

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**22-064**

**PROPRIETARY NAME REVIEW(S)**

**CONSULTATION RESPONSE**

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

<b>DATE RECEIVED:</b> November 30, 2006	<b>DESIRED COMPLETION DATE:</b> March 23, 2007	<b>OSE REVIEW #:</b> 2006-914
<b>DATE OF DOCUMENT:</b> July 24, 2006	<b>PDUFA DATE:</b> May 25, 2007	

**TO:** Badrul Chowdhury, MD  
Director, Division of Pulmonary and Allergy Products  
HFD-570

**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:** Xyzal  
(Levocetirizine Dihydrochloride) Tablets  
5 mg

**DA#:** 22-064

**SPONSOR:** UCB Pharma, Inc.

**RECOMMENDATIONS:**

1. DMETS has no objections to the use of the proprietary name, Xyzal. This is considered a final decision. However, if the approval of this application is delayed beyond 90 days from the signature date of this document, the name must be re-evaluated. A re-review of the name will rule out any objections based upon approval of other proprietary or established names from the signature date of this document.
2. 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.
3. DDMAC finds the proprietary name, Xyzal, 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 Sammie Beam, Project Manager, at 301-796-0080.

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: December 27, 2006

NDA#: 22-064

NAME OF DRUG: Xyzal  
(Levocetirizine Dihydrochloride) Tablets  
5 mg

NDA SPONSOR: UCB Pharma, Inc.

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

**I. INTRODUCTION:**

This review was written in response to a request from the Division of Pulmonary and Allergy Products (HFD-570), for a re-review of the proprietary name, Xyzal, regarding potential name confusion with other proprietary or established drug names. The proposed proprietary name, Xyzal, was found acceptable in DMETS' initial review of the name (OSE Consult #05-0312, dated August 14, 2006). Revised container labels, carton and insert labeling were provided for review and comment as well.

PRODUCT INFORMATION

Xyzal (levocetirizine dihydrochloride), is a selective H<sub>1</sub>-receptor antagonist indicated for the treatment of the following conditions: seasonal allergic rhinitis, perennial allergic rhinitis, and chronic idiopathic urticaria. The recommended initial dose is \_\_\_\_\_ For patients with renal impairment, the recommended dose is 2.5 mg \_\_\_\_\_ for a creatinine clearance of 30 to 49 mL/min or \_\_\_\_\_ for those with a creatinine clearance less than 30 mL/min. Patients with end-stage renal disease (creatinine clearance less than 10 mL/min) and patients undergoing hemodialysis should not receive Xyzal. Xyzal will be available as 5 mg scored tablets in bottles of 30-count and 180-count tablets as well as boxes of 30-count tablets (3 blister cards of 10 tablets).

Levocetirizine dihydrochloride is currently marketed by UCB Pharma, Inc. in numerous foreign countries under the proprietary names Xyzal and Xyzall and in Germany as Xusal.

## II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of the internet, several standard published drug product reference texts<sup>1,2</sup> as well as several FDA databases<sup>3,4</sup> for existing drug names which sound-alike or look-alike to “Xyzal” 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<sup>5</sup>. The Saegis<sup>6</sup> 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. Prescription studies were not repeated for this second review. Following completion of these initial steps, an overall risk assessment is conducted that does not evaluate the name alone. The assessment considers the findings from above and more importantly integrates post-marketing experience in assessing the risk of name confusion, product label/labeling, and product packaging. Because it is the product that is inserted into the complex and unpredictable U.S. healthcare environment, all product characteristics of a drug must be considered in the overall safety evaluator risk assessment.

### A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name, Xyzal. 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, Xyzal, acceptable from a promotional perspective.
2. The Expert Panel identified six proprietary names that were thought to have the potential for confusion with Xyzal. These products are listed in Table 1 (see page 4), along with the dosage forms available and usual dosage.

**Appears This Way  
On Original**

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

<sup>2</sup> Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

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

<sup>4</sup> Phonetic and Orthographic Computer Analysis (POCA)

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

<sup>6</sup> Data provided by Thomson & Thomson’s SAEGIS™ Online Service, available at [www.thomson-thomson.com](http://www.thomson-thomson.com)

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

Product Name	Dosage form(s), Established name	Usual adult dose	Other
Xyzal	Levocetirizine dihydrochloride Tablets 5 mg	Seasonal allergic rhinitis, perennial allergic rhinitis, and chronic idiopathic urticaria. <i>Adults and children 12 years of age and older:</i>  _____  _____  _____	N/A
Lozol	Indapamide Tablets 1.25 mg and 2.5 mg	<u>Hypertension:</u> 1.25 mg once daily, gradually increase dose to 5 mg once daily, if necessary. <u>Edema of congestive heart failure:</u> 2.5 mg once daily, dose may be increased to 5 mg once daily, if necessary.	LA/SA
Zymar	Gatifloxacin Ophthalmic solution 0.3% (2.5 mL and 5 mL bottles)	<u>Bacterial conjunctivitis caused by susceptible strains of organisms:</u> <i>Days 1 and 2:</i> 1 drop in affected eye(s) every 2 hours while awake, up to 8 times per day; <i>Days 3 through 7:</i> 1 drop up to 4 times per day while awake.	LA/SA
Tyzeka	Telbivudine Tablets 600 mg	<u>Chronic hepatitis B:</u> 600 mg once daily. <i>Dose adjustment for renal insufficiency:</i> crcl 30-49 mL/min, 600 mg every 48 hours; crcl less than 30 mL/min (not on dialysis) 600 mg every 72 hours; end-stage renal disease, 600 mg every 96 hours.	LA
Tyzine Nasal Drops and Nasal Spray	0.1% solution Tetrahydrozoline Hydrochloride 15 mL and 30 mL bottles	<u>Nasal Congestion:</u> Adults: 2-4 drops or 3-4 sprays in each nostril as needed, not more than every 3 hours.	LA
Tyzine Pediatric Nasal Drops	0.05% solution Tetrahydrozoline Hydrochloride 15 mL bottles	Children (6 & older): 2-4 drops in each nostril as needed, not more than every 3 hours.	LA
/	/	/	LA
Xepol (Orphan Drug)	Human immune globulin (Additional product information not available)	<u>Post polio syndrome</u> (Dosing information not available)	LA
<p>* Frequently used, not all-inclusive.  ** L/A (look-alike), S/A (sound-alike)  ***Name pending approval. Not FOI releasable.</p>			

## B. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proposed proprietary name, Xyzal, the primary concerns relating to look-alike and/or sound-alike confusion with Xyzal are: Lozol, Zymar, Tyzeka, Tyzine, \_\_\_\_\_, and Xepol.

Upon further analysis of the names Tyzeka, Tyzine, \_\_\_\_\_, and Xepol, it was determined that these names would not be reviewed further because they lack convincing look-alike/sound-alike similarities with Xyzal in addition to having differentiating product characteristics such as indication of use and strength. Additionally, Tyzine and \_\_\_\_\_ have a route of administration that differs from Xyzal. Furthermore, Xepol is an orphan drug made in Sweden and product characteristics and dosing information for this product are not readily available.

The remaining names are discussed in detail below.

1. Lozol (indapamide) was identified as a name with similar appearance and sound to Xyzal. Lozol is a thiazide diuretic indicated for the treatment of hypertension and edema of congestive heart failure. The usual recommended dose is 1.25 mg to 5 mg once daily.

The letter "L" in Lozol may look similar to the letter "X" in Xyzal when scripted. Additionally, both names contain five letters and have the letters "z" and "l" in the same positions which contributes to the look-alike similarities between the names. Furthermore, the last three letters of both names ("zol" vs. "zal") may look similar because the second letter "o" in Lozol may look similar to the letter "a" in Xyzal when scripted. However, Xyzal contains the downstroke letter "y" which may help to differentiate the names orthographically. Additionally, the letters "o" and "y", which share the same location (second position) in each name, look different when scripted (see below).



Xyzal may sound similar to Lozol when spoken. Both names contain two syllables and end with syllables that have a similar sound ("ZÄL" vs. "ZÖL"). However, their beginning syllables sound distinctly different ("XY" vs. "LÖ") which may help to differentiate the names when spoken.

Lozol and Xyzal share several overlapping product characteristics such as dosage form (tablet), frequency of administration (once daily), and dose (2.5 mg and 5 mg) which may contribute to confusion between the names. However, they differ in strength (1.25 mg and 2.5 mg vs. 5 mg) which may help to differentiate the names. For example, an order for Lozol would have to indicate the strength since it is available in two strengths (1.25 mg and 2.5 mg). Likewise, a prescription for a 2.5 mg dose of Xyzal may state "Take one-half tablet daily" since the 5 mg tablet must be broken in half to obtain a 2.5 mg dose. Similarly, a prescription for Lozol 5 mg may state "Take 2 tablets daily" since the highest strength available is 2.5 mg. In cases where only the dose is specified

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

and not the tablet strength (i.e. Xyzal 2.5 mg or Lozol 5 mg) the orthographic differences between the names will minimize the potential for confusion. Although there are some overlapping product characteristics, the orthographic and phonetic differences between the name pair will minimize the potential to confuse the names.

2. Zymar was identified as a name with similar sound and appearance to Xyzal. Zymar (gatifloxacin) is an ophthalmic antibiotic indicated for the treatment of bacterial conjunctivitis. The recommended dose is: days 1 and 2, one drop instilled into the affected eye(s) every 2 hours while awake (up to 8 times per day); and on days 3 through 7, one drop instilled into the affected eye(s) up to four times per day while awake.

The letters “Z” and “m” in Zymar may look similar to the letters “X” and “z” in Xyzal, respectively, when scripted. Additionally, both names contain five letters and have the letters “y” and “a” in the same positions which contributes to the look-alike similarities between the names. However, the ending letter “l” in Xyzal has an upstroke which may help to differentiate the names.



Xyzal may sound similar to Zymar when spoken. Both names contain two syllables and begin with syllables that have a similar sound (“XY” vs. “ZY”). However, their ending syllables sound distinctly different (“ZÖL” vs. “MÄR”) which may help to differentiate the names when spoken.

Zymar and Xyzal have many different product characteristics. They differ in indication of use (bacterial conjunctivitis vs. seasonal and perennial allergies), dosage form (ophthalmic solution vs. tablet), strength (0.3% vs. 5 mg), route of administration (instillation into eye vs. oral) and frequency of administration (every 2 hours on days 1 and 2 followed by up to 4 times per day on days 3 through 7 vs. once daily). However, both products are similar in that each is available in only one strength. As such, a prescription may be written for these products without specifying a strength. Nevertheless, it is likely that a prescription for either of these products will contain other information that will help to differentiate the products. For example, a prescription for Zymar will probably specify a route of administration and directions for use (e.g., “Instill one drop into the affected eye(s) as directed”). Furthermore, Zymar is administered multiple times per day (two to eight times per day) whereas Xyzal is administered only once daily. Although there are some phonetic and orthographic similarities between the names, the numerous different product characteristics will minimize the potential to confuse Xyzal with Zymar.

### III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In the review of the container labels, carton and insert labeling of Xyzal, DMETS has focused on safety issues relating to possible medication errors. DMETS has identified the following areas of improvement which might minimize potential user error.

3 Page(s) Withheld

       Trade Secret / Confidential

✓ Draft Labeling

       Deliberative Process

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50703118! 12; 36; 52! QN  
ESVH! TBGFUZ! PGGJDF! SFWFXFS

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50703118! 12; 45; 22! QN  
ESVH! TBGFUZ! PGGJDF! SFWFXFS

Dbspm l pmr vj t u  
50703118! 12; 4; ; 48! QN  
ESVH! TBGFUZ! PGGJDF! SFWFXFS

# REQUEST FOR CONSULTATION

(Division/Office):

**Director, Division of Medication Errors and  
Technical Support (DMETS), HFD-420  
WO22, RM 4447**

FROM:

Lori Garcia, R.Ph., Regulatory Project Manager  
Division of Pulmonary and Allergy Products

DATE  
November 28, 2006

IND NO.

NDA NO.  
NDA 22-064

TYPE OF DOCUMENT  
Original NDA

DATE OF DOCUMENT  
July 24, 2006

NAME OF DRUG  
Xyzal (levocetirizine)

PRIORITY CONSIDERATION  
S

CLASSIFICATION OF DRUG

DESIRED COMPLETION DATE  
March 23, 2007

NAME OF FIRM: UCB Inc.

## REASON FOR REQUEST

### I. GENERAL

- |  |  |   |
|--|--|---|
| <input type="checkbox"/> NEW PROTOCOL                  | <input type="checkbox"/> PRE--NDA MEETING        | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER                              |
| <input type="checkbox"/> PROGRESS REPORT               | <input type="checkbox"/> END OF PHASE II MEETING | <input type="checkbox"/> FINAL PRINTED LABELING                                     |
| <input type="checkbox"/> NEW CORRESPONDENCE            | <input type="checkbox"/> RESUBMISSION            | <input type="checkbox"/> LABELING REVISION  |
| <input type="checkbox"/> DRUG ADVERTISING              | <input type="checkbox"/> SAFETY/EFFICACY         | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE                                |
| <input type="checkbox"/> ADVERSE REACTION REPORT       | <input type="checkbox"/> PAPER NDA               | <input type="checkbox"/> FORMULATIVE REVIEW   |
| <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION | <input type="checkbox"/> CONTROL SUPPLEMENT      | <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): <b>Trade name review</b> |
| <input type="checkbox"/> MEETING PLANNED BY            |  |   |

### II. BIOMETRICS

STATISTICAL EVALUATION BRANCH

STATISTICAL APPLICATION BRANCH

- TYPE A OR B NDA REVIEW  
 END OF PHASE II MEETING  
 CONTROLLED STUDIES  
 PROTOCOL REVIEW  
 OTHER (SPECIFY BELOW):

- CHEMISTRY REVIEW  
 PHARMACOLOGY  
 BIOPHARMACEUTICS  
 OTHER (SPECIFY BELOW):

### III. BIOPHARMACEUTICS

- DISSOLUTION  
 BIOAVAILABILITY STUDIES  
 PHASE IV STUDIES

- DEFICIENCY LETTER RESPONSE  
 PROTOCOL-BIOPHARMACEUTICS  
 IN-VIVO WAIVER REQUEST

### IV. DRUG EXPERIENCE

- PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL  
 DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES  
 CASE REPORTS OF SPECIFIC REACTIONS (List below)  
 COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP

- REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY  
 SUMMARY OF ADVERSE EXPERIENCE  
 POISON RISK ANALYSIS

### V. SCIENTIFIC INVESTIGATIONS

CLINICAL

PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS: Please perform DMETS review of new NDA 22-064 for Xyzal (levocetirizine) 5mg Tablet. Previous DMETS review done under IND 72,233 (review dated 8/15/06). The entire NDA is available in the EDR. If you have any questions, please contact me at 301-796-1212.

PDUFA DATE: May 25, 2007

ATTACHMENTS: Draft Package Insert, Container and Carton Labels

CC: Archival IND NDA 22-064

HFD-570 Division File

D-570 RPM

D-570 Reviewers and Team Leaders

NAME AND PHONE NUMBER OF REQUESTER

Lori Garcia

METHOD OF DELIVERY (Check one)

DFS ONLY

MAIL

HAND

SIGNATURE OF RECEIVER

SIGNATURE OF DELIVERER

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

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Lori Garcia

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**CONSULTATION RESPONSE**

**DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT  
OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY  
(DMETS; WO22 M/S 4447)**

**DATE RECEIVED:**

November 17, 2005

**DOCUMENT DATE:**

October 6, 2005

**DESIRED COMPLETION DATE:**

**OSE REVIEW #:** 05-0312

**TO:** Badrul Chowdhury, M.D.  
Director, Division of Pulmonary and Allergy Products  
HFD-570

**THROUGH:** Alina R. Mahmud, RPh, MS, Team Leader  
Denise Toyer, PharmD, Deputy Director  
Carol Holquist, RPh, Director  
Division of Medication Errors and Technical Support, HFD-420

**FROM:** Tina M. Tezky, Pharm.D., Safety Evaluator  
Division of Medication Errors and Technical Support, HFD-420

**PRODUCT NAME:**

Xyzal  
(Levocetirizine Dihydrochloride) Tablets  
5 mg

**IND SPONSOR:** UCB Pharma, Inc.

**IND#:** 72,233

**RECOMMENDATIONS:**

1. DMETS has no objections to the use of the proprietary name, Xyzal. This is considered a tentative decision and the firm should be notified that this name with its associated labels and labeling must be re-evaluated upon submission of the NDA and approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary or established names from the signature date of this document.
2. Container labels, carton and insert labeling were not submitted for review and comment. Please submit the labels and labeling when available for review and comment.
3. DDMAC finds the proprietary name, Xyzal, 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 Diane Smith, Project Manager, at 301-796-0538.

**Division of Medication Errors and Technical Support (DMETS)  
Office of Surveillance and Epidemiology  
HFD-420; WO22, M/S 4447  
Center for Drug Evaluation and Research**

**PROPRIETARY NAME REVIEW**

**DATE OF REVIEW:** November 28, 2005

**IND#:** 72,233

**NAME OF DRUG:** Xyzal™ (Levocetirizine Dihydrochloride) Tablets  
5 mg

**IND HOLDER:** UCB Pharma, Inc.

**I. INTRODUCTION:**

This consult was written in response to a request from the Division of Pulmonary and Allergy Products (HFD-570) for a review of the proprietary name, "Xyzal", regarding potential name confusion with other proprietary and/or established drug names. Container labels, carton, and insert labeling were not provided for review and comment at this time.

**PRODUCT INFORMATION**

Xyzal (levocetirizine dihydrochloride) is an oral H<sub>1</sub>-histamine receptor antagonist indicated for the treatment of seasonal allergic rhinitis and perennial allergic rhinitis. Levocetirizine dihydrochloride is currently marketed by UCB Pharma, Inc. in numerous foreign countries under the proprietary names Xyzal and Xyzall and in Germany as Xusal. The usual dosage range is 2.5 mg to 5 mg once daily. Xyzal will be available in 5 mg scored tablets.

**II. ADVERSE EVENT REPORTING SYSTEM (AERS) FINDINGS**

Since Xyzal is currently marketed in numerous countries outside the U.S., DMETS searched the FDA Adverse Event Reporting System for cases of medication errors associated with Xyzal, Xyzall, and Xusal. Sixteen cases were reported to the Agency. Fourteen cases describe adverse events and two cases involved an attempted suicide. None of the cases pertained to a medication error relating to name confusion or label/labeling issues.

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### III. RISK ASSESSMENT

The medication error staff of DMETS conducted a search of several standard published drug product reference texts<sup>1,2</sup> as well as several FDA databases<sup>3,4</sup> for existing drug names which sound-alike or look-alike to Xyzal 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<sup>5</sup>. The SAEGIS™ Online service<sup>6</sup> 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 Xyzal. 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 with the name, Xyzal, in regard to promotional claims.
2. The expert panel identified eight proprietary names that were thought to have the potential for confusion with Xyzal. Two additional names, Zylol and Kytril, were identified names with potential similarity through the FDA prescription studies. These products are listed in Table 1 (see page 4), along with the available dosage forms and usual dosage.

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On Original**

<sup>1</sup> 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.

<sup>2</sup> Facts and Comparisons, online version, Facts and Comparisons, St. Louis, Missouri.

<sup>3</sup> 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.

<sup>4</sup> Phonetic and Orthographic Computer Analysis (POCA).

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

<sup>6</sup> Data provided by Thomson & Thomson's SAEGIS™ Online service, available at [www.thomson-thomson.com](http://www.thomson-thomson.com)

Table 1: Potential Sound-Alike/Look-Alike Names Identified for Xyzal

Product Name	Dosage form(s), Established name	Usual adult dose	Other
Xyzal (UCB)	Levocetirizine dihydrochloride tablets 5 mg	2.5 mg – 5 mg once daily	
Xyzal (UCB) Foreign <sup>†</sup>	Levocetirizine dihydrochloride tablets 5 mg	2.5 mg – 5 mg once daily.	LA/SA
Xyzal (UCB) Foreign <sup>††</sup>	Levocetirizine dihydrochloride tablets 5 mg	2.5 mg – 5 mg once daily.	LA/SA
Xusal (UCB) Germany	Levocetirizine dihydrochloride tablets 5 mg	2.5 mg – 5 mg once daily.	LA/SA
Zylol (Teva) Isreal	Allopurinol Tablets 100 mg, 300 mg Allopurinol Powder for Injection 500 mg	200 mg – 600 mg daily, in single or divided doses.	LA
Zazole Rx	Terconazole Vaginal Cream 0.4%, 0.8%	Insert one applicatorful vaginally QHS for 3 consecutive days.	SA
Xiral Rx (no longer marketed)	Chlorphenamine/pseudoephedrine/ methscopolamine Tablets 8 mg/120 mg/2.5 mg	Allergic rhinitis, cold symptoms, sinusitis	LA/SA
Vexol Rx	Rimexolone Ophthalmic Suspension 1%	1-2 drops every hour to QID.	SA
Xyrem CIII – restricted access	Sodium Oxybate Oral Solution 500 mg/mL	6 – 9 grams/day: half at bedtime, while in bed, and the second half 4 hours later.	LA
Kefzol Discontinued	Cefazolin Injection 250 mg, 500 mg, 1 gm, 10 gm, 20 gm 500 mg/50 mL, 1 gm/50 mL	500 mg – 1 g every 6 – 8 hours depending on indication. Renal adjustments are necessary.	LA
Kytril Rx	Granisetron Tablets 1 mg, 2 mg Granisetron Oral Solution 2 mg/10 mL Granisetron Injection 0.1 mg/mL, 1 mg/mL	2 mg PO 1 hour before chemotherapy or radiation. 10 mcg/kg IV 30 minutes before chemotherapy. 1 mg IV immediately before induction anesthesia	LA
*Frequently used, not all-inclusive. **LA (look-alike), SA (sound-alike)			

<sup>†</sup>Bulgaria, Czech Republic, Denmark, Finland, Hungary, Indonesia, Ireland, Italy, Netherlands, Norway, Philippines, Poland, Portugal, Republic of Korea, Saudi Arabia, Singapore, Slovak Republic, South Africa, Switzerland, Taiwan, Thailand, Turkey, United Kingdom

<sup>††</sup>Austria, Belgium, France

## 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 Xyzal 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 122 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 Xyzal (see page 5). 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 style="text-align: center;">Xyzal 5mg take 1 tablet daily # 30</p>	<p>Xyzal 5 mg Take one tablet daily, dispense 30.</p>
<p>Inpatient RX:</p> <hr/> <p style="text-align: center;"><del>Xyzal 5mg one po qd</del></p>	

2. Results:

One respondent from the inpatient study interpreted the proposed name as Xytril, which looks like the currently marketed U.S. product, Kytril. Another respondent from the inpatient study commented, "Xytral looks like Xylol". Xylol is a colorless flammable volatile liquid hydrocarbon used as a solvent. However the name Xylol looks and sounds similar to Zylol, the proprietary name for allopurinol marketed in Israel. A third respondent in the verbal prescription study commented, "The name reminds me of a multiple vitamin in the Visol family, e.g. Poly vi sol, Tri vi sol. It implies that the product is a vitamin. I don't know what this product is used for, but if it's not a vitamin, the name is better changed that doesn't give the vitamin connotation". The remaining incorrect name interpretations were misspelled/phonetic variations of "Xyzal". See Appendix A for the complete listing of interpretations from the verbal and written studies.

C. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name Xyzal, the primary concerns relating to look-alike and sound-alike confusion with Xyzal are Xyzal, Xyzall, Xusal, Zylol, Zazole, Xiral, Vexol, Xyrem, Kefzol, and Kytril.

Upon further review of the names Xyzal, Xyzall, and Xusal, it was determined that these are proprietary names used in numerous foreign countries to market the identical drug product, levocetirizine dihydrochloride. Thus, we are not concerned that these names will cause confusion.

The name Zylol was not reviewed further because it is not marketed in the U.S. and it has numerous differentiating product characteristics such as the product strength, dosage formulation, indication for use, and frequency of administration.

Per conversation with the manufacturer, Hawthorn Pharmaceuticals (888-455-5253), the product Xiral is no longer manufactured and there are no generic equivalents. Therefore Xiral will not be reviewed further.

The name Xyrem was not reviewed further due to a lack of convincing look-alike/sound-alike similarities with Xyzal in addition to numerous differentiating product characteristics such as restricted access, product strength, indication for use, frequency of administration, and dosage form.

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, one respondent from the inpatient study interpreted the proposed name as Xytril, which looks like the currently marketed U.S. product, Kytril. One additional respondent from the inpatient written study commented that the proposed name looks similar to Xylol, which looks and sounds similar to the foreign marketed product, Zylol. DMETS is not concerned with the similarity of this name pair for the reasons mentioned above. A third respondent in the verbal prescription study commented, "The name reminds me of a multiple vitamin in the Visol family, e.g. Poly vi sol, Tri vi sol. It implies that the product is a vitamin. I don't know what this product is used for, but if it's not a vitamin, the name is better changed that doesn't give the vitamin connotation". DMETS acknowledges the respondents concern; however, we believe the likelihood for confusion is minimal due to lack of convincing look-alike and sound-alike similarities, since it is unlikely a patient or healthcare provider will prescribe or ask for "Visol". The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Xyzal.

1. Zazole was identified as having sound-alike potential with Xyzal. Zazole (terconazole) is a vaginal antifungal agent indicated for the treatment of vulvovaginal candidiasis. It is available as a 0.4% vaginal cream in 45 gm tubes and a 0.8% vaginal cream in 20 gm tubes. The usual dose of Zazole is one applicatorful vaginally every day at bedtime for three consecutive days.

The sound-alike similarities stem from the fact that Zazole and Xyzal share the same number of syllables (two) and each respective syllable has a strong phonetic likeness, (ZAZ- vs. XYZ-) and (-OLE vs. -AL).

Although the products have a strong phonemic similarity and they can have an overlapping dosing interval (once daily), differing product characteristics will help avert the potential for confusion between the two drug names. Zazole and Xyzal differ with respect to dosage form (vaginal cream vs. tablet), available strengths (0.4%, 0.8% vs. 5 mg), and route of administration (vaginal vs. oral). Since Zazole is available in two different strengths (0.4% and 0.8%) and two different packaging sizes (20 grams and 45 grams), the indication of one or both of these differing characteristics will help minimize the potential for confusion between Zazole and Xyzal. Additionally, many pharmacies store topical and oral products in separate

locations. DMETS believes the product differences decrease the potential for name confusion between Zazole and Xyzal.

2. Vexol was identified as a name with similar sound to Xyzal. This similarity depends upon how they are pronounced. Vexol (rimexolone) is an ophthalmic anti-inflammatory corticosteroid indicated for post-operative inflammation and anterior uveitis. Vexol is available as a 1% ophthalmic suspension in 5 mL and 10 mL bottles. The typical dose is 1 – 2 drops into the affected eye(s) every one to six hours.

Vexol and Xyzal contain the same number of syllables (two) and the second syllable of each name sounds identical (-OL vs. -AL), which contributes to the phonetic similarities of this name pair. However, the first syllable (VEX- vs. XYZ-) provides a phonetic differentiation between the two names. Additionally, the two products have differing product characteristics, such as dosage form (ophthalmic suspension vs. tablet), route of administration (ophthalmic vs. oral), dosage strength (1% vs. 5 mg), and frequency of administration (1 – 2 drops every one to six hours vs. once daily). Due to the phonetic and product differences, DMETS believes the potential for name confusion between Vexol and Xyzal is minimal.

3. Kefzol was identified as a name with similar appearance to Xyzal. Kefzol (cefazolin) is a first generation cephalosporin indicated for the treatment of susceptible infections. Kefzol has been discontinued by the manufacturer; however, generic cefazolin is available as 250 mg, 500 mg, 1 g, 10 g and 20 g vials and as 500 mg/50 mL and 1 g/50 mL premixed minibags. Kefzol is usually dosed at 500 mg – 1 gram every 6 to 8 hours depending on the indication and severity of infection.

The endings of the two names (-ZOL vs. -ZAL) look similar when scripted, which contributes to the look-alike similarities between Kefzol and Xyzal. The beginning (KEF- vs. XY-) can also look similar when written poorly or quickly because the “X” can resemble a “K” and the “Y” can resemble the “F” portion of the name (see sample below). However, different product characteristics such as dosage form (injection vs. tablet), available strength (250 mg, 500 mg, 1 g, 10 g, 20 g vs. 5 mg), route of administration (injection vs. oral), and frequency of administration (every 6 to 8 hours vs. once daily) may help distinguish between the two products. DMETS believes the product differences will help to minimize name confusions between Kefzol and Xyzal.

*Xyzal*  
*Kefzol*

4. Kytril and Xyzal were found to have look-alike similarities. Kytril (granisetron) is an antiemetic indicated for the prevention of chemotherapy induced nausea (CINV) and vomiting and for the prevention of post-operative nausea and vomiting (PONV). Kytril is available as 1 mg tablets, as 2 mg/10 mL oral solution, and as 0.1 mg/mL and 1 mg/mL injection. The usual dose for CINV is 2 mg orally 1 hour before

chemotherapy or radiation or 10 mcg/kg intravenously 30 minutes before treatment. The usual dose of Kytril for PONV is 1 mg intravenously immediately before induction anesthesia.

Kytril and Xyzal contain two overlapping letters in similar positions in each name (KYTRIL vs. XYZAL), which may contribute to the look-alike characteristics of the two names. Additionally, the initial letters (K- vs. X-) can look similar when scripted. Furthermore, if the "Z" in Xyzal is written without a downstroke and is crossed, it has a strong likeness to a lower case "T" (see writing sample below). Additionally, the two products also share some product characteristics, such as dosage form (tablet) and route of administration (oral).

However, differing strengths (1 mg, 2 mg, 2 mg/10 mL 0.1 mg/mL, 1 mg/mL vs. 5 mg) and frequency of administration (before chemotherapy or anesthesia vs. once daily) will help differentiate Kytril and Xyzal. Furthermore, the strength of Kytril would be required prior to dispensing since it is available in multiple strengths. DMETS believes the potential for confusion between Kytril and Xyzal is minimal due to the aforementioned reasons.

*Xyzal*  
*Kytril*

**Appears This Way  
On Original**

Appendix A – DMETS Prescription Study Results for Xyzal

**Inpatient**

Xyzal  
Xytol  
Xyfal

**Outpatient**

Xyzal  
Xyzal  
Xyzal

**Voice**

Zyzol  
Zyzol  
Zyzol  
Zisol

(Comment: The name reminds me of a multiple vitamin in the Visol family, e.g. Poly vi sol, Tri vi sol. It implies that the product is a vitamin. I don't know what this product is used for, but if it's not a vitamin, the name is better changed that doesn't give the vitamin connotation.)

Xyzal  
Xytal  
XYTAL  
Xyzal  
Xytal  
Xytal

(Xytal looks like xylol)

Xyzol  
Xytal  
Xytal  
Xyzal  
Xyzal  
Xyzal  
Xyzal  
Xyzal  
Xytril  
Xyzal  
Xyzal  
Xyzal  
Xyzal

Xyzal  
Xyaaail  
Xyzal  
Xyzal  
Xyzal

Xyzal  
Xyzal  
Xyzal  
Xyzal  
Xygral  
Xygal  
Xyral  
Xyzal  
Xyzal  
Xyral  
Xyzal  
Xyzal

Zysol  
Xixol  
Zyzol  
Zyzol

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