

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER: 21-301

APPROVAL LETTER



NDA 21-301

Jones Pharma Incorporated
Attention: Nancy Cafmeyer
Vice President of Regulatory Affairs
1945 Craig Road
St. Louis, Missouri 63146

Dear Ms. Cafmeyer:

Please refer to your new drug application (NDA) dated July 28, 2001, received July 28, 2001, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Levoxyl® (levothyroxine sodium tablets, USP) 25, 50, 75, 88, 100, 112, 125, 137, 150, 175, 200 and 300 mcg strengths.

We acknowledge receipt of your submissions dated December 14, 2000, January 29, February 27, March 8, 14; and 19, April 5 and 6, and May 2, 11, 14, and 15, 2001.

This new drug application provides for the use of Levoxyl (levothyroxine sodium tablets, USP) for hypothyroidism and suppression of thyroid-stimulating hormone.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text. Accordingly, the application is approved effective on the date of this letter.

Regarding the in vitro dissolution study submitted on July 28, 2000, for this application we have the following recommendation:

With respect to your proposed in vitro dissolution specification for the drug product, we note you that you used the USP 24 monograph with specification of not less than 70% in 45 minutes. However, we recommend that the appropriate specification should be not less than 80% (Q=(b)()) in 15 minutes.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert, immediate container and carton labels submitted May 15, 2001). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no

more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 21-301." Approval of this submission by FDA is not required before the labeling is used.

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 FR 66632). We are waiving the pediatric study requirement for this action on this application.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Steve McCort, Regulatory Project Manager, at (301) 827-6415.

Sincerely,

{See appended electronic signature page}

David G. Orloff, M.D.
Director
Division of Metabolic and
Endocrine Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research

**APPEARS THIS WAY
ON ORIGINAL**