

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
22-417

OTHER ACTION LETTER(s)



NDA 22-417

COMPLETE RESPONSE

Abbott Laboratories
Attention: Mary Konkowski
Manager, Global Pharmaceutical Regulatory Affairs
Dept. PA76/ Bldg. AP30-1E
200 Abbott Park Road
Abbott Park, IL 60064-6157

Dear Ms. Konkowski:

Please refer to your new drug application (NDA) dated December 19, 2008, received December 19, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for NORVIR® (ritonavir) 100mg tablets.

We also acknowledge receipt of your submissions dated January 23, 2009, January 28, 2009, January 29, 2009, February 5, 2009, February 9, 2009, February 13, 2009, March 10, 2009, March 31, 2009, April 27, 2009, May 14, 2009, June 3, 2009, July 17, 2009, July 24, 2009, August 4, 2009, August 5, 2009, September 4, 2009, September 11, 2009, September 15, 2009, September 22, 2009, September 24, 2009, September 29, 2009, October 1, 2009, and October 5, 2009, October 7, 2009, and October 13, 2009.

We have completed the review of your application and have determined that we cannot approve this application in its present form. We have described below our reasons for this action and, where possible, our recommendations to address these issues.

FACILITY INSPECTIONS

During a recent inspection of the Abbott GmbH manufacturing facility in Ludwigshafen, Germany for this application, our field investigator conveyed deficiencies to the representative of the facility. Satisfactory resolution of these deficiencies is required before this application may be approved.

SAFETY UPDATE

When you respond to the above deficiencies, include a safety update as described at 21 CFR 314.50(d)(5)(vi)(b). The safety update should include data from all nonclinical and clinical studies/trials of the drug under consideration regardless of indication, dosage form, or dose level.

1. Describe in detail any significant changes or findings in the safety profile.

2. When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:
 - Present new safety data from the studies/clinical trials for the proposed indication using the same format as the original NDA submission.
 - Present tabulations of the new safety data combined with the original NDA data.
 - Include tables that compare frequencies of adverse events in the original NDA with the retabulated frequencies described in the bullet above.
 - For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.
3. Present a retabulation of the reasons for premature trial discontinuation by incorporating the drop-outs from the newly completed trials. Describe any new trends or patterns identified.
4. Provide case report forms and narrative summaries for each patient who died during a clinical trial or who did not complete a trial because of an adverse event. In addition, provide narrative summaries for serious adverse events.
5. Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original NDA data.
6. Provide updated exposure information for the clinical studies/trials (e.g., number of subjects, person time).
7. Provide a summary of worldwide experience on the safety of this drug. Include an updated estimate of use for drug marketed in other countries.
8. Provide English translations of current approved foreign labeling not previously submitted.

OTHER

Within one year after the date of this letter, you are required to resubmit or take one of the other actions available under 21 CFR 314.110. If you do not take one of these actions, we will consider your lack of response a request to withdraw the application under 21 CFR 314.65. A resubmission must fully address all the deficiencies listed. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

Under 21 CFR 314.102(d), you may request a meeting or telephone conference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a meeting, submit your meeting request as described in the FDA's *Guidance for Industry - Formal Meetings Between the FDA and Sponsors or Applicants*, May 2009 at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM153222.pdf>.

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

If you have any questions, call Amalia Himaya, Regulatory Project Manager, at (301) 796-3391.

Sincerely,

{See appended electronic signature page}

Debra Birnkrant, M.D.
Director
Division of Antiviral Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22417

ORIG-1

ABBOTT
LABORATORIES

RITONAVIR

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

/s/

JEFFREY S MURRAY

10/16/2009