DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-471/S-014
NDA 22-052/S-005

Cornerstone Therapeutics Inc.
1255 Crescent Green Drive
Suite 250
Cary, NC 27518

Attention: Brian Dickson, MD
Chief Medical Officer

Dear Dr. Dickson:

Please refer to your supplemental new drug applications dated May 22, 2009, and received May 22, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zyflo (zileuton) tablets and Zyflo CR (zileuton) extended-release tablets.

We also acknowledge receipt of your submissions dated July 06, 08, 21, and 23, 2009.

These Prior Approval Labeling supplemental new drug applications provide for the following additions and revisions to the package insert and to the patient package insert:

1. Neuropsychiatric Events was added as a separate subsection to the PRECAUTIONS section of the package insert for Zyflo and to the WARNINGS AND PRECAUTIONS section of the highlights and to the full prescribing information section of the package insert for Zyflo CR.

2. A statement instructing patients to notify their physician if neuropsychiatric events occur while using Zyflo was added to the Information for Patients subsection of the package insert and to the possible side effects section of the patient package insert.

3. The following statement “Cases of sleep disorders and behavior changes have also been reported” was added to the ADVERSE REACTIONS, Post-Marketing Experience subsection.

We have completed our review of these applications, as amended. These applications are approved, effective on the date of this letter, for use as recommended in the content of labeling [21 CFR 314.50(1)] in structured product labeling (SPL) format submitted on July 21 and 23, respectively.

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/oc/datacouncil/spl.html, that is identical in content to the enclosed labeling (text for the package inserts and text for the patient package inserts submitted on July 21 and 23, respectively). Upon receipt, we will transmit those versions to the National Library of Medicine for

public dissemination. For administrative purposes, please designate this submission, "**SPL for approved NDA 22-052/S-005; NDA 20-471/S-014.**"

In addition, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed the revised product labeling and has determined that it contains significant updated risk information relating to your drug product. We are hereby informing you that all promotional materials for your drug product that include representations about your drug product should be revised to include the new risk information immediately. *See* 21 CFR 314.70(a)(4), 601.12(a)(4). These revisions should include prominent disclosure of the important new information described in the PRECAUTIONS section that appears in the revised package labeling. Please submit a written response to this request within one week of receipt of this letter, stating whether you intend to comply with this request, to the Food and Drug Administration, Center for Drug Evaluation and Research, Division of Drug Marketing, Advertising, and Communications by facsimile at (301) 847-8444 or at 5901-B Ammendale Road, Beltsville, MD 20705.

For more information about submission of promotional materials to DDMAC, see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Sadaf Nabavian, Regulatory Project Manager, at (301) 796-2777.

Sincerely,

{See appended electronic signature page}

Badrul A. Chowdhury, M.D., Ph.D.
Director
Division of Pulmonary and Allergy Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure: Approved Labeling

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

/s/

BADRUL A CHOWDHURY
08/21/2009