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AstraZeneca

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Dockets Management Branch
HFA-305
Food and Drug Administration
5630 Fishers Lane
Rm. 1061
Rockville, MD 20852

JAN 24 2001

2521 '0 JAN '5 A9:58

Re: Docket No. 99N-3088
RIN 0910-AB33
Marketing Exclusivity and Patent Provisions for Certain Antibiotic Drugs

Dear Sir or Madam:

Reference is made to the FDA's proposed rule published in the Federal Register of January 24, 2000, to exempt marketing applications for certain antibiotic drug products from the regulatory provisions governing marketing exclusivity. The proposal would apply to marketing applications for drug products containing an antibiotic drug that was subject of a marketing application received by the FDA before November 2 1, 1997, the effective date of the Food and Drug Administration Modernization Act of 1997.

Reference is also made to a January 22, 2001 telephone conversation between the FDA's Mr. Wayne Mitchell and the undersigned regarding a submission that AstraZeneca made to the FDA's Division of Anti-Infective Drug Products on January 22, 1999. In that submission, AstraZeneca Pharmaceuticals LP indicated that our drug product, MERREM® I.V. (meropenem for injection), NDA No. 50-706, should be classified as an "anti-infective" and not an antibiotic as defined previously by Section 507 [357](a) of the Federal Food, Drug and Cosmetic Act. Mr. Mitchell indicated that FDA is in the process of finalizing the proposed rule, and he requested that AstraZeneca submit a copy of our January 22, 1999 document to the above-referenced Docket for consideration as soon as possible.

Accordingly, attached is a copy of our January 22, 1999 submission to the FDA's Division of Anti-Infective Drug Products regarding the classification of MERREM® I.V. As noted in the document cover letter, microorganisms do not produce the structural component of the active ingredient of MERREM® I.V. that imparts the capacity to inhibit or destroy microorganisms. The synthesis of meropenem, and all intermediates in the synthetic pathway, cannot be manufactured by fermentation and is described in the MERREM® I.V., NDA No. 50-706 and in Sumitomo's DMF #10322. The January 22, 1999 submission also provided a review article by S. Coulton and E. Hunt (Progress in Medicinal Chemistry 1996; 33:99-145) that discusses the chemistry and biology of carbapenems. In this article, meropenem is characterized as a totally synthetic non-natural carbapenem, providing further evidence that MERREM® I.V. does not meet the strict definition of an antibiotic.

US Regulatory Affairs
AstraZeneca Pharmaceuticals LP
1800 Concord Pike PO Box 8355 Wilmington DE 1985043355

AZ0010 (8/00)

99N-3088

The confidentiality of this submission, and all information contained herein, is claimed by AstraZeneca under all applicable laws and regulations. Disclosure of any such information is not authorized without the prior written authorization of AstraZeneca.

I trust this information is helpful. If you have any questions or comments, please do not hesitate to contact me, or in my absence, Ms. Darci Bertelsen at (302) 886-7355.

Sincerely,

Barry D. Sickels
Director, Regulatory Affairs
(302) 886-5895
(302) 886-2822 (fax)

BDS/DLB/mrsc
Enclosure

ZENECA
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SENT VIA UNITED PARCEL SERVICE

JAN 2 2 1999

Gary K. Chikami, M.D.
Director
Division of Anti-Infective
Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research
Food and Drug Administration
HFD No. 520, Document Control Room
920 1 Corporate Boulevard
Rockville, MD 20850

Dear Dr. Chikami:

Re: MERREM® I.V. (meropenem for injection)
NDA SO-706
Request for Drug Classification

Zeneca is writing in regards to an unresolved issue from 1993. At the request of Zeneca Pharmaceuticals (ZENECA), FDA pre-assigned an NDA number to the MERREM? I.V. (meropenem for injection) NDA on May 7, 1993. The MERREM I.V. NDA was inadvertently assigned a 50-series number (NDA 50-706). The original NDA for MERREM I.V. was submitted on October 28, 1993 by ZENECA under section 505(b) of the Federal Food, Drug and Cosmetic Act.

During a conversation initiated by Dr. Kathleen A. Creedon, (Microbiologist, Division of Anti-Infective Drug Products) on November 3, 1993, she noted that the NDA was submitted under section 505. Dr. Creedon commented that the NDA number was incorrectly cited since 50-series numbers are reserved for antibiotics, as defined by section 507.[357](a) of the Act, and that drugs which are submitted under section 505 should be designated with 20-series NDA numbers. In the November 4, 1993 telephone conversation between Dr. Creedon and ZENECA, Dr. Creedon stated if MERREM I.V. was submitted under section 505 it should be referred to as an anti-infective, and that the NDA number for MERREM I.V. could be reassigned to the 20-series numbers upon the submission of documentation which proved that MERREM I.V. does not fit the definition of an antibiotic.

Section 507.[357](a) of the Federal Food, Drug and Cosmetic Act defined an antibiotic as: *"any drug (except drugs for use in animals other than humans) composed wholly or partly of any kind of penicillin, streptomycin, chlortetracycline, chloramphenicol, bacitracin, or any other drug intendedfor use by man containing any quantify of any chemical substance which is produced by a micro-organism and which has fhe capacity to inhibit or destroy micro-organisms in dilute solution (including the chemically synthesized equivalent of any such substance) or any derivative thereof."* ZENECA is aware that section 507 has been repealed; however, the repeal of this section did not change the definition for antibiotic classification (see FDA Guidance for Industry and Reviewers: Repeal of section 507 of the Federal Food, Drug and Cosmetic Act [May 1998] referring to new section 201(j)(j) of the Act).

The structural component of the active ingredient of MERREM I.V. that imparts the capacity to inhibit or destroy micro-organisms is not produced by micro-organisms. The synthesis of meropenem, along with all intermediates in the synthetic pathway, cannot be manufactured by fermentation and is described in the MERREM I.V. NDA 50-706 and in the Sumitomo meropenem Drug Master File (DMF #10322). In addition, the attached review article written by S. Coulton discusses the chemistry and biology of carbapenems. In this article meropenem is characterized as a totally synthetic non-natural carbapenem. These documents provide evidence that MERREM I.V. does not meet the strict definition to be classified as an antibiotic.

Correspondence to FDA, dated December 3, 1993 requested that the MERREM I.V. NDA number be reassigned to a non 50-series NDA number, and the NDA be filed under section 505(b). Subsequently, the NDA was filed by FDA under section 507, and no further communication regarding this issue has been received.

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By means of this correspondence, ZENECA again respectfully requests that the MERREM I.V. NDA be re-assigned a 20-series NDA number and be classified as an anti-infective drug.

We will be contacting the FDA Project Manager shortly to discuss this matter. If you have any questions *or* comments, please do not hesitate to contact me.

Sincerely,

Gerald L. Limp
Manager, Marketed Products Group
Drug Regulatory Affairs Department
(302) 886-8017
(302) 886-2822 (fax)

GLL/DLB/jr
Enclosure

Desk Copy: Ms. Maureen P. Dillon-Parker, HFD No. 520