# APPROVAL LETTER

NDA 19-943

MAR 30 1995

TAP Pharmaceuticals, Inc.
Attention: Aruna Dabholkar, M.D.
Regulatory Products Manager
2355 Waukegan Road
Deerfield, IL 60015

Dear Dr. Dabholkar:

Please refer to your December 30, 1988, new drug application and your resubmission dated March 30, 1994, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lupron® (leuprolide acetate) Depot, 3.75 mg.

We acknowledge receipt of your amendments dated May 20, July 29, and November 1, 1994; January 9, February 13 and 15, and March 9, 24, and 29, 1995.

This new drug application provides for the treatment of anemia caused by uterine leiomyomata in women who fail iron therapy.

We have completed the review of this application including the submitted draft labeling and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the March 29, 1995, draft labeling. Accordingly, the application is approved effective on the date of this letter.

We also remind you of your commitment dated March 24, 1995, to perform a Phase 4 pharmacokinetic study as described in our telefacsimile of March 22, 1995.

The final printed labeling (FPL) must be identical to the March 29, 1995, draft labeling. Marketing the product with FPL that is not identical to this draft labeling may render the product misbranded and an unapproved new drug.

Please submit fifteen copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy weight paper or similar material. For administrative purposes this submission should be designated "FINAL PRINTED LABELING" for approved NDA 19-943. Approval of this labeling by FDA is not required before it is used.

Should additional information relating to the safety and effectiveness of the drug become availabl revision of that labeling may be required.

Please submit three copies of the introductory promotional material that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional material and the package insert, directly to:

Food and Drug Administration
Division of Drug Marketing, Advertising and Communications,
HFD-240
5600 Fishers Lane
Rockville, Maryland 20857

Please submit one market package of the drug when it is available.

Under section 736(a)(1)(B)(ii) of the Prescription Drug User Fee Act of 1992, this letter triggers the remaining 50% of the fee assessed for this application. You will receive an invoice for the amount due within the next month. Payment will be due within 30 days of the date of the invoice.

Should you have any questions, please contact:

Lana L. Pauls, M.P.H.
Consumer Safety Officer
Telephone: (301) 443-3510

Sincerely yours,

3/30/95

Solomon Sobel, M.D.
Director
Division of Metabolism and
Endocrine Drug Products (HFD-510)
Office of Drug Evaluation II
Center for Drug Evaluation and Research

| Name | Title | Date | Signature |
|---|---|---|---|
| Enid Galliers | SCSO | 3-24-95 | |
| Annette Bey, M.D. | Medical Officer | 3-29-95 | |
| Philip Corfman, M.D. | Supervisory Medical Officer | 03-23-95 | |
| Chien-Hua Niu, Ph.D. | Chemist | 3-23-95 | |
| Yuan-yuan Chiu, Ph.D. | Supervisory Chemist | 3-23-95 | |
| Krishan Raheja, D.V.M., Ph.D.. | Pharmacologist | 3-24-95 | |
| Alexander Jordan, Ph.D. | Supervisory Pharmacologist | 3/24/95 | |
| Solomon Sobel, M.D. | Division Director | 3/28/95 | |

cc:
Original NDA
HF-2/MEDWATCH (with draft labeling)
DISTRICT OFFICE
HFD-003/MLumpkin
HFD-80 (+ draft labeling & exclusivity checklist)
HFD-426/HAhn/JHunt
HFD-500/LRipper (with draft labeling)
HFD-510
HFD-510/ABey, PCorfman, CNiu, YYChiu, Kraheja, AJordan
HFD-713/DMarticello/ENevius
HFD-510/LPauls/03.21.95/N19943AP.001
HFI-20/SCruzan

APPROVAL (AP)

Concurrences: (see above)

NDA # 19-943 Drug LUPRON (LEUPROLIDE ACETATE) DEPOT

Applicant TAP PHARMACEUTICALS SO SAN PAULO Phone 3-3510

| | Arrange package in the following order: | Check or Comment |
|---|---|---|
| 1. | ACTION LETTER with supervisory signatures | A.P ✓ AE ____ NA ____ |
| 2. | ACTION PACKAGE TRACKING FORM | |
| 3. | Completed copy of this CHECKLIST in package | Chem/Ther Types 6S |
| 4. | LABELING (package insert and labels). (If final or revised draft, include copy of previous version with ODE's comments and state where in action package the Division's review is located. If Rx-to-OTC switch, include current Rx PI and HFD-210 review of OTC insert.) | Draft ____ Final ✓ Revised Draft ____ |
| 5. | SUMMARY BASIS OF APPROVAL. (Copy of previous version with ODE's comment as well as disk, FPL and sign-off sheet must accompany revised or final version. If no SBA, include memo stating what reviews will be used as SBA equivalent.) | SBA ____ N/A Revised SBA ____ SBA Equivalent ____ |
| 6. | PATENT INFORMATION ✓ | EXCLUSIVITY CHECKLIST ✓ |
| 7. | Debarment Certification (Copy of applicant's certification for all NDAs submitted on or after June 1, 1992) | ✓ |
| 8. | DIVISION DIRECTOR'S MEMO (If more than 1 review for any 1 discipline, separate reviews with a sheet of colored paper. Any conflicts between reviews must have resolution documented.) | N/A |
| | GROUP LEADER'S MEMO | ✓ |
| | PEDIATRIC PAGE | N/A |
| | MEDICAL REVIEW | ✓ |
| | SAFETY UPDATE REVIEW | ✓ |
| | STATISTICAL REVIEW | ✓ |
| | BIOPHARMACEUTICS REVIEW | ✓ |
| | PHARMACOLOGY REVIEW (Include pertinent IND reviews) | ✓ |
| | Statistical Review of Carcinogenicity Study(ies) | ✓ |
| | CHEMISTRY REVIEW | ✓ |
| | Date EER completed 3/22/95 (attach signed form or CIRTS printout); FUR needed ____ requested ____ | OK ✓ No ____ |
| | Have the methods been validated? | Yes (attach) ____ No N/A |
| | Environmental Assessment Review | N/A |
| | MICROBIOLOGY REVIEW | N/A |
| | Has the monograph been approved? | Yes ____ No ✓ |
| 9. | Statement on status of DSI's AUDIT OF PIVOTAL CLINICAL STUDIES (If AE or AP ltr, explain if not satisfactorily completed. Attach a COMIS printout of DSI status.) | N/A N/A |
| 10. | CORRESPONDENCE and MEMOS OF TELECONS | ✓ |
| 11. | MINUTES OF MEETINGS | ✓ |
| | Date of End-of-Phase II Meeting | N/A |
| | Date of pre-NDA Meeting | N/A |
| 12. | ADVISORY COMMITTEE MEETING MINUTES or, if not available, 48-Hour Info Alert or pertinent section of transcript | Minutes ✓ Info Alert ____ Transcript ____ No mtg ____ |
| 13. | FEDERAL REGISTER NOTICES; OTC or DESI DOCUMENTS | ____ |
| 14. | If approval letter, has ADVERTISING MATERIAL been reviewed? If no and this is an AP with draft labeling letter, has advertising material already been requested? | Yes ____ No ✓ Yes, documentation attached ____ No, included in AP ltr ✓ |
| 15. | Have all disciplines completed their reviews? If no, what review(s) is/are still pending? | Yes ✓ No ____ |
| 16. | Integrated Summary of Safety | ✓ |
| 17. | NDA (especially Medical/Statistical) Summary | ✓ |