DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-905

Quintiles BRI
Attention: Joy K. Bates, RN, BSN
Manager, Regulatory Affairs
1801 Rockville Pike, Suite 300
Rockville, Maryland 20852

SEP 10 1998

Dear Ms. Bates:

Please refer to your new drug application (NDA) dated March 10, 1998, received March 10, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Arava (leflunomide) Tablets, 10 mg, 20 mg, and 100 mg.

We acknowledge receipt of your submissions dated April 20, 21, 24, and 27; May 1(2), 5(2), 6, 7, 15, 22(2), 26, and 27(2); June 2, 3, 11, 15(2), 16, 17, 19, 23(2), 24(3), 26, and 30; July 1, 2(3), 6, 9(2), 10(2), 13, 14, 15, 17(2), 21, and 28; August 4(2), 11, 13, 14, 21, 28, and 31, and September 1 and 10, 1998. The user fee goal date for this application is September 10, 1998.

This new drug application provides for the use of Arava (leflunomide) Tablets, 10 mg, 20 mg, and 100 mg, in adults for the treatment of active rheumatoid arthritis (RA) to reduce signs and symptoms and to retard structural damage as evidenced by X-ray erosions and joint space narrowing.

We have completed the review of this application, as amended, 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 enclosed marked-up draft labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed marked-up draft labeling. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

As previously discussed, you may use the existing stock of carton and container labels. However, we remind you to change the storage statement for the carton and container labels at the next printing to read as follows:

Store at 25° C (77° F); excursions permitted to 15 - 30° C (59 - 86° F) [see USP Controlled Room Temperature]. Protect from light.

Please submit 20 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 "FPL for approved NDA 20-905." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your Phase 4 commitments specified in your submission dated September 10, 1998. These commitments, along with any completion dates agreed upon, are listed below.

Protocols, data, and final reports related to these commitments should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. If an IND is not required to meet a Phase 4 commitment, please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21 CFR 314.82(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print.

Please send one copy to the Division of Anti-Inflammatory, Analgesic and Ophthalmic Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

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

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Sandra N. Cook, Project Manager, at (301) 827-2090.

Sincerely,

Robert J. DeLap, M.D., Ph.D.
Director
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Enclosure