

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number **21-397**

21-423

21-424

ADMINISTRATIVE DOCUMENTS

CORRESPONDENCE

**ITEM 13.
PATENT AND MARKET EXCLUSIVITY INFORMATION**

**Time Sensitive Patent Information
Pursuant to 21 C.F.R. 314.53
for
sNDA for Neuropathic Pain**

The following is provided in accordance with the Drug Price Competition and Patent Term Restoration Act of 1984:

- Trade Name: Neurontin®
 - Active Ingredient: 1-(aminomethyl)-1-cyclohexaneacetic acid
 - Strengths: 100, 300, 400 mg capsules; 600, 800 mg tablets
 - Dosage Form: Capsules and tablets for oral administration
 - Approval Date: December 30, 1993 (capsules)
October 9, 1998 (tablets)
-

U.S. Patent Number: 4,894,476

Expiration Date: May 2, 2008
• PED November 2, 2008

Type of Patent: Drug Substance (Active Ingredient)

Assignee: Warner-Lambert Company

U.S. Patent Number: 5,025,035

Expiration Date: October 12, 2010
• PED April 12, 2011

Type of Patent: Method of Use

Assignee: Warner-Lambert Company

U.S. Patent Number: 5,084,479
Expiration Date: January 2, 2010
• PED July 2, 2010
Type of Patent: Method of Use
Assignee: Warner-Lambert Company

U.S. Patent Number: 5,792,796
Expiration Date: August 11, 2015
• PED February 11, 2016
Type of Patent: Method of Use
Assignee: Warner-Lambert Company

U.S. Patent Number: 6,054,482
Expiration Date: April 25, 2017
• PED October 25, 2017
Type of Patent: Composition
Assignee: Goedecke Aktiengesellschaft
U.S. Agent: Warner-Lambert Company

The undersigned declares that U.S. 4,894,476 covers a crystal form of Neurontin® (gabapentin) (1-(aminomethyl)-1-cyclohexaneacetic acid), that U.S. 5,025,035, U.S. 5,084,479 and U.S. 5,792,796 cover methods of use of Neurontin® (gabapentin) (1-(aminomethyl)-1-cyclohexaneacetic acid), and that U.S. 6,054,482 covers a pharmaceutical composition of Neurontin® (gabapentin) (1-(aminomethyl)-1-cyclohexaneacetic acid). Neurontin® is approved under section 505 of the Federal Food, Drug, and Cosmetic Act.

Date:

July 30, 2001

Charles W. Ashbrook
Assistant General Patent Counsel
Pharmaceutical Patents
Warner-Lambert Company
Registration No. 27,610

MEMORANDUM OF TELECON

Date: May 22, 2002

Application Number: N 21-397/ 21-423/ 21-424

Between:

Drusilla Scott, Regulatory WRA
Steve Gracon, WRA
Robin Pitts, WRA
Alexandra Fernandes, WRA
Edwina Koto, WRA
Howard Bockbrader, Clinical Sciences
Jeff Robbins, Clinical Biostatistics
Kevin Chartier, Clinical Biostatistics
David Wesche, Clinical Sciences
Elizabeth Garofalo, Clinical Development
Valerie Flapan, Legal
John Marino, Marketing
Preston Holley, Clinical Development

Representing Pfizer/Parke-Davis

And:

Sharon Hertz, M.D.
Bob Rappaport, M.D.
Cynthia McCormick, M.D.
Tim McGovern, Ph.D.
Suresh Doddapaneni, Ph.D.
Suliman Al-Fayoumi, Ph.D.
Stella Grosser, Ph.D.
Tom Permutt, Ph.D.
Kim Compton, Project Manager
Division of Anesthetic, Critical Care, and
Addiction Drug Products; HFD-170

Subject: Neurontin Label Clarifications

The sponsor was contacted to discuss and clarify Agency proposed changes forwarded to the sponsor by the Division (with the input of HFD-120).

Overall recommendations included to change "gabapentin" to "neurontin" throughout where appropriate.

The sponsor requested the re-insertion of the word ~~neuralgia~~ in the indication section (as in ~~the~~ indication). Dr. McCormick indicated that the term "neuralgia" is defined as nerve pain and therefore the treatment of pain was implied in the indication of

“postherpetic neuralgia.” She stated that if the sponsor wanted to re-insert the ~~word~~, they would need more convincing justification as they have not supported an indication of ~~the~~.

Minor changes were agreed to in the Description, Clinical Studies, Precautions, and Drug Interactions section sections.

The sponsor agreed to re-work the Adverse Events section with regard to the ~~word~~ patient data.

The Dosage and Administrations section was changed to reflect doses up to 3600mg/day in the text and the table provided for dosage adjustment based on renal function. It was agreed that the Agency would provide specific language to the sponsor for these sections, as well as language for Dosing in the Elderly.

**APPEARS THIS WAY
ON ORIGINAL**

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Kimberly Compton
5/23/02 05:24:55 PM
CSO

**APPEARS THIS WAY
ON ORIGINAL**

Number of Pages
Redacted 76



Draft Labeling
(not releasable)

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

Application Information		
NDA 21-397 NDA 21-423 NDA 21-424	Efficacy Supplement Type SE-	Supplement Number
Drug: Neurontin (gabapentin) capsules, tablets and oral solution		Applicant: Pfizer/Parke-Davis
RPM: Kim Compton	HFD-170	Phone # 301-827-7432
Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)		Reference Listed Drug (NDA #, Drug name):
❖ Application Classifications:		
• Review priority		<input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority
• Chem class (NDAs only)		6S
• Other (e.g., orphan, OTC)		
❖ User Fee Goal Dates		June 7, 2002 (N 21-397) June 17, 2002 (N 21-423/21-424)
❖ Special programs (indicate all that apply)		<input checked="" type="checkbox"/> None Subpart H <input type="checkbox"/> 21 CFR 314.510 (accelerated approval) <input type="checkbox"/> 21 CFR 314.520 (restricted distribution) <input type="checkbox"/> Fast Track <input type="checkbox"/> Rolling Review
❖ User Fee Information		
• User Fee		<input checked="" type="checkbox"/> Paid
• User Fee waiver		<input type="checkbox"/> Small business <input type="checkbox"/> Public health <input type="checkbox"/> Barrier-to-Innovation <input type="checkbox"/> Other
• User Fee exception		<input type="checkbox"/> Orphan designation <input type="checkbox"/> No-fee 505(b)(2) <input type="checkbox"/> Other
❖ Application Integrity Policy (AIP)		
• Applicant is on the AIP		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• This application is on the AIP		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• Exception for review (Center Director's memo)		
• OC clearance for approval		
❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification and certifications from foreign applicants are co-signed by U.S. agent.		<input checked="" type="checkbox"/> Verified
❖ Patent		
• Information: Verify that patent information was submitted		<input checked="" type="checkbox"/> Verified
• Patent certification [505(b)(2) applications]: Verify type of certifications submitted		21 CFR 314.50(i)(1)(i)(A) <input type="checkbox"/> I <input type="checkbox"/> II <input type="checkbox"/> III <input type="checkbox"/> IV 21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii)
• For paragraph IV certification, verify that the applicant notified the patent holder(s) of their certification that the patent(s) is invalid, unenforceable, or will not be infringed (certification of notification and documentation of receipt of notice).		<input type="checkbox"/> Verified

❖ Exclusivity (approvals only)	
• Exclusivity summary	X ✓
• Is there an existing orphan drug exclusivity protection for the active moiety for the proposed indication(s)? Refer to 21 CFR 316.3(b)(13) for the definition of sameness for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification!	() Yes, Application # _____ (X) No
❖ Administrative Reviews (Project Manager, ADRA) (indicate date of each review)	
General Information	
❖ Actions	
• Proposed action	(X) AP () TA () AE () NA
• Previous actions (specify type and date for each action taken)	
• Status of advertising (approvals only)	(X) Materials requested in AP letter () Reviewed for Subpart H
❖ Public communications	
• Press Office notified of action (approval only)	() Yes (X) Not applicable
• Indicate what types (if any) of information dissemination are anticipated	(X) None () Press Release () Talk Paper () Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable))	
• Division's proposed labeling (only if generated after latest applicant submission of labeling)	X
• Most recent applicant-proposed labeling	
• Original applicant-proposed labeling	X
• Labeling reviews (including DDMAC, Office of Drug Safety trade name review, nomenclature reviews) and minutes of labeling meetings (indicate dates of reviews and meetings)	DDMAC did not write a review, but did OK the draft label sent to the sponsor 5/23/02.
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	
❖ Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	Not supplied-Approved Product
• Applicant proposed	
• Reviews	
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	N/A
• Documentation of discussions and/or agreements relating to post-marketing commitments	
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	
❖ Memoranda and Telecons	X
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	
• Pre-NDA meeting (indicate date)	
• Pre-Approval Safety Conference (indicate date; approvals only)	
• Other	

❖ Advisory Committee Meeting	
• Date of Meeting	N/A
• 48-hour alert	
❖ Federal Register Notices, DESI documents, NAS, NRC (if any are applicable)	
Summary Application Review	
❖ Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) (indicate date for each review)	X (May 23, 2002)
Clinical Information	
❖ Clinical review(s) (indicate date for each review)	X (HFD-170, May 24, 2002) ✓ X (HFD-120, April 11, 2002)
❖ Microbiology (efficacy) review(s) (indicate date for each review)	N/A
❖ Safety Update review(s) (indicate date or location if incorporated in another review)	Included in HFD-170 Clinical Review (see above)
❖ Pediatric Page (separate page for each indication addressing status of all age groups)	X
❖ Statistical review(s) (indicate date for each review)	X (May 24, 2002) ✓
❖ Biopharmaceutical review(s) (indicate date for each review)	X (HFD-170, May 6, 2002) X (HFD-170, addendum, May 13, 2002) X (HFD-120, May 14, 2002)
❖ Controlled Substance Staff review(s) and recommendation for scheduling (indicate date for each review)	N/A
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	N/A
• Bioequivalence studies	
CMC Information	
❖ CMC review(s) (indicate date for each review)	X (May 13, 2002)
❖ Environmental Assessment	
• Categorical Exclusion (indicate review date)	
• Review & FONSI (indicate date of review)	
• Review & Environmental Impact Statement (indicate date of each review)	See May 13, 2002 CMC Reviews
❖ Micro (validation of sterilization & product sterility) review(s) (indicate date for each review)	N/A
❖ Facilities inspection (provide EER report)	N/A (Approved Drug Product) Date completed: () Acceptable () Withhold recommendation
❖ Methods validation	N/A (Approved Drug Product) () Completed () Requested () Not yet requested
Nonclinical Pharm/Tox Information	
❖ Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	X (May 21, 2002)
❖ Nonclinical inspection review summary	
❖ Statistical review(s) of carcinogenicity studies (indicate date for each review)	
❖ CAC/ECAC report	

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: <http://www.fda.gov/cder/pdufa/default.htm>

1. APPLICANT'S NAME AND ADDRESS

Parke-Davis Pharmaceutical Research
Division of Warner-Lambert Company
2800 Plymouth Rd
Ann Arbor, MI 48105

4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER

21-397 (Type 6 NDA)

5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?

YES NO

IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW:

THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:

(APPLICATION NO. CONTAINING THE DATA.)

2. TELEPHONE NUMBER (Include Area Code)

(734) 622-1819

3. PRODUCT NAME

Neurontin (gabapentin)

6. USER FEE I.D. NUMBER

4163

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory)

A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE (See item 7, reverse side before checking box.)

THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act (See item 7, reverse side before checking box.)

THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act (See item 7, reverse side before checking box.)

THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY (Self Explanatory)

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION?

YES NO

(See Item 8, reverse side if answered YES)

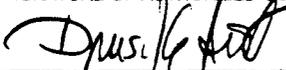
Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
CBER, HFM-99
1401 Rockville Pike
Rockville, MD 20852-1448

Food and Drug Administration
CDER, HFD-94
and 12420 Parklawn Drive, Room 3046
Rockville, MD 20852

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE



TITLE

Director, Worldwide Regulatory Affairs

DATE

July 31, 2001

USER FEE VALIDATION SHEET

NDA # 21-424 Supp. Type & # N000 UFID # 4193
 (e.g., N000, SLR001, SE1001, etc.)

1. YES NO User Fee Cover Sheet Validated? MIS_Elements Screen Change(s):

2. YES NO **APPLICATION CONTAINS CLINICAL DATA?**
 (Circle YES if NDA contains study or literature reports of what are explicitly or implicitly represented by the application to be adequate and well-controlled trials. Clinical data do not include data used to modify the labeling to add a restriction that would improve the safe use of the drug (e.g., to add an adverse reaction, contraindication or warning to the labeling).

REF IF NO CLINICAL DATA IN SUBMISSION, INDICATE IF CLINICAL DATA ARE CROSS REFERENCED IN ANOTHER SUBMISSION.
21-397

3. YES NO SMALL BUSINESS EXEMPTION

4. YES NO WAIVER GRANTED

5. YES NO NDA BEING SPLIT FOR ADMINISTRATIVE CONVENIENCE (other than bundling).
 If YES, list all NDA #s, review division(s) and those for which an application fee applies.

NDA #	Division	<input checked="" type="radio"/> Fee	<input checked="" type="radio"/> No Fee
<u>N21-397</u>	<u>HFD-170</u>	Fee	No Fee
<u>N21-423</u>	<u>HFD-170</u>	Fee	<input checked="" type="radio"/> No Fee

6. YES NO **BUNDLING POLICY APPLIED CORRECTLY? No Data Entry Required**
 (Circle YES if application is properly designated as one application or is properly submitted as a supplement instead of an original application. Circle NO if application should be split into more than one application or be submitted as an original instead of a supplement. If NO, list resulting NDA #s and review division(s).

NDA #	Division	NDA #	Division
N _____	HFD- _____	N _____	HFD- _____

7. P S PRIORITY or STANDARD APPLICATION?

[Signature] / 8-20-01 [Signature] / 8/21/01
 PM Signature / Date CPMS Concurrence Signature / Date

USER FEE VALIDATION SHEET

NDA # 21-423 Supp. Type & # N000 UFID # 4194
(e.g., N000, SLR001, SE1001, etc.)

1. YES NO User Fee Cover Sheet Validated? MIS Elements Screen Change(s):

2. YES NO **APPLICATION CONTAINS CLINICAL DATA?**
(Circle YES if NDA contains study or literature reports of what are explicitly or implicitly represented by the application to be adequate and well-controlled trials. Clinical data do not include data used to modify the labeling to add a restriction that would improve the safe use of the drug (e.g., to add an adverse reaction, contraindication or warning to the labeling).

REF YES NO IF NO CLINICAL DATA IN SUBMISSION, INDICATE IF CLINICAL DATA ARE CROSS REFERENCED IN ANOTHER SUBMISSION.
21-397

3. YES NO **SMALL BUSINESS EXEMPTION**

4. YES NO **WAIVER GRANTED**

5. YES NO **NDA BEING SPLIT FOR ADMINISTRATIVE CONVENIENCE (other than bundling).**
If YES, list all NDA #s, review division(s) and those for which an application fee applies.

NDA #	Division	<input checked="" type="radio"/> Fee	<input type="radio"/> No Fee
N <u>21-397</u>	HFD- <u>170</u>	<input type="radio"/> Fee	<input checked="" type="radio"/> No Fee
N <u>21-424</u>	HFD- <u>170</u>		

6. YES NO **BUNDLING POLICY APPLIED CORRECTLY? No Data Entry Required**
(Circle YES if application is properly designated as one application or is properly submitted as a supplement instead of an original application. Circle NO if application should be split into more than one application or be submitted as an original instead of a supplement. If NO, list resulting NDA #s and review division(s).

NDA #	Division	NDA #	Division
N _____	HFD- _____	N _____	HFD- _____

7. P S **PRIORITY or STANDARD APPLICATION?**

PM Signature / Date

CPMS Concurrence Signature / Date

2/14/00

8/21/01

USER FEE VALIDATION SHEET

NDA # 21-397 Supp. Type & # N000 UFID # 4163
(e.g., N000, SLR001, SE1001, etc.)

1. YES NO User Fee Cover Sheet Validated? MIS_Elements Screen Change(s):

2. YES NO APPLICATION CONTAINS CLINICAL DATA?
(Circle YES if NDA contains study or literature reports of what are explicitly or implicitly represented by the application to be adequate and well-controlled trials. Clinical data do not include data used to modify the labeling to add a restriction that would improve the safe use of the drug (e.g., to add an adverse reaction, contraindication or warning to the labeling).

REF IF NO CLINICAL DATA IN SUBMISSION, INDICATE IF CLINICAL DATA ARE CROSS REFERENCED IN ANOTHER SUBMISSION.

3. YES NO SMALL BUSINESS EXEMPTION

4. YES NO WAIVER GRANTED

5. YES NO NDA BEING SPLIT FOR ADMINISTRATIVE CONVENIENCE (other than bundling). If YES, list all NDA #s, review division(s) and those for which an application fee applies

NDA #	Division	Fee	<input checked="" type="radio"/> No Fee
N <u>21-424</u>	HFD- <u>170</u>	Fee	<input checked="" type="radio"/> No Fee
N <u>21-423</u>	HFD- <u>170</u>	Fee	<input checked="" type="radio"/> No Fee

6. YES NO BUNDLING POLICY APPLIED CORRECTLY? No Data Entry Required
(Circle YES if application is properly designated as one application or is properly submitted as a supplement instead of an original application. Circle NO if application should be split into more than one application or be submitted as an original instead of a supplement. If NO, list resulting NDA #s and review division(s).

NDA #	Division	NDA #	Division
N <u>21-423</u>	HFD- <u>170</u>	N <u>21-424</u>	HFD- <u>170</u>

7. P S PRIORITY or STANDARD APPLICATION?

/s/ _____ Date 8/13/01
PM Signature / Date

/s/ _____ Date 8/13/01
CPMS Concurrence Signature / Date

Exclusivity Checklist

NDA: 21-397/21-423/21-424				
Trade Name: Neurontin				
Generic Name: gabapentin				
Applicant Name: Pfizer/Parke-Davis				
Division: HFD-170				
Project Manager: Kim Compton				
Approval Date: May 24, 2002				
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
c. If yes, what type? (SE1, SE2, etc.)	N/A			
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.				
Explanation:				
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:				
Explanation:				
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.				
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.				
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 (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.	Yes	X	No	
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," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).				
Drug Product	Neurontin Capsules			
NDA #	20-235			

Drug Product	Neurontin Tablets			
NDA #	20-882			
Drug Product	Neurontin Oral Solution			
NDA #	21-216, 21-129			
2. Combination product.	Yes		No	X
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 <u>any one</u> 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 "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).				
IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS. 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	X	No	
IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS.				
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	X	No	
If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCKS.				
Basis for conclusion:				
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? Literature could not support new indication alone (per Medical Officer, 5/23/02)	Yes		No	X
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	X
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	X
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 (Efficacy), Study #:	945-211			

Investigation #2 (Efficacy), Study #:	945-295			
Investigation #3 (Safety), Study #:	945-210			
Investigation #4 (Safety), Study #:	945-224			
Investigation #5 (Safety), Study #:	945-306			
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	<input type="checkbox"/>	No	X
Investigation #2	Yes	<input type="checkbox"/>	No	X
Investigation #3	Yes	<input type="checkbox"/>	No	X
Investigation #4	Yes	<input type="checkbox"/>	No	X
Investigation #5	Yes	<input type="checkbox"/>	No	X
If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:				
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?				
	Yes	<input type="checkbox"/>	No	X
If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:				
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"): All listed in 2(c) are "new".				
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? Yes				
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? Yes				
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	<input type="checkbox"/>	No	X
If yes, explain:				

Completed by: Kim Compton, Regulatory Project Manager with the assistance of Sharon Hertz, M.D., Medical Officer.

Concurred by: Cynthia McCormick, M.D., Division Director

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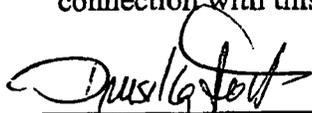
Cynthia McCormick
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**APPEARS THIS WAY
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Item 16 (revised)
NDA 21-397
Neurontin (gabapentin) Capsules

DEBARMENT CERTIFICATION
[FD&C Act 306(k)(1)]

Pfizer hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.



Drusilla L. Scott, PhD
Director, Regulatory Strategy and Policy

May 29, 2002

Date

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N 21-397/ 21-423/ 21-424 Neurontin Capsules, Tablets and Oral Solution

For review of Financial Disclosure see the main Clinical Review of these NDAs by Dr. Sharon Hertz (dated May 23, 2002, pg. 18, sect. 5.5)

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Pfizer will submit

1. new datasets to support the change in indication by the end of November
2. updated ISS by December 20, 2001.
3. revised labeling by mid January, 2002.

Medical Officer concurs with these timelines.

Judit Milstein
Regulatory Project Manager

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Judith Milstein
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MEMORANDUM OF TELECON

DATE: October 5, 2001

APPLICATION NUMBER: NDA 21-397 (NDA 21-423, NDA 21-424)

DRUG: Neurontin (gabapentin)

BETWEEN:

Name: Stephen Gracon, DVM – Regulatory Affairs
Robin Pitts, RPh – Regulatory Affairs
Drusilla Scott, PhD – Regulatory Affairs
Lloyd Knapp, PharmD – Clinical Development
Michael Poole, MD – Clinical Development
Kevin Chartier, PhD – Biostatistics
Jeff Robbins – Biostatistics
Douglas Y. Shapiro, MD, PhD – Clinical Development
Marie Ulrey – Development Operations
Thomas Purcell, MS – Clinical Communications
Sue Kolberg – Programming
Kjersten Ingolfsrud - Programming

Representing: Parke-Davis/Pfizer
Phone: 877-300-8186, #929261

AND

Name: Sharon Hertz, M.D., Medical Reviewer
Laura Governale, Pharm.D., Regulatory Project Manager
Division of Anesthetic, Critical Care, and Addiction Drug Products
HFD-170

SUBJECT: Presentation of adverse event profiles

.....

A teleconference was held today to outline the proposal for the format of the adverse event tables for NDA 21-397 (NDA 21-423, NDA 21-424). It was agreed between the sponsor and Dr. Hertz that the adverse event tables will be reconstructed to capture the dose at which the adverse event occurred. In addition, the dose ranges depicting the highest dose achieved will be reconstructed to reflect at which dose the adverse event occurred. The sponsor will submit a draft of the adverse event tables by fax on Tuesday, October 9, 2001, to obtain the Division's concurrence before executing the proposal.

Laura Governale, Pharm.D.
Regulatory Project Manager

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MEMORANDUM OF TELECON

DATE: October 3, 2001

APPLICATION NUMBER: NDA 21-397, NDA 21-423, NDA 21-424

DRUG: Neurontin (gabapentin)

BETWEEN:

Name: Drusilla Scott, Ph.D.
Representing: Director, Regulatory Strategy and Registration
Phone: 734-622-1819

AND

Name: Sharon Hertz, M.D., Medical Reviewer
Laura Governale, Pharm.D., Regulatory Project Manager
Division of Anesthetic, Critical Care, and Addiction Drug Products
HFD-170

SUBJECT: Integrated safety dataset; presentation of adverse event profiles

.....

The sponsor was told to submit the integrated safety dataset to the FDA by Friday, October 5, 2001, in order for the application to be filed. The sponsor should also fax/e-mail a table of the variables included in the dataset by Thursday, October 4, 2001.

In addition, the sponsor will submit a proposal of the marked table presentation for the adverse event profiles later this afternoon. A telecon will be scheduled for Friday, October 5, 2001, at 2:00 PM to discuss in detail the format of the adverse event presentation. The presentation should include a correlation between the adverse event and the dose at which the adverse event occurred.

The sponsor agreed to provide the integrated safety dataset and the table of variables by the above mentioned timelines.

Laura Governale, Pharm.D.
Regulatory Project Manager

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Laura Governale
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MEMORANDUM OF TELECON

DATE: August 13-14, 2001

APPLICATION NUMBER: NDA 21-397

BETWEEN:

Name: Drusilla Scott, Ph.D.
Steve Gracon, Ph.D.

Representing: Pfizer/Parke-Davis

Phone: 734-622-1819

AND

Name: Laura Governale, Pharm.D., Regulatory Project Manager
Division of Anesthetic, Critical Care, and Addiction Drug Products
HFD-170

SUBJECT: New NDA's needed for tablet and solution dosage forms

.....

The sponsor was advised to submit two new NDA's for the tablet and oral solution dosage forms for Neurontin® (gabapentin). The new NDA's may be cross-referenced to NDA 21-397 for Neurontin® Capsules. A form 356(h) should also accompany each new NDA.

The sponsor agreed to comply.

Laura Governale, Pharm.D.
Regulatory Project Manager

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FDA Links Searches Check Lists Tracking Links Calendars Reports Help

PEDIATRIC PAGE (Complete for all original application and all efficacy supplements)

NDA Number: 021397 **Trade Name:** NEURONTIN (GABAPENTIN)100/300/400 MG CAP
Supplement Number: 000 **Generic Name:** GABAPENTIN
Supplement Type: N **Dosage Form:**
Regulatory Action: OP **COMIS Indication:**
Original NDA Action Date: 8/7/01

Indication # 1 Management of Postherpetic Neuralgia

Comments (if any): This indication is not significant in the pediatric population, so studies of the use of this product for this indication in pediatric patients are being waived.

Ranges for This Indication

<u>Lower Range</u>	<u>Upper Range</u>	<u>Status</u>	<u>Date</u>
0 years	16 years	Waived	

Comments: See comment above.

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Signature

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Date

5/22/02

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FDA Links Searches Check Lists Tracking Links Calendars Reports Help

PEDIATRIC PAGE (Complete for all original application and all efficacy supplements)

NDA Number: 021423 **Trade Name:** NEURONTIN (GABAPENTIN) TABLETS
Supplement Number: 000 **Generic Name:** GABAPENTIN
Supplement Type: N **Dosage Form:** _____
Regulatory Action: OP **COMIS Indication:** _____
Original NDA Action Date: 8/17/01

Indication # 1 Management of Postherpetic Neuralgia

Comments (if any): -

Ranges for This Indication

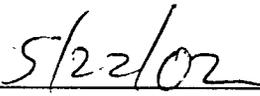
<u>Lower Range</u>	<u>Upper Range</u>	<u>Status</u>	<u>Date</u>
0 years	16 years	Waived	

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Signature



Date



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FDA Links Searches Check Lists Tracking Links Calendars Reports Help

PEDIATRIC PAGE (Complete for all original application and all efficacy supplements)

NDA Number: 021424 Trade Name: NEUROTIN (GABAPENTIN) ORAL SOLUTION
 Supplement Number: 000 Generic Name: GABAPENTIN
 Supplement Type: N Dosage Form: _____
 Regulatory Action: OP COMIS Indication: _____
 Original NDA Action Date: 8/17/01

Indication # 1 Management of Postherpetic Neuralgia

Comments (if any):

Ranges for This Indication

<u>Lower Range</u>	<u>Upper Range</u>	<u>Status</u>	<u>Date</u>
0 years	16 years	Waived	

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