CHEM REVIEW

MAR 23 1995

DIVISION OF METABOLISM AND ENDOCRINE DRUG PRODUCTS

Review of Chemistry, Manufacturing and Controls

NDA #: 19-943
Chemistry Review #: 3 Date Reviewed: March 23, 1995

Submission Type	Document Date	CDER Date	Assigned Date
Original	12/30/88	1/9/89	1/9/89
Resubmission	3/30/94	3/31/94	4/5/94

Name & Address of Applicant: TAP Pharmaceuticals, Inc.
Bannockburn Lake Office Plaza
Deerfield, IL 60015

Drug Product Name:

Proprietary: Lupron Depot
Nonproprietary/Established/USAN: Leuprolide acetate for depot suspension
Code Name: TAP-144, TAP-144-SR
Chem.Type/Ther.Class: 3S

Pharmacological Category/Indication: Gonadotropin releasing hormone (GnRH) agonist to be used for the treatment of leiomyoma uteri (uterine fibroids)

Dosage Form: Lyophilized microsphere powder
Strengths: 3.75 mg leuprolide acetate
Route of Administration: Intramuscular injection
Dispensed: __X__ Rx ____ OTC

Conclusions and Recommendation:

The FUR for the estalished cGMP of Mitsui Plant and Shonan Plant, Takeda Chemical Industries, Japan and Abbott Laboratories, USA is acceptable by the Office of Compliance (dated March 22, 1995). Because there is no more pending CMC issued, this application is approvable from chemistry viewpoint.

Chien-Hua Niu, Ph.D.
Review Chemist

cc: Org. NDA
HFD-510/Division File
HFD-510/CHNiu/3/23/95/Disc NDA/NDA19943.003
HFD-510/LPauls
HFD-510/YYChiu
R/D init by: 3/23/95

DIVISION OF METABOLISM AND ENDOCRINE DRUG PRODUCTS

Review of Chemistry, Manufacturing and Controls

FEB 15 1995

NDA #: 19-943
Chemistry Review #: 2

Date Reviewed: February 15, 1995

Submission Type	Document Date	CDER Date	Assigned Date
Original	12/30/88	1/9/89	1/9/89
Resubmission	3/30/94	3/31/94	4/5/94

Name & Address of Applicant: TAP Pharmaceuticals, Inc.
Bannockburn Lake Office Plaza
Deerfield, IL 60015

Drug Product Name:

Proprietary: Lupron Depot
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Dosage Form: Lyophilized microsphere powder
Strengths: 3.75 mg leuprolide acetate
Route of Administration: Intramuscular injection
Dispensed: __X__ Rx ____ OTC

Conclusions and Recommendation:

Lupron Depot 3.75 mg used for the treatment of uterine fibroids is exactly the same as that employed for the treatment of endometriosis under NDA #20-011. The chemistry and manufacturing controls of Lupron Depot, 3.75 mg, has been previously reviewed and found satisfactory (see Chem. Rev. #1 for NDA #19-943). Moreover, the estalished cGMP of Mitsui Plant and Shonan Plant, Takeda Chemical Industries, Japan and Abbott Laboratories, USA is acceptable by the Office of Compliance. The application is approvable from chemistry viewpoint although another acceptable FUR for the acceptable EER is needed.

Chien-Hua Niu, Ph.D.
Review Chemist

cc: Org. NDA
HFD-510/Division File
HFD-510/CHNiu/2/9/95/Disc NDA/NDA19943.002
HFD-510/LPauls
HFD-510/YYChiu
R/D init by: 2/15/95

ORIGINAL APR 17 1989

REVIEW OF CHEMISTRY AND MANUFACTURING CONTROL

NDA # 19,943

Division: DMEDP, HFD-510
Chemistry Review: # 1

Sponsor: Takeda-Abbott Research and Development
Address: Abbott Park
North Chicago, Il. 60064

Date Completed: 4/17/89

Product Name(s):

Proprietary:	Lupron Depot^{R}
Non-proprietary:	Leuprolide acetate for depot suspension
USAN:	Leuprolide acetate
Code name/number:	TAP-144, TAP-144-SR

Dosage Form and Route of Administration:
Lyophilized microsphere powder containing 3.75 mg leuprolide acetate to be suspended in a diluent for intramuscular injection.

Structural Formula and Chemical Name:
Leuprolide Acetate

5-oxo-L-propyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosyl-D-leucyl-L-leucyl-L-arginyl-N-ethyl-L-prolinamide acetat

Initial Submission: December 30, 1988

Rec'd by CDB: January 9, 1989

Related Documents: IND (Lupron Depot, Abbott Laboratories)
NDA 19,010 (Lupron, Abbott Laboratories)
NDA 19,732 [Lupron Depot (7.50 mg), Takeda-Abbott R & D]

Remarks:
Lupron Depot, 3.75 mg, is indicated in the treatment of leiomyoma uteri (uterine fiborids) for a period of up to 6 months. Therapy may be preoperative prior to myomectomy or hysterectomy or it may provide symptomatic relief for the perimenopausal woman who does not desire surgery.

Conclusion and Recommendation:
Lupron Depot 3.75 mg is manufactured by the identical process as described for the approved drug, Lupron Depot, 7.5 mg. The only difference is the quantity of lupron depot microspheres filled into the vial. Therefore, the drug is approvable from chemistry viewpoint. Additional information should be requested (See draft letter).

Chien-Hua Niu, Ph.D.
Review Chemist

cc: IND/NDA Orig.
HFD-510
HFD-102/Kumkumian
HFD-510/CHNiu/4/17/89/Wang #0814c
R/D init. by: 4/19/89

NDA 19-943
Lupron® Depot (leuprolide acetate)
TAP Pharmaceuticals, Inc.

Environmental Impact Assessment Report (EIAR)

Included in the chemistry review dated April 17, 1989

NDA 19-943
Lupron® Depot (leuprolide acetate)
TAP Pharmaceuticals, Inc.

Microbiology Review

No microbiology review is required per discussion with the reviewing chemist, Dr. Chien-hua Niu.

NDA 19-943
Lupron® Depot (leuprolide acetate)
TAP Pharmaceuticals, Inc.

DSI Investigations

No DSI investigations are required per discussion with the original medical officer on this application, Dr. Lisa Rarick.