

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-462

Correspondence



IND 40,061

Eli Lilly and Company
Attention: Elizabeth C. Sloan, Ph.D.
Director, Oncology, U.S. Regulatory Affairs
Lilly Corporate Center
Indianapolis, IN 46285

Dear Dr. Sloan:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act (the Act) for ALIMTA (LY231514 Disodium) Injectable.

We also refer to your April 10, 2002, request for fast track designation and for step-wise submission of sections of a New Drug Application supplemental new drug application under section 506 of the Act (rolling submission).

We have reviewed your request and have concluded that it meets the criteria for fast track designation. Therefore, we are designating ALIMTA (LY231514 disodium) Injection for malignant pleural mesothelioma as a fast track product.

We are granting fast track designation for the following reasons:

1. Malignant pleural mesothelioma is a life-threatening disease with no effective standard therapy.
2. In a randomized controlled study of ALIMTA in combination with cisplatin versus single agent cisplatin, ALIMTA demonstrated a survival benefit in chemo-naïve patients with malignant pleural mesothelioma.

We have also reviewed your request for step-wise submission of sections of an NDA a supplemental new drug application for the indication described above and have concluded that the proposed plan, described in your request, for its step-wise submission is acceptable.

If you pursue a clinical development program that does not support use of ALIMTA (Ly232514 disodium) Injectable for Malignant Pleural Mesothelioma, we will not review the application or accept step-wise submission of sections of an NDA a supplemental new drug application under the fast track program.

IND 40,061

Page 2

If you have any questions, call Debra Vause, Regulatory Project Manager, at 301-594-5724.

Sincerely,

~~/s/~~ *{See appended electronic signature page}*

Richard Pazdur, M.D.

Director

Division of Oncology Drug Products

Office of Drug Evaluation I

Center for Drug Evaluation and Research

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/s/

Richard Pazdur ;
6/10/02 07:29:16 PM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Office of Orphan Products Development (HF-35)
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857
(301) 827-3666

August 28, 2001

Eli Lilly and Company
Lilly Corporate Center
Indianapolis, IN 46285

Attention: John Worzalla
Associate Regulatory Consultant

Dear Mr. Worzalla:

Reference is made to your request for orphan-drug designation dated May 21, 2001, of pemetrexed disodium for the treatment of malignant pleural mesothelioma (request #01-1451), submitted pursuant to Section 526 of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 360bb).

We have completed the review of this request and have determined that pemetrexed disodium qualifies for orphan designation for the treatment of malignant pleural mesothelioma. Please note that it is pemetrexed disodium and not its formulation that has received orphan designation. You have notified us that you are currently developing pemetrexed disodium under the proposed trade name ALIMTA[®]

Please be advised that if pemetrexed disodium is approved for an indication broader than the orphan designation, your product might not be entitled to exclusive marketing rights pursuant to Section 527 of the FDCA (21 U.S.C. 360cc). Therefore, prior to final marketing approval, sponsors of designated orphan drugs are requested to compare the designated orphan indication with the proposed marketing indication and to submit additional data to amend their orphan designation prior to marketing approval if warranted.

Finally, please notify this Office within 30 days of submission of a marketing application for the use of pemetrexed disodium as designated. Also an annual progress report must be submitted within 14 months after the designation date and annually thereafter until a marketing application is approved (21 CFR 316.30). If you need further assistance in the development of your product for marketing, please feel free to contact Robert Pratt, PharmD at (301) 827-0990.

Please refer to this letter as official notification of designation and congratulations on obtaining your orphan drug designation.

Sincerely yours,

/s/

Marlene E. Haffner, MD, MPH
Rear Admiral, United States Public Health Service
Director, Office of Orphan Products Development

EXCLUSION FROM USER FEES FOR ORPHAN DRUGS

NDA Number: 21-462
USER FEE ID#: 4249
Sponsor: Eli Lilly and Company
Indication: Malignant Pleural Mesothelioma

This NDA is for an orphan product. According to section 736(a)(1)(E) of the FD&C Act, orphan drugs are not subject to application fees for a rare disease or condition as long as the application does not include any indication that is not designated as an orphan disease. NDA 21-462 for Alimta (pemetrexed) is only for the single indication of malignant pleural mesothelioma.

Attached on the following pages is a copy of the communication (dated 28 August 2001) from the Office of Orphan Products Development of the FDA granting Orphan Drug Designation for Alimta (pemetrexed) for the indication of malignant pleural mesothelioma.

**APPEARS THIS WAY
ON ORIGINAL**

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: <http://www.fda.gov/cder/pdufa/default.htm>

1. APPLICANT'S NAME AND ADDRESS Eli Lilly and Company Lilly Corporate Center Indianapolis, IN 46285 c/o Debasish F. Roychowdhury, M.D. Director, U.S. Regulatory Affairs	4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER NDA 21-462
2. TELEPHONE NUMBER (Include Area Code) (317) 433-6604	5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM. IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW: <input checked="" type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION. <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO: _____ (APPLICATION NO. CONTAINING THE DATA).
3. PRODUCT NAME Alimta (pemtrexed)	6. USER FEE I.D. NUMBER 4249

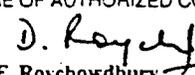
7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

<input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory)	<input type="checkbox"/> A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE (See item 7, reverse side before checking box.)
<input checked="" type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act (See item 7, reverse side before checking box.)	<input type="checkbox"/> THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act (See item 7, reverse side before checking box.)
<input type="checkbox"/> THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY (Self Explanatory)	

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? YES NO
(See Item 8, reverse side if answered YES)

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services Food and Drug Administration CDER, HFM-99 1401 Rockville Pike Rockville, MD 20852-1448	Food and Drug Administration CDER, HFD-94 and 12420 Parklawn Drive, Room 3046 Rockville, MD 20852	An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.
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SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE  Debasish F. Roychowdhury	TITLE Director, U.S. Regulatory Affairs	DATE September 30, 2002
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FILING COMMUNICATION

NDA 21-462

Eli Lilly & Company
Attention: John F. Worzalla
Regulatory Research Scientist, U.S. Regulatory Affairs
Lilly Corporate Center
Indianapolis, IN 46285

Dear Mr. Worzalla:

Please refer to your September 29, 2003 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Alimta® (pemetrexed, LY231514).

We also refer to your submissions dated October 24, November 22, December 6, 2002; January 10, 28, February 13, 27, March 24, 27, April 3, May 9, 12, 29, June 18, 26, July 29, 30, August 8, 15, 21, 28, September 2, 3, 4, 9, 12, 15, 16, 19, 22, 29, October 6, 7, 20, and November 4, 5, 6, and 7, 2003.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application will be filed under section 505(b) of the Act on November 29, 2003 in accordance with 21 CFR 314.101(a).

At this time, we have not identified any potential filing review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review.

If you have any questions, call Patty Garvey, Regulatory Project Manager, at (301) 594-5766.

Sincerely,


{See appended electronic signature page}

Dotti Pease
Chief, Project Management Staff
Division of Oncology Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

Patricia Garvey
11/19/03 01:41:35 PM
Signed for Dotti Pease



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-462

Eli Lilly & Company
Attention: John F. Worzalla
Regulatory Research Scientist, U.S. Regulatory Affairs
Lilly Corporate Center
Indianapolis, IN 46285

Dear Mr. Worzalla:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Alimta® (pemetrexed, LY231514)

Review Priority Classification: Priority (P)

Date of Application: September 29, 2003

Date of Receipt: September 30, 2003

Our Reference Number: NDA 21-462

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on November 29, 2003 in accordance with 21 CFR 314.101(a). If we file the application, the user fee goal date will be March 31, 2003.

Under 21 CFR 314.102(c), you may request a meeting with this Division (to be held approximately 90 days from the above receipt date) for a brief report on the status of the review but not on the ultimate approvability of the application. Alternatively, you may choose to receive a report by telephone.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application. Address all communications concerning this NDA as follows:

NDA 21-462

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U.S. Postal Service:

Center for Drug Evaluation and Research
Division of Oncology Drug Products, HFD-150
Attention: Division Document Room, 3067
5600 Fishers Lane
Rockville, Maryland 20857

Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Oncology Drug Products, HFD-150
Attention: Document Room 3067
1451 Rockville Pike
Rockville, Maryland 20852

If you have any questions, call Patty Garvey, Regulatory Project Manager, at (301) 594-5766.

Sincerely,


(See appended electronic signature page)

Richard Pazdur
Director
Division of Oncology Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

Dotti Pease
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signing for Richard Pazdur, M.D.