CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 21-342

PHARMACOLOGY REVIEW(S)

REVIEW & EVALUATION OF PHARMACOLOGY/TOXICOLOGY DATA:

Key Words: levothyroxine-sodium, Levo-T, hypothroidism

Reviewer: Karen Davis-Bruno; Ph.D.; Supervisory Pharmacologist
Division of Metabolic & Endocrine Drug Products; HFD-510
Review completion: 6/21/01
Review #1
Submission Date: 5/1/01

NDA21-342

Information to the sponsor: no
Sponsor: Mova Pharmaceutical Corporation; Caguas, PR
Drug: Levo-T (levothyroxine sodium)
Relevant NDAs: [redacted], 21-210, [redacted], 21-301, IND [redacted]
Drug class: synthetic thyroid hormone
Clinical formulation: tablet of 25, 50, 75, 88, 100, 112, 125, 150, 175, 200, 300 mcg

Indication: replacement or supplemental therapy for hypothyroidism
Route: oral
Previous Clinical Experience: Extensive with currently approved and marketed products

Introduction and Drug History: Levothyroxine has been marketed extensively for many years in both a tablet and injectable form. The indication is for replacement of thyroid hormone in hypothyroidism. Under a Federal Register notice of August 14, 1997 (Volume 62, Number 157) current products will be branded mislabeled as of August 2001 in the absence of approved NDA and removed from the market. The prior lack of stability and batch to batch variability in these products as a class was the impetus for this legislation.

Studies reviewed within this submission: none, preclinical data was not submitted

Overall Summary and Evaluation: Levothyroxine has been marketed extensively for many years. The replacement indication for naturally occurring thyroid hormone indicates little safety concern. Potential problems may arise from inappropriate dosing or manufacturing impurities/degradation products. Prior experience suggests that proper monitoring can minimize the associated safety risk. The toxicity of thyroid hormone has been well documented in published literature.

Safety evaluation: There are no preclinical safety issues with this product provided proper individualized replacement dosing is performed with adequate monitoring and appropriate product stability demonstrated.

Recommendations: approval

Cc:HFD510/Davis-Bruno/McCort

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/s/

Karen Davis-Bruno
6/21/01 12:40:16 PM
PHARMACOLOGIST
Pharm/Tox AP

APPEARS THIS WAY
ON ORIGINAL