

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-303/S-001

APPROVABLE LETTER



NDA 21-303/S-001

Shire Pharmaceutical Development, Inc.
Attention: Raj Kishore, Ph.D.
1901 Research Blvd., Suite 500
Rockville, MD 20850

Dear Dr. Kishore:

Please refer to your supplemental new drug application (NDA) dated October 26, 2001, received October 26, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ADDERALL XR™ (Mixed Salts of a Single-Entity Amphetamine Product) Extended-release Capsule.

We also acknowledge receipt of your submission dated January 29, 2002.

This supplement provides for the following three additional strengths: 5 mg, 15 mg and 25 mg.

We have completed the review of this application, as amended, and it is approvable. Before this application may be approved, however, it will be necessary for you to submit the following:

1. Revised labeling under the DOSAGE AND ADMINISTRATION section:

With the addition of the 5, 15 and 25 mg capsules, physicians will have greater flexibility in titrating patients, and the labeling should be amended to reflect this. Therefore, the following statement should be included:

'In children with ADHD who are 6 years of age and older and are either starting treatment for the first time or switching from another medication, start with 5mg or 10 mg once daily in the morning; daily dosage may be raised in increments of 5 mg or 10 mg at weekly intervals.'

2. A commitment to submit the draft container labels as soon as they become available.

3. We ask you to adopt the following dissolution method and specifications for all six strengths (5, 10, 15, 20, 25 and 30 mg) of Adderall XR capsules:

Apparatus: USP Apparatus II (paddle) at _____
Media: _____
Specifications: _____

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

Within 10 days after the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

The drug product may not be legally marketed until you have been notified in writing that the application is approved.

If you should have any questions, please call Ms. Anna Marie Homonnay, R.Ph., Regulatory Health Project Manager, at (301) 594-5535.

Sincerely,

{See appended electronic signature page}

Russell Katz, M.D.
Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Russell Katz
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