Benign nodules and nontoxic multinodular goiter*: Goal TSH suppression 0.1 mU/L to either 0.5 mU/L or 1 mU/L	SA
Lonox	Diphenoxylate hydrochloride and atropine sulfate Tablet 2.5 mg/0.025 mg	Adjunctive therapy in the management of diarrhea: Two tablets four times per day. Reduce dosage once control is achieved.	LA
Lidex	Fluocinonide Cream, ointment, solution and gel 0.05%	Inflammatory and pruritic dermatologic conditions: Apply a thin film to the affected area 2 to 4 times daily depending on the severity of the condition.	

Lovenox	Enoxaparin sodium Sterile solution for injection Prefilled Syringes: 30 mg/0.3 mL, 40 mg/0.4 mL, 60 mg/0.6 mL, 80 mg/0.8 mL, 100 mg/1 mL, 120 mg/0.8 mL, 150 mg/1 mL Multidose vial: 300 mg/3 mL vial (100 mg/mL)	Given subcutaneously. Deep vein thrombosis (DVT) prophylaxis: *Hip replacement surgery*: 30 mg twice daily or 40 mg daily; *Knee replacement*: 30 mg twice daily; *Abdominal surgery*: 40 mg once daily; *Medical patients with severely restricted mobility during acute illness*: 40 mg once daily; DVT treatment: 1 mg/kg/dose every 12 hours or 1.5 mg/kg once daily. Unstable angina or non-Q-wave MI: 1 mg/kg twice daily in conjunction with oral aspirin.	LA/SA
Fluoxetine (established name)	Fluoxetine hydrochloride Tablets: 10 mg and 20 mg Capsules: 10 mg, 20 mg, and 40 mg Oral solution: 20 mg/5 mL	Depression, Obsessive-Compulsive Disorder, Bulimia: 20 mg per day in the morning; may increase after several weeks by 20 mg per day increments; maximum 80 mg per day. Doses greater than 20 mg may be given once daily or divided twice daily. Lower doses of 5 mg to 10 mg per day have been used for initial treatment. Panic disorder: Initially, 10 mg per day. After 1 week, increase to 20 mg per day.	LA/SA
Luveris	Lutropin Alfa Powder for injection, lyophilized 82.5 units/vial (Delivers 75 units lutropin alfa after reconstitution)	Follicle stimulation: 75 units subcutaneously daily until adequate follicular development is noted; maximum duration of treatment: 14 days; to be used concomitantly with follitropin alfa.	LA/SA
Zyvox	Linezolid Tablets: 400 mg and 600 mg Powder for oral suspension: 100 mg/5 mL (after reconstitution) Injection (2 mg/mL): 100 mL, 200 mL and 300 mL ready to use bags	Treatment of infections caused by susceptible strains of the designated organisms: Dosage range: 400 mg to 600 mg orally or intravenously for 10 to 28 days depending on the type of infection being treated.	LA/SA
Loprox	Ciclopirox Cream: 0.77% Gel: 0.77% Shampoo: 1% Suspension, topical: 0.77%	*Suspension and cream:* Tinea pedis, tinea cruris and tinea corporis; cutaneous candidiasis; and tinea versicolor. Apply twice daily, gently massage into affected areas; if no improvement after 4 weeks, re-evaluate the diagnosis. *Gel:* Tinea pedis and tinea corporis; seborrheic dermatitis of the scalp. Apply twice daily, gently massage into affected areas and surrounding skin, if no improvement after 4 weeks of treatment, re-evaluate the diagnosis. *Shampoo:* Seborrheic dermatitis of the scalp in adults. Apply to wet hair, lather, and leave in place for about 3 minutes; rinse. Repeat twice weekly for 4 weeks; allow a minimum of 3 days between applications.	LA/SA

* Frequently used, not all-inclusive.
** L/A (look-alike), S/A (sound-alike)
***Name pending approval. Not FOI releasable.

B. 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 Luvox CR 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 126 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 Luvox CR (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. A total of 37 participants that were surveyed responded to these studies.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Outpatient RX: Luvox CR 100 mg #15 1 capsule at bedtime	"Luvox CR 100 mg Dispense Number 15 One capsule at bedtime"
Inpatient RX: Luvox CR 100mg, 1 capsule at bedtime	

2. Results:

None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed U.S. product. However, two respondents in the inpatient prescription study omitted the modifier "CR" and misinterpreted the name as "Luvox". See Appendix A (page 14) for the complete listing of interpretations from the verbal and written studies.

C. ADVERSE EVENT REPORTING SYSTEM (AERS) and DQRS DATABASE SEARCHES

Although the NDA for Luvox was withdrawn on September 3, 2003[7], generically equivalent products are currently available from various manufacturers. Since the sponsor proposes to use the root name, Luvox, the FDA *Adverse Event Reporting System* (AERS) and the *Drug Quality Reporting System* (DQRS) databases were searched for all postmarketing cases concerning medication errors associated with Luvox and fluvoxamine.

[7] Decision Support System (DSS), accessed June 29, 2006.

AERS was searched using the MedDRA High Level Group Term "Medication Error" (the Preferred Term "Intentional Overdose" was excluded) and the product names "Luvox" and "fluvoxamine maleate". Additionally, the DQRS database was searched for medication error cases concerning Luvox and fluvoxamine.

Using this search strategy, eleven medication error cases (n=11) were retrieved. Of the eleven cases, ten cases concerned name confusion between Luvox or fluvoxamine with another name: fluvoxamine and fluoxetine (n=4), Luvox and Levoxyl (n=1), Luvox and Lasix (n=3), and Luvox and Lovenox (n=2). The remaining case (n=1) involved the dispensing of the wrong strength of Luvox (Luvox 100 mg tablets were dispensed instead of the prescribed 50 mg tablets).

- Luvox Brand Name Confusion (n=6)

  Five of the brand name confusion cases cited reporter's concerns with the potential to confuse the name Luvox with either Lasix, Lovenox, or Levoxyl due to look-alike and/or sound-alike similarities between these names. The fifth case reported that "several close dispensing errors" occurred because Luvox looks like Lasix when written. The case report narratives are listed in Appendix B (page 15).

- Established Name Confusion (n=4)

  Four of the name confusion cases dealt with look-alike and/or sound-alike confusion between the established names Fluvoxamine and Fluoxetine. In one of the four cases, fluoxetine 10 mg tablets were dispensed instead of fluvoxamine 100 mg tablets and was taken by the patient. No patient harm was reported. In the second case, there was confusion between fluoxetine and fluvoxamine; however the error was discovered before the medication was dispensed. The third case describes a situation in which fluoxetine 100 mg twice per day was ordered but upon further investigation, the pharmacist discovered that the drug ordered should have been fluvoxamine. Subsequently, the order was clarified and the error did not reach the patient. The final case describes the potential to confuse the names fluvoxamine and fluoxetine due to similarities between the names. The case report narratives are listed in Appendix B (page 15).

- Wrong strength dispensed (n=1)

  One case describes a situation in which Luvox 100 mg tablets were dispensed instead of the prescribed Luvox 50 mg tablets and the patient took the wrong dose for two weeks; there was no patient harm. The case report narrative is listed in Appendix B (page 15).

D. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name Luvox CR, the primary concerns relating to look-alike and sound-alike confusion with Luvox CR are: Luvox, Lasix, Levoxyl, Lovenox, Lonox, Luveris, Zyvox, Loprox, Lidex, and ——→ There is also look-alike and sound-alike concern about confusion between the established names, fluvoxamine and fluoxetine.
DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was confirmation that Luvox CR could be confused with Luvox. Two respondents from the verbal prescription study misinterpreted the name as "Luvox" without the inclusion of

the modifier "CR". 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. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Luvox CR.

Upon further analysis, the names Lonox, Luveris, Zyvox, Loprox, and Lidex will not be reviewed further because they lack convincing look-alike and/or sound-alike similarities to Luvox in addition to having different product characteristics such as indication of use, dosage form and/or product strength.

Additionally, postmarketing surveillance has demonstrated that the names Lasix, Levoxyl, and Lovenox are of concern due to look-alike/sound-alike similarities with Luvox. However, the reports concerning proprietary name confusion between Luvox and Lasix, Levoxyl, or Lovenox were received within the first several years of introduction of Luvox in 1994 and may have been due to unfamiliarity with Luvox. Furthermore, due to name recognition of Luvox, orders may still be written for Luvox in lieu of writing out the generic name, fluvoxamine. Prescription data from Verispan shows tha[redacted] Although practitioners are still prescribing fluvoxamine by the branded name, Luvox, DMETS has not received any new reports of confusion between Luvox and Lasix, Levoxyl, or Lovenox since 1995. Thus, DMETS does not believe that the addition of the modifier "CR" to the name Luvox will pose any additional look-alike/sound-alike concerns with the names Lasix, Levoxyl and Lovenox. Therefore, these names will not be reviewed further. However, DMETS will continue to monitor for errors between those names and Luvox or Luvox CR (once approved).

1. Look-Alike and Sound-Alike Name Confusion with Luvox CR

   a. Luvox was identified as a name that poses potential comfusion with Luvox CR. Luvox was discontinued in 2003; however, the generic equivalent, fluvoxamine maleate (an immediate-release dosage form) is readily available from various manufacturers. In 2006, data from Verispan indicates that[redacted]

      Although, Luvox CR is technically not a product line extension of Luvox (because it has been discontinued), since fluvoxamine is still being prescribed as Luvox DMETS must also review the name as a product line extension. Post-marketing experience has shown that medication errors may occur when introducing product line extensions especially when there is an overlap in strengths, dosing interval, and a knowledge deficit with respect to the introduction of the new extended-release formulation. DMETS anticipates this to be a problem despite the fact that the branded product Luvox is no longer marketed. Luvox CR and Luvox overlap in established name (Fluvoxamine Maleate), indication of use (obsessive compulsive disorder), product strength (100 mg), route of administration (oral), dosage form (tablet) and dose (100 mg to 300 mg). The fact that both formulations have overlapping product characteristics compounds the potential for

[8] Verispan Vector One®: National, 2002-2007, data extracted Jan 2007. Source Files: VONA TAYLOR 01-17-2007 06-0193 Fluvoxamine Use Rxs.xl.

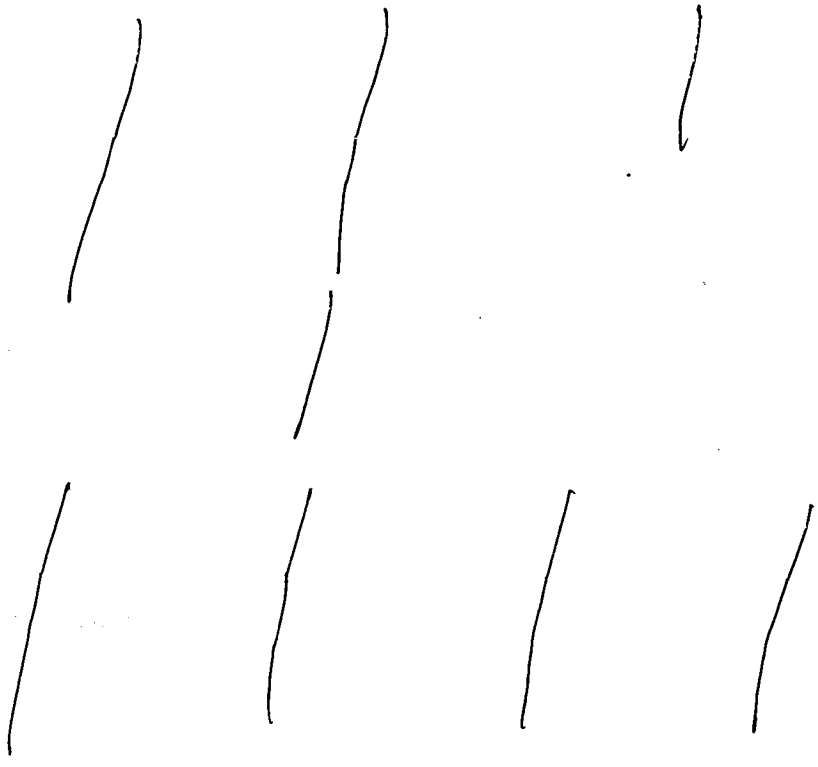
*****Proprietary Information: Data not FOI releasable.**

confusion between the existing immediate release fluvoxamine and the proposed Luvox CR. These product similarities are concerning because of the number of prescriptions still being written for "Luvox."

Although the proposed name contains a modifier, "CR", it may not serve as a deterrent in the misinterpretation of the name. For example, two respondents in the written inpatient prescription study misinterpreted the prescription as "Luvox" without the inclusion of the modifier "CR". Thus, if the modifier "CR" was omitted from a prescription, the generic immediate-release fluvoxamine may be substituted. The omission of modifiers from prescription orders are a common source of error.[9]

Confusion between proposed extended-release dosage forms and their currently marketed immediate-release dosage forms are common upon the introduction of an extended-release dosage form to the marketplace because there is a knowledge deficit with respect to the new formulation. In order to minimize medication errors and confusion, DMETS recommends the sponsor launch an educational campaign to inform practitioners of the existence of this new product and to the fact that it has overlapping characteristics with the currently marketed fluvoxamine immediate-release products. Practitioners need to be forewarned of these similarities before being exposed to new prescriptions of Luvox CR.

b. Luvox CR has the potential to look like ***



[9] Lesar, Timothy S. Prescribing Errors Involving Medication Dosage Forms. J Gen Intern Med. 2002;17:579-87.

*** **Name pending approval. Not FOI releasable.**

2. The Modifier "CR" may not convey the right dosing frequency to a healthcare practioner

With respect to the modifier "CR", DMETS is concerned that the modifier may be ambiguous and not convey the differences between the immediate-release (once or twice daily dosing) and extended-release (once daily dosing) products. We recognize that the accepted practice to convey differences in product formulations is to include an appropriate modifier. However, there are currently seven prescription products listed in the Orange Book that use the "CR" modifier (Paxil CR, Ambien CR, Dynacirc CR, Afeditab CR, Sinemet CR, Norpace CR and Coreg CR). The recommended frequency of administration for five of these products is once daily (Paxil CR, Ambien CR, Dynacirc CR, Afeditab CR and Coreg CR), twice daily for Norpace CR, and two or three times per day for Sinemet CR. Since the currently marketed products have a wide range of dosing intervals, this suffix does not convey to healthcare practitioners that the product frequency of administration should be once daily. To compound the confusion, there is an overlapping dose (100 mg), strength (100 mg) and frequency of administration (once daily) for Luvox CR and the currently existing fluvoxamine maleate immediate-release products. Thus, in order to avoid ambiguity over the dosing interval for Luvox CR, it is

3. Established Name

The sponsor proposes to utilize "[redacted]" to describe this formulation (i.e., fluvoxamine maleate [redacted] capsule). However, [redacted] is not a recognized dosage form in the United States Pharmacopeia. We recommend consulting Richard Lostritto, Chair of the CDER Labeling and Nomenclature Committee (LNC), on the correct nomenclature for this product.

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In the review of the container labels and insert labeling of Luvox CR, DMETS has attempted to focus on safety issues relating to possible medication errors. DMETS has identified several areas of possible improvement, which might minimize potential user error.

A. GENERAL COMMENTS

1. As currently presented, the labels for both strength[redacted]

*** **Name pending approval. Not FOI releasable.**

3 Page(s) Withheld

1 Trade Secret / Confidential

_____ Draft Labeling

_____ Deliberative Process

Inpatient	Outpatient	Verbal
Luvox	Luvor CR	Luvox CR
Luvox	Luvox CR	Luvox CR
Luvox CR	Luvox CR	Luvox CR
Luvox CR	Luvox CR	Luvox CR
Luvox CR	Luvox CR	Luvox CR
Luvox CR	Luvox CR	Luvox ER
Luvox CR	Luvox CR	
Luvox CR	Luvox CR	
Luvox CR	Luvox CR	
Luvox CR		
Luvox CR		
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Luvox CR		
Luvox CR		
Luvox CR		
Luvox DR		

Appendix B

Source Case Number Date of Report	Type of Error	Narrative	Outcome
AERS Report #: 1623358 05/16/1995	Wrong Strength	Patient was prescribed Luvox 50 mg (1 qd) and received 100 mg tablets. Patient took the 100 mg dose for approximately two weeks before the error was determined. During this time, the physician increased the dose and patient experienced daytime sedation.	No patient harm.
DQRS Accession#: 022364 01/25/1996	Wrong Drug	Several close dispensing errors because of the name Luvox. When written by the average MD, many times it is nearly indistinguishable from Lasix.	Not reported.
AERS ISR#: 3942787-8-00-01 04/26/02	Wrong Drug	Fluoxetine and fluvoxamine need extra scrutiny to assure no confusion. This is especially important with oral orders. I know the strengths would seem to preclude this happening, but it nearly happened in our pharmacy.	Error was discovered before the medication was dispensed.
AERS ISR#: 4187360-4-00-01 07/28/03	Wrong Drug	Misfill of prescription for Fluvoxamine 100 mg tabs with Fluoxetine 10 mg tabs.	The medication was taken by the patient but there was no patient harm.
AERS ISR#: 4821375-5-00-01 07/29/05	Wrong Drug	"A PA ordered fluoxetine 100 mg po bid via the hospital's computer system for a newly admitted patient. Upon verification , the RPh called the PA to discuss the dose but he had left for the day. She was told by the nurse that the patient was ordered this as an outpatient by an out of state psychiatrist. This drug/dose was also listed on the H&P. The RPh still disputed the dose. The patient's wife said she might have a tablet in the car which she brought in for the RPh to ID. The drug was fluvoxamine 100 mg. The on call physician was contacted to clarify the order. In this case the error did not reach the patient due to the pharmacist's intervention. The RPh did not attempt to verify the order but if she had, the Meditech dosage check would not allow the order to be filled."	The error did not reach the patient.
DQRS Accession#: U 019672 06/23/1994	Potential Error	"The reporter is concerned that the similarity of the generic names Fluoxetine and the new drug Fluvoxamine is going to be very confusing and create a potential for errors especially since both are antidepressants and have similar indications."	N/A
AERS ISR#: 4453186-7-00-01 03/02/1995	Potential Error	"A new antidepressant by Solvay is Luvox 100 mg is easily mistaken for Lasix 100 mg. This is a potential med error that should be able to be reduced with a name change."	N/A
AERS ISR#: 4622204-5-00-01 03/03/1995	Potential Error	"This product's name (Luvox) is similar to Lovenox. This poses a serious potential for medication errors. Luvox versus Lovenox."	N/A
DQRS Accession#: D 120251 11/03/1995	Potential Error	"The reporter states the product names (Luvox and Lovenox) are too similar in sound and spelling. There is potential for a drug mix-up."	N/A
AERS ISR#: 4516128-1-00-01 11/29/1995	Potential Error	"Similar names. Orally, if the "L" on the end of the name Levoxyl is not heard, it would sound like Luvox.	N/A
AERS ISR#: 4532849-9-00-01 05/24/1995	Potential Error	"Luvox, the brand name for Fluvoxamine, when written out, looks extremely similar to the brand name of Furosemide which is Lasix."	N/A

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/s/

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1/31/2007 03:34:29 PM
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