

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**50-813**

**PROPRIETARY NAME REVIEW(S)**

**CONSULTATION RESPONSE**

**DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT  
OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY  
(DMETS; HFD-420, White Oak Building 22, Mail Stop 4447)  
Center for Drug Evaluation and Research**

<b>DATE RECEIVED:</b> November 1, 2007	<b>DESIRED COMPLETION DATE:</b> December 15, 2007	<b>OSE REVIEW #:</b> 2007-2280
<b>DATE OF DOCUMENT:</b> October 5, 2007	<b>PDUFA DATE:</b> January 23, 2008	

**TO:** Janice Soreth, MD  
Director, Division of Anti-Infective and Ophthalmology Products

**THROUGH:** Kristina Arnwine, PharmD, Team Leader  
Denise Toyer, PharmD, Deputy Director  
Carol Holquist, RPh, Director  
Division of Medication Errors and Technical Support

**FROM:** Tselaine Jones Smith, PharmD, Safety Evaluator  
Division of Medication Errors and Technical Support

<b>PRODUCT NAME:</b> Moxatag Ampicillin Extended-release Tablets 250mg	<b>NDA APPLICANT:</b> MiddleBrook Pharmaceuticals
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- RECOMMENDATIONS:**
1. DMETS has no objections to the use of the proprietary name, Moxatag. This is considered a final decision. However, if the approval of the NDA is delayed beyond 90 days from the 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 this date forward.
  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 finds the proprietary name, Moxatag, 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 that is sent to the sponsor concerning this review. If you have further questions or need clarifications, please contact Anne Crandall, OSE Project Manager, at 301-796-2282.

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

**PROPRIETARY NAME, LABEL, AND LABELING REVIEW**

**DATE OF REVIEW:** January 16, 2008

**NDA #:** 50-813

**NAME OF DRUG:** Moxatag  
Amoxicillin Extended-release Tablets  
775 mg

**NDA HOLDER:** MiddleBrook Pharmaceuticals

**I. INTRODUCTION:**

This review was written in response to a request from the Division of Anti-Infective and Ophthalmology Products, for assessment of the proprietary name, Moxatag, regarding potential name confusion with other proprietary or established drug names. Container labels and carton and package insert labeling were for review and comment at this time.

**PRODUCT INFORMATION**

Moxatag is a once-a-day amoxicillin regimen for the treatment of tonsillitis and/or pharyngitis secondary to *Streptococcus pyogenes* in adolescents and adults. Moxatag utilizes Pulysys™ (pulsatile release) to provide prolonged concentrations of amoxicillin enabling once-daily dosing. The recommended dose for tonsillitis and/or pharyngitis is 775 mg once daily for ten days with food. Moxatag is available as a 775 mg tablet.

**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 Moxatag 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.

<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)

In addition, DMETS conducted three prescription studies consisting of two written inpatient prescription studies and a 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. Following completion of these initial components, 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)

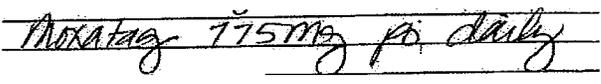
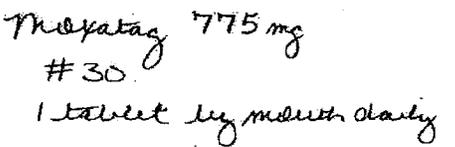
An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name, Moxatag. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and 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, Moxatag, acceptable from a promotional perspective.
2. The Expert Panel identified twelve proprietary names that were thought to have the potential for confusion with Moxatag.

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 Moxatag 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 outpatient prescription and an inpatient prescription were written, each consisting of a combination of marketed and unapproved drug products and a prescription for, each consisting of a combination of marketed and unapproved drug products and a prescription for Moxatag (see page 4). These orders were optically scanned and delivered to a random sample of the participating health professionals via e-mail. In addition, one of the requisition orders was recorded on voice mail. The voice mail message was 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 ORDERS	VERBAL ORDER
<u>Inpatient Sample:</u> 	Moxatag Take 1 tablet by mouth daily
<u>Outpatient Sample:</u> 	

2. Results:

None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed U.S. product. 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, Moxatag, the following twelve names were identified as having the potential to look and/or sound similar to Moxatag: Mycolog, Novolog, Ultratag, Mexitil, Moxilin, Mexate AQ, Maxaquin, Moxalactam, Moxam, Moxitab (Thailand), Moxatid and Maxidex.

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

Upon analysis of the aforementioned names, we determined that the all twelve names Mycolog II, NovoLog, Ultratag, Mexitil, Moxilin, Mexate AQ, Maxaquin, Moxalactam, Moxam, Moxitab, Moxatid (Thailand) and Maxidex will not be considered further for the following reasons:

- In addition to lacking orthographic and phonetic similarities with Moxatag: NovoLog, Ultratag and Maxidex do not share product characteristics such as product strength, frequency of administration, route of administration, patient population, therapeutic class, unit of measure and/or dosage formulation.
- The name Moxatid was found in Micromedex, listed as amoxicillin trihydrate manufactured by Marksman Pharmaceuticals in Bangladesh. However, no additional information about the product can be found in Micromedex or other commonly used drug references such as, the online versions of Facts and Comparison, Clinical Pharmacology, the Orange Book, and RedBook 2006.
- Myocolog II (nystatin and triamcinolone acetonide topical ointment) is listed in Clinical Pharmacology on-line as a product that is no longer actively marketed in the United States. However, generic nystatin and triamcinolone acetonide is available as 15 gram,

30 gram, 60 gram, 120 gram and 454 gram 0.1% topical cream and as a 0.1% topical ointment. Mycolog II and Moxatag do not share product characteristics such as product strength, indication of use, frequency of administration, route of administration, patient population, therapeutic class and/or dosage formulation

- Maxaquin (lomefloxacin hydrochloride), Moxam (moxalactam sodium) and Moxalactam are products that are no longer actively marketed in the United States. There are no generic equivalents available for Maxaquin, Moxam or Moxalactam. Furthermore, in addition to lacking orthographic similarities with Moxatag, Maxaquin, Moxam and Moxalactam do not share product characteristics such as strength, dosage form, route of administration and indication of use.
- Mexitil (mexiletine hydrochloride) is listed in Clinical Pharmacology on-line as a product that is no longer actively marketed in the United States. However, generic mexiletine hydrochloride is available as 150 mg, 200 mg and 250 mg capsules and as a 25 gram, 100 gram and 1 gram powder. Mexiletine does not share product characteristics with Moxatag such as strength, indication of use, frequency of administration and patient population.
- Moxilin (amoxicillin) is listed in Clinical Pharmacology on-line as a product that is no longer actively marketed in the United States. However, generic amoxicillin is available as 250 mg and 500 mg capsules; 125 mg, 250 mg and 400 mg chewable tablets; 875 mg tablets; and 125 mg/5 mL, 200 mg/5 mL, 250 mg/5mL and 400 mg/5 mL powder for suspension. Amoxicillin and Moxatag differ with respect to their frequency of administration and strength.
- Mexate AQ (methotrexate sodium) is listed in Drugs @FDA as a product that is no longer actively marketed in the United States. However, methotrexate sodium is available as 2.5 mg tablets, 1 gram powder for solution and 25 mg/mL solution. This product does not share product commonalities with Moxatag such as indication of use, frequency of administration, indication of use, strength and dosage form (powder for solution, solution).
- Moxitab (amoxicillin trihydrate) was identified as a foreign product (Thailand). It is amoxicillin trihydrate which is available as 250 mg and 500 mg tablets. This product does not share product commonalities such as prescription status, dosing frequency, strength and indication of use.

Thus, DMETS does not object to the use of the proprietary name Moxatag.

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

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

#### A. GENERAL COMMENTS

We had concerns regarding the proposed established name

However, we note that the chemistry review has addressed our concerns, and has determined that the established name will be "Amoxicillin Extended-release Tablets" which is consistent with USP nomenclature. We concur with the chemistry recommendation.

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**B. CONTAINER LABEL (30 Count)**

1. Ensure that the established name is at least  $\frac{1}{2}$  the size of the proprietary name in accordance with 21 CFR 201.10(g)(2).
2. Relocate the prominent product strength presented in the upper right corner of the label to be presented directly underneath the established name. This strength is commensurate with the size of the proprietary name. Delete the statement "775 mg Tablets" that is currently presented underneath the established name. As currently presented, the product strength under the established name is not prominent enough, and the product strength presented in the right corner is duplicative.
3. The low color-contrast of the black font and purple background utilized for the NDC number and net quantity make the information difficult to read. Revise the color scheme in order to increase readability.
4. Delete the blue color block at the bottom of the principal display panel. This will allow for increased size of the strength immediately following the established name. Additionally, as currently presented this color block distracts from and competes with the presentation of the strength.

**C. BLISTER CARD (Trade and Professional Sample 10 Count)**

1. Ensure that the established name is at least  $\frac{1}{2}$  the size of the proprietary name in accordance with 21 CFR 201.10(g)(2).
2. The low color-contrast of the black font on the purple background and the black font on the blue background make the information difficult to read. Revise the color scheme in order to increase readability.
3. Relocate the prominent product strength presented in the upper right corner of the label to be presented directly underneath the established name. This strength is commensurate with the size of the proprietary name. Delete the statement "775 mg Tablets" that is currently presented underneath the established name. As currently presented, the product strength under the established name is not prominent enough, and the product strength presented in the right corner is duplicative.
4. The product strength presented on the spine of the folder as well as the product strength presented underneath the established name should read "775 mg per tablet" to ensure that health care practitioners and patients do not think the entire contents of the blister pack contains 775 mg .
5. Delete the blue color block at the bottom of the principal display panel. This will allow for increased size of the strength immediately following the established name. Additionally, as currently presented this color block distracts from and competes with the presentation of the strength.
6. Each blister should be individually labeled with the brand name, established name and product strength so that the product remains accurately labeled if the blister card is cut apart or altered in any manner.

7. Delete the statement "1 tablet per blister cavity" as it is not necessary, and only adds clutter to the label.
8. On the Professional Sample, increase the prominence of the statement "Professional Sample-Not for Sale."

D. BLISTER CARD TRAY (Trade and Professional Sample)

1. Ensure that the established name is at least  $\frac{1}{2}$  the size of the proprietary name in accordance with 21 CFR 201.10(g)(2).
2. The low color-contrast of the black font on the purple background and the black font on the blue background make the information difficult to read. Revise the color scheme in order to increase readability.
3. Relocate the prominent product strength presented in the upper right corner of the label to be presented directly underneath the established name. This strength is commensurate with the size of the proprietary name. Delete the statement "775 mg Tablets" that is currently presented underneath the established name. As currently presented, the product strength under the established name is not prominent enough, and the product strength presented in the right corner is duplicative.
4. We note that in some locations on the labeling the strength does not appear immediately after the established name. Please relocate and present in accordance with D-3.
5. Delete the blue color block at the bottom of the principal display panel. This will allow for increased size of the strength immediately following the established name. Additionally, as currently presented this color block distracts from and competes with the presentation of the strength.
6. On the Professional Sample, increase the prominence of the statement "Professional Sample-Not for Sale."

E. BLISTER CARD [One (1) Count Professional Sample]

1. Ensure that the established name is at least  $\frac{1}{2}$  the size of the proprietary name in accordance with 21 CFR 201.10(g)(2).
2. The low color-contrast of the black font and purple background utilized for the NDC number and net quantity make the information difficult to read. Revise the color scheme in order to increase readability.
3. Relocate the prominent product strength presented in the upper right corner of the label to be presented directly underneath the established name. This strength is commensurate with the size of the proprietary name. Delete the statement "775 mg Tablets" that is currently presented underneath the established name. As currently presented, the product strength under the established name is not prominent enough, and the product strength presented in the right corner is duplicative.

4. Delete the blue color block at the bottom of the principal display panel. This will allow for increased size of the strength immediately following the established name. Additionally, as currently presented this color block distracts from and competes with the presentation of the strength.
5. Include the statement "Professional Sample-Not For Sale" on the principal display panel, and increase the prominence of this statement.

F. PACKAGE INSERT LABELING

No comment at this time.

**Appendix A: Prescription Study Results for Moxatag**

<b>Inpatient</b>	<b>Outpatient</b>	<b>Voice</b>
Moxatag	moxatag	Moxatag
Moxatag	Moxatag	Moxitag
Moxatag	Moxatag	Amoxitag
Moxatag	Moxatag	Moxatag
Moxatag	Moxatag	Moxitag
Moxatag	Moxatag	Moxatag
Moxatag	Moxatag	
Moxatag		

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/s/

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Kristina Arnwine  
1/17/2008 09:51:03 AM  
DRUG SAFETY OFFICE REVIEWER  
Also signing for Tselaine Jones-Smith

Denise Toyer  
1/17/2008 10:07:50 AM  
DRUG SAFETY OFFICE REVIEWER  
Also signing for Carol Holquist, DMETS Director in her  
absence