CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20646

ADMINISTRATIVE DOCUMENTS

Memorandum

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research

DATE: September 23, 1997

FROM: Paul Leber, M.D.
Director,
Division of Neuropharmacological Drug Products
HFD-120

SUBJECT: Gabitril™ Filmtab® [tiagabine HCl] NDA 20-646

TO: File NDA 20-646
&
Robert Temple, M.D.
Director, Office of New Drug Evaluation 1

This memorandum conveys my formal recommendation to the file that pending NDA 20-646 (declared approvable on October 31, 1996) be approved.

My views on the probity of the substantive findings and facts that speak to the safety and efficacy of tiagabine's use as adjunctive (i.e., add-on) therapy in the management of partial seizures[1] will be found in my memorandum to the file of October 22, 1996.

In making this affirmative recommendation, I am mindful that the Division's Review Team, led by Dr. Katz, is, albeit with one important exception[2], also satisfied that Gabitril will be safe for use and effective

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[1] Whether or not tiagabine had an effect, as the sponsor wished to claim, on the incidence of secondarily generalized seizures occurring in patients suffering a primary seizure was not known at the time of the approvable action because the firm had failed to conduct the necessary conditional analysis. This analysis has now been completed and it fails to provide evidence of such an effect.

[2] Dr. Katz's reservations about approving the NDA, resolved now at least insofar as the current application is concerned, were not about the safety and efficacy of the lots of drug product that underwent evaluation in clinical trials, but about the specifications requested by the firm for the upper allowable limits for 3 degradants that develop over time in the "to be marketed formulation of Gabitril."

in use under the conditions of use enumerated in the draft of product labeling attached to the approval action letter being forwarded to the Office for issuance.

Issues pending at the time of the approvable action and their resolution

1. The claimed use for Gabitril

As a result of the null findings of the conditional analysis we asked them to perform, the firm now acknowledges that there is a lack of evidence

Accordingly, the Division review team and the firm are in agreement that Gabitril will be approved for use as an add-on treatment for partial seizures.

2. Clarification of the nature of Mental Status Changes associated with the use of tiagabine.

At the time the approvable action was taken, the review team was dissatisfied with the extent to which the firm had investigated and characterized various adverse events associated with tiagabine's use, not so much because the events involved represented ones so serious as to preclude tiagabine's marketing, but because the quality of the description provided in the NDA made them difficult, (actually virtually impossible) to describe in clinically meaningfully terms in product labeling. The approvable action letter, among other requests and instructions, advised the firm that although the NDA was "approvable," further evaluation, characterization, and tabulation of the adverse events reported in association with the use of tiagabine would be required.

The limits sought by the firm exceed those ordinarily allowed under IH Guidance in marketed products. Dr. Katz is concerned, not because of an affirmative finding of risk, or because of a known capacity of these degradants to cause injury, but because an approval of the firm's request would allow users of Gabitril to be exposed to higher levels of 3 substances that have not, as far as we know, ever been systematically evaluated for their capacity to cause harm in humans. Dr. Katz explicates his views on this matter in detail in his 9/11/97 memorandum to the file; I offer my own views in the concluding section of this memorandum.

The Division review team is now persuaded that it has a sufficiently clear understanding of the nature of the adverse clinical events reported in the original NDA to be persuaded that they are described accurately, in clinically understandable terminology, in the version[3] of product labeling under which the Division recommends the NDA be approved. How the firm worked to clarify the adverse reaction information is recounted in Dr. Burkhart's memorandum[4] to the file of 8/21/97.

3. The risk of withdrawal emergent seizures

Although there is no compelling statistically significant evidence of a tiagabine withdrawal associated increment (relevant to a patient's baseline state) in seizure activity, an analysis of the data proposed by Dr. Burkhart suggests that such seizures may occur. In light of the fact that withdrawal emergent seizures are a safety issue, the fact that the consistently observed directional differences cannot be declared statistically significant is ignorable; moreover, it is widely held that sudden withdrawal of an AED may precipitate seizures. Accordingly, I am persuaded that there is merit in Dr. Katz's recommendation (his memorandum of 9/11/97, page 4) that the finding of withdrawal emergent increment in seizure activity be mentioned in product labeling in the Warning Section where generic advice is given urging prescribers to avoid sudden AED withdrawal.

4. Safety Update Assessment

The review[5] of the firm's safety update reveals no major previously un-identified risk of tiagabine.

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[3] that is, the labeling attached to the approval action letter being forwarded to the Office for signature.

[4] Dr. Burkhart is Chief of the Division's Safety Unit.

[5] Because Dr. Balian no longer works in the Division, the task of reviewing the firm's post approvable safety update was assigned to Dr. Knudsen who works under the immediate supervision of Dr. Burkhart.

The additional clinical experience reported upon in Safety Update II is, as the following table documents, relatively meager, however. There were only about 90 new patients; however, because of continuing use by patients already on treatment, there was a net gain of approximately 20 % in the total patient time reported upon (i.e., from 3231 to 3831 patient-years).

Tabular outline of the Safety Updates

Update	submis-sion date	cut off date[s]	Cumulative Numbers & PYs included	Division safety reviewer
Safety Update I (available prior to approvable action	3/1/96	11/30/95 for Abbott 8/31/95 Novo	N= 2999 [PYs= 3231]	John Balian
Safety Update II	3/31/97	8/3/96 [general] 10/15/96 pregnancy 12/31/96 deaths	N = 3091 [PYs =3831]	James Knudsen
Rash specific report	8/8/97		N.A.	James Knudsen

Dr. Knudsen has concluded, and Dr. Burkhart concurs in this judgment, that there are no findings that would cause the agency to revise its basic conclusion that tiagabine is safe for use as add-on treatment for the management of partial seizures.

The review of Safety Update II, however, did lead to a re-examination of the database for reports of serious rash. The sponsor assisted in this evaluation by providing, in their letter of 8/8/97: 1) a comparison of the numbers of patients reporting a rash as an adverse event in Safety Updates I and II, 2) the results of a search for patients who discontinued tiagabine treatment and had a rash identified as either a primary or secondary cause for the discontinuation, 3) detailed reports on the clinical features of all cases so identified, 4) a list of the subset of treatment emergent rashes considered "serious."

As a result of these efforts, 4 patients were identified who developed a serious rash on tiagabine (3205 with vesiculobullous rash, 2102 with Stevens Johnson Syndrome, 520 and 11343 both with a maculopapular rashes).

Although I am mindful that Dr. Burkhart believes the evidence is insufficient to require that product labeling identify any unique type of rash as being associated with the use of tiagabine, I believe it is, the weakness of the evidence notwithstanding, reasonable to do so, in part because although there is but one case of SJS [6], there is a second patient who developed a vesiculobullous rash that, although not identified as such, might have been an erythema multiforme variant. Accordingly, I believe, given an appropriate and candid acknowledgement of the tenuous nature of the link, mention of rash associated discontinuations should be made in the Precautions Sections of labeling.

5. Labeling

Dr. Katz's memorandum of 9/11/97 describes how the draft labeling being forwarded with the approval action letter was developed and how it

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[6] A 9 year old boy, receiving 3 AEDs in addition to tiagabine, developed SJS. Tiagabine's causal role is clearly arguable because the patient had been on tiagabine, without evidence of rash, for almost 2 years; it was only within weeks of the addition of the 3 other AEDs, (see page 12 of Dr. Knudsen's 7/25/97 review), that SJS developed.

differs from the draft issued as an attachment to the approvable action letter. Since the time that he issued his memorandum, some additional changes have been made to the draft, but none are of a kind that warrant comment on my part

Two other issues discussed by Dr. Katz do require comment.

6. Proprietary Name

When the Division initially sought its counsel about the use of the name, Gabitril, CDER's Labeling and Nomenclature Committee raised no objection to it. In a memorandum (June 23, 1997) specifically identifying two product names that might arguably be confused with Gabitril, the Division sought to confirm this advice. By memorandum of 8/18/97, the Committee informed the Division that it now considers the name unacceptable in light of the fact that the generic name of Neurontin is gabapentin.

> (WL/PD, the marketers of Neurontin, had written to complain about the choice, citing a WHO resolution presumably condemning the use of Proprietary Names that are linked to "receptors." I now gather from informal conversations with Dr. Katz that Dr. Boring has said the referenced document is not binding upon the agency.)

I have no strong opinion on this matter. Like Dr. Katz, I personally find the name Gabitril acceptable. To be clear, this does not mean that I am unconcerned about prescribing errors, only that I think it unlikely that this name will cause them to become more common.

7. Degradant Tolerances.

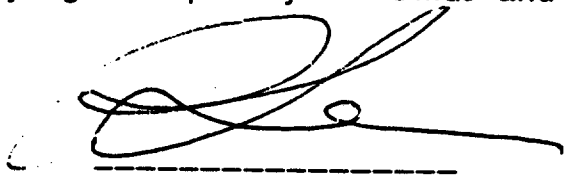
In the interval between the time Dr. Katz issued his 9/11/97 memorandum and the time at which this memorandum is being written, the Division review team and the Office have reached agreement on the upper limits that will be set for 3 degradants that appear in the to-be-marketed formulation of Gabitril. (See footnote #2). These limits are intended to ensure that at the product expiry date being granted (i.e,.18 months), the

levels of the 3 degradants will be at or close to the maximum levels of unknown impurity permitted in a drug product under IH guidances without "qualification." It was also agreed that the sponsor would be advised that a longer expiry (i.e., 24 months) would not be granted until the firm conducted , and submitted satisfactory findings, from a number of additional tests (these are enumerated in Dr. Fitzgerald's 9/18/97 to the file)

Because agreement was reached, I will not "weigh in" on the process of degradant "qualification" by animal toxicity testing to the extent I might have had the matter vis a vis this NDA not been resolved. It should suffice to state that I find the criticisms offered by Dr. Katz (memorandum of 9/11/97) concerning "qualification" of degradants by animal testing on target and compelling. My views on the paramount importance of human testing notwithstanding, I am mindful that agency policies reflect compromises about the interpretations of existing law and, as such, are rarely entirely satisfying to any of the parties who frame them, let alone those who are, at same later point in time, obliged to enforce them.

Conclusion and Recommendation

The information provided in the Gabitril NDA has been found upon review, and in consultation with the Office of New Drug Evaluation I, to satisfy current regulatory requirements for its approval. Accordingly, the Division recommends that the NDA be approved under the manufacturing specifications and conditions of use jointly agreed upon by the Office and Division.



Paul Leber, M.D.
September 23, 1997.

cc:

NDA 20-646
HFD-120
Katz
Burkhart
Knudsen
Rouzer-Kammeyer
Ware
Rapprot
Rzeszotarski
HFD-710
Sahlroot.

APPEARS THIS WAY
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MEMORANDUM

DATE: 9/16/97

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

TO: Director
Division of Neuropharmacological Drug Products/HFD-120

File, NDA 20-646

SUBJECT: Appropriateness of GABITRIL as a tradename

As noted in my supervisory memo dated 9/11/97, questions have been raised about the appropriateness of permitting Abbott Laboratories to name their product GABITRIL (tiagabine). Specifically, the Labeling and Nomenclature Committee concluded that there was a significant potential for confusion between this product and Neurontin (gabapentin), a marketed drug for the same indication, based on the similarities between the trade name GABITRIL and the USAN name gabapentin. Further, Warner-Lambert, the owner of Neurontin, stated in a letter to the Division that granting permission to Abbott for the use of the name GABITRIL would violate a WHO Nomenclature Resolution.

On 9/15/97, I spoke with Dan Boring, Chair of the Labeling and Nomenclature Committee, to determine exactly what our responsibilities are vis-a-vis the WHO Resolution. Indeed, there does exist a WHO Resolution that discourages the use of portions of the generic name in tradenames, and USAN agrees that this should be discouraged.

However, Mr. Boring informed me that we have no legal basis to impose these restrictions, and further, that we ordinarily object to such a usage only when it poses a (potential) risk to the public or when such use is clearly misleading. My understanding, therefore, was that we ordinarily would not object strenuously to the use of a portion of the generic name in the tradename solely on the basis of the WHO Resolution.

Given this understanding, I see no reason to alter my initial recommendation that the name GABITRIL be permitted.

Russell Katz, M.D.

Cc:
NDA 20-646
HFD-120
HFD-120/Leber/Katz/Ware

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PATENT INFORMATION

We, Abbott Laboratories, certify that the drug, Tiagabine Hydrochloride, is claimed in U.S. Patent Numbers 5,010,090 and 5,354,760. The patents were issued April 23, 1991 and October 11, 1994 and are presently set to expire October 7, 2008 and March 24, 2012, respectively.

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EXCLUSIVITY SUMMARY for NDA # 20-646 SUPPL #_____

Trade Name Gabritril® tablets Generic Name tiagabine hydrochloride
Applicant Name Abbott Laboratories HFD-120

Approval Date _____

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 questions about the submission.

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

   b) Is it an effectiveness supplement?

   YES /___/ NO /_X_/

   If yes, what type? (SE1, SE2, etc.) _____

   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 /_X_/ NO /___/

   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:

_____

_____

Form OGD-011347 Revised 8/7/95; edited 8/8/95
cc: Original NDA Division File HFD-85 Mary Ann Holovac

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 8.

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?

YES /___/ NO /_X_/

If yes, NDA #_____ Drug Name_____

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

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 8 (even if a study was required for the upgrade).

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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 /___/ NO /_X_/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # _____ _____

NDA # _____ _____

NDA # _____ _____

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 /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # _____ _____

NDA # _____ _____

NDA # _____ _____

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. 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 /___/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

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.

   For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

   (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 /___/

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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 8:**

_____

_____

(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 /___/

If yes, explain: _____

_____

(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 /___/

If yes, explain: _____

_____

(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:

Investigation #1, Study # _____

Investigation #2, Study # _____

Investigation #3, Study # _____

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 /___/
Investigation #3	YES /___/	NO /___/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

NDA # _____ Study #_____
NDA # _____ Study #_____
NDA # _____ Study #_____

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 /___/
Investigation #3	YES /___/	NO /___/

If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:

NDA # _____ Study #_____
NDA # _____ Study #_____
NDA # _____ Study #_____

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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"):

Investigation #_, Study # _____

Investigation #_, Study # _____

Investigation #_, Study # _____

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

IND # ____ YES /___/ NO /___/ Explain: _____

_____

Investigation #2

IND # ____ YES /___/ NO /___/ Explain: _____

_____

(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?

Investigation #1

YES /___/ Explain _____ NO /___/ Explain _____

_____ _____

_____ _____

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Investigation #2 !

YES /___/ Explain _____ ! NO /___/ Explain _____

_____ ! _____

_____ ! _____

(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 /___/

If yes, explain: _____

_____

_____

_____

Jackie Ware
Jackie Ware, Pharm.D.
Regulatory Management Officer

10/21/96
Date

Paul Leber, M.D.
Division Director

9/23/97
Date

APPEARS THIS WAY
ON ORIGINAL

file:tiagexcl.wpc

cc: Original NDA Division File HFD-85 Mary Ann Holovac

DRUG STUDIES IN PEDIATRIC PATIENTS
(To be completed for all NME's recommended for approval)

NDA # 20-646 Trade (generic) names Gabitril (tiagabine) tablets HCl

Check any of the following that apply and explain, as necessary, on the next page:

____ 1. A proposed claim in the draft labeling is directed toward a specific pediatric illness. The application contains adequate and well-controlled studies in pediatric patients to support that claim.

____ 2. The draft labeling includes pediatric dosing information that is not based on adequate and well-controlled studies in children. The application contains a request under 21 CFR 210.58 or 314.126(c) for waiver of the requirement at 21 CFR 201.57(f) for A&WC studies in children.

____ a. The application contains data showing that the course of the disease and the effects of the drug are sufficiently similar in adults and children to permit extrapolation of the data from adults to children. The waiver request should be granted and a statement to that effect is included in the action letter.

____ b. The information included in the application does not adequately support the waiver request. The request should not be granted and a statement to that effect is included in the action letter. (Complete #3 or #4 below as appropriate.)

____ 3. Pediatric studies (e.g., dose-finding, pharmacokinetic, adverse reaction, adequate and well-controlled for safety and efficacy) should be done after approval. The drug product has some potential for use in children, but there is no reason to expect early widespread pediatric use (because, for example, alternative drugs are available or the condition is uncommon in children).

____ a. The applicant has committed to doing such studies as will be required.

____ (1) Studies are ongoing.
____ (2) Protocols have been submitted and approved.
____ (3) Protocols have been submitted and are under review.
____ (4) If no protocol has been submitted, on the next page explain the status of discussions.

____ b. If the sponsor is not willing to do pediatric studies, attach copies of FDA's written request that such studies be done and of the sponsor's written response to that request.

____ 4. Pediatric studies do not need to be encouraged because the drug product has little potential for use in children.

✓ 5. If none of the above apply, explain.

Explain, as necessary, the foregoing items:

Pediatric studies should be done after approval. The drug product has potential for widespread pediatric use, even though alternative drug products are available.

The sponsor should be advised that PK, safety and efficacy studies are lacking.

If the sponsor plans to establish that pubertal onset begins at the same (or sufficiently similar) in children & adults and that the behavior of the drug is sufficiently similar in both populations (considering factors of safety and efficacy) then adult studies can be relied upon. In Certain case, pediatric PK and safety will need to be established in children by studies in that population.

Cynthia McCormick MD 9/11/96

Signature of Preparer Date

cc: Orig NDA
HFD-120/Div File
NDA Action Package

Consult #833 (HFD-120)

The Committee considered the likelihood of confusion between the proposed proprietary names GABITRIL and SABRIL. The Committee felt there was a high potential for confusion between these names. However, the Committee notes that both of these names are the subject of pending applications. Usually, the first approval will retain all name privileges, and the second approval may be asked to change their name. Unfortunately, since all applications are confidential, there does not exist a satisfactory method for alerting the concerned parties that a potential conflict exists unless a waiver of confidentiality regarding the trademarks is supplied by both sponsors.

The Committee also considered the likelihood of confusion between the proprietary name GABITRIL and the non-proprietary name gabapentin. The Committee felt there is a high potential for confusion between these names also.

Given the factors in this consult, the Committee felt it might be easiest to ask GABITRIL to submit some other name choices, citing the gabapentin conflict. If the sponsor is unwilling to consider alternates, then the Division might ask the sponsors of SABRIL and GABITRIL to submit waivers of confidentiality regarding the trademarks, and discuss the conflicts with each sponsor.

Overall, the Committee finds the name GABATRIL to be unacceptable.

P C Boring 8/18/97, Chair
CDER Labeling and Nomenclature Committee

REQUEST FOR PROPRIETARY/ESTABLISHED NAME REVIEW

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

From: Paul Leber, M.D., Director
Division of Neuropharmacological Drug Products, HFD-120

Date: June 23, 1997

Application/ Status	Proprietary Name	Trademark Registration Status/ Countries Registered (if known)	Company Tradename	Other Proprietary Names by Same Firm for Companion Products	USAN, dosage form, dosage strength, dosing schedule	Indication for Use
NDA 20-646 (review action pending; user fee due date is 10/1/97)	Gabitril™ Filmtab®	Assume name is not trademark registered since ™ is used in labeling.	Gabitril/ Sponsor: Abbott	None	tiagabine; tablets; 4mg, 12mg, 16mg, 20mg; 4mg-32mg/day in 2-4 divided doses	anti-convulsant

APPEARS THIS WAY
ON ORIGINAL

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

Comments from submitter (concerns, observations, etc.):

The division requests that the nomenclature committee re-evaluate the above 3 proprietary and established names, concurrently, for the following reasons:

1. We have recently received correspondence (a copy is attached) from Parke-Davis advising us of their concern for the potential confusion between the trademark Gabitril and the generic name gabapentin.

2. We are unsure if the committee considers the names of not yet approved products when making their evaluations, and given the time difference between the 2 original consults for and for Gabitril, consult #654 dated 8/22/96, we think it prudent to ask for their re-evaluation at this time. We note that in both original nomenclature consults (#319 and #654), the committee found no reason to find the proposed names unacceptable.

Review actions are pending for both NDA and NDA 20-646 (Gabitril). The Division is currently reviewing dated 5/29/97, and submitted in response to the Agency's April 28, 1995 not approvable letter, and Abbott's resubmission to NDA 20-646, dated 3/31/97, and submitted in response to the Agency's October 31, 1996 approvable letter. Both of these resubmissions have a six month review clock with user fee due dates of 11/29/97 and 10/1/97, respectively.

Additionally, we anticipate, this week, receipt of a new original NDA Tablets, a new dosage form of the currently approved product, by

We would appreciate the committee's response to this consult by July 31, 1997 in order that we might have sufficient lead time to consider your recommendation and to meet our user fee due dates.

Thank you in advance for your assistance in this difficult matter.

cc: Original NDA
HFD-120 Division File
HFD-120/Leber/Katz/Ware 6/27/97
file: 20427nam.c2; 20646nam.c3; 20235nam.c2

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

Consult #654

GABITRIL (tiagabine HCl tablets)

The LNC noted the following look alike/sound alike conflicts with the trademark: HABITROL and captopril. However, the Committee believes there is a low potential for confusion with the other names. There are no apparent misleading or fanciful aspects with the proposed name.

The LNC has no reason to find the proposed name unacceptable.

D Kboing 8/22/96, Chair
CDER Labeling and Nomenclature Committee

APPEARS THIS WAY
ON ORIGINAL

APPEARS THIS WAY
ON ORIGINAL

502

MEMORANDUM DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: October 17, 1995

FROM: Paul Leber, M.D.
Director, Division of Neuropharmacological Drug Products, HFD-120

SUBJECT: Request for assessment of a Trademark for a Proposed Drug Product

TO: Dr. Dan Boring
Chair, Labeling and Nomenclature Committee, (HFD-530)

Proposed Trademark: Tibex® Tablets; IND 36,579

Established name: tiagabine HCl 4 mg, 12 mg, 16 mg, 20mg tablets

Indication and Use: Treatment of epilepsy

Attached is correspondence dated September 27, 1995, from the sponsor providing for documentation to support their proposed trademark (Attachment I).

Please review and comment on whether the trademark is considered acceptable.

The sponsor has planned to submitt the NDA on October 31, 1995.

CSO Contact: Robin M. Pitts, R.Ph.; 594-5504

APPEARS THIS WAY
ON ORIGINAL

cc:
IND 36,579
HFD-120/Div File
HFD-120/PLeber/RKatz/CMcCormick/RPitts
Doc #ind\i36,579\nomen.con

APPEARS THIS WAY
ON ORIGINAL

APPEARS THIS WAY
ON ORIGINAL

Consult #502 (HFD-120)

TIBEX Tiagabine Hydrochloride Tablets

eview revealed several names which sound like or look like the proposed
: Tobrex, Tibexin, Ticrex. The Committee believes that Tibexin and
Ticrex are no longer in use, and, due to differences in dosage forms, does not believe there is a significant potential for confusion involving Tobrex and the proposed name.

The Committee has no reason to find the proposed name unacceptable at this time but reserves their recommendation until after a USAN is selected and the proposed name is submitted to the Committee for reconsideration. Furthermore, the Committee notes the proposed name has been submitted for review very early in the review process (IND stage). Under such circumstances, the Committee routinely recommends the proposed name be re-evaluated once an NDA has been submitted and the application is closer to approval since the universe of potential sound-alike/look-alike proprietary names is constantly changing.

CDER Labeling and Nomenclature Committee

D L Boring, Chair