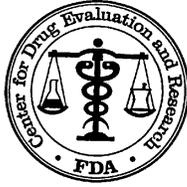


**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

203696Orig1s000

STATISTICAL REVIEW(S)



U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Translational Sciences
Office of Biostatistics

STATISTICAL REVIEW AND EVALUATION

CLINICAL STUDIES

NDA#: 203696/N0000

Drug Name: Lupaneta Pack (Leuprolide Acetate for depot suspension 3.75 mg injection monthly and Norethindrone Acetate 5 mg tablet for oral once daily)

Indication(s): Initial management of the painful symptoms of endometriosis and for management of recurrence of symptoms

Applicant: Abbott Endocrine Inc

Date(s): Submission Date: 02/15/2012
PDUFA Due Date: 12/15/2012

Review Priority: Standard

Biometrics Division: Division of Biometrics 3

Statistical Reviewer: Xin Fang, Ph.D., Statistical Reviewer

Concurring Reviewers: Mahboob Sobhan, Ph.D., Statistical Team Leader

Medical Division: Division of Reproductive and Urological Drug Products

Clinical Team: Ronald J. Orleans, MD., Clinical Reviewer
Lisa Soule, MD., Clinical Team Leader

Project Manager: Kimberly A. Shiley

Keywords: NDA review, clinical study

BACKGROUND

This submission is a 505(b)(1) NDA application in support of Lupaneta Pack for the treatment of initial management of the painful symptoms of endometriosis and for management of recurrent symptoms. The efficacy and safety of Lupaneta Pack are referred to the Agency approved NDA 020011/S-021, sNDA 020708/S-011, and ANDA 091090.

According to the meeting minutes dated Dec. 9, 2011 under (b) (4), the Agency agreed with the sponsor to cross-reference the historical Lupron NDAs to support this application.

CONCLUSION

There was no new efficacy data submitted in support of this submission. Therefore, no statistical review was necessary.

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/s/

XIN FANG
11/15/2012

MAHBOOB SOBHAN
11/15/2012

STATISTICS FILING CHECKLIST FOR A NEW NDA/BLA

NDA Number: 203-696/0000 **Applicant:** Abbott Endocrine Inc **Stamp Date:** 02/15/2012

Drug Name: leuprolide acetate for depot suspension and norethindrone acetate tablets **NDA/BLA Type:** Original/Standard **Indication:** initial management of the painful symptoms of endometriosis and for management of recurrence of symptoms

On **initial** overview of the NDA/BLA application for RTF:

	Content Parameter	Yes	No	NA	Comments
1A	Paper Submission: Index is sufficient to locate necessary reports, tables, data, etc.			X	
1B	Electronic Submission: Indexing and reference links within the electronic submission are sufficient to permit navigation through the submission, including access to reports, tables, data, etc.	X			
2	ISS, ISE, and complete study reports are available (including original protocols, subsequent amendments, etc.)			X	
3	Safety and efficacy were investigated for gender, racial, and geriatric subgroups investigated.			X	
4	Data sets in EDR are accessible and conform to applicable guidances (e.g., existence of define.pdf file for data sets).			X	

IS THE STATISTICAL SECTION OF THE APPLICATION FILEABLE? **YES**

Content Parameter (possible review concerns for 74-day letter)	Yes	No	NA	Comment
Designs utilized are appropriate for the indications requested.			X	
Endpoints and methods of analysis are specified in the protocols/statistical analysis plans.			X	
Interim analyses (if present) were pre-specified in the protocol and appropriate adjustments in significance level made. DSMB meeting minutes and data are available.			X	
Appropriate references for novel statistical methodology (if present) are included.			X	
Safety data organized to permit analyses across clinical trials in the NDA/BLA.			X	
Investigation of effect of dropouts on statistical analyses as described by applicant appears adequate.			X	

Information requests for the Applicant: None at this time.

File name: 5_Statistics Filing Checklist for a New NDA_203696

STATISTICS FILING CHECKLIST FOR A NEW NDA/BLA

Background:

The sponsor, Abbott Endocrine Inc, is seeking approval of co-packaged product containing Lupron Depot and norethindrone acetate tablets in the treatment of endometriosis. The proposed two products are:

- 1 month 3.75 mg inj/5 mg tablets (30 tablets/bottle) kit
- 3 month 11.25 mg inj/5 mg tablets (90 tablets/bottle) kit

Lupron Depot 3.75 mg for 1-month administration and Lupron Depot 11.25 mg for 3-month administration were approved in September 21, 2001 under sNDA 020011/S-021 and sNDA 020708/S-011, respectively. The norethindrone acetate was approved for the treatment of secondary amenorrhea, endometriosis, and abnormal uterine bleeding due to hormonal imbalance in the absence of organic pathology, such as submucous fibroids or uterine cancer under ANDA 091090 in July 21, 2010.

No new efficacy data were submitted. In the meeting held on Nov. 10, 2011 under (b) (4) meeting minutes dated Dec. 9, 2011), the Agency agreed with the sponsor to “cross-reference the historical Lupron NDAs that supported the approval of the Lupron add-back indication and that no documents need to be included in Module 2, 4, and 5 for the proposed Lupron co-pack NDA.”

Sponsor’s Efficacy Results:

Statistical review of efficacy is not necessary at this time. The efficacy of the co-packed leuprolide acetate for depot suspension and norethindrone acetate tablets will be cross-referenced to NDA 020011, 020708, and ANDA 091090.

Xin Fang, Ph.D.	04/09/2012
Reviewing Statistician	Date
Mahboob Sobhan, Ph.D.	04/09/2012
Supervisor/Team Leader	Date

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/s/

XIN FANG
04/16/2012

MAHBOOB SOBHAN
04/26/2012