CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-402/SCM-001/S-002/S-003/S-004/S-005

APPROVAL LETTERS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-402/S-005

MAR 16 2000

Whitehall-Robins Healthcare
Attention: Sharon Heddish
Vice President, Regulatory Affairs Worldwide
5 Giralda Farms
Madison, NJ 07940-0871

Dear Ms. Heddish:

Please refer to your supplemental new drug application dated May 14, 1999, received May 17, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Advil Migraine Liqui-Gels (solubilized ibuprofen), 200 mg.

We acknowledge receipt of your communications dated September 8, November 19 and 23, and December 14, 1999; January 21 and 24, February 15 and March 9, and 14, 2000.

This supplemental new drug application provides for the use of Advil Migraine Liqui-Gels (solubilized ibuprofen), 200 mg for treatment of migraine.

We have completed the review of this supplemental 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 enclosed agreed upon labeling text. Accordingly, the supplemental new drug application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed draft labeling text, and must be formatted consistent with the requirements of 21 CFR 201.66. Please be advised that, under the "Inactive ingredients" heading, you may replace the listing of the ink components (black iron oxide, lechitin, pharmaceutical glaze and simethicone) with the term "pharmaceutical ink."

Please submit 20 copies of the FPL as soon as it is available, in no case 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 supplement NDA 20-402/S-005." Approval of this submission by FDA is not required before the labeling is used.

Should additional information relating to the safety and effectiveness of the drug become available, further revision of the labeling may be required.

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 one copy 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. For administrative purposes, this submission should be sent to the NDA and should be identified as new correspondence to approved supplement 20-402/S-005.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

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 regarding this application, please contact Kerry Rothschild, Esq., Regulatory Project Manager, at 301-827-2284.

Sincerely

/S/

Charles Ganley, M.D.
Director
Division of Over-The-Counter Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

/S/

Russell Katz, M.D.
Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-402/S-003

FEB 5 1999

Whitehall-Robins
Attention: Hulon McCain
Director, Regulatory Affairs
Five Giralda Farms
Madison, NJ 07940-0871

Dear Dr. McCain:

Please refer to your supplemental new drug application dated September 30, 1998, received October 5, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Advil Liqui-Gels (solubilized ibuprofen) capsules, 200mg.

Please refer also to your amendment to your additional communications dated January 26 and February 5 (two), 1999.

The User Fee goal date for this supplemental new drug application is February 5, 1999.

This supplemental new drug application proposes that the packaging components for the bottles and blisters be changed to those currently approved under NDA 19-898 for Advil Tablets, 200 mg. It further provides for a pouch packaging configuration. Draft labeling was also submitted.

We have completed the review of this supplemental new drug application 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 enclosed labeling text. Accordingly, the supplemental new drug application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling text. 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 20 copies of the FPL as soon as it is available, in no case 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 supplement NDA 20-402/S-003." Approval of this submission by FDA is not required before the labeling is used.

We also request that you consider reformatting the labeling as outlined in the February 27, 1997 FEDERAL REGISTER notice "Over-the Counter Human Drugs; Proposed Labeling Requirements" (62 FR 9024). Note, however, that the proposed labeling requirements and the draft prototype label are subject to change pending finalization of this rule.

Should additional information relating to the safety and effectiveness of the drug become available, further revision of the labeling may be required.

This approval affects only those changes specifically submitted in this supplemental new drug application. Other changes that may have been approved or are pending evaluation are not affected.

Please submit three copies of the introductory promotional material 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 the Division of Over-the-Counter Drug Products and two copies of both the promotional material and the labeling directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

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 regarding this application, please contact Kerry Rothschild, Esq., Project Manager, at (301)827-2284.

Sincerely yours,

/S/

Debra L. Bowen, M.D.
Acting Director
Division of Over-the-Counter Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Enclosure: Approved labeling text

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-402/S-002

Whitehall-Robins Healthcare
Attention: Sharon C. Heddish
Vice President, Worldwide Regulatory Affairs
Five Giralda Farms
Madison, New Jersey 07940-0871

FEB 23 1998

Dear Ms. Heddish:

Please refer to your supplemental new drug application dated December 10, 1996, received December 11, 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Provel® (ibuprofen green oblong liquigel), 200 mg.

We acknowledge receipt of your submissions dated July 21 and September 10, 1997; and January 13 and February 20 and 23, 1998.

This supplemental new drug application provides for revisions to the approved labeling: (1) removal of the "take with food" direction, (2) modification of the Provel® labeling to be consistent with Advil labeling, and (3) conversion to "drug facts" style labeling.

We have completed the review of this supplemental new drug application, including the submitted draft labeling, 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 enclosed draft labeling. Accordingly, the supplemental new drug application is approved effective on the date of this letter.

As stated in your letter dated February 23, 1998, the final printed labeling (FPL) will be identical to the enclosed draft labeling. Marketing the product with FPL that is not identical to this draft labeling may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case 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 "FINAL PRINTED LABELING" for approved NDA 20-402/S-002. Approval of this submission by FDA is not required before the labeling is used.

Should additional information relating to the safety and effectiveness of the drug become available, revision of the labeling may be required.

In addition, please submit three copies of the introductory promotional material 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 material and the package insert directly to:

Food and Drug Administration
Division of Drug Marketing, Advertising and Communications
HFD-40
5600 Fishers Lane
Rockville, Maryland 20857

Should a letter communicating important information about this drug product (i.e., a "Dear Doctor" letter) be issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20852-9787.

Please submit one market package of the drug product when it is available.

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, please contact Stephanie Mason, Project Manager, at (301) 827-2222.

Sincerely yours,

/S/

Debra L. Bowen, M.D.
Director
Division of Over-the-Counter Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

ENCLOSURE

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-402/SCM-001/S-002/S-003/S-004/S-005

APPROVABLE LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-402/SCM-001

MAY - 2 1997

Whitehall-Robins Healthcare
Atten: Rich Cuprys
Assistant Vice President, Regulatory Affairs
5 Giralda Farms,
Madison, NJ 07940

Dear Mr. Cuprys:

Please refer to your November 11, 1996, supplemental new drug application, received November 13, 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Provel(R) (Ibuprofen Liquigels), 200 mg.

This supplemental application provides for an alternate packaging and testing site and modifications to the stability testing program.

We have completed the review of this supplemental application, and it is approvable. Before this application may be approved, however, it will be necessary for you to satisfactorily address the following deficiencies:

1. Please provide your acceptance testing and specifications for the packaging materials and bulk drug product at the proposed packaging site upon receipt. If they are received with a Certificate of Analysis (COA), only a specific identification test need to be performed. Otherwise, full testing is required.

2. The post approval stability program calls for testing of one additional batch per year after the initial first three batches at yearly test intervals. Please note that the stability testing at reduced level than that in the currently approved stability protocol requires submission of a prior approval supplement. The stability testing. should be performed in accordance with the approved stability protocol in the NDA.

3. The post approval stability commitment should cover testing of all drug product packaging configurations and package sizes, i.e., the smallest and largest of each packaging configuration. Use of bracketing to reduce the extent of testing is acceptable.

4. The stability commitment should also include the following:

To withdraw from the market any lots found to fall outside the approved specifications for the drug product or immediately discuss it with the reviewing division if the deviation is a single occurrence that does not affect the safety and efficacy of the drug product and provide justification for the continued distribution of that batch.

Additionally, we have the following information request:

Please provide information on the packaging equipment at the proposed site as to whether or not it is similar to that used at the currently approved packaging site Wyeth-Ayerst, Rouses Point, NY.

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.120. In the absence of any such action FDA may proceed to withdraw the supplemental application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

If you have any questions, please contact Stephanie Mason, Project Manager, for the Division of Over the Counter Drug Products, 301-827-2275.

Sincerely,

/S/

Hasmukh B. Patel, Ph.D.
Chemistry Team Leader,
Division of New Drug Chemistry III
Center for Drug Evaluation and Research