ANDA 74-984 December 20, 1999

Purepac Pharmaceutical Co.
Attention: Joan Janulis, R.A.C.
200 Elmora Avenue
Elizabeth, NJ 07207

Dear Madam:

This is in reference to your abbreviated new drug application dated October 11, 1996, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Diltiazem Hydrochloride Extended-release Capsules USP (Once-a-Day Dosage), 120 mg, 180 mg, 240 mg and 300 mg.

Reference is also made to your amendments dated November 13, 1996; January 31, and October 2, 1997; April 21, 1998; and July 9, September 23, September 30, and November 12, 1999.

This letters supercedes the previous approval letter dated December 20, 1999.

The listed drug product (RLD) referenced in your application, Cardizem CD Capsules of Carderm Capital L.P., is subject to periods of patent protection which will expire on March 26, 2008, (U.S. patent 5,002,776); November 14, 2011 (U.S. patent 5,364,620); August 8, 2012 (U.S. patent 5,439,689); January 16, 2007 (U.S. patent 4,894,240); and May 20, 2011 (U.S. patents 5,470,584 and 5,286,497). 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 Diltiazem Hydrochloride Extended-release Capsules USP, (Once-a-Day Dosage) will not infringe on any of the listed patents or that the patents are otherwise invalid. Section 505(j)(5)(B)(iii) of the Act provides that approval of an abbreviated application shall be made effective immediately unless an action is brought before the expiration of forty-five (45) days from the date the notice provided under paragraph (2)(B)(i) is received. You have notified the agency that Purepac Pharmaceutical Co. (Purepac) has complied with the requirements of Section 505(j)(2)(B) of the Act and that as a result Hoechst Marion Roussel, Inc. initiated a patent infringement suit against you in United States District Court for the District of New Jersey involving your notification on patent 5,439,689 (the ‘689 patent), [Hoechst Marion Roussel,

Inc. and Carderm Capital L.P. v. Faulding Inc. and Purepac Pharmaceutical Co., Civil Action No. 97-516]. You have also notified the agency that a settlement agreement between Purepac and the plaintiffs over Civil Action 97-516 (the '689 patent) was effected on May 3, 1999, and that the 30-month statutory stay on final approval during which the agency was prohibited from approving your application pending resolution of the above referenced litigation expired on July 10, 1999.

The agency was unable to grant final approval to your application on July 10, 1999, because an abbreviated application for the same drug product containing a Paragraph IV Certification under Section 505(j)(2)(A)(vii)(IV) was previously approved on July 9, 1998 (Cartia XT Capsules of Andex Corp), thus becoming eligible for 180 days of generic drug exclusivity. We refer you to the agency's guidance document entitled "180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments" (June 1998) for additional information on this topic. As a result, your application became eligible for final approval beginning 180 days after the first commercial marketing of the drug product under the former application; i.e., December 20, 1999.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved. The Division of Bioequivalence has determined your Diltiazem Hydrochloride Extended-release Capsules USP (Once-a-Day Dosage), 120 mg, 180 mg, 240 mg, and 300 mg, to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Cardizem CD Capsules, 120 mg, 180 mg, 240 mg, and 300 mg, respectively, of Carderm Capital L.P.). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application. The "interim" dissolution test and tolerances are:

> The Dissolution testing should be conducted in 900 ml of 0.1 N HCl at 37 degrees C using USP apparatus 2 (paddle) at 100 rpm. The test product should meet the following specifications :
>
> | Time (hr) | Interim Specification (% dissolved) |
> |---|---|
> | 1 | [ ] |
> | 6 | [ ] |
> | 12 | [ ] |
> | 18 | [ ] |

The "interim" dissolution test and tolerances should be finalized by submitting dissolution data for the first three production size batches in a supplemental application. A "Special Supplement - Changes Being Effected" (zero) should be submitted when there are no revisions to the interim specifications or when the final specifications are tighter than the interim specifications. In all other instances a Prior Approval supplement should be submitted.

Under section 506(A) of the Act, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth 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.

Sincerely yours,

Douglas L. Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research