ANDA 75-189/S-001, S-002 September 24, 2001

TEVA Pharmaceuticals USA
Attention: Deborah A. Jaskot
1090 Horsham Road
PO Box 1090
North Wales, PA 19454

Dear Madam:

This is in reference to your supplemental new drug applications dated August 28, 2001, submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act for Nabumetone Tablets, 500 mg and 750 mg.

Reference is also made to the Tentative Approval letter for Nabumetone Tablets 500 mg and 750 mg issued by this office on December 24, 1998, and to the approval letter for Nabumetone Tablets 500 mg dated May 26, 2000.

These supplemental applications, submitted as ″Prior Approval Supplements-Expedited Review Requested,″ provide for the final approval of Nabumetone Tablets 750 mg:

S-001 An additional strength – Nabumetone Tablets 750 mg; and

S-002 Revised labeling to incorporate the 750 mg tablet strength.

We have completed the review of these supplemental abbreviated applications and have concluded that the 750 mg strength of the drug product is safe and effective for use as recommended in the submitted labeling. Accordingly, the supplemental applications are approved. The Division of Bioequivalence has determined your Nabumetone Tablets, 750 mg, to be bioequivalent and therefore therapeutically equivalent to the listed drug (Relafen Tablets, 750 mg, of SmithKline Beecham Pharmaceuticals). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

The listed drug product (RLD) noted above and referenced in your application, Relafen Tablets of SmithKline Beecham Pharmaceuticals, is subject to a period of patent protection which expires on December 13, 2002, (U.S. Patent No. 4,420,639 [the '639 patent]). Your application contains a patent certification under Section 505(j)(2)(A)(vii)(IV) of the Act stating that your manufacture, use, or sale of this drug product will not infringe on the '639 patent or that the patent is

otherwise invalid. You further informed the agency that litigation is currently underway in the United States District Court for the District of Massachusetts involving a challenge to the '639 patent (SmithKline Beecham Corporation, and Beecham Group, p.l.c. v. Teva Pharmaceuticals USA, Civil Action No. 97 CV12541 RCL). Thus, this approval is partially based upon the Agency's recognition that the 30-month period identified in Section 505(j)(5)(B)(iii) of the Act, during which time FDA was precluded from approving your application, has expired.

As noted in the Agency's publication entitled "Approved Drug Products with Therapeutic Equivalence Evaluations" (the "Orange Book"), an abbreviated new drug application for Nabumetone Tablets, 750 mg strength, was approved for Copley Pharmaceuticals Inc. (Copley) on June 6, 2000. This application also contained a Paragraph IV Certification and was the first application received by the Agency for the 750 mg strength. Upon approval, Copley became eligible for 180 days of market exclusivity for the 750 mg strength which would be triggered by the occurrence of one of the two events stated below. The Act provides that approval of a subsequent abbreviated new drug application such as yours that also contains a Paragraph IV Certification under Section 505(j)(2(A)(vii)(IV) and that provides for approval of the same drug product as that for which another abbreviated application containing a Paragraph IV Certification was previously received, shall be made effective not earlier than:

1. One hundred and eighty (180) days after the date the Secretary receives notice from the applicant of the previous application that commercial marketing of the drug product approved in that application has commenced, or

2. the date of a decision of a court holding the patent which is the subject of the certification to be invalid or not infringed; whichever option occurs first [Section 505(j)(5)(B)(iv)].

Based upon the regulations cited above, this supplemental application for Nabumetone Tablets 750 mg would not be eligible for final approval until one of the precipitating events has occurred. However, you have notified the Agency that the 180-day exclusivity for this drug product commenced on August 27, 2001, upon the first comemrcial marketing of the product under Copley's application. Furthermore, you have also notified the agency that as the owner of both the Copley and the Teva ANDAs, you are selectively transferring the remainder of Copley's 180-day generic drug exclusivity awarded under Copley's ANDA 75-179 to Teva under this application.

We remind you that you must comply with the requirements for an approved abbreviated application described in 21 CFR 314.80-81

and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

We request that you submit, in duplicate, any proposed advertising or promotional copy that you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-40). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-40) with a completed Form FD-2253 at the time of their initial use.

The material submitted is being retained in our files.

Sincerely yours,

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research