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**Application Number 21-216**

**APPROVAL LETTER**



Food and Drug Administration  
Rockville, MD 20857

NDA 21-216  
NDA 20-235/S-015  
NDA 20-882/S-002  
NDA 21-129/S-005

OCT 12 2000

Parke-Davis Pharmaceutical Research  
Division of Warner-Lambert Company  
For Parke Davis Pharmaceuticals Limited  
Attention: Janeth L. Turner, R.N., B.S.N.  
2800 Plymouth Road, P.O. Box 1047  
Ann Arbor, MI 48106-1047

Dear Ms. Turner:

Please refer to your new drug application (NDA 21-216) and to your supplemental new drug applications (NDA 20-235/S-015, NDA 20-882/S-002) dated December 14, 1999, received December 15, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Neurontin (gabapentin) oral solution, Neurontin (gabapentin) capsules, and Neurontin (gabapentin) tablets.

Reference is also made to your labeling supplement (NDA 21-129/S-005) dated October 11, 2000, received October 12, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Neurontin (gabapentin) oral solution.

We acknowledge receipt of your additional correspondence and amendments to NDA 21-216, NDA 20-235/S-015, and NDA 20-882/S-002 dated:

April 14, 2000  
May 11, 2000  
August 1, 2000

August 9, 2000  
August 16, 2000  
August 21, 2000

August 25, 2000  
October 3, 2000

These applications provide for the use of Neurontin as adjunctive therapy in the treatment of partial seizures in pediatric patients age 3 years and above.

We have completed the review of these applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon enclosed labeling text. Accordingly, the application is approved effective on the date of this letter.

### Labeling

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

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Please submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative purposes, this submission should be designated "FPL for approved NDA 21-216 and approved supplemental NDA 20-235/S-015, NDA 20-882/S-008, NDA 21-129/S-005." Approval of these submissions by FDA is not required before the labeling is used.

### Supersede

We have reviewed the content of the following labeling supplements, and we note that these changes have been incorporated in the enclosed labeling text. Therefore, the supplemental applications listed below have been superseded, and will be retained in our files with no further action.

Supplement Number:	Date Submitted:
NDA 20-235/S-008	May 19, 1997 (Initial submission) June 25, 1997 (amendment)
NDA 20-235/S-010	May 26, 1998 (Initial submission) June 16, 1998 (amendment)
NDA 20-235/S-013	July 30, 1999 (Initial submission)
NDA 20-882/S-001	July 30, 1999 (Initial submission)
NDA 20-882/S-003	June 21, 2000 (Initial submission)
NDA 20-882/S-004	June 21, 2000 (Initial submission)
NDA 21-129/S-001	June 21, 2000 (Initial submission)
NDA 21-129/S-002	June 21, 2000 (Initial submission)
NDA 21-129/S-003	June 21, 2000 (Initial submission)

### Phase 4 Commitment

We remind you of your post marketing commitment specified in your submission dated October 3, 2000 and in an e-mail dated October 5, 2000. This commitment, along with any completion dates agreed upon, is listed below.

In the above referenced correspondences, you agreed to conduct a repeated-dose neonatal/juvenile rat study to assess gabapentin's developmental neurotoxicity. You also stated that you would submit the protocol to FDA for review prior to study initiation and anticipate completion of the study by 4<sup>th</sup> quarter 2002.

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Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. If an IND is not required to meet your post marketing commitments, please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21 CFR 314.81(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these post marketing commitments must be clearly designated "Post Marketing Commitments."

In addition, we acknowledge that with this approval, all Phase 4 Commitments, described in our December 30, 1993 approval letter for Neurontin (gabapentin) capsules (NDA 20-235), have been fulfilled.

#### **Pediatrics**

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 FR 66632). We note that you have fulfilled the pediatric study requirement at this time.

#### **Promotional Materials**

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-42  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20857

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**Other**

We remind you that you must comply with the requirements for an approved NDA as set forth under 21 CFR 314.80 and 314.81. To comply with these regulations, all 7-day and 15-day alert reports, periodic adverse drug experience (ADE) reports, field alerts, annual reports, supplements, and other submissions should be addressed to NDA 21-129 for Neurontin (gabapentin) oral solution rather than NDA 21-216. In the future, no submissions should be made to NDA 21-216 except for final printed labeling as described earlier in this letter.

If you have any questions, call Jacqueline H. Ware, Pharm.D., Regulatory Management Officer, at (301) 594-5533.

Sincerely,

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

Enclosure

**APPEARS THIS WAY  
ON ORIGINAL**