

The Division of Medication Error Prevention and Analysis (DMEPA) evaluated the container label, carton labeling, outer wrap foil pouch and insert labeling to identify vulnerabilities that could lead to medication errors. Our findings indicate that the design and the presentation of information on the proposed labels, labeling and outer wrap foil pouch appear to be vulnerable to confusion that could lead to medication errors. We specifically note that the principal display panel is cluttered because of too much information and the directions for use in the insert labeling are incomplete and may lead to inappropriate use of this product. Furthermore, we remain concerned about the packaging of Cetraxal in LDPE vials and the potential that this configuration may cause confusion and increase the risk of wrong route of administration errors associated with this product. To address these concerns, the Applicant has embossed the word "Cetraxal" on one side of the vial along with the established name and strength. Although we remain unsure of the effectiveness of this strategy since embossed information is difficult to read on LDPE material, DMEPA aligns with the Division to allow the marketing of this product as it is currently proposed.

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Representatives from DDMAC and DMEPA were in attendance at the April 15, 2009, internal labeling meeting. Their suggestions have been incorporated into the revised, final labeling where appropriate.

## 12. Labeling

NDA 21-918 is recommended for approval for the treatment of acute otitis externa due to susceptible isolates of *Pseudomonas aeruginosa* or *Staphylococcus aureus* with the labeling submitted by the applicant on April 27, 2009, and found in this Cross-Discipline Team Leader Review (see Appendix 1).

## 13. Recommendations/Risk Benefit Assessment

### RECOMMENDED REGULATORY ACTION:

NDA 21-918 is recommended for approval for the treatment of acute otitis externa due to susceptible isolates of *Pseudomonas aeruginosa* or *Staphylococcus aureus*.

The labeling submitted by the applicant on April 27, 2009, and found in this Cross-Discipline Team Leader Review (see Appendix 1) is acceptable for approval.

### RISK BENEFIT ASSESSMENT:

The application supports the safety and efficacy of Cetraxal (ciprofloxacin otic solution) 0.2%

Medical Officer/Cross-Discipline Team Leader Review  
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NDA 21-918 AZ  
Cetraxal (ciprofloxacin otic solution) 0.2%

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for the treatment of acute otitis externa due to susceptible isolates of *Pseudomonas aeruginosa* or *Staphylococcus aureus*.

In the per protocol population of Study CIPROT III/ 03 IA 02, clinical cure was achieved at the end of a 7-day treatment in 70% (173/247) for the CETRAXAL™ treated group versus 60% (147/243) for the control treated group. The non-inferiority (within a 10% margin) of Cetraxal (ciprofloxacin otic solution) 0.2% therapy to comparator therapy neomycin and polymyxin B sulfates and hydrocortisone (PNH) otic solution was demonstrated for the treatment of otitis externa in both the clinical intent to treat and clinical per protocol populations.

The most common treatment-emergent adverse reactions in Clinical Trial CIPROT III/ 03 IA 02 in ciprofloxacin treated subjects were fungal otitis externa (otomycosis) and headache, both at 3%. Other common adverse reactions seen in 2% of ciprofloxacin treated subjects were nasopharyngitis, ear pruritis, and ear pain.

The package insert, carton, foil wrap, and single use container are adequate to avoid confusion and decrease the risk of wrong route of administration errors.

CMC, Pharmacology/Toxicology, Clinical Pharmacology, and Product Quality Microbiology have recommended approval for this application.

The Biostatistics consultative review states that study CIPROT III/ 03 IA 02 demonstrated the non-inferiority (within a 10% margin) of Cetraxal (ciprofloxacin otic solution) 0.2% therapy to comparator therapy neomycin and polymyxin B sulfates and hydrocortisone (PNH) otic solution for the treatment of otitis externa in both the clinical intent to treat and clinical per protocol populations.

Clinical Microbiology and the Medical Officer recommend approval.

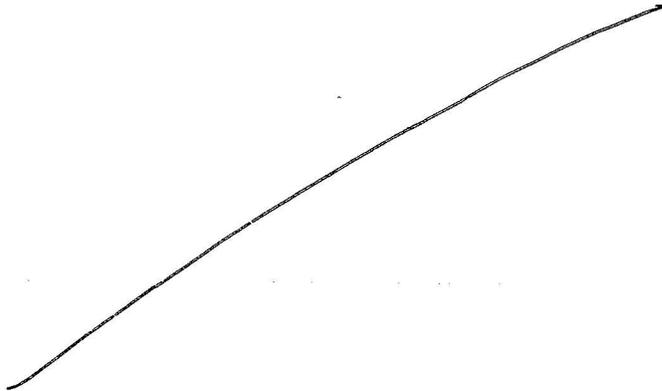
**RECOMMENDATION FOR POSTMARKETING RISK MANAGEMENT ACTIVITIES:**

There are no additional proposed risk management actions except the usual postmarketing collection and reporting of adverse experiences associated with the use of the drug product.

## Appendix 1

Per the April 27, 2009, submission,

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### 1.14.1.3 Draft Labeling Text

- Please note the following: The draft labeling text being provided is the same text that was sent to the sponsor on April 27, 2009 by Sumita Samanta. The Sponsor accepted all changes in the draft label that was provided by the FDA.

8 Page(s) Withheld

       Trade Secret / Confidential (b4)

       Draft Labeling (b4)

       Draft Labeling (b5)

       Deliberative Process (b5)

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/s/

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4/29/2009 10:56:59 AM  
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