DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 76-563

SEP 12 2006

KV Pharmaceutical Company
Attention: Angel L. Rodriguez
Director, Regulatory Affairs
2503 South Hanley Road
St. Louis, MO 63144-2555

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated December 9, 2002, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Diltiazem Hydrochloride Extended-release Capsules USP, (Once-a-Day Dosage), 420 mg. Your amendment dated December 16, 2003 provided for the addition of Diltiazem Hydrochloride Extended-release Capsules USP, (Once-A-Day Dosage) 120 mg, 180 mg, 240 mg, 300 mg, and 360 mg.

Reference is also made to your amendments dated December 31, 2003; March 12, September 30 and November 10, 2004; November 18 and December 21, 2005; and April 18, July 21, July 26, and August 2, 2006. We also acknowledge your correspondence dated January 24, and April 3, 2003; and January 23 and February 9, 2004, pertaining to the patent issues listed below.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that your Diltiazem Hydrochloride Extended-release Capsules USP, (Once-A-Day Dosage) 120 mg, 180 mg, 240 mg, 300 mg, 360 mg, and 420 mg are safe and effective for use as recommended in the submitted labeling. Accordingly the ANDA is approved, effective on the date of this letter. The Division of Bioequivalence has determined your Diltiazem Hydrochloride Extended-release Capsules USP (Once-a-Day Dosage), 120 mg, 180 mg, 240 mg, 300 mg, 360 mg, and 420 mg to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug, Tiazac Extended-release Capsules, 120 mg, 180 mg, 240 mg, 300 mg, 360 mg and 420 mg, respectively, of Biovail Corporation International.

Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your ANDA. The "interim" dissolution specifications are as follows:

> Dissolution Testing should be conducted in 900 mL of water at 37°C using USP Apparatus I (Basket) at 100 rpm. All strengths of the drug product should meet the following "interim" specifications:

Time (hours)	Percent Dissolved
2	NMT (b)(4)
4	(b)(4)
8	(b)(4)
12	(b)(4)
16	NLT (b)(4)

The "interim" dissolution test(s) and tolerances should be finalized by submitting dissolution data from the first three production size batches. These data should be submitted as a "Special Supplement - Changes Being Effected" when there are no revisions to be made to the "interim" specifications, or when the final specifications are tighter than the "interim" specifications. In all other instances, the information should be submitted in the form of a Prior Approval Supplement.

The reference listed drug (RLD) upon which you have based your ANDA, Tiazac, Extended-release Capsules, 120 mg, 180 mg, 240 mg, 300 mg, 360 mg, and 420 mg of Biovail Corporation International (Biovail), is subject to a period of patent protection. As noted in the agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"), U.S. Patent No. 5,529,791 (the '791 patent), is scheduled to expire on June 25, 2013.

Your ANDA contains a paragraph IV certification to the '791 patent under section 505(j)(2)(A)(vii)(IV) of the Act stating that the patent is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Diltiazem Hydrochloride Extended-release Capsules USP under this ANDA. Section 505(j)(5)(B)(iii) of the act provides that approval of an ANDA shall be made effective immediately, unless an action was brought against KV Pharmaceutical Company (KV) for infringement of the listed '791 patent. This action must have been brought against KV prior to the expiration of 45 days from

the date the notice you provided under section 505 (j)(2)(B)(i) was received by the NDA/patent holder(s). You have notified the agency that KV complied with the requirements of section 505(j)(2)(B) of the Act, and that litigation was initiated against KV with respect to the 420 mg strength only in the United States District Court for the Eastern District of Missouri [Biovail Laboratories, Inc., a Corporation of Barbados vs. KV Pharmaceutical Company, a Delaware Corporation, Civil Action No. 4:03CV541-DJS]. You have also notified the agency that this suit was subsequently dismissed without prejudice by the same District Court on September 23, 2003. You have also informed the agency that no legal action was brought against KV with respect to the 120 mg, 180 mg, 240 mg, 300 mg, and 360 mg strengths within the statutory 45-day period.

With respect to 180-day generic drug exclusivity for the 420 mg strength drug product, the agency has concluded that KV was the first ANDA applicant to submit a substantially complete ANDA with a paragraph IV certification. Therefore, with this approval, KV is eligible for 180-days of generic drug exclusivity for Diltiazem Hydrochloride Extended-release Capsules USP (Once-a-Day Dosage), 420 mg. This exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the Act, will begin to run from the earlier of the commercial marketing or court decision dates identified in section 505(j)(5)(B)(iv). Please submit correspondence to this ANDA informing the agency of the date the exclusivity begins to run.[1] We note that 180-day exclusivity for the 120 mg, 180 mg, 240 mg, 300 mg and 360 mg strength drug products, previously awarded to another ANDA holder has expired.

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

Postmarketing reporting requirements for this ANDA 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.

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[1]Because your ANDA was filed before the date of enactment of the Medicare Prescription Drug, Improvement and Modernization Act (MMA) (Public Law 108-173) on December 8, 2003, this reference to the 180-day exclusivity provision is to the section of the Act as in effect prior to December 8, 2003. See MMA § 1102(b)(1).

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Division of Drug Marketing, Advertising, and Communications with a completed Form FDA 2253 at the time of their initial use.

You have the option to provide additional dissolution data after the ANDA has been approved. Any information submitted to meet the conditions requested in this letter is considered a "Post Approval Commitment Response." To alert the Office of Generic Drug staff to the fact that you are providing post approval commitment information, please designate your submission in your cover letter as "POST APPROVAL COMMITMENT RESPONSE."

Sincerely yours,

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