CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

80-600

Generic Name: Folic Acid 1mg Tablets

Sponsor: West-ward, Inc.

Approval Date: March 31, 1972

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

80-600

CONTENTS

Reviews / Information Included in this ANDA Review.

Approval Letter(s)	X
Tentative Approval Letter(s)	
Final Printed Labeling	X
CSO Labeling Review(s)	X
Medical Officer Review(s)	
Chemistry Review(s)	X
Microbiology Review(s)	
Bioequivalence Review(s)	
Administrative Document(s)	X
Correspondence	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

80-600

APPROVAL LETTER

NDA 80-600

AF 31-015

West-ward, Inc.
Attention: Mr. Edward Green
745 Eagle Green
Bronx, New York 10456

MAR 31 1972

Gentlemen:

Reference is made to your abbreviated new drug application dated August 25, 1971, submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Folic Acid Tablets, 1 mg.

Reference is also made to your communication dated January 18, 1972, containing control information and printed package inserts.

We have completed the review of this abbreviated new drug application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved.

Any significant change in the conditions outlined in this abbreviated new drug application requires an approved supplemental application before the change may be made, except for changes made in conformance with other provisions of Section 130.9 of the new drug regulations.

This Administration should be advised of any change in the marketing status of this drug.

The enclosures summarize the conditions relating to the approval of this application.

Sincerely yours,

Paul A. Bryan, M.D. 3/30/72

Paul A. Bryan, M.D.
Director
Drug Efficacy Study Implementation
Project Office
Bureau of Drugs

cc:
NYK-DO
Dup
BD-100 BD-69 BD-67
BD-22 BD-242 BD-310
JHEilert/JLMeyer/REJoyce:3/20/72
R/D init. MAClark, JLMeyer 3/27/72
Final typing bhy 3/28/72
Approval
Enclosures
Conditions of Approval of a New Drug Application
Records and Reports Requirement

JHEilert 3-29-72

MAClark MD 3/30/72

JLMeyer 3/30/72

REJoyce 3/30/72

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

80-600

FINAL PRINTED LABELING

FOLIC ACID

Ref 3-20-72

APPROVED 31 MAR 1972 RAL

DESCRIPTION: Folic Acid, $C_{19}H_{19}N_7O_6$, is a yellow or yellowish orange, odorless, crystalline powder, very slightly soluble in water.

ACTION: Folic acid is rapidly but preferentially absorbed from the small intestine. It is almost completely absorbed orally, even in the presence of the malabsorption associated with tropical sprue. Folic acid (pteroylglutamic acid) is not active as such in the mammalian organism. Rather it is enzymatically reduced in the body to tetrahydrofolic acid, the coenzyme which is concerned with nearly all, or possibly all, mammalian metabolic systems in which there is a transfer of a one carbon unit, viz., $-CH_3$, -CHO. $-CH=NH$.

INDICATIONS: Folic acid is effective in the treatment of megaloblastic anemias due to a deficiency of folic acid as may be seen in tropical or non-tropical sprue, in anemias of nutritional origin, pregnancy, infancy, or childhood.

WARNINGS: Folic acid alone is improper therapy in the treatment of pernicious anemia and other megaloblastic anemias where vitamin B_{12} is deficient.

PRECAUTIONS: Folic acid especially in doses above 1.0 mg. daily may obscure pernicious anemia, in that hematologic remission may occur while neurological manifestations remain progressive.

ADVERSE REACTIONS: Allergic sensitization has been reported following both oral and parenteral administration of folic acid.

DOSAGE AND ADMINISTRATION —
Oral administration: Folic acid is well absorbed and may be administered orally with satisfactory results except in severe instances of intestinal malabsorption.

Usual therapeutic dosage: In adults: 0.25 mg. to 1.0 mg. daily. **In children (regardless of age):** 0.25 to 1.0 mg. daily. Resistant cases may require larger doses.

Maintenance dosage: When clinical symptoms have subsided and the blood picture has become normal, a maintenance dose of 0.1 mg. to 0.25 mg. daily should be used, but never less than 0.1 mg. per day. Patients should be kept under close supervision and adjustment of the maintenance dose made if relapse appears imminent.

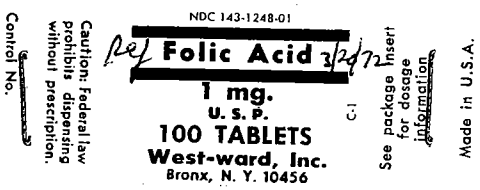
In the presence of alcoholism, pregnancy, hemolytic anemia, anticonvulsant therapy, or chronic infection, the maintenance dose should be at least doubled.

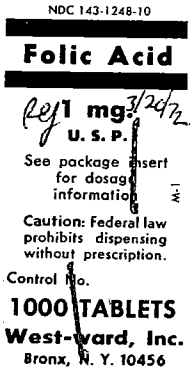
HOW SUPPLIED: Tablets 1 mg. scored in bottles of 100 and 1000.

CAUTION: Federal law prohibits dispensing without prescription.

West-ward Inc.
October, 1971

ANDA 80-600
Original
Rec'd 8-30-71
Reviewed by RLyyco 3/20/72





CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

80-600

CSO LABELING REVIEW(S)

REVIEW OF FPL

DATE COMPLETED: 2-15-72

ANDA #: 80-600

F.R. DATE: 4-9-71

CO. NAME: West-Ward Incorporated
745 Eagle Avenue
Bronx, N. Y. 10456

NAME OF DRUG: Trade:
& Folic Acid Tablets 1 mg.
Generic: (scored in bottles of 100 and 1,000)

DATE OF SUBMISSION: 1-18-72

TYPE OF SUBMISSION: FPL and data for chemist

CLINICAL EVALUATION:

1. Review of Studies:

Chemist to review

2. Review of Labeling:

FPL conforms to requirements
Container labels accepted in M.O. review of 9-6-71

CONCLUSION:

1. FPL approvable.

2. Chemist to review.

RECOMMENDATIONS:

1. Approve FPL.

2. Chemist to review.

John H. Eilert, M.D.

cc:
Dup.
BD-69
JHEilert/rt/2-16-72

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

80-600

CHEMISTRY REVIEW(S)

REVIEW OF ANDA

Date Completed: 9/6/71

ANDA #: 80-600
F.R. Statement Date: 4/9/71
Co. Name: West-ward, Inc.
Bronx, N.Y.

NAME OF DRUG: Trade:
Generic: Folic Acid Tablets, 1 mg.

DATE OF SUBMISSION: 8/25/71

TYPE OF SUBMISSION: ANDA

CLINICAL EVALUATION:

1. Review of Studies: Bioavailability studies submitted as required in NF XIII dissolution and disintegration data meet standards.

   Manufacturing and control data to be analyzed by chemist.

2. Review of Labeling: Package insert and immediate labeling conform to Federal Register statement requirements.

   However, it is recommended that " [redacted] be changed to "How Supplied". Explanation should be requested of varied tablet strength, 0.1 mg., 0.25 mg. and 1 mg. when only 1 mg. is listed on application.

   In Dosage & Administration, delete references to [redacted] as this is a tablet dosage form.

CONCLUSIONS: Bioavailability studies acceptable. Manufacturing-control data require chemist appraisal. Elucidation of differing tablet strengths necessary.

RECOMMENDATIONS:
1. Chemist appraisal
2. Tablet strength variance to be explained.
3. Package insert [redacted] to be changed to "How Supplied." and delete references to [redacted]

M. Clark MD for
John H. Eilert, M.D.

cc:
Dup
BD-100
BD-69
JHEilert/bhy 9/9/71

REVIEW OF RESUBMISSION OF ORIGINAL ANDA

DATE COMPLETED: 11/4/71

ANDA#: 80-600

F.R. Date: 4/9/71
West Ward Incorporated
The Bronx, N.Y.

NAME OF DRUG: Trade & Generic Folic Acid Tablets, 1 mg.

DATE OF SUBMISSION: 10/27/71

TYPE OF SUBMISSION: 1. Insert revision)
2. Chemist data) Response to FDA 10/4/71 letter.

CLINICAL EVALUATION:

L. Review of Studies: To be evaluated by chemist.

2 Review of Labeling: Revised insert (October, 1971) conforms to FDA 10/4/71 request.

CONCLUSION: 1. Approvable insert.

2 Studies require chemist appraisal.

RECOMMENDATION: 1. Chemist to review

2. Approve insert, and request FPL.

John H. Eilert, M.D.

CC:
Dup.
BD-100
BD 69
JHEilert/mc 11/4/71

ABBREVIATED NEW DRUG APPLICATION (X) SUPPLEMENT | Date Received 4-9-71 | NDA Number 80-600

Name and Address of Applicant (City and State)
West-Ward
Bronx, New York 10456

Original XX
Amendment
Supplement
Other

Name of Drug	Nonproprietary Name
Folic Acid	Folic Acid

Purpose of Supplement

DATE(s) of Submission(s)

Pharmacological Category	How Dispensed	NDA Number
Hematopoietic Vitamin	[X] Rx [ ] OTC	31-015
Dosage Form(s)	Potency(ies)	Related IND/NDA/MF
Tablet	1 mg.	

[ ] Satisfactory Labeling
Date Due M.O.R. (Dr. Eilert)

[ ] Satisfactory Components, Composition, Manufacturing and Controls
Date Due See Below

[ ] Satisfactory Biologic Availability
Date Due Not required.
Is data on current formulation? YES [ ] NO [ ]

[ ] Satisfactory Probably or Possibly Effective Indications (if in labeling)
Date data Due None

Establishment Inspection	Recalls
TWX 3-17-71---Satisfactory	

Is relabeling of drug in commercial channels required? [ ] YES [X] NO
If so, what level:

Remarks

1. Labeling requires revision
2. Folic Acid Powder Residue on Ignition Test not performed and assay doesn't follow USP method.
3. Tablets-Content uniformity doesn't follow USP method.

Conclusions

LTR. to firm requesting: 1. Label Revision
2. Proper tests

R.E. Joyce 9/29/71

Reviewer	Signature	Date Completed
R.E. Joyce		9-16-71

CHEMIST'S REVIEW FOR ABBREVIATED NEW DRUG APPLICATION OR SUPPLEMENT

Federal Register Statement Date: 4-9-71

Original ☒ Resubmission
Supplement ☐

Name and Address of Applicant (City and State)

west-Ward, Inc.
Bronx, New York 10456

NDA Number: 80-600

Supplement Date and Number:

Amendment Date(s):

Other Date(s):

Name of Drug	Nonproprietary Name
Folic Acid	Folic Acid

Purpose of Supplement

AF Number: 31-005

Related IND/NDA/MF(s):

Pharmacological Category	How Dispensed	Dosage Form(s)	Potency(ies)
Hematopoietic Vitamin	☒ Rx ☐ OTC	Tablet	1 mg.

Satisfactory ☐ Labeling
Date Due Satisfactory M.O.R. 11-4-71 Dr. Eilert

Satisfactory ☐ Components, Composition, Manufacturing and Controls
Date Due See below

Sat factory ☐ Biologic Availability
Date Due Not required
Is data on current formulation? YES ☐ NO ☐

Satisfactory ☐ Probably or Possibly Effective Indications (if in labeling)
Date data Due

Establishment Inspection	Recalls
E.I. 3-17-71 Satisfactory	

Is relabeling of drug in commercial channels required? ☐ YES ☐ NO
If so, what level:

Remarks

1. Require FPL
2. Require data to substantiate use of different content uniformity test.

Conclusions

Rev. w/f 1 and 2

R. E. Joyce 12-2-71 REJoyce 12/7/71

CHECKLIST & REVIEW FOR ABBREVIATED NEW DRUG APPLICATION (OR SUPPLEMENT)

Federal Register Statement Date: 4/9/71

NDA Number: 80-600

Name and Address of Applicant (City and State)

st-ward Inc.
ronx, N.Y. 10456

Original: ____
Amendment: X
Supplement: ____
Other: ____

Name of Drug	Nonproprietary Name
	Folic Acid

DATE(s) of Submission(s)

Purpose of Supplement

Pharmacological Category	How Dispensed	AF Number
Vitamin	[X] Rx [ ] OTC	
Dosage Form(s)	**Potency(ies)**	**Related IND/NDA/MF**
Tablet	1.0 mg.	

Satisfactory [ ] Labeling
Date Due Satisfactory M.O.R. of 9/6/71 and 2/15/72

Satisfactory [ ] Components, Composition, Manufacturing and Controls
Date Due Adequate

Satisfactory [ ] Biologic Availability
Date Due N.A.
Is data on current formulation? YES [ ] NO [ ]

Satisfactory [ ] Probably or Possibly Effective Indications (if in labeling)
Date data Due ____

Establishment Inspection	Recalls
EI 3/17/71 Satisfactory	

Is relabeling of drug in commercial channels required? [ ] YES [ ] NO
If so, what level:

Remarks

1. Labeling satisfactory
2. Firm will follow USP content uniformity test procedure.

Conclusions

Approval letter to issue

R. E. Joyce Joyce 3/30/72 3/20/72

Reviewer | Signature | Date Completed

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

80-600

ADMINISTRATIVE DOCUMENTS

orig

NOTICE OF APPROVAL
NEW DRUG APPLICATION OR SUPPLEMENT

NDA NUMBER: 80-600

DATE APPROVAL LETTER ISSUED: 31 MAR 1972

TO: Press Relations Staff *(CE-300)*

FROM:
- [X] Bureau of ~~Medicine~~ Drugs
- [ ] Bureau of Veterinary Medicine

ATTENTION

Forward original of this form for publication only after approval letter has been issued and the date of approval has been entered above.

TYPE OF APPLICATION
- [ ] ORIGINAL NDA
- [X] ABBREVIATED ORIGINAL NDA
- [ ] SUPPLEMENT TO NDA

CATEGORY
- [X] HUMAN
- [ ] VETERINARY

TRADE NAME *(or other designated name)* AND ESTABLISHED OR NONPROPRIETARY NAME *(if any)* OF DRUG

Folic Acid

DOSAGE FORM: Tablet

HOW DISPENSED
- [X] RX
- [ ] OTC

ACTIVE INGREDIENT(S) *(as declared on label. List by established or nonproprietary name(s) and include amount(s), if amount is declared on label.)*

Folic Acid 1.0 mg.

NAME OF APPLICANT *(Include City and State)*

West-ward Incorporated
745 Eagle Avenue
Bronx, New York 10456

APPEARS THIS WAY ON ORIGINAL

PRINCIPAL INDICATION OR PHARMACOLOGICAL CATEGORY

Vitamin

COMPLETE FOR VETERINARY ONLY

ANIMAL SPECIES FOR WHICH APPROVED

COMPLETE FOR SUPPLEMENT ONLY

CHANGE APPROVED TO PROVIDE FOR

FORM PREPARED BY

NAME: Ronald E. Joyce

DATE:

FORM APPROVED BY

NAME: Jack L. Meyer

DATE:

FD FORM 1642 (7/69) PREVIOUS EDITION MAY BE USED UNTIL SUPPLY IS EXHAUSTED.

[DESI 5897; Docket No. FDC-D-265; NDA 5-897, etc.]

FOLIC ACID PREPARATIONS, ORAL AND PARENTERAL FOR THERAPEUTIC USE

Drugs for Human Use; Drug Efficacy Study Implementation

The Food and Drug Administration has evaluated reports received from the National Academy of Sciences-National Research Council, Drug Efficacy Study Group, on the following folic acid preparations:

1. a. Folvite Elixir; 5 mg. folic acid per 5 cc.;

b. Folvite Tablets; 5 mg. and 20 mg. folic acid per tablet; and

c. Folvite Parenteral Solution; sodium folate equivalent to 15 mg. folic acid per cc.; marketed by Lederle Laboratories, Pearl River, New York 10965 (NDA 5-897).

2. Folic Acid Tablets; 5 mg. per tablet; marketed by Eli Lilly and Co., Box 618, Indianapolis, Indiana 46206 (NDA 6-135).

3. Folic Acid Injection; 15 mg. folic acid, as the sodium salt, per cc.; marketed by S. F. Durst and Co., Inc., 5317 North Third Street, Philadelphia, Pennsylvania 19120 (NDA 6-338).

In addition to the above products, folic-acid preparations for therapeutic use are marketed by other firms. A partial list of other suppliers of folic acid preparations limited to prescription dispensing, as indicated in readily available reference sources, is as follows:

BA Pharmaceutical Co., Division of Bergher Distributing Co.
American Pharmaceutical Co.
American Drug Products.
American Quinine Co.
Approved Pharmaceutical Corp.
Arcum Pharmaceutical Corp.
Associated Labs., Inc.
Barre Drug Co., Inc., The.
Barry-Martin Pharmaceuticals, Inc.
Bell Pharmacal Co.
Carroll Chemical Co., The.
Columbia Medical Co.
Consolidated Midland Corp., CMC Research Division.
Corvit Pharmaceuticals.
Daniels, Robert and Co., Inc.
DuMont Pharmacal Co.
Evron Pharmaceutical Co., Inc.
Faraday Laboratories, Inc.
Gold Leaf Pharmacal Co., Inc.
Gotham Pharmaceutical Co., Inc.
Halsey Drug Co., Inc.
Harvey Labs., Inc.
Jan Labs.
Kirkman Labs., Inc.
Lannett Co., Inc.
Lit Drug Co.
Lustgarten Laboratories, Inc.
Mifflin, McCambridge Co., Inc.
Penhurst Pharmacal Co.
Pharmex, Inc.
Preston Franklin Pharmacal Co.
Richlyn Labs.
Robinson Laboratory, Inc.
Spencer-Mead, Inc.
Stanlabs, Inc.
Supreme Pharmaceutical Co., Inc.
Thompson, Wm. T., Co.
Towne, Paulson and Co., Inc.
Upjohn Research Corp.
Vi-More Products Co.
West-Ward, Inc.
Williams Chemical Co.
Winsale Drug Co.

The drugs are regarded as new drugs (21 U.S.C. 321(p)). Supplemental new-drug applications are required to revise the labeling in and to update previously approved applications providing for such drugs. A new-drug application is required from any person marketing such drugs without approval.

The Food and Drug Administration is prepared to approve new-drug applications and supplements to previously approved new-drug applications under conditions described in this announcement.

A. *Effectiveness classification.* The Food and Drug Administration has considered the Academy reports, as well as other available evidence, and concludes that:

1. Folic acid is effective for the treatment of megaloblastic anemias of tropical and nontropical sprue, nutritional origin, pregnancy, infancy, and childhood.

2. There is a lack of substantial evidence that folic acid is effective for the following labeled indications: "macrocytic anemias associated with pellagra and similar deficiency states" and such vague, unspecific conditions as "macrocytic anemia of gastrointestinal origin" and "megaloblastic anemias other than pernicious anemia."

The Food and Drug Administration also concludes that there is no evidence that doses of folic acid greater than 1 mg. daily have greater efficacy than do those of 1 mg. Further, the usual therapeutic dose, oral or parenteral, should be 0.25 mg. to 1.0 mg. daily, and the maintenance dose should ordinarily be 0.1 to 0.25 mg. daily. Administration of higher doses greatly increases the possibility of masking vitamin B-12 deficiencies and the insidious development of or precipitation of neurological manifestations and/or lesions.

Preparations supplying no more than 0.1 mg. folic acid daily continue to be regarded as dietary supplements (21 CFR 3.42) and may be prescribed when a maintenance dose of 0.1 mg. a day is indicated.

B. *Form of drug.* Folic acid preparations are in (1) tablet form suitable for oral administration and contain no less than 0.15 mg. and no more than 1.0 mg. folic acid per tablet or (2) solution form suitable for parenteral administration in the dosages recommended in the labeling guidelines below.

C. *Labeling conditions.* 1. The label bears the statement "CAUTION: Federal law prohibits dispensing without prescription."

2. The drug is labeled to comply with all requirements of the Act and regulations promulgated thereunder, and those parts of its labeling indicated below are substantially as follows: (Optional additional information, applicable to the drug, may be proposed under other appropriate paragraph headings and should follow the information set forth below.)

FOLIC ACID

DESCRIPTION

(To be supplied by the manufacturer. This is to be confined to an appropriate description of the physical and chemical properties of the drug, and the formulation.)

ACTIONS

(To be supplied by the manufacturer. This is to be confined to an appropriate statement of the demonstrated pharmacologic/physiologic actions of the active ingredients of the drug in humans. When the mode of action has not been determined, this should be clearly indicated.)

INDICATIONS

Folic acid is effective in the treatment of megaloblastic anemias due to a deficiency of folic acid as may be seen in tropical or nontropical sprue, in anemias of nutritional origin, pregnancy, infancy, or childhood.

WARNINGS

Folic acid alone is improper therapy in the treatment of pernicious anemia and other megaloblastic anemias where vitamin B_{12} is deficient.

PRECAUTIONS

Folic acid especially in doses above 1.0 mg. daily may obscure pernicious anemia, in that hematologic remission may occur while neurological manifestations remain progressive.

ADVERSE REACTIONS

Allergic sensitization has been reported following both oral and parenteral administration of folic acid.

DOSAGE AND ADMINISTRATION

Oral administration: Folic acid is well absorbed and may be administered orally with satisfactory results except in severe instances of intestinal malabsorption.

Parental administration: Intramuscular, intravenous, and subcutaneous routes may be used if the disease is exceptionally severe, or if gastrointestinal absorption may be, or is known to be, impaired.

Usual therapeutic dosage: In adults: 0.25 mg. to 1.0 mg. daily. *In Children (regardless of age):* 0.25 to 1.0 mg. daily. Resistant cases may require larger doses.

Maintenance dosage: When clinical symptoms have subsided and the blood picture has become normal, a maintenance dose of 0.1 mg. to 0.25 mg. daily should be used, but never less than 0.1 mg. per day. Patients should be kept under close supervision and adjustment of the maintenance dose made if relapse appears imminent.

In the presence of alcoholism, pregnancy, hemolytic anemia, anticonvulsant therapy, or chronic infection, the maintenance dose should be at least doubled.

D. *Previously approved applications.* 1. Each holder of a "deemed approved" new-drug application (i.e., an application which became effective on the basis of safety prior to October 10, 1962) for such drug is requested to seek approval of the claims of effectiveness and bring the application into conformance by submitting supplements containing:

a. Revised labeling as needed to conform to the labeling conditions described herein for the drug, and complete current container labeling, unless recently submitted.

b. Updating information as needed to provide for an oral dosage form containing no less than ~~0.15~~ 0.1 mg. and no more than 1.0 mg. folic acid per tablet or a

parenteral dosage form containing an amount appropriate for administration as described herein, and to make the application current in regard to items 6 (components), 7 (composition), and 8 (methods, facilities, and controls) of the new-drug application form FD–356H to the extent described for abbreviated new-drug applications, § 130.4(f), published in the FEDERAL REGISTER April 24, 1970 (35 F.R. 6574). (One supplement may contain all the information described in this paragraph.)

2. Such supplements should be submitted within the following time periods after the date of publication of this notice in the FEDERAL REGISTER:

a. 60 days for revised labeling; or, for those products which must be reformulated, 180 days for revised labeling fully in accord with this announcement, provided claims for which substantial evidence of effectiveness is lacking are deleted within 60 days. The supplements should be submitted under the provisions of § 130.9 (d) and (e) of the new-drug regulations (21 CFR 130.9) which permit certain changes to be put into effect at the earliest possible time.

b. 180 days for updating information.

3. Marketing of the drug may continue until the supplemental applications submitted in accord with the preceding subparagraphs 1 and 2 are acted upon, provided that the labeling of the preparation shipped within the jurisdiction of the Act is in accord with the labeling conditions described in this announcement within the time periods described in subparagraph 2a.

E. *New applications.* 1. Any person who distributes or intends to distribute such drug which is intended for the conditions of use for which it has been shown to be effective, as described under A1 above, should submit an abbreviated new-drug application meeting the conditions specified in § 130.4(f) (1) and (2), published in the FEDERAL REGISTER April 24, 1970 (35 F.R. 6574). Such applications should include proposed labeling which is in accord with the labeling conditions described herein.

2. Distribution of any such preparation currently on the market without an approved new-drug application may be continued provided that:

a. Within 60 days from the date of publication of this announcement in the FEDERAL REGISTER, the labeling of such preparation shipped within the jurisdiction of the Act is in accord with the labeling conditions described herein, except that if the preparation must be reformulated, 180 days will be allowed for the dosage recommendations to be in accord with this announcement.

b. The manufacturer, packer, or distributor of such drug submits, within 180 days from the date of this publication, a new-drug application to the Food and Drug Administration.

c. The applicant submits within a reasonable time additional information that may be required for the approval of the application as specified in a written communication from the Food and Drug Administration.

d. The application has not been ruled incomplete or unapprovable.

F. *Opportunity for a hearing.* 1. The Commissioner of Food and Drugs proposes to issue an order under section 505(e) of the Federal Food, Drug, and Cosmetic Act withdrawing approval of all new-drug applications and all amendments and supplements thereto providing for the indications for which substantial evidence of effectiveness is lacking as described in paragraph A2 of this announcement. An order withdrawing approval of the applications will not issue if such applications are supplemented, in accord with this notice, to delete such indications. Promulgation of the proposed order would cause any such drug for human use offered for the indications for which substantial evidence of effectiveness is lacking, to be a new drug for which an approved new-drug application is not in effect. Any such drug then on the market would be subject to regulatory proceedings.

2. In accordance with the provisions of section 505 of the Act (21 U.S.C. 355) and the regulations promulgated thereunder (21 CFR Part 130), the Commissioner will give the holders of any such applications, and any interested person who would be adversely affected by such an order, an opportunity for a hearing to show why such indications should not be deleted from labeling. A request for a hearing must be filed within 30 days after the date of publication of this notice in the FEDERAL REGISTER. A request for a hearing may not rest upon mere allegations or denials, but must set forth specific facts showing that a genuine and substantial issue of fact requires a hearing, together with a well-organized and full-factual analysis of the clinical and other investigational data the objector is prepared to prove in a hearing. Any data submitted in response to this notice must be previously unsubmitted and include data from adequate and well-controlled clinical investigations (identified for ready review) as described in § 130.12(a)(5) of the regulations published in the FEDERAL REGISTER of May 8, 1970 (35 F.R. 7250). Carefully conducted and documented clinical studies obtained under uncontrolled or partially controlled situations are not acceptable as a sole basis for approval of claims of effectiveness, but such studies may be considered on their merits for corroborative support of efficacy and evidence of safety. If a hearing is requested and justified by the response to this notice, the issues will be defined, a hearing examiner will be named, and he shall issue a written notice of the time and place at which the hearing will commence.

G. *Unapproved use or form of drug.* 1. If the article is labeled or advertised for use in any condition other than those provided for in this announcement, it may be regarded as an unapproved new drug subject to regulatory proceedings until such recomended use is approved in a new-drug application, or is otherwise in accord with this announcement.

2. If the article is proposed for marketing in another form or for use other than the use provided for in this announcement, appropriate additional information as described in § 130.4 or § 130.9 of the regulations (21 CFR 130.4, 130.9) may be required, including results of animal and clinical tests intended to show whether the drug is safe and effective.

Representatives of the Administration are willing to meet with any interested person who desires to have a conference concerning proposed changes in the labeling set forth herein. Requests for such meetings should be made to the Office of Scientific Evaluation at the address given below, within 30 days after the publication of this notice in the FEDERAL REGISTER.

A copy of the NAS–NRC report has been furnished to each firm referred to above. Any other interested person may obtain a copy by request to the appropriate office named below.

Communications forwarded in response to this announcement should be identified with the reference number DESI 5397, directed to the attention of the following appropriate office, and addressed (unless otherwise specified) to the Food and Drug Administration, 5600 Fishers Lane, Rockville, Maryland 20852:

Supplements (identify with NDA number): Office of Scientific Evaluation (BD–100), Bureau of Drugs.

Original abbreviated new-drug applications (identify as such): Drug Efficacy Study Implementation Project Office (BD–5), Bureau of Drugs.

Request for Hearing (identify with Docket number): Hearing Clerk, Office of General Counsel (GC–1), Room 6–62, Parklawn.

All other communications regarding this announcement: Drug Efficacy Study Implementation Project Office (BD–5), Bureau of Drugs.

Requests for NAS–NRC report: Press Relations Office (CE–200), 200 C Street SW., Washington, D.C. 20204.

This notice is issued pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (secs. 502, 505, 52 Stat. 1050–53, as amended; 21 U.S.C. 352, 355) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 2.120).

Dated: March 19, 1971.

SAM D. FINE,
Associate Commissioner for Compliance.

[FR Doc.71–4952 Filed 4–8–71;8:46 am]

[DESI 10423]

LEVALLORPHAN TARTRATE INJECTION

Drugs for Human Use; Drug Efficacy Study Implementation

The Food and Drug Administration has evaluated a report received from the National Academy of Sciences-National Research Council, Drug Efficacy Study Group, on the following drug for intravenous use:

Lorfan Injection, containing levallorphan tartrate; Roche Laboratories, Division of Hoffman-LaRoche, Inc., 340 Kingsland Street, Nutley, New Jersey 07110 (NDA 10–423).

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

80-600

CORRESPONDENCE

3 SEP 1971

NDA 80-600
AF 31-015

West-Ward, Inc.
Attention: Mr. Edward Green
745 Eagle Avenue
Bronx, New York 10456

Gentlemen:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

NAME of DRUG: Folic Acid Tablets, 1 mg.

DATE of APPLICATION: August 25, 1971

DATE of RECEIPT: August 30, 1971

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the NDA number shown above.

Sincerely yours,

Paul A. Bryan, M.D. 9/3/71

Paul A. Bryan, M.D.
Director
Drug Efficacy Study Implementation
Project Office
Bureau of Drugs

cc:
HFK-BO
Dup
BD-69
BD-67
BD-22
BD-310
JLMeyer/wlb/9-2-71
Ack

JLMeyer 9/2/71

NDA 80-600
AF 31-015

OCT 4 [redacted]

West-Ward, Inc.
Attention: Mr. Edward Green
745 Eagle Avenue
Bronx, New York 10456

Gentlemen:

Reference is made to your abbreviated new drug application dated August 25, 1971, submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Folic Acid Tablets, 1 mg.

We have completed our review of this abbreviated new drug application. However, before we are able to reach a final conclusion, the following additional information is necessary:

1. Revised Package Insert:

   a) DOSAGE and ADMINISTRATION section: Delete reference to _____

   b) _____ Change heading to "HOW SUPPLIED". Reference is made to 0.1 mg. and 0.25 mg. tablets. Please clarify.

2. Please clarify the following deviations from the USP XVIII monographs.

   a) Folic Acid Powder
      1) Residue on Ignition Test is not performed.

      2) Assay is not performed according to procedure.

   b) Folic Acid Tablet
      1) The Content Uniformity test does not follow USP XVIII procedure.

Please submit the above information promptly.

Sincerely yours,
Carl A. Bryan, M.S. 10/4/71
RE Joyce 9/29/71
Paul A. Bryan, M.D.
Director
Drug Efficacy Study Implementation
Project Office
Bureau of Drugs
10/4/71

Dup
BD-69 BD-67 BD-22
BD-242 BD-100
JEilert/JLMeyer/REJoyce 9-16-71
R/D init by MAClark/JLMeyer9-24-71
Final typing/wlb/9-29-71
Rev w/f JLMeyer 10/1/71

JEilert 9-30-71

cc:
NYK-DO

M. Clark MD 10/4/71

REV. W/F E

RESUBMISSION
NDA ORIG AMENDMENT

Orig

West-ward, Incorporated

745 EAGLE AVENUE BRONX, N. Y. 10456

PERSONALLY SUBMITTED BY
Edward Green
Rec'd from Wendy Bruce 80-60
D. Greene
10-28-71

NDA 80-600

October 27, 1971

Paul A. Bryan, M.D.
Director
Drug Efficacy Study Implementation
Project Office
Bureau of Drugs
Food and Drug Administration
Rockville, Maryland 20852

Dear Dr. Bryan:

This is in answer to your letter of October 4, 1971 with reference to our abbreviated new drug application for Folic Acid Tablets 1 mg.

The information requested follows the numbering sequence of your letter.

1. a and b Enclosed is a printer's proof of the package insert with the Dosage and Administrative section and the _____ revised in accordance with your recommendations. If satisfactory we will send you 12 copies of the final printed copy.

2. a. Folic Acid Powder

1) Please amend our application to include the Ignition Test.

2) Please amend our application to follow the U.S.P. XVIII assay procedure.

b. Folic Acid Tablet

1) The actual method for determining the Content Uniformity is herewith attached. This is a relatively simple method which we can apply since we make the tablets ourselves and have full knowledge of the excipients which do not introduce any error. We have verified the reliability of the method by checking the results against those obtained using the Official U.S.P. method. The results agree well within acceptable limits.

We trust you will find the above satisfactory.

RECEIVED
OCT 29 1971
BUREAU OF DRUGS

Sincerely,
West-ward, Inc.

Edward Green

Edward Green
Technical Director

EG/eb
encl.

DEC 17 1971

Salmon

ANDA 80-600
AF 31-015

West-Ward, Inc.
Attention: Mr. Edward Green
745 Eagle Avenue
Bronx, New York 10456

Gentlemen:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Folic Acid Tablets, 1 mg.

Reference is also made to your communication dated October 27, 1971, containing requested information and proofs of revised labeling.

We have completed the review of this abbreviated new drug application as submitted with draft labeling. However, before the application may be approved, it will be necessary for you to submit final printed labeling. The labeling should be identical in content to the draft copy.

Please submit twelve copies of the final printed labeling.

It is also requested that you submit a commitment to follow the USP XVIII content uniformity test or data to substantiate the claim that the alternate procedure is comparable to the USP XVIII procedure.

Please submit the above information promptly.

Sincerely yours,

Paul A. Bryan M.D. 12/16/71

Paul A. Bryan, M.D.
Director
Drug Efficacy Study Implementation
Project Office
Bureau of Drugs

cc:
NYK-DO
Dup.
BD-67
BD-69 OMRandell,md 12/16/71
BD-22
BD-100 JLMeyer 12/15/71
BD-242
JHEilert/JLMeyer/REJoyce 12-2-71 REJoyce 12/7/71
Initialed by JLMeyer 12-3-71
rt 12-7-71
Approvable

Filed 12-13-71

SALMON

E

ORIG

ORIGINAL FPL

West-ward, Incorporated

745 EAGLE AVENUE BRONX, N. Y. 10456

ANDA 80-600

January 18, 1972

Paul A. Bryan, M.D.
Director
Drug Efficacy Study Implementation
Project Office
Bureau of Drugs
Food and Drug Administration
Rockville, Maryland 20852

Dear Dr. Bryan:

This is in answer to your letter of December 17, 1971 with reference to our abbreviated new drug application for Folic Acid Tablets 1 mg.

As requested we are enclosing 12 final printed copies of the package insert, identical to the draft copy submitted with our letter of October 27, 1971.

Further as requested we herewith commit ourselves to follow the U.S.P. XVIII content uniformity test.

We trust you will find the above satisfactory.

Sincerely,
West-ward, Inc.

Edward Green

EG/eb
encl.

Edward Green
Technical Director

RECEIVED
JAN 26 1972
BUREAU OF DRUGS