

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-488

Correspondence



NDA 21-488

INFORMATION REQUEST LETTER

Atrix Laboratories
Attention: Johanna J. Matz
Regulatory Affairs Project Leader
2579 Midpoint Drive
Fort Collins, CO 80525-4417

Dear Ms. Matz:

Please refer to your April 13, 2002 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Eligard™ (leuprolide acetate for injectable suspension) received on April 16, 2002.

We are reviewing the chemistry, manufacturing and controls section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

1. Please revise the "Marketed Product Post-Approval Stability Commitment" to the following.
 - a. Atrix Laboratories, Inc. commits to place the first three production batches of ELIGARD™ 30 mg on stability per the approved protocol, followed by a minimum of one batch per year. The generated data will be submitted to the agency periodically in Annual Reports.
 - b. Commits to withdraw from the market any lot that falls out of specification during shelf life of the drug product. If the applicant has evidence that the deviation is a single occurrence that does not affect the safety and efficacy of the drug product, Atrix Laboratories Inc. will immediately discuss it with the agency.
 - c. Where future changes to the CMC for the ELIGARD™ 30 mg drug product requires support of stability evaluation, representative batches will be placed on stability per the approved protocol.
 - d. The expiration dating period for the product may be extended in an annual report if the first three production batches tested by the approved protocol meets established specifications.
2. Please submit three copies of the Methods Validation package including a list of samples and equipment, which will be provided for the analysis of the methods.

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If you have any questions, call Archana Reddy, M.P.H., Regulatory Project Manager, at 301-827-4260.

Sincerely,

{see appended ~~/S/~~ electronic signature page}

David Lin, Ph.D.
Chemistry Team Leader, DNDC II for the
Division of Reproductive and Urologic Drug
Products, HFD-580
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

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/s/

David T. Lin
1/21/03 04:11:18 PM
I concur.



NDA 21-488

INFORMATION REQUEST LETTER

Atrix Laboratories
Attention: Johanna J. Matz
Regulatory Affairs Project Leader
2579 Midpoint Drive
Fort Collins, CO 80525-4417

Dear Ms. Matz:

Please refer to your April 13, 2002 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Eligard™ (leuprolide acetate for injectable suspension) received on April 16, 2002.

We are reviewing the chemistry, manufacturing and controls section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

1. Provide representative _____ to justify comparability of the impurity profiles for the drug substance obtained from _____
2. Provide the polydispersity data obtained in the stability studies for drug product batches #1276, #1317, #1352 and #1444.
3. Based on the stability data provided, we recommend an 18-month expiration dating period for the drug product.
4. Provide water content data for the syringe A component of the drug product during stability testing.
5. A study similar to Study #50270 performed at _____ °C to evaluate the degradants in the Syringe B component of the drug product should be performed using batches containing drug substance from _____. In addition, this study should also be performed for Syringe A.
6. Table 53 appears to incorrectly list drug product lot # 1277 instead of 1276, and 1318 instead of 1317. Clarify these discrepancies. In addition, please include data from drug product containing drug substance obtained from _____ into this table.

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Page 2

If you have any questions, call Archana Reddy, M.P.H., Regulatory Project Manager, at
301- 827 - 4260.

Sincerely,

 {see appended electronic signature page}

David Lin, Ph.D.
Chemistry Team Leader, DNDC II for the
Division of Reproductive and Urologic Drug
Products, HFD-580
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

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/s/

David T. Lin
1/9/03 03:28:58 PM
I concur.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-488

Atrix Laboratories, Inc.
Attention: Johanna Matz
Regulatory Affairs Project Leader
2579 Midpoint Drive
Fort Collins, CO 80525

Dear Ms. Matz:

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: Eligard™ (leuprolide acetate) 30 mg injection suspension
Review Priority Classification: Standard (S)
Date of Application: April 13, 2002
Date of Receipt: April 16, 2002
Our Reference Number: NDA 21-488

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on June 14, 2002, in accordance with 21 CFR 314.101(a). If the application is filed, the primary user fee goal date will be February 16, 2003.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 FR 66632). If you have not already fulfilled the requirements of 21 CFR 314.55 (or 601.27), please submit your plans for pediatric drug development within 120 days from the date of this letter unless you believe a waiver is appropriate. Within approximately 120 days of receipt of your pediatric drug development plan, we will review your plan and notify you of its adequacy.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will make a determination whether to grant or deny a request for a waiver of pediatric studies during the review of the application. In no case, however, will the determination be made later than the date action is taken on the application. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov/cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" (PPSR) in addition to your plans for pediatric drug development described above. We recommend that you submit a Proposed Pediatric Study Request within 120 days from the date of this letter. If you are unable to meet this time frame but are interested in pediatric exclusivity, please notify the division in writing. FDA generally will not accept studies submitted to an NDA before issuance of a Written Request as responsive to a Written Request. Sponsors should obtain a Written Request before submitting pediatric studies to an NDA. If you do not submit a PPSR or indicate that you are interested in pediatric exclusivity, we will review your pediatric drug development plan and notify you of its adequacy. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

Under 21 CFR 314.102(c) of the new drug regulations, you may request an informal conference 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 application's ultimate approvability. Alternatively, you may choose to receive such a report by telephone.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application. All communications concerning this NDA should be addressed as follows:

U.S. Postal/Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Reproductive and Urologic Drug Products, HFD-580
Attention: Division Document Room
5600 Fishers Lane
Rockville, Maryland 20857

If you have any questions, call Archana Reddy, M.P.H., Regulatory Project Manager, at (301) 827-4260.

Sincerely,

{See appended electronic signature page}

Margaret Kober, R.Ph.
Acting Chief, Project Management Staff
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Margaret Kober
4/26/02 03:21:51 PM



NDA 21-488

INFORMATION REQUEST LETTER

Atrix Laboratories
Attention: Johanna J. Matz
Regulatory Affairs Project Leader
2579 Midpoint Drive
Fort Collins, CO 80525-4417

Dear Ms. Matz:

Please refer to your April 13, 2002 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Eligard™ (leuprolide acetate for injectable suspension) 30 mg.

We also refer to your submission dated October 29, 2002.

We are reviewing the Labeling section of your April 13, 2002 submission and have the following attached labeling comments. We request a prompt written response to the attached labeling comments in order to continue our evaluation of your NDA.

If you have any questions, call Archana Reddy, M.P.H., Regulatory Project Manager, at 301- 827 - 4260.

Sincerely,

{See appended electronic signature page}

Daniel Shames, M.D.
Division Director
Division of Reproductive and Urologic Drug
Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Cc: Enclosure

19 pages redacted from this section of
the approval package consisted of draft labeling

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/s/

Daniel A. Shames
1/27/03 10:04:36 AM