CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

125290

SUMMARY REVIEW

Cross-Discipline Team Leader Review

Date	8/13/09
From	Billy Dunn, MD
Subject	Cross-Discipline Team Leader Review
NDA/BLA # **Supplement#**	125290 0.14
Applicant	Novartis
Date of Submission	6/15/09
PDUFA Goal Date	8/14/09
Proprietary Name / Established (USAN) names	Extavia/Interferon beta-1b
Dosage forms / Strength	0.25 mg subcutaneous injection
Proposed Indication(s)	Relapsing multiple sclerosis
Recommended:	Approval

1. Introduction

Extavia is a drug product proposed by Novartis for the treatment of relapsing forms of multiple sclerosis to reduce the frequency of clinical exacerbations.

This BLA was originally submitted on 5/6/08 and on 6/5/09 a complete response action was issued for the original application. Please refer to my original review dated 6/3/09 for a complete discussion of the original application. Issues cited in the complete response pertained to labeling and the Risk Evaluation And Mitigation Strategy (REMS).

The sponsor submitted on 6/15/09 a response to the complete response action letter. Labeling information and a REMS along with supporting REMS documentation were included in the current submission. Accordingly, only the relevant disciplines have been involved in the review of this new material. Prior first cycle reviews from unaffected disciplines remain valid and were confirmed with the various reviewers. Please refer to those reviews for any issues related to the original application.

The review team for this submission included the following primary reviewers:

CMC – Ralph Bernstein, PhD
Microbiology – Bo Chi, PhD
DRISK (REMS) – Jessica Diaz, BSN, RN
DRISK (Patient Labeling) – Sharon Mills, BSN, RN, CCRP
DMEPA – Laura Pincock, PharmD

I discuss below the key conclusions of each reviewer and provide my recommendations regarding this submission.

8. Safety

This sponsor has submitted a Medication Guide-only REMS along with its supporting documentation. Ms. Diaz has reviewed this REMS and has found it acceptable. There are no outstanding clinical safety issues.

9. Advisory Committee Meeting

N/A

10. Pediatrics

N/A

11. Other Relevant Regulatory Issues

N/A

12. Labeling

The proposed label for Extavia is informed by the label of currently approved Betaseron, with appropriate changes. Ms. Mills made several comments and recommendations in her review of the Medication Guide and Patient Instructions for Use that were communicated to and negotiated with the sponsor. Dr. Pincock reviewed the carton and container labeling submitted by the sponsor and found it acceptable. Previous issues related to inclusion in labeling of (b) (4) with regard to Extavia and Betaseron have been resolved in discussions with the sponsor. Labeling negotiations with the sponsor have been completed and the label as agreed to by the sponsor is acceptable. There are no outstanding labeling issues.

13. Recommendations/Risk Benefit Assessment

I recommend approval of this application.

2. Background

Please see my original review.

3. CMC/Device

Dr. Bernstein reviewed this submission and engaged the sponsor in a series of discussions and negotiations regarding appropriate quality assurance oversight over the manufacturing process and carton and container labeling. These have been resolved and there are no outstanding CMC issues. Upon approval, Dr. Bernstein is recommending a post-marketing commitment to develop an analytical test method for use in release and stability testing of the drug product to control of the size of the IFN /HAS complexes to ensure product quality. A detailed discussion of this PMC and full language describing its requirements may be found in Dr. Bernstein's review.

4. Nonclinical Pharmacology/Toxicology

N/A

5. Clinical Pharmacology/Biopharmaceutics

N/A

6. Clinical Microbiology

Dr. Chi reviewed this submission and found it acceptable. There are no outstanding microbiology issues. Upon approval, Dr. Chi is recommending three post-marketing commitments to monitor endotoxin for the (b) pool, to collect bioburden data for (b) (4) pools maintained at 2-8 degree C for thirty days, and to use 100 mL sample volume instead of 10 mL for the pre-filtration bioburden test. A detailed discussion of these PMCs and full language describing their requirements may be found in Dr. Chi's review.

7. Clinical/Statistical- Efficacy

N/A