CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 020844

ADMINISTRATIVE/CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-844

JUL 20 1998

R.W. Johnson Pharmaceutical Research Institute
Attention: Michael H. Kaufman
Associate Director, Regulatory Affairs
920 Route 202 South
P.O. Box 300
Raritan, New Jersey 08869-0602

Dear Mr. Kaufman:

Please refer to your new drug application (NDA) dated July 31, 1997, received August 1, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Topamax (topiramate capsules) Sprinkle Capsules 15 mg, 25 mg, and 50 mg. (Please refer to the Nomenclature section of this letter for comments regarding nomenclature.)

We acknowledge receipt of your additional correspondence and amendments dated:

August 12, 1997	December 4, 1997	April 21, 1998	May 22, 1998
August 18, 1997	December 24, 1997	May 6, 1998	June 24, 1998
October 29, 1997	January 27, 1998	May 15, 1998	

The user fee goal date for this application is August 1, 1998.

This original new drug application provides for a sprinkle capsule formulation of topiramate, a new dosage form, as adjunctive therapy for the treatment of adults with partial onset seizures.

We have completed the review of this application, as amended, and it is approvable. Before this application may be approved, however, it will be necessary for you to respond to the following requests or comments.

Labeling

The attachment to this letter provides a draft of the labeling that the Agency asks you to adopt for Topamax Sprinkle upon approval of this application. Although sections of this proposal are taken verbatim from the labeling proposed by you in your December 24, 1997 amendment, other sections have been revised. Please note that we have embedded several "Notes to Sponsor" in the text of the attached draft labeling, requesting further revisions or clarifications.

If additional information relating to the safety or effectiveness of this drug becomes available before we receive the final printed labeling, revision of that labeling may be required.

Nomenclature

We have been advised by the CDER Labeling and Nomenclature Committee that "sprinkle capsules" are not a recognized dosage form descriptor in the USP, but that the term "sprinkle" may be used as a descriptive term in conjunction with the proprietary name to form the proprietary name for this product. Accordingly, we request that you adopt, as the established name for this new dosage form, topiramate capsules, and suggest the following presentation of proprietary and established names in labeling, Topamax (topiramate capsules) Sprinkle Capsules. This request is reflected throughout this letter and in the attached draft labeling.

Biopharmaceutics

1. We ask that the following final dissolution methodology and specification be adopted for Topamax (topiramate capsules) Sprinkle Capsules 15 mg, 25 mg, and 50 mg:

   Apparatus: USP Apparatus II (paddle)
   Agitation: rpm
   Medium: mL
   Specification: Q = at minutes

2. We note that your application included a request for waiver of bioequivalence studies for the Topamax (topiramate capsules) Sprinkle Capsules 15 mg and 25 mg. Based on review of the data and rationale provided, your request for waiver of bioequivalence studies is granted for the Topamax (topiramate capsules) Sprinkle Capsules 15 mg and 25 mg.

Chemistry, Manufacturing, and Controls (CMC)

1. Please provide a certificate of analysis for a representative batch of the because the referenced drug master file is a type 1 DMF and does not contain CMC information on this container. Please also provide letters of authorization for the DMFs of the used in the manufacturing of the If this information has been previously submitted in this NDA, please provide its location(s).

2. The drug product specifications should include a identity specification and test for the drug substance extracted from the sprinkle capsule. The two identity tests provided do not assure the identity of the drug substance in the sprinkle An individual exception to the Agency's stereochemistry policy was allowed for the tablets in NDA 20-505/Topamax (topiramate) Tablets.

3. In any future application, please include the in-process controls, which were stated in the batch records of this application, as a separate text section in the CMC portion of the application.

4. Your acceptance testing of the capsules should include an identity test for the printing ink used as identifier.

5. The expiration dating period for Topamax (topiramate capsules) Sprinkle Capsules is 24 months when packaged and stored as per the original NDA submission.

Promotional Material

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-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Within 10 days after the date of this letter, you are required to amend the 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 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.

The drug product may not be legally marketed until you have been notified in writing that the application is approved.

If you have any questions, contact Jacqueline H. Ware, Pharm.D., Regulatory Management Officer, at (301) 594-2850.

Sincerely yours,

/S/ /S/ 7/20/92

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

APPEARS THIS WAY
ON ORIGINAL

cc:
Archival NDA 20-844 /S/ 7/10/98
HFD-120/Div. Files /S/ 7/14/98
HFD-120/Leber/Katz/Tresley/Ware /S/ 7/10/98
HFD-120/Guzewska/Zarifa/Fitzgerald /S/ 7/9/98
HFD-860/Sahajwalla/Mahmood /S/ 7/9/98
HFD-345/Viswanathan/Yau
HFD-002/ORM
HFD-101/ADRA
HFD-95/DDMS
HFD-40/DDMAC (with labeling)
HFD-810/DNDC Division Director
DISTRICT OFFICE

Drafted by: jhw/June 29, 1998
Initialed by:
final:
filename: 29844AE.LTR

APPROVABLE (AE)

APPEARS THIS WAY
ON ORIGINAL

PATENT AND EXCLUSIVITY INFORMATION

For patent information regarding TOPAMAX® (topiramate) please refer to our approved NDA 20-505, Item 13 (Volume 2.1) submitted on December 29, 1994 and subsequently approved on December 24, 1996. There is no patent information filed on the sprinkle capsule formulation.

Exclusivity Summary for NDA 20-844

Exclusivity Summary Form

EXCLUSIVITY SUMMARY FOR NDA # **20-844** SUPPL #_____

Trade Name: **Topamax Sprinkle** Generic Name: **topiramate capsules**

Applicant Name: **R. W. Johnson Pharmaceutical Research Institute**

HFD#: **HFD-120** Approval Date If Known: 10/26/98

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. *An exclusivity determination will be made for all original applications, but only for certain supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following question about the submission.*

a) Is it an original NDA? YES/_X_/ NO /___/

b) Is it an effectiveness supplement? YES /___/ NO /_X_/

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")
YES /__/ NO /_X_/

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

---

d) Did the applicant request exclusivity? YES /__/ NO /_X_/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 4.

2. *Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule, previously been approved by FDA for the same use? (Rx to OTC switches should be answered NO - please indicate as such)* YES /__/ NO /_ X _/

If yes, NDA # Drug Name

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 4.

Exclusivity Summary for NDA 20-844

3. *Is this drug product or indication a DESI upgrade?* YES /___/ NO /_ **X** _/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 4 (even if a study was required for the upgrade).

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES.

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety. YES /_ **X** __/ NO /__/

If yes, NDA # **20-505** Drug Name: **Topamax (topiramate) Tablets**

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.) YES /___/ NO /_ **X** _/

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 4. IF "YES" GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS.

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations?
(The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) **If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a).** If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation. YES /__/ NO /_ **X** _/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 4.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be

sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement? YES /__/ NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 4:**

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application? YES /___/ NO /__/

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO. YES /___/ NO /___/

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product? YES /___/ NO /__/

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /__/ NO /__/ Investigation #2 YES /__/ NO /__/

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /__/ Investigation #2 YES /___/ NO /__/

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Exclusivity Summary for NDA 20-844

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1 YES /__/ NO /___/

Investigation #2 YES /__/ NO /___/

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /__/

Signature: /S/ ***Date:*** 11/5/98

Title: Project Manager

Signature of Office/Division Directo

Signature: /S/ ***Date:*** 11/6/98

APPEARS THIS WAY
ON ORIGINAL

Form OGD-011347 Revised 8/27/97
cc: Original NDA Division File HFD-93 Mary Ann Holovac

PEDIATRIC PAGE

(Complete for all original application and all efficacy supplements)

NDA/BLA Number:	20844	**Trade Name:**	TOPAMAX(TOPIRAMATE)SPRINKLE CAPS 50/25/1
Supplement Number:		**Generic Name:**	TOPIRAMATE
Supplement Type:		**Dosage Form:**	CAP
Regulatory Action:	AP	**Proposed Indication:**	As adjunctive therapy for treatment of adults with partial onset seizures.

IS THERE PEDIATRIC CONTENT IN THIS SUBMISSION? NO

What are the INTENDED Pediatric Age Groups for this submission?

____NeoNates (0-30 Days)____Children (25 Months-12 years)
____Infants (1-24 Months) ____Adolescents (13-16 Years)

Label Status -
Formulation Status -
Studies Needed -
Study Status -

Are there any Pediatric Phase 4 Commitments in the Action Letter for the Original Submission? NO

COMMENTS:

This Page was completed based on information from a PROJECT MANAGER/CONSUMER SAFETY OFFICER, JACKIE WARE

/S/

Signature

10/26/98

Date

APPEARS THIS WAY
ON ORIGINAL

DEBARMENT CERTIFICATION

The R.W. Johnson Pharmaceutical Research Institute certifies that we did not and will not use in any capacity the services of any person debarred under subsections 306 (a) or 306 (b) of the Federal Food Drug and Cosmetic Act in connection with this New Drug Application.

APPEARS THIS WAY
ON ORIGINAL

COPY

MEMORANDUM

DATE: October 5, 1998

FROM: Deputy Director
Division of Neuropharmacological Drug Products/HFD-120

TO: File, NDA 20-844

SUBJECT: Supervisory Review of Response to Approvable Letter for NDA 20-844, for Topiramate Sprinkle Capsules

On 7/28/98, the Division issued an Approvable letter to R.W. Johnson Pharmaceutical Research Institute for NDA 20-844, which proposed a new dosage form (a sprinkle capsule) of topiramate. In that letter, the following issues/requests were noted:

1) Draft labeling, with embedded comments, was included

2) The Nomenclature Committee requested that the sponsor adopt the following presentation of proprietary and established names: Topamax (topiramate capsules) Sprinkle Capsules

3) We requested the sponsor adopt specific dissolution specifications

4) Several CMC requests were made.

5) Promotional materials were requested.

On 8/26/98, the sponsor responded to the Approvable letter. This response has been reviewed by Dr. Zarifa, chemist (review dated 9/9/98).

They have agreed to the requests of the Nomeclature Committee, and have agreed to adopt the proposed dissolution specifications. Dr. Zarifa has recommended that the NDA be approved, and the labeling is acceptable.

For these reasons, I recommend that the application be approved with the attached labeling.

/S/

Russell Katz, M.D.

cc:
NDA 20-844
HFD-120
HFD-120/Katz/Leber/Ware/Zarifa

APPEARS THIS WAY
ON ORIGINAL

TELEPHONE CONTACT MEMORANDUM

NDA/IND #:	**NDA 20-844**
DATE:	May 5, 1998
PRODUCT NAME:	Topiramate Sprinkle Capsules
FIRM NAME:	R.W. Johnson
CONVERSATION WITH:	Kathy Glamkowski
TELEPHONE #:	(908)704-4756 Ext. 5360
FDA Contact:	Mona Zarifa

I called to discuss the proposed limits for impurities in the drug product specifications. I pointed out that the limit for and for other impurity (each) have no supporting data in the NDA. Justification for these limits is needed based on batch analysis results for the finished product and corresponding drug substance. Ms. Glamkowski said she will send an amendment with the justification.

/S/

Mona Zarifa, Review Chemist

INIT: MG/
CC: HFD-120 Div. File

Filename: 20844.Tel

TELEPHONE CONTACT MEMORANDUM

NDA/IND #:	**NDA 20-844**
DATE:	May 19, 1998
PRODUCT NAME:	Topiramate Sprinkle Capsules
FIRM NAME:	R.W. Johnson
CONVERSATION WITH:	Kathy Glamkowski
TELEPHONE #:	(908)704-4756 Ext. 5360
FDA Contact:	Mona Zarifa

I called to discuss the May 5 amendment sent in response to the request for information per our previous telephone conversation on May 5, 1998. I pointed out that the amendment contained batch results on the drug substance and Topiramate tablets. Batch results on the sprinkle dosage form are still lacking. I also asked about the chiral identity test for the drug substance as extracted from the sprinkle Ms. Glamkowski said she will provide the information ASAP.

/S/

Mona Zarifa, Review Chemist

INIT: MG/
CC: HFD-120 Div. File

Filename: 2084401.Tel

875

REQUEST FOR PROPRIETARY/ESTABLISHED NAME REVIEW

OUTGOING

AUG 22 1997

To: CDER Labeling and Nomenclature Committee
Attention: Dan Boring, R.Ph., Ph.D., Chair
HFD-530
9201 Corporate Blvd, Room N461

From: HFD-120 - Division of Neuropharmacological Drug Products

JAN 28 1998

Paul Leber, M.D., Director /S/ - 8/19/97

Date: August 18, 1997

Application Status (IND/NDA/ANDA): NDA 20-844

RECEIVED JAN 3 /S/

Proposed Proprietary Name: Topamax Sprinkle Capsules

Trademark registration status/Countries registered(if known): Registered but country unknown

Company tradename: **R.W. Johnson**

Other proprietary names by same firm for companion products: Topamax Tablets (NDA 20-505)

United States Adopted Name, dosage form, strength and dosing schedule:
Topiramate, Sprinkle Capsules, 15 mg, 25 mg, and 50 mg, 400 mg/day in two divided doses

Indication for use:
Adjunctive therapy for the treatment of adults with partial onset seizures.

Comments from submitter (concerns, observations, etc.):
None

Meetings of the Committee are scheduled for the 4th Tuesday of each month. Please submit this form at least one week before the meeting. Responses will be as timely as possible.
Rev. 2/97

cc
NDA 20-844
HFD-120/Division File
HFD-120/CSO/JWare

Consult #875 (HFD-120)

TOPAMAX Sprinkle Capsule topiramate capsules

TOPAMAX is the proprietary name of an already approved product and was not evaluated. The term "sprinkle" may be used as a descriptive term in conjunction with the proprietary name to form the proprietary designation for this product. However, "sprinkle capsules" are not a recognized dosage form descriptor in the USP. It is recommended that the established name be (topiramate capsules) sprinkle.

The Committee has no reason to find the proposed proprietary name unacceptable, however, the established name should be modified as indicated.

/S/ 1/28/98, Chair
CDER Labeling and Nomenclature Committee

PM REVIEW OF NDA LABELING FOR NDA 20-844

NDA# **20-844**

Date Review Completed: **8-OCT-98**

Supplement #:

Date of Submission: **26-AUG-98**

Applicant's Name & Address: **R.W. Johnson Pharmaceutical Research Institute**
920 Route 202 South, P.O. Box 300
Raritan, New Jersey 08869

Product Trade Name: **Topamax Sprinkle Capsule**
Product Generic Name: topiramate

Dosage Form & Strength: **15mg, 25mg, and 50 mg capsules**

Pharmacologcial Category &/or Indication: **Anticonvulsant**

Material Reviewed:
1. FDA draft approvable labeling dated 7/20/98
2. Sponsor's proposed draft labeling submitted 8/26/98

Evaluation: (See Attached Review Notes)

Recommendation:
With concurrence from the clinical and biopharmaceutical reviewers, an approval letter should issue.

/S/ 10/14/98
Jacqueline H. Ware, Pharm.D.
Project Manager

Concur /S/ for 10/14/98
John S. Purvis
Chief, PM Staff

cc:
Archival NDA 20-844
HFD-120 Division Files
HFD-120/Leber/Katz/Ware /S/ 10/15/98

filename: C:\My Documents\WPFILES\jwndas\N20844\labelrev.doc

PM REVIEW OF NDA LABELING FOR NDA 20-844

Review Notes

I. LABELING COMPARISON

The FDA draft approvable labeling, which accompanied the 7/20/98 FDA approvable letter for NDA 20-844, was electronically compared line-by-line to the sponsor's proposed draft labeling submitted 8/26/98 in response to the 7/20/98 FDA approvable letter and labeling.

II. LABELING CHANGES **(See attachment for specific notes.)**

When the 7/20/98 draft approvable labeling was compared to the 8/26/98 sponsor's proposed draft labeling, the following changes were noted and are listed below by section:

Section	Note #	FDA Draft Approvable Labeling dated 7/20/98	Sponsor's Proposed Draft Labeling dated 8/26/98	Project Manager Comment
DESCRIPTION	Note #1			editorial letter case change
DESCRIPTION	Note #2			deletion of reference to 50mg capsule
CLINICAL STUDIES	Note #3			addition
INDICATIONS & CONTRA-INDICATIONS	Note #4			editorial letter case change
WARNINGS	Note #5			editorial deletion
WARNINGS	Note #6			editorial change for clarity
PRECAUTIONS	Note #7			Response to FDA "Note to Sponsor" referencing 21 CFR 201.57(f)(2)
PRECAUTIONS	Note #8			Explanation of revision provided under reference 1 of 8/26/98 submission.

PM REVIEW OF NDA LABELING FOR NDA 20-844

Section	Note #	FDA Draft Approvable Labeling dated 7/20/98	Sponsor's Proposed Draft Labeling dated 8/26/98	Project Manager Comment
PRECAUTIONS	Note #9			editorial deletion
DRUG ABUSE & DEPENDENCE & OVERDOSAGE	Note #10			editorial deletion
DOSAGE & ADMINISTRATION	Note #11			
DOSAGE & ADMINISTRATION	Note #12			editorial letter case change
HOW SUPPLIED	Note #13			editorial letter case change
HOW SUPPLIED	Note #14			deletion of reference to 50mg capsule
HOW SUPPLIED	Note #15			
Patient Information Sheet	Note #16			Editorial change
Patient Information Sheet	Note #17			Editorial change

IV. COMMENTS:

1. The changes identified as Notes #1, #3, #4, #5, #6, #9, #10, #12, #13, #16, and #17 are minor editorial changes.

2. The changes identified as Notes #2 and #14 should be included in the draft approval labeling for topiramate capsule for completeness. The sponsor should be advised that it is acceptable to remove these references when creating final printed labeling for this product if the 50 mg dosage strength will not be marketed.

3. No other changes were noted in the sponsor's proposed draft labeling.

V. CONCLUSIONS:

1. The sponsor's proposed draft labeling incorporates all of the substantive changes, except that identified in Note #8, provided in the Agency's draft approvable labeling dated 7/20/98.

2. The changes identified as Notes #7 and #8 require review by the clinical and biopharmaceutical reviewers to determine the accuracy and acceptability of this information.

CONCLUSIONS (continued):

3. The change identified as Note #11 is acceptable because this labeling is for the topiramate capsule dosage form only; any reference to the appropriate use of the tablet should be deleted.

4. The change identified as Note #15 is acceptable per the July 1998 Guidance for Industry on Implementation of Section 126 of the FDA Modernization Act of 1997 – Elimination of Certain Labeling Requirements.

5. The changes identified as Notes #1, #3, #4, #5, #6, #9, #10, #12, #13, #16, and #17 are minor editorial changes and are acceptable.

23 Page(s) Redacted

DRAFT LABELING