

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

022503Orig1s000

OTHER ACTION LETTERS



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22503

COMPLETE RESPONSE

CorePharma, LLC
215 Wood Avenue
Middlesex, NJ 08846-2554

Attention: Kimberly Ernst
Senior Director, Regulatory Affairs

Dear Ms. Ernst:

Please refer to your New Drug Application (NDA) dated August 18, 2009, received August 20, 2009, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Metaxalone Tablets, 640.

We acknowledge receipt of your amendments dated June 18, and July 18, 2013.

The June 18, 2013, submission constituted a complete response to our June 11, 2010, action letter.

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

FACILITY INSPECTIONS

Our field investigator could not complete inspection of the CorePharma manufacturing facility at Middlesex, NJ because the facility was not ready for inspection. Satisfactory inspection is required before this application may be approved. Please notify us in writing when this facility is ready for inspection.

LABELING

We reserve comment on the proposed labeling until the application is otherwise adequate. If you revise labeling, your response must include updated content of labeling [21 CFR 314.50(10)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

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 other actions available under 21 CFR 314.110. If you do not take one of these actions, we may consider your lack of response a request to withdraw the application under 21 CFR 314.65. You may also request an extension of time in which to resubmit the application. 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 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 Carol F. Hill, Senior Regulatory Health Project Manager, at (301) 796-1226.

Sincerely,

{See appended electronic signature page}

Badrul A. Chowdhury, M.D., Ph.D.
Director
Division of Pulmonary, Allergy, and Rheumatology
Products
Office of Drug Evaluation II
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/

BADRUL A CHOWDHURY
12/18/2013



NDA 22-503

COMPLETE RESPONSE

CorePharma LLC
215 Wood Avenue,
Middlesex, NJ 08846

Attention: Prakash Kulkarni, PhD
Chief Scientific Officer

Dear Dr. Kulkarni:

Please refer to your New Drug Application (NDA) dated August 18, 2009, received August 21, 2009, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for TRADENAME (metaxalone) Tablets, 640 mg.

We acknowledge receipt of your submissions dated October 20, and 26, November 25, 2009, January 06, March 01, and 19, April 21, and 27, June 01, 2010.

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

FACILITY INSPECTIONS

During a recent inspection of the CorePharma manufacturing facility in Middlesex, NJ 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.

PATENT CERTIFICATION

We remind you of the requirement to comply with applicable regulatory requirements regarding patent certification as described in our May 27, 2010, email.

LABELING

Submit draft labeling that incorporates revisions in the attached labeling. In addition, submit updated content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at

<http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>.

To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version.

Please submit draft carton and container labeling revised as shown in the comments below that were previously conveyed to you in a Discipline Review Letter dated May 28, 2010.

1. The labels and labeling include a proprietary name (b) (4) which we found unacceptable and communicated this decision to you via a letter dated May 27, 2010. The container labels and package insert should be revised to remove all instances of the proposed proprietary name (b) (4).
2. Your logo on the principal display panel of the container labels is large, distracting, and competes for prominence with both the proposed proprietary name and established name of the drug. Delete or reduce the size of your logo and relocate it away from the proposed proprietary name and established name so that it does not compete with prominence with the proposed proprietary name or the established name.
3. The 'Rx Only' statement and the net quantity statement '100 Tablets' (b) (4) is distracting from more vital information on the PDP of your container labels such as the name of the product and the strength. Decrease the prominence of these statements by un-bolding the font or decreasing the size of the statement.
4. The usual dose is located on the side panel of the container labels. Revise this statement to include the word (b) (4) at the beginning of the statement. The revised statement should read "**USUAL DOSAGE:** The recommended dose for adults and children over 12 years of ages is one tablet (640 mg) three to four times a day".
5. The side panel of the container labels instructs pharmacists to (b) (4) however this product should also be dispensed in a container that is also unless otherwise specified by the patient. Revise the statement to read "Dispense in a well-closed child-resistant container".

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:
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- 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.
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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 Ramani Sista, Regulatory Project Manager, at (301) 796-1236.

Sincerely,

{See appended electronic signature page}

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

ENCLOSURE: Package Insert

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22503	ORIG-1	COREPHARMA LLC	(b) (4) 640MG (METAXALONE)

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
06/11/2010