

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20-743

ADMINISTRATIVE DOCUMENTS



NDA 20-743

Dermik Laboratories, Inc.
Attention: Ronald F. Panner
500 Arcola Road
Collegeville, PA 19426

JUN 20 1997

Dear Mr. Panner:

Please refer to your pending September 30, 1996, new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Noritate® (metronidazole cream) Cream, 1%.

We also refer to your amendments dated October 10 and 28, November 1, 13, 14 (two) and 22, December 2, 13, 19 and 20, 1996, January 31, February 4, 5 and 14, and April 9 and 14, 1997.

To complete our review of the chemistry section of your submission, we request the following:

1. The critical steps in the manufacturing process of the drug product have not been adequately identified. All critical parameters should be identified.
2. Prior to packaging, a test/specification for globule size should be proposed. This will assure a consistent cream and viscosity.
3. It would be advisable to also include viscosity and pH as in-process specifications prior to packaging the drug product.
4. It should be noted that the retention time of the major peak in the chromatogram of the sample solution, which corresponds to that of the reference solution, is not a desirable identity test. The sole proposed identity method of the drug substance in the dosage form is not adequate. Refer to the guidances for industry to identify a more suitable identity test.
5. Since the NDA has not included a protocol for reprocessing the drug product due to foreseeable deviations from specifications, including information about the maximum holding times and storage conditions before reprocessing, and additional controls used, any reprocessing of this drug product would require a preapproval supplement. A statement should be submitted to the pending application which states that no reprocessing of the drug product will be done prior to approval from the FDA.

6. The NDA does not provide the number of tubes that should be obtained for release and stability testing of the drug product in its final packaging. The sampling process, as well as the number of samples per production batch and selection of sub-samples for analyses, should be provided.

7. Utilization of microscopic examination would assure the agency that early phase separation of the cream does not occur, and will further provide data regarding the precipitation/crystallization of the drug substance in the dosage form.

8. The homogeneity specifications are not adequate. Specifications that address the distribution of the drug substance throughout the container/closure system would be more appropriate.

9. A summary of the container/closure system compatibility with the drug product should be provided.

10. A stability update should be provided to support the desired expiration dating period.

11. The post-approval stability commitment should be revised to include the commitment that the first three post-approval commercial lots of Noritate® Cream will be placed into the stability program.

12. It has been noted that different release and stability specifications have been submitted. However, a single set of regulatory specifications should be provided.

13. An acceptable MV package should be provided. Please refer to the facsimile dated April 28, 1997, for details.

14. In the description section of the package insert submitted to the FDA on 1/31/97, the product name placement should be changed to read as follows:

15. Mock up copies of the carton and tube labels were provided in volume 1.7 of the original submission. The product name placement on the carton and tube label should be changed to read as follows:

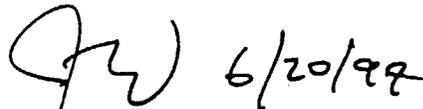
NDA 20-743

Page 3

We would appreciate your prompt written response so we can continue our evaluation of your NDA.

If you have any questions, please contact Olga Cintron, Project Manager, at (301) 827-2020.

Sincerely yours,

Handwritten signature of Jonathan K. Wilkin and the date 6/20/99.

Jonathan K. Wilkin, M.D.

Director

Division of Dermatologic and Dental Drug
Products

Office of Drug Evaluation V

Center for Drug Evaluation and Research

NDA 20-743

Page 4

cc:

Original NDA 20-743

HFD-540/Div. Files

HFD-540/CSO/O. Cintron

HFD-540/Division Director/Wilkin *WD 6/11/97*

HFD-540/Chem/Higgins *JGA 5/12/97*

HFD-830/ONDC Division Director/Chen

HFD-540/Chemistry Team Leader/DeCamp

Drafted by: JGH/May 12, 1997/

Initialed by:

final:

INFORMATION REQUEST (IR)